LBA1 Plenary Session

Randomized trial of standard chemotherapy alone or combined with atezolizumab as adjuvant therapy for patients with stage III deficient DNA mismatch repair (dMMR) colon cancer (Alliance A021502; ATOMIC).

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Background: Standard adjuvant chemotherapy of stage III colon cancer consists of a fluoropyrimidine plus oxaliplatin. In patients (pts) with stage III colon cancer and deficient mismatch repair (dMMR), the benefit of an immune checkpoint inhibitor combined with adjuvant chemotherapy is unknown. The phase III ATOMIC trial (NCT02912559) was conducted to determine whether atezolizumab (atezo), an anti-PD-L1 antibody, can improve pt outcomes when added to adjuvant 5-fluorouracil, leucovorin plus oxaliplatin (mFOLFOX6) in pts with stage III dMMR tumors. **Methods:** We conducted an NCI-sponsored, multicenter and randomized phase III trial in pts with surgically resected stage III dMMR colon adenocarcinoma (any T, $N_{1,2}$ M_0). Pts, age > 12 years (yr), were accrued at NCTN sites and the German AIO. Tumor dMMR was determined by local immunohistochemistry and centrally verified. Pts were randomized 1:1 to mFOLFOX6 plus atezo (840 mg IV q2 weeks) for 12 cycles (6 months)[mo] followed by atezo monotherapy for 13 cycles (12 mo total) versus mFOLFOX6 alone for 12 cycles. Randomization stratification factors were N-stage (N_1/N_{1c} vs N_2), T-stage (T_1-T_3 vs T_4) and site (proximal vs distal). The primary endpoint was disease-free survival (DFS); secondary endpoints were overall survival and adverse event (AE) profile (CTCAE, PRO-CTCAE). Primary efficacy analysis was done in the intent-to-treat population; DFS was compared by arm (stratified log-rank test). Hazard ratio (HR) and 95% confidence interval (CI) were calculated using a stratified Cox model; 3-yr DFS was determined by Kaplan-Meier method. Among 700 pts., 165 DFS events with two interim analyses (50% , 75% of events) yielded 90% power to detect HR 0.6 (3-yr DFS 75% vs. 84.2%) assuming exponential survival and 1-sided alpha (0.025). **Results:** From 9/2017 to 1/2023, 712 pts were randomized (1 pediatric) to either atezo plus mFOLFOX6 (n= 355; atezo arm) or mFOLFOX6 (n= 357). Median pt age was 64 yr. 55.1% were female. Among tumors, 83.8% were proximal, 46.1% were clinical low risk ($T_{1-3}N_1$) and 53.9% high risk (T_4 and/or N_2). At the second interim analysis, median pt follow-up was 37.2 mo (interquartile range, 24.2 to 55.5) and 124 DFS events were observed. Three-year DFS was 86.4 % (95% CI, 81.8 to 89.9) in the atezo arm and 76.6 % (95% CI, 71.3 to 81.0) in the mFOLFOX6 arm (HR, 0.50; 95% CI, 0.35 to 0.72). Stratified log-rank p-value was <0.0001, crossing the pre-specified efficacy boundary of 0.009. Efficacy for the atezo arm was consistent across subgroups, including pts >70 yr and low- and high-risk groups. Treatment-related > grade 3 AEs occurred in 71.7 % of pts in the atezo arm vs 62.1 % in the mFOLFOX6 arm. **Conclusion:** The addition of atezolizumab to mFOLFOX6 significantly improved DFS and should be considered the new adjuvant standard of care for patients with dMMR stage III colon cancer. Support: U10CA180821, U10CA180882, U24CA196171; Genentech, a member of the Roche group; https://acknowledgments.alliancefound.org. Clinical trial information: NCT02912559. Research Sponsor: National Cancer Institute; U10CA180882; Genentech.

LBA2 **Plenary Session**

NIVOPOSTOP (GORTEC 2018-01): A phase III randomized trial of adjuvant nivolumab added to radio-chemotherapy in patients with resected head and neck squamous cell carcinoma at high risk of relapse.

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Background: The standard of care (SOC) over the past two decades for resected locally advanced SCCHN (LA-SCCHN) with high-risk of relapse is adjuvant cisplatin-radiotherapy (CRT). Despite these definitive treatments, many patients develop recurrence, indicating that more effective treatments are needed. This study evaluated the addition of nivolumab (NIVO) to SOC CRT compared to SOC CRT alone after surgery. **Methods:** NIVOPOSTOP is an international randomized, open-label Phase 3 trial (NCT03576417). Main inclusion criteria were patients $<$ 75 years, ECOG PS 0-1, with resected LA-SCCHN of the oral cavity, oropharynx (OPC), hypopharynx or larynx at high-risk of relapse defined by presence of nodal extra capsular extension and/or positive tumor margins, $\geq$4 nodal involvements, multiple peri-neural invasion. The primary endpoint was Disease Free Survival (DFS); key secondary endpoints include overall survival (OS) and safety. Patients were randomized 1:1 after surgery to receive Arm A SOC 66 Gy RT and cisplatin (100 mg/m2 every 3 weeks (Q3W) for three cycles) or Arm B NIVO 240 mg, followed by SOC CRT with 3 cycles of NIVO 360 mg Q3W, and followed by 6 cycles of NIVO 480 mg Q4W. Treatment allocation was done by minimization for centers and p16 status. To detect a HR of events of 0.65 at 2-sided alpha error 0.05 and power 90%, 230 events were required. Analysis was performed when this required number of events was reached (cutoff date April 30, 2024). **Results:** A total of 680 patients were randomized. DFS analysis was based on 666 patients randomized before the cutoff date (334 in Arm A vs 332 in Arm B; intent-to-treat analysis) and 252 events at a median follow-up of 30.3 months (IQR 16.0; 44.9). Baseline characteristics were balanced between both arms. DFS was significantly improved across PD-L1 all-comers with adjuvant NIVO + CRT vs. CRT alone (HR 0.76 (95% CI, 0.60-0.98); stratified log rank test p value = 0.034). The 3-year DFS was 52.5% (95% CI, 46.2-58.4%) with CRT vs. 63.1% (57-68.7%) with NIVO + CRT. The analysis of OS will occur when the required number of deaths will be reached (currently 158 and required 283 deaths). The compliance with CRT was similar in both arms. Safety analysis up to 9 months after CRT was based on patients who received at least one administration of treatment. Patients experiencing grade 4 adverse events were less frequent in patients receiving CRT vs. NIVO + CRT (5.6% vs. 13.1% until 100 days after CRT and then 0% vs. 1.2% up to 9 months), and treatment related deaths occurred in 0.7% and 0.6% of patients, respectively. **Conclusions:** Adjuvant NIVO added to CRT after surgery provided a statistically and clinically meaningful DFS improvement in PD-L1 all-comers patients. This is the first time in over 2 decades that a therapy demonstrated superiority over SOC CRT in patients with resected LA-SCCHN at high-risk of relapse. Clinical trial information: NCT03576417. Research Sponsor: Bristol Myers Squibb.

LBA3 **Plenary Session**

Results from VERIFY, a phase 3, double-blind, placebo (PBO)-controlled study of rusfertide for treatment of polycythemia vera (PV).

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Background: PV is characterized by red blood cell overproduction. Rusfertide is a subcutaneous (SC), self-injected, first-in-class peptide hepcidin mimetic that decreases erythrocytosis. VERIFY (NCT05210790) is a global, ongoing phase 3 study designed to assess rusfertide vs PBO in phlebotomy (PHL)-dependent patients (pts) with PV receiving standard of care (SOC) therapy. **Methods:** In VERIFY Part 1a (Weeks [Wks] 0-32), pts requiring frequent PHL with or without stable cytoreductive therapy (CRT) to control hematocrit (Hct) were randomized (1:1) to receive once-weekly rusfertide or PBO. Pts were stratified by concurrent PV therapy. All pts completing Part 1a were eligible for open-label rusfertide in Part 1b (Wks 32-52). Pts who completed Part 1b were eligible to continue receiving rusfertide. The primary efficacy endpoint was the proportion of pts achieving a clinical response (ie, absence of PHL eligibility and no PHLs from Wks 20-32, and Part 1a completion). Key secondary endpoints (Wks 0-32) included mean number of PHLs, proportion of pts with Hct <45%, and mean change from baseline at end of Part 1a (Wk 32) in the (1) PROMIS Fatigue Short Form 8a (SF-8a) total T-score and (2) MFSAF v4.0 Total Symptom Score (TSS). **Results:** A total of 293 pts (male, 73.0%; median age, 57 [27-86] years) were randomized to receive rusfertide (n=147) or PBO (n=146). In the rusfertide and PBO groups, 56.5% (n=83) and 55.5% (n=81) of pts, respectively, received concurrent CRT. During Wks 20-32, significantly more pts in the rusfertide group (76.9%) achieved a clinical response vs PBO (32.9%) ($p<0.0001$). The mean (SE) number of PHLs (Wks 0-32) was 0.5 (0.2) with rusfertide vs 1.8 (0.2) with PBO ($p<0.0001$). More pts treated with rusfertide maintained Hct <45% from Wks 0-32 vs PBO (rusfertide, 62.6%; PBO, 14.4%; $p<0.0001$). For patient-reported outcomes (PROs), pts treated with rusfertide demonstrated a statistically significant improvement in the PROMIS Fatigue SF-8a total T-score and MFSAF TSS ($p<0.03$). During Part 1a, the most common treatment-emergent adverse events (AEs) in the rusfertide and PBO groups, respectively, were injection site reactions (55.9% and 32.9%), anemia (15.9% and 4.1%), and fatigue (15.2% and 15.8%). Serious AEs occurred in 3.4% (rusfertide) and 4.8% (PBO) of pts; none were considered related to rusfertide. During Part 1a, new malignancies were reported in 1 (rusfertide) and 7 (PBO) pts. **Conclusions:** In pts with PV receiving SOC, rusfertide resulted in a statistically significant reduction in the mean number of PHLs and improved Hct control. Rusfertide is the first investigational agent to target the hepcidin pathway to control Hct and the first agent to prospectively demonstrate a statistically significant improvement in the PROMIS Fatigue SF-8a and MFSAF PROs in pts with PV. Rusfertide had a safety and tolerability profile consistent with rusfertide in prior studies. Clinical trial information: NCT05210790. Research Sponsor: Protagonist Therapeutics, Inc.

LBA4 Plenary Session

Camizestrant + CDK4/6 inhibitor (CDK4/6i) for the treatment of emergent *ESR1* mutations during first-line (1L) endocrine-based therapy (ET) and ahead of disease progression in patients (pts) with HR+/HER2− advanced breast cancer (ABC): Phase 3, double-blind ctDNA-guided SERENA-6 trial.

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Background: *ESR1* mutations (*ESR1*m) constitutively activate the estrogen receptor (ER) and are the most common mechanism of acquired resistance to aromatase inhibitor (AI) + CDK4/6i. Molecular monitoring by ctDNA analysis can detect the emergence of *ESR1*m during 1L AI + CDK4/6i. Camizestrant, the next-generation selective ER degrader (SERD) and complete ER antagonist, has shown anti-tumor activity in pts with and without detectable *ESR1*m. SERENA-6 is the first global registrational Phase 3 trial assessing a ctDNA-guided approach to detect the emergence of *ESR1*m during 1L AI + CDK4/6i to inform a switch in therapy ahead of disease progression. **Methods:** Pts with HR+/HER2− ABC who had received ≥6 months of 1L AI (anastrozole/letrozole) + CDK4/6i (abemaciclib/palbociclib/ribociclib) were enrolled and had ctDNA tested for *ESR1*m every 2–3 months, coinciding with routine imaging. At *ESR1*m detection, pts without evidence of disease progression were randomized 1:1 to switch to camizestrant (75 mg) with continued CDK4/6i (type and dose maintained) + placebo for AI vs continuing AI + CDK4/6i + placebo for camizestrant. The primary endpoint was investigator-assessed PFS (per RECIST v1.1). Prespecified interim analysis data cutoff was Nov 28, 2024. **Results:** 3,256 eligible pts were surveilled for *ESR1*m using ctDNA until 315 eligible pts were randomized to switch to camizestrant (n=157) or continue with AI (n=158). All pts remained on the same CDK4/6i. ~50% of randomized pts had *ESR1*m detected at the first ctDNA test. Baseline characteristics were well balanced between treatments. After 171 PFS events, hazard ratio for PFS was 0.44 (95% CI 0.31–0.60, $p<0.00001$; median PFS 16.0 vs 9.2 months). PFS benefit was consistent across subgroups. PFS rate at 12 months was 60.7% (95% CI 51.1–69.0) vs 33.4% (95% CI 24.9–42.2) and at 24 months was 29.7% (95% CI 19.0–41.2) vs 5.4% (95% CI 0.7–18.2). PFS2 hazard ratio was 0.52 (95% CI 0.33–0.81; 27% maturity). OS is immature (12%). Camizestrant + CDK4/6i was well tolerated with safety consistent with the known profiles of camizestrant, and of each CDK4/6i. Rates of treatment discontinuation due to adverse events were 1.3% for camizestrant and 1.9% for AI. **Conclusions:** Camizestrant + CDK4/6i guided by emergence of *ESR1*m during 1L AI + CDK4/6i in pts with HR+/HER2− ABC resulted in a statistically significant and clinically meaningful improvement in PFS. SERENA-6 is the first global Phase 3 trial to demonstrate clinical utility of using ctDNA to detect and treat emerging resistance, ahead of disease progression. These findings represent a potential new treatment strategy to optimize and improve 1L patient outcomes. Clinical trial information: NCT04964934. Research Sponsor: AstraZeneca.

LBA5 Plenary Session

Event-free survival (EFS) in MATTERHORN: A randomized, phase 3 study of durvalumab plus 5-fluorouracil, leucovorin, oxaliplatin and docetaxel chemotherapy (FLOT) in resectable gastric/gastroesophageal junction cancer (GC/GEJC).

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Background: FLOT is a perioperative standard of care (SoC) in resectable GC/GEJC, yet recurrence rates remain high. Immune checkpoint inhibitors are approved in combination with chemotherapy in metastatic GC/GEJC, but not in the perioperative setting. The randomized, double-blind, global, Phase 3 MATTERHORN study (NCT04592913) assesses the combination of perioperative durvalumab (D) + FLOT vs placebo (P) + FLOT in participants (pts) with locally advanced, resectable GC/GEJC. The primary endpoint is EFS. Pathologic complete response (pCR) and overall survival (OS) are key secondary endpoints. The trial previously showed a statistically significant gain in pCR for D + FLOT. Here, we report efficacy and safety from the pre-planned interim analysis 2. **Methods:** Pts aged ≥18 years with histologically confirmed, resectable (Stage II–IVa per American Joint Committee on Cancer 8th edition) untreated G/GEJ adenocarcinoma were randomized 1:1 to D 1500 mg or P every 4 weeks (Q4W) on Day 1 + FLOT on Days 1 and 15 for 4 cycles (2 cycles each neoadjuvant/adjuvant), followed by D 1500 mg or P on Day 1 Q4W for 10 cycles. Pts were stratified by Asia vs non-Asia, clinical lymph node status (positive vs negative) and programmed cell death ligand-1 Tumor Area Positivity score (≥1% vs <1%). Data cutoff was Dec 20, 2024. EFS (time from randomization to progression, local or distant recurrence, or death) superiority for D + FLOT vs P + FLOT was assessed in all randomized pts by a stratified log-rank test (2-sided significance level threshold: 0.0239) on data according to RECIST v1.1 per BICR and/or locally by pathology testing. **Results:** In total, 948 pts were randomized to receive D + FLOT (n=474) or P + FLOT (n=474); median (m) follow-up duration was 31.5 months (mo). Demographic/baseline characteristics were generally similar across treatment arms. D + FLOT demonstrated a statistically significant improvement in EFS vs P + FLOT (hazard ratio [HR] 0.71; 95% confidence interval [CI], 0.58–0.86; p<0.001), mEFS was not reached (NR) with D + FLOT vs 32.8 mo with P + FLOT. The 24-mo EFS rate was higher for D + FLOT vs P + FLOT (Table). mOS was NR for D + FLOT vs 47.2 mo for P + FLOT (HR 0.78; 95% CI, 0.62–0.97; p=0.025; 33.9% maturity) and will be formally assessed at the final analysis. Maximum Grade 3 or 4 adverse event rates were similar between treatment arms; D + FLOT did not delay surgery or initiation of adjuvant therapy vs P + FLOT. **Conclusion:** D + FLOT demonstrated a statistically significant improvement in EFS vs P + FLOT in pts with resectable GC/GEJC, with an encouraging OS trend. These results support D + FLOT as a potential new global SoC for resectable GC/GEJC. Clinical trial information: NCT04592913. Research Sponsor: AstraZeneca.

	D + FLOT (n=474)	P + FLOT (n=474)
mEFS (95% CI), mo	NR (40.7–NR)	32.8 (27.9–NR)
EFS rate (95% CI), %		
12 mo	78.2 (74.1–81.7)	74.0 (69.7–77.8)
24 mo	67.4 (62.9–71.6)	58.5 (53.8–63.0)

LBA109 **Oral Abstract Session**

Sacituzumab govitecan (SG) + pembrolizumab (pembro) vs chemotherapy (chemo) + pembro in previously untreated PD-L1–positive advanced triple-negative breast cancer (TNBC): Primary results from the randomized phase 3 ASCENT-04/ KEYNOTE-D19 study.

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Background: Although PD-1/PD-L1 inhibitors plus chemo have expanded treatment options for previously untreated PD-L1–positive advanced TNBC, there still remains a critical unmet need to improve outcomes. SG previously demonstrated significant clinical benefit in pretreated metastatic TNBC (mTNBC). We report results from the ASCENT-04/KEYNOTE-D19 study in patients with previously untreated, PD-L1–positive (CPS ≥ 10; 22C3 assay) locally advanced unresectable or mTNBC. **Methods:** Patients were randomized 1:1 to SG (10 mg/kg IV, day 1 & 8) + pembro (200 mg, day 1, max 35 cycles) in 21-day cycles or chemo (gemcitabine + carboplatin, paclitaxel, nab-paclitaxel) + pembro until disease progression or unacceptable toxicity. Randomization was stratified by curative treatment-free interval, geography, and prior exposure to anti–PD-(L)1 therapy in the curative setting. Primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR). Key secondary endpoints include overall survival (OS); objective response rate (ORR) and duration of response (DOR) by BICR; and safety. **Results:** 443 patients were randomized at a 1:1 ratio: 221 to SG + pembro and 222 to chemo + pembro. The median follow-up was 14 mo. SG + pembro showed a significant improvement in PFS by BICR compared with chemo + pembro (hazard ratio [HR], 0.65; 95% CI, 0.51-0.84; P = .0009; Table). Median DOR was 16.5 mo for SG + pembro vs 9.2 mo for chemo + pembro (Table). Although OS data were immature, a positive early trend in OS improvement was also noted. The most frequent (≥ 10% of patients) grade ≥ 3 treatment-emergent adverse events (TEAEs) with SG + pembro were neutropenia (43%) and diarrhea (10%); and with chemo + pembro were neutropenia (45%), anemia (16%), and thrombocytopenia (14%). **Conclusions:** SG + pembro led to a statistically significant and clinically meaningful improvement in PFS vs chemo + pembro with durable responses, no new safety concerns for SG or pembro, and a lower rate of treatment discontinuation due to TEAEs in patients with previously untreated, PD-L1–positive advanced TNBC. These data support the use of SG + pembro as a potential new standard of care treatment in this patient population. Clinical trial information: NCT05382286. Research Sponsor: Gilead Sciences, Inc.

Efficacy, BICR, intent-to-treat	SG + pembro (n = 221)	Chemo + pembro (n = 222)
Median PFS (95% CI), mo	11.2 (9.3-16.7)	7.8 (7.3-9.3)
HR (95% CI); *P*-value (adjusted for randomization stratification factors)	0.65 (0.51-0.84); *P* = .0009	
ORR (95% CI), %	59.7 (52.9-66.3)	53.2 (46.4-59.9)
Median DOR (95% CI), mo	16.5 (12.7-19.5)	9.2 (7.6-11.3)
Safety (TEAEs), all treated, n (%)	**n = 221**	**n = 220**
Any grade; grade ≥ 3	220 (> 99); 158 (71)	219 (> 99); 154 (70)
Led to dose reduction	78 (35)	96 (44)
Led to any treatment discontinuation	26 (12)	68 (31)

LBA500 **Oral Abstract Session**

De-escalated neoadjuvant taxane plus trastuzumab and pertuzumab with or without carboplatin in HER2-positive early breast cancer (neoCARHP): A multicentre, open-label, randomised, phase 3 trial.

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Background: Neoadjuvant taxane, carboplatin and trastuzumab plus pertuzumab is associated with excellent treatment outcomes. The neoCARHP study aimed to evaluate the efficacy and safety of a de-escalated neoadjuvant taxane plus trastuzumab and pertuzumab with or without carboplatin in HER2-positive early breast cancer. **Methods:** The neoCARHP was a multicenter, open-label, randomized non-inferiority phase 3 trial conducted in 15 hospitals. Eligible patients were ≥18 years old with untreated, stage II-III, invasive HER2-positive breast cancer. Patients were stratified by nodal and hormone receptor status and randomized (1:1) to receive six 3-week cycles of an investigator-selected taxane (docetaxel, paclitaxel or nab-paclitaxel) plus trastuzumab (8 mg/kg loading dose, then 6 mg/kg every 3 weeks) and pertuzumab (840 mg loading dose, then 420 mg every 3 weeks), with carboplatin (TCbHP; AUC 6 mg/mL per min) or without carboplatin (THP). The primary endpoint was the pathological complete response (pCR) rate in the breast and axilla (ypT0/is ypN0), assessed in the modified intent-to-treat (mITT) population (all randomised patients who received at least one dose of study medication). The primary efficacy analysis was performed using the Cochran-Mantel-Haenszel χ^2 test(stratified by nodal and hormone receptor status), with a prespecified non-inferiority margin of -10%. Assuming a pCR rate of 62.8% for each group, 774 patients would provide 80% power at a one-sided significance level of 0.025, with an assumed 5% dropout rate. Safety was assessed in all patients who received the study drug. The trial is registered with ClinicalTrials.gov (NCT04858529), and adjuvant phase follow-up is ongoing. **Results:** Between April 30, 2021, and August 27, 2024, 774 patients were enrolled and randomized (387 per group), with 766 included in the mITT population (382 in THP and 384 in TCbHP). 245 (64.1% [95% CI 59.2-68.8]) patients in the THP group achieved pCR, compared with 253 (65.9% [61.0-70.5]) patients in the TCbHP group (absolute difference -1.8%, 95% CI -8.5 to 5.0; odds ratio 0.93, 95% CI 0.69 to 1.25; p=0.0089). Patients receiving THP had fewer grade 3–4 adverse events (79 of 382 [20.7%] vs 133 of 384 [34.6%]) and serious adverse events (5 of 382 [1.3%] vs 18 of 384 [4.7%]) compared with those receiving TCbHP. The most common grade 3-4 adverse events with THP were neutropenia (26 of 382 [6.8%] vs 63 of 384 [16.4%] with TCbHP), leukopenia (21 [5.5%] vs 57 [14.8%]) and diarrhoea (10 [2.6%] vs 16 [4.2%]). No treatment-associated deaths occurred. **Conclusions:** THP provided non-inferior pCR rates and improved tolerability compared with TCbHP. Omitting carboplatin could be an efficacious de-escalated neoadjuvant strategy in the presence of dual HER2 blockade for patients with HER2-positive early breast cancer. Clinical trial information: NCT04858529. Research Sponsor: National Natural Science Foundation of China; 82171898; National Natural Science Foundation of China; 82303848.

LBA509 Rapid Oral Abstract Session

NRG-BR003: A randomized phase III trial comparing doxorubicin plus cyclophosphamide followed by weekly paclitaxel with or without carboplatin for node-positive or high-risk node-negative TNBC.

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Background: NRG-BR003 is a phase III, randomized trial evaluating whether the addition of carboplatin (carbo) to an adjuvant chemotherapy regimen of doxorubicin/cyclophosphamide (AC) followed by paclitaxel (P) will improve invasive disease-free survival (IDFS) compared to AC followed by P when administered to patients (pts) with operable node-positive or high-risk node-negative triple-negative breast cancer (TNBC). **Methods:** Eligible pts had operable node-positive or high-risk node-negative TNBC and were randomized to receive dose-dense (DD) AC every 2 weeks for 4 cycles followed by weekly P (80 mg/m2) for 12 doses or the same regimen with carbo AUC of 5 IV every 3 weeks for 4 cycles. Stratification factors were number of positive nodes (0, 1-3, 4-9, 10+) and BRCA mutation status (positive; negative; or unknown). The study was designed to detect a hazard ratio (HR) in IDFS at 0.67 with the addition of carbo. The stratified log-rank test was used for the primary analysis. Secondary endpoints include DRFI, OS, BCFS, and RFI. **Results:** 769 pts were randomized to control arm (n=385) and carbo arm (n=384) from June 2015 to May 2022. Patient characteristics include age >50 (66%), primary tumors >2 cm (70%), node-positive (69%), and g*BRCA* pathogenic variants (9%). Delivery of AC was balanced between arms and P delivery was not compromised by co-administration of carbo with a mean of 11.3 doses (sd=2.1) of P with a relative total dose intensity (RTDI) at 0.97 in the control arm and 11.0 doses (sd=2.3) and a RTDI at 0.95 in the carbo arm. At data cutoff (2/28/25), median follow-up was 79.4 mos. IDFS events were reported in 92 pts (23.9%) in the control group and 76 (19.8%) in the carbo group. The stratified log-rank test p-value was 0.097, not meeting the prespecified significance of 0.049; the HR was 0.77 (95% CI, 0.57-1.05). The 5-year IDFS (95% CI) was 77.8% (73.7%-82.2%) vs 82.9% (79.2%-86.9%), respectively. HR was similar across patient subgroups, including germline *BRCA* and nodal status. Grade ≥3 treatment-related AE rates were 51.1% in the control group and 72.9% in the carbo group. Grade 5 events were 0.8% vs 0.8%, respectively. **Conclusions:** The addition of carbo to P following DD AC for adjuvant therapy of node-positive or high-risk node-negative TNBC did not result in a statistically significant improvement in IDFS, DRFI, or OS. However, it increased grade ≥3 treatment-related AE rates. Although not meeting criteria for efficacy across the entire study population, results support planned translational research to identify subsets of pts who may benefit from carbo. Clinical trial information: NCT02488967. Research Sponsor: National Cancer Institute; U10CA180868; National Cancer Institute; U10CA180822; National Cancer Institute; UG1CA189867; National Cancer Institute; U24CA196067.

Secondary efficacy results of DRFI and OS.

End Points	Treatment	5-year Event-free Rate (95% CI)	HR (95% CI)
DRFI			
	AC→P	84.4% (80.7-88.2)	1
	AC→P+Carbo	88.7% (85.5-92.0)	0.74 (0.50-1.10)
OS			
	AC→P	84.4% (80.8-88.3)	1
	AC→P+Carbo	87.7% (84.4-91.2)	0.81 (0.56-1.16)

LBA1000 Oral Abstract Session

Vepdegestrant, a PROTAC estrogen receptor (ER) degrader, vs fulvestrant in ER-positive/human epidermal growth factor receptor 2 (HER2)–negative advanced breast cancer: Results of the global, randomized, phase 3 VERITAC-2 study.

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Background: Vepdegestrant, an oral PROTAC (PROteolysis TArgeting Chimera) ER degrader, showed encouraging clinical activity and was well tolerated in a phase 1/2 study in pretreated patients (pts) with aBC, and is the first PROTAC to be evaluated in a phase 3 trial (VERITAC-2). **Methods:** Eligible pts (aged ≥18 y) had ER+/HER2- aBC, 1 prior line of a cyclin-dependent kinase (CDK)4/6 inhibitor plus endocrine therapy (ET) and ≤1 additional line of ET (most recent ET given for ≥6 mo before disease progression); pts with prior chemotherapy in the advanced setting or prior fulvestrant were excluded. Pts were randomized 1:1 to vepdegestrant 200 mg orally once daily continuously or fulvestrant 500 mg intramuscularly (days 1 and 15 of cycle 1; day 1 of subsequent cycles); pts were stratified by *ESR1* mutation status and presence of visceral disease. The primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR) in pts with *ESR1* mutations (*ESR1m*) and all pts. Overall survival (OS) was a key secondary endpoint. PFS was tested by stratified 1-sided log-rank. Median PFS (mPFS) was estimated by Kaplan-Meier method and hazard ratio (HR) by a stratified Cox proportional hazard model; study was designed to detect HR<0.60 with 88% power in pts with *ESR1m* and HR<0.67 with 92.5% power in all pts (1-sided α=0.01875). **Results:** 624 pts (median age: 60.0 y [range 26–89]) were randomized (n=313 vepdegestrant; 311 fulvestrant); 43.3% had *ESR1m* tumors (n=136 vepdegestrant; 134 fulvestrant). PFS by BICR was significantly longer with vepdegestrant vs fulvestrant among pts with *ESR1m* (174 events, HR=0.57 [95% CI 0.42–0.77]; *P*=0.0001); mPFS (95% CI) was 5.0 mo (3.7–7.4) vs 2.1 (1.9–3.5). PFS by BICR in all pts was not significantly different (384 events, HR=0.83 [95% CI 0.68–1.02]; *P*=0.0358); mPFS (95% CI) was 3.7 mo (3.6–5.3) vs 3.6 (2.2–3.8). OS data are immature (20% of targeted events in all pts). In 619 treated pts, treatment-emergent adverse events (TEAEs) were mostly grade 1/2. Grade ≥3 TEAEs occurred in 23.4% of pts in the vepdegestrant arm (vs 17.6% fulvestrant). The most common TEAEs in the vepdegestrant arm were fatigue (26.6% vs 15.6% fulvestrant), increased ALT (14.4% vs 9.8%), increased AST (14.4% vs 10.4%) and nausea (13.5% vs 8.8%). TEAEs led to discontinuation of vepdegestrant in 2.9% of pts (vs 0.7% fulvestrant). **Conclusions:** Vepdegestrant demonstrated statistically significant and clinically meaningful improvement in PFS vs fulvestrant in the *ESR1m* population. No statistically significant improvement in PFS was observed in the all-pt population. Vepdegestrant was generally well tolerated with low discontinuation rates due to TEAEs. Results support vepdegestrant as a potential oral treatment option for previously treated pts with *ESR1m* ER+/HER2- aBC. Clinical trial information: NCT05654623. Research Sponsor: Arvinas Operations, Inc.

LBA1005 Oral Abstract Session

A double-blind placebo controlled randomized phase III trial of fulvestrant and ipatasertib as treatment for advanced HER2-negative and estrogen receptor positive (ER+) breast cancer following progression on first line CDK 4/6 inhibitor and aromatase inhibitor: The CCTG/BCT MA.40/FINER study (NCT04650581).

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Background: Standard first line therapy in ER+/ HER2 negative endocrine sensitive metastatic breast cancer (MBC) is a CDK4/6 inhibitor plus AI. Upon progression the majority of patients will receive further endocrine based therapy. Alterations in PI3K/AKT pathway genes are a known mechanism of endocrine resistance – either *de novo* or acquired. The MA.40 trial evaluated the efficacy and safety of the AKT inhibitor ipatasertib versus placebo plus fulvestrant in the metastatic breast cancer (MBC) setting immediately post progression on 1st line CDK4/6 inhibitor and AI. **Methods:** This phase III, randomized, double-blind trial enrolled pre/peri/postmenopausal women and men with ER+/HER-2 negative MBC. Patients were randomly assigned 1:1 to receive ipatasertib plus fulvestrant versus (vs) placebo plus fulvestrant. Stratification factors included: AKT pathway altered (*PIK3CA*, *AKT1*, and/or *PTEN* genomic alteration(s)) vs wild-type/unknown and endocrine resistance (primary vs secondary). Primary objective: To compare investigator assessed PFS (RECIST 1.1) between treatment arms in the ITT population. Pre-specified secondary analysis: PFS in the AKT pathway altered cohort using a hierarchical procedure. The FoundationOne Liquid cfDNA NGS assay was utilized to assess genomic alterations in the AKT pathway for stratification. **Results:** 250 participants (females 247/males 3) were enrolled from Canada, Australia and New Zealand between January 2021 and May 2024. Baseline characteristics between arms were balanced. 44.4% of the study population had AKT pathway alteration(s) per cfDNA assay. Median follow-up 15.2 months(mo); proportion remaining on protocol treatment at time of analysis 21.0% ipatasertib vs 11.3% placebo arm. Median PFS ITT ipatasertib vs placebo arms were: 5.32 mo (95% CI: 3.58 to 5.62 mo) vs 1.94 mo (95% CI: 1.84 to 3.22) [HR 0.61, 95% CI: 0.46 to 0.81; p= 0.0007] and in the AKT pathway altered cohort: 5.45 mo (95% CI: 3.55 to 11.01) vs 1.91 mo (95% CI: 1.77 to 3.48) [HR = 0.47, 95% CI: 0.31 to 0.72; p= 0.0005]. Grade 3 or higher adverse events (AE) ipatasertib vs placebo arms (%):37.1 vs 27.4. Grade 3 or higher non haematological treatment related AE $>$ 1% ipatasertib vs placebo arms: diarrhea (16% vs 0%); fatigue (3% vs 0%); vomiting (2% vs 0), rash (2% vs 0%). Treatment discontinuation due to AEs ipatasertib vs placebo arms: 6.5% vs 0.8%. **Conclusions:** Ipatasertib plus fulvestrant significantly prolongs PFS compared to placebo/fulvestrant in patients with hormone receptor–positive MBC post progression on 1st line CDK 4/6 inhibitor and AI. Follow-up and additional analyses continue. Supported by Hoffmann-La Roche Ltd, CCS grant #707213. Clinical trial information: NCT04650581. Research Sponsor: Canadian Cancer Society (CCS); 707213.

LBA1008 **Oral Abstract Session**

Trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for first-line (1L) treatment of patients (pts) with human epidermal growth factor receptor 2–positive (HER2+) advanced/metastatic breast cancer (a/mBC): Interim results from DESTINY-Breast09.

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Background: DESTINY-Breast09 (NCT04784715) is a global, randomized Phase 3 study assessing the efficacy and safety of 1L T-DXd ± P vs THP in 1157 pts with HER2+ a/mBC. The CLEOPATRA study established THP as standard of care in this setting over a decade ago. **Methods:** Eligible pts had centrally confirmed HER2+ (IHC 3+ or ISH+) a/mBC and no prior chemotherapy or HER2-directed therapy for a/mBC ([neo]adjuvant HER2-directed therapy / chemotherapy with a disease-free interval of >6 months [mo] and ≤1 line of endocrine therapy for metastatic disease permitted). Pts were randomized 1:1:1 to T-DXd 5.4 mg/kg (+ placebo), T-DXd + P, or THP, stratified by de-novo vs recurrent disease, and hormone receptor (HR) and *PIK3CA* mutation status. In this planned interim analysis, data for T-DXd + P vs THP are presented; the T-DXd + placebo arm remains blinded until final PFS analysis. The primary endpoint was progression-free survival (PFS) by blinded independent central review (BICR) in the intent-to-treat population. Other endpoints included overall survival (OS), PFS by investigator (INV), objective response rate (ORR), duration of response (DOR), and safety. **Results:** Among the pts randomized to T-DXd + P (n=383) and THP (n=387), 52% had de-novo disease and 54% had HR+ status; demographic and disease characteristics were well balanced. At this interim data cutoff (Feb 26, 2025; median follow up 29 mo; 38% mature for PFS), T-DXd + P significantly improved PFS by BICR (hazard ratio 0.56; 95% CI 0.44, 0.71; P<0.00001) and INV (Table). PFS benefit was consistent across all subgroups. OS data were immature. Median response duration with T-DXd + P exceeded 3 years (Table). Grade ≥3 treatment-emergent adverse events (TEAEs) occurred in 63.5% and 62.3%, and serious TEAEs in 27.0% and 25.1%, of pts in the T-DXd + P and THP groups, respectively. Adjudicated drug-related interstitial lung disease/pneumonitis occurred in 46 (12.1%; predominantly Gr 1/2; n=2 [0.5%] Gr 5) pts who received T-DXd + P, and 4 (1.0%; all Gr 1/2) who received THP. **Conclusion:** T-DXd + P demonstrated a statistically significant and clinically meaningful improvement in PFS vs THP that was consistently observed across all subgroups and may represent a new 1L standard of care in HER2+ a/mBC; no new safety signals were identified. Clinical trial information: NCT04784715. Research Sponsor: AstraZeneca; Daiichi Sankyo.

	T-DXd + P (n=383)	THP (n=387)
Median PFS by BICR (95% CI), mo	40.7 (36.5, NC)	26.9 (21.8, NC)
Hazard ratio (95% CI) vs THP	0.56 (0.44, 0.71); P<0.00001	–
24-mo PFS rate (95% CI), %	70.1 (64.8, 74.8)	52.1 (46.4, 57.5)
Median PFS by INV (95% CI), mo	40.7 (36.5, NC)	20.7 (17.3, 23.5)
Hazard ratio (95% CI) vs THP	0.49 (0.39, 0.61)	–
Confirmed ORR by BICR (95% CI), %	85.1 (81.2, 88.5)	78.6 (74.1, 82.5)
Complete response rate, %	15.1	8.5
Median DOR by BICR (95% CI), mo	39.2 (35.1, NC)	26.4 (22.3, NC)

NC, not calculable.

LBA1512 Rapid Oral Abstract Session

Anesthesia type during surgery for treatment of biologically aggressive cancers: Results of the GA-CARES randomized, multicenter trial.

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Background: Surgical resection is a widely used treatment for cancer. Patients can be "seeded" with their own cancer cells during surgery, with the immune response to these circulating cancer cells influencing recurrence risk. Numerous preclinical and retrospective studies have suggested that propofol-based anesthesia may be superior to volatile halogenated ethers with respect to cell-mediated immunity, implantation of circulating tumor cells and cancer-related outcomes. Due to the above, an expert Consensus panel called for large, randomized trials on this topic. **Methods:** To test the hypothesis that propofol-based anesthesia leads to better cancer-related outcomes, adults at five U.S. sites scheduled for resection of biologically aggressive malignancies from the pancreas, esophagus, lung, stomach, bile ducts, liver, bladder, or peritoneal surface were randomly assigned to receive either propofol or a volatile agent for maintenance of general anesthesia. Data sources included the National Death Index (gold standard for vital status in the US), NY Cancer Registry, and hospital electronic medical records. The primary and key secondary endpoints were overall survival and disease-free survival, respectively. Assuming a 5% absolute difference in 2-year overall survival rates (85% vs 90%) between study arms, power using a planned two-sided log-rank test with type I error of 0.05 (no planned interim analyses) was calculated to be 97.4% based on a target enrollment of 1,800 subjects (final n=1,826). **Results:** The study population was diverse with 41.6% females, 22.1% non-whites, and 6.0% Latinos. Most patients were over 65 years of age and were at higher risk for surgery with approximately 85% classified as ASA 3 or 4. Adherence to the study protocol was very high with 95.9% of patients receiving the assigned anesthetic drug exclusively. Through up to 60 months of follow-up (median 40, IQR 22-60 months), 708 (40.2%) patients died in the intent-to-treat (ITT) population (n=1763). In contrast to our hypothesis, propofol-treated patients did not exhibit better survival (propofol 359 deaths/881 [40.7%] vs. volatile 349 deaths/882 [39.6%]; hazard ratio 1.07; 95%CI 0.92-1.24; P=0.371). In the per-protocol population (n=1411), significantly more patients randomized to propofol died through the prespecified 2-year follow-up (25.5% vs. 20%; hazard ratio 1.31; 95%CI 1.05-1.64; p=0.017). Results were similar for disease-free survival and were consistent across numerous prespecified subgroups. **Conclusions:** Our large, multicenter trial shows that propofol-based anesthesia is not effective at improving cancer-related outcomes in patients who undergo resection of biologically aggressive malignancies; paradoxically, its use might result in worse outcomes compared with volatile anesthesia. Clinical trial information: NCT03034096. Research Sponsor: None.

LBA1551 Poster Session

Cancer Care Beyond Walls (CCBW): A randomized pragmatic trial of home-based versus in-clinic cancer therapy administration.

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Background: Traditional cancer therapy is primarily delivered in clinical settings, imposing logistical, emotional, and financial burdens, particularly on rural and underserved patients. While international studies have demonstrated the safety of home-based chemotherapy, no randomized U.S. trials have evaluated this approach. Mayo Clinic's CCBW program aims to expand access to high-quality cancer care by providing in-home cancer treatment, lab testing, telemedicine, remote patient monitoring, command center and paramedic support. This pragmatic randomized controlled trial evaluates feasibility and impact of home-based versus in-clinic cancer directed therapy on patient preference, acceptability, safety, and patient-reported outcomes. **Methods:** Adult patients (ECOG 0-2) receiving chemotherapy or hormonal therapy at Mayo Clinic Florida were randomized 1:1 after confirmation of treatment tolerance in clinic to receive (1) home-based care for 24 weeks or (2) in-clinic care for 8 weeks followed by home-based care for 16 weeks. Target accrual is 200 patients. A planned interim analysis after 50 enrollments assessed accrual, data completeness, technical challenges, safety, and study outcomes. The primary endpoint is patient ratings of their overall cancer care experience (0–10 scale, CAHPS Cancer Care Survey) at 8 weeks. 200 patients provide 80% power to detect a 0.45 standard deviation difference in mean ratings between arms with a 2-sided 2-sample t-test (α=0.05) and 20% missing data rate. Secondary endpoints are patient preference, comfort with home infusions, treatment worthwhileness, functional/symptom assessments (EORTC QLQ-F17, PRO-CTCAE, GP5), grade $\geq$3 AEs, hospitalizations, and overall survival. Cost is a tertiary endpoint. The trial is IRB-approved (#23001719) and registered (NCT05969860). **Results:** Enrollment began 8/23/23. As of 2/21/25, 52 patients (26 per arm) were enrolled and 36 started protocol treatment. Common cancers were breast (38%), colorectal (21%), prostate (19%), and multiple myeloma (14%). 64% (28/44) of patients were female; 84% identified as White, 14% as Black, and 2% as multiple races. Median distance to clinic was 20 miles (range 2-66). After 8 weeks, patients in both arms rated their overall cancer care experience highly (mean [SD]=9.69 [0.85] versus 9.54 [0.66] for home-based vs. in-clinic care, n=26). After 24 weeks, 73% preferred home-based care, 18% had no preference, and 9% preferred in-clinic care; 100% felt comfortable with home infusions. No grade $\geq$3 AEs related to location of care have occurred. **Conclusions:** Early findings support the feasibility, safety, and high patient acceptability of home-based cancer therapy. No safety concerns related to care location were observed and most patients preferred home-based treatment. Ongoing accrual and analysis will assess clinical outcomes and cost implications. Clinical trial information: NCT05969860. Research Sponsor: Mayo Clinic.

LBA2000 **Oral Abstract Session**

Efficacy and safety of STUPP regimen with or without anlotinib for newly diagnosed glioblastoma: Results of a multicenter, double-blind, randomized phase II trial.

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Background: The standard STUPP regimen (radiotherapy with temozolomide [TMZ] followed by adjuvant TMZ) remains limited in efficacy for newly diagnosed glioblastoma (GBM). Anlotinib, a multi-kinase inhibitor targeting tumor angiogenesis and proliferation, showed promising progression-free survival (PFS) in a prior single-arm trial (NCT04119674). This multicenter, double-blind, randomized phase II trial (NCT04959500) evaluates STUPP plus anlotinib versus STUPP plus placebo. **Methods:** Eligible patients (≥18 years, ECOG ≤2) are randomized 1:1 to receive anlotinib (10 mg/day, days 1–14 per 21-day cycle) or placebo alongside TMZ-based chemoradiotherapy (54–60 Gy). Patients undergo six TMZ cycles and eight anlotinib/placebo cycles after radiotherapy, then receiving anlotinib/placebo until disease progression or unacceptable toxicity. Key exclusions include brainstem-only tumors, prior GBM therapy, IDH1/2 mutations, or significant intracranial hemorrhage. The primary endpoint is Independent Review Committee (IRC)-assessed PFS. Secondary endpoints include overall survival (OS), investigator-assessed PFS, objective response rate (ORR), and safety. With 150 patients (targeting 110 PFS events), the study has 80% power to detect a hazard ratio of 0.58, at a two-sided alpha level of 5%. Efficacy is analyzed in intent-to-treat populations using Kaplan-Meier estimates and log-rank tests, with ORR 95% CIs calculated via exact binomial methods. **Results:** A total of 153 patients were randomized in this study, 77 patients were in the anlotinib group and 76 patients were in the placebo group. Baseline characteristics were balanced. In the anlotinib (ALTN) and placebo (PLB) group, the median age was 55.4 and 55.1 years, 64 and 62 patients had an ECOG PS of 0-1, rate of MGMT methylation was 32.47% and 31.58%, respectively. The median follow-up duration was 27.53 months (95% CI 25.46-29.93) and 31.05 months (95% CI 26.25, 32.72) in the ALTN and PLB group. The median PFS evaluated by IRC was 9.89 months (95% CI 9.10, 11.56) in the ALTN group, 5.85 months (95% CI 3.58, 7.69) in the PLB group [HR 0.59 (95% CI 0.42,0.85), p= 0.0043]. The ORR evaluated by IRC was 16.88% (95% CI 9.31,27.14) in the ALTN group, 5.26% (95% CI 1.45,12.93) in the PLB group [p= 0.0220]. The most frequent grade 3 or higher toxicities in the ALTN and PLB group were thrombocytopenia (7.79% vs 1.32%), neutropenia (6.49% vs 3.95%), lymphocyte count decreased (6.49% vs 7.89%), white blood cell count decreased(6.49% vs 2.63%) and hypertension (5.19% vs 0%). **Conclusion:** This study had reached the primary endpoint of PFS evaluated by IRC, further data will be analyzed based on molecular pathology when OS data is mature. The combination of ALTN and STUPP regimen showed very good efficacy and favorable safety profile in patients with newly diagnosed GBM, with a simple and feasible treatment process. Clinical trial information: NCT04959500. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

LBA2512 Rapid Oral Abstract Session

The phase II NIBIT-ML1 study of nivolumab plus ipilimumab and ASTX727 or nivolumab plus ipilimumab in PD-1 resistant metastatic melanoma: Tumor methylation landscape and correlation with clinical outcomes.

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Background: In the NIBIT Foundation-sponsored phase Ib NIBIT-M4 study, we firstly showed that the hypomethylating agent (HMA) guadecitabine (guade), a prodrug of decitabine (D), followed by ipilimumab (I) was safe with promising clinical and immunologic activity in cutaneous metastatic melanoma (MM) patients (pts) (Di Giacomo, *Clin Cancer Res* 2019; Noviello, *Nat Commun 2023*). Thus, we further explored the activity of HMA combined with checkpoint inhibitors in the NIBIT-ML1 trial in which we investigated the efficacy of guade plus I+nivolumab (I+N) in PD-1/PDL-1-resistant MM and NSCLC pts. The primary analysis and the correlation between tumor methylome and immune contextures with the MM Cohort clinical outcome will be presented. **Methods:** The NIBIT Foundation NIBIT-ML1 is a multicenter, run-in, phase II randomized, non-comparative study (Simon two stages optimal design), in unresectable Stage III/IV MM (Cohort A) and NSCLC (Cohort B) pts progressing to PD-1/PDL-1 as last treatment. A Monitoring Committee reviewed safety data throughout the study. A trial amendment replaced guade with ASTX727, an oral fixed-dose combination of D with cedazuridine. Following a safety run-in of 6 pts, 36 eligible MM pts were randomized (1:1) to ASTX727 plus I+N or to I+N. Primary objective was immune(i)-ORR, according to a centralized radiologic assessment, defined as the proportion of pts with an iBOR of confirmed iCR/iPR. Secondary were: safety, DCR and PFS. Tumor methylation and immune contextures of serial tumor biopsies at baseline (W0) and on-treatment (W12 and/or W19) were investigated by EPIC Array and RNAseq. **Results:** Run-in phase: 6 Stage IV MM pts received guade (2 pts) or ASTX727 (4 pts) plus I+N. No DLT occurred. Three PR, 2 SD, and 1 PD were observed. Stage I: 36 Stage III (3)/IV (33) MM pts, received ASTX727 plus I+N (ARM A) or I+N (ARM B). ORR was 33% (2 CR, 4 PR) and 17% (3 PR) in ARM A and B; DCR was 56% in ARM A and 39% in ARM B. Both ARMs met the Stage I Simon design. The 1-year PFS rate was 43% and 11% for ARM A and B. With no overlapping toxicities, 1 DLT (G5 macrophage activation syndrome) was reported in ARM A. G3/4 TRAEs were 72% and 50% in ARM A and B, respectively, and G3/4 irAEs were 39% in ARM A and 44% in ARM B. A time-dependent reduction in tumor methylation levels in run-in and ARM A pts was observed, with more hypomethylated probes in on-treatment *vs* baseline tumors. Integrative methylation and transcriptomic analyses showed a promotion of immune regulatory genes, T and B cell activation in on-treatment tumors of ARM A pts. Enrichment of immune pathways was found in the Run-in and in ARM A responder pts. **Conclusions:** Treatment with ASTX727 plus I+N is feasible and has meaningful clinical and immunologic activity in PD-1 refractory MM pts. Clinical trial information: NCT04250246. Research Sponsor: None.

LBA3500 Oral Abstract Session

First-line encorafenib + cetuximab + mFOLFOX6 in BRAF V600E-mutant metastatic colorectal cancer (BREAKWATER): Progression-free survival and updated overall survival analyses.

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Background: BREAKWATER (NCT04607421) is an open-label, global, randomized, phase 3 study evaluating first-line (1L) encorafenib + cetuximab (EC) ± chemotherapy (chemo) vs standard of care (SOC; chemo ± bevacizumab) in BRAF V600E-mutant metastatic colorectal cancer (mCRC). The study previously met one of its dual primary endpoints (EPs) demonstrating clinically meaningful and statistically significant improvement in confirmed objective response rate (ORR) by blinded independent central review (BICR) in the ORR subset. These results were the basis for the FDA accelerated approval of EC+mFOLFOX6 for BRAF V600E-mutant mCRC, including in the 1L, under Project Frontrunner. Here, we report the primary analysis of progression-free survival (PFS) by BICR, updated interim analysis of OS, updated safety, and other analyses. **Methods:** Eligible patients (pts) with untreated BRAF V600E-mutant mCRC were randomized 1:1:1 to receive EC, EC+mFOLFOX6, or SOC; EC arm enrollment was closed after a protocol amendment. Dual primary EPs: ORR and PFS by BICR (EC+mFOLFOX6 vs SOC); key secondary EP: OS (EC+mFOLFOX6 vs SOC). **Results:** 637 pts were randomized to EC, EC+mFOLFOX6, or SOC. Baseline demographics and disease characteristics were generally balanced between arms. EC+mFOLFOX6 (data cutoff: Jan 6, 2025) demonstrated a clinically meaningful and statistically significant PFS improvement vs SOC, meeting the other dual primary EP; HR=0.53 (95% CI 0.407, 0.677; P<0.0001); median PFS 12.8 vs 7.1 mo. OS was clinically meaningful and statistically significant vs SOC; HR=0.49 (95% CI 0.375, 0.632; P<0.0001); median OS 30.3 vs 15.1 mo. Median PFS and OS in the EC arm were 6.8 and 19.5 mo. These data and response data for all randomized pts are shown in the table. Serious treatment-emergent adverse events occurred in 30%, 46%, and 39% of pts in the safety analysis set. Safety was consistent with that known for each agent. **Conclusions:** BREAKWATER demonstrated clinically meaningful and statistically significant PFS and OS improvements with EC+mFOLFOX6 vs SOC and manageable toxicities. EC+mFOLFOX6 is potentially practice changing as the new SOC. Clinical trial information: NCT04607421. Research Sponsor: Pfizer.

	EC n=158	EC+mFOLFOX6 n=236	SOC n=243	EC+mFOLFOX6 vs SOC HR (95% CI) P-value[a]
Median PFS[b], mo	6.8	12.8	7.1	0.53
(95% CI)	(5.7, 8.3)	(11.2, 15.9)	(6.8, 8.5)	(0.407, 0.677) <0.0001
Median OS, mo	19.5	30.3	15.1	0.49
(95% CI)	(17.6, 22.5)	(21.7, NE)	(13.7, 17.7)	(0.375, 0.632)<0.0001
ORR,[b] %	45.6	65.7	37.4	
(95% CI)	(38.0, 53.3)	(59.4, 71.4)	(31.6, 43.7)	
Median DOR[b], mo	7.0	13.9	10.8	
(95% CI)[c]	(4.2, 11.6)	(10.9, 18.5)	(7.6, 13.4)	
DOR[b] ≥6 mo, n (%)[c]	29 (40.3)	110 (71.0)	38 (41.8)	
DOR[b] ≥12 mo, n (%)[c]	15 (20.8)	54 (34.8)	16 (17.6)	
Median time to response,[b] wk	6.6	7.0	7.3	
(range)[c]	(4.3-86.4)	(5.1-103.6)	(5.4-48.0)	

[a]1-sided stratified log rank test.
[b]By BICR.
[c]Responders: n=72, n=155, and n=91.
DOR, duration of response.

LBA3502 Oral Abstract Session

Anlotinib versus bevacizumab added to standard first-line chemotherapy among patients with RAS/BRAF wild-type, unresectable metastatic colorectal cancer: A multicenter, prospective, randomised, phase 3 clinical trial (ANCHOR trial).

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Background: Anti-VEGF antibodies combined with chemotherapy remain first-line treatment for unresectable metastatic colorectal cancer (mCRC), but no randomised trials have evaluated oral VEGFR-TKI plus chemotherapy in this setting. **Methods:** In this Chinese multicenter, randomised, non-inferiority, phase 3 trial, treatment-naïve RAS/BRAF wild-type mCRC patients with MDT-assessed unresectable metastases were 1:1 randomised to receive anlotinib (12mg, QD, days 1-14) or bevacizumab (7.5mg/kg, IV, day 1), both combined with oxaliplatin (130mg/m^2, IV, day 1) and capecitabine (anlotinib group:850mg/m2, bevacizumab group 1000mg/m^2, BID, days 1-14) in 3-week cycles. After 4-8 induction cycles, maintenance therapy with anlotinib or bevacizumab plus capecitabine continued until progression/unacceptable toxicity. Stratification factors were tumor location (right/left) and prior adjuvant chemotherapy (yes/no). Primary endpoint was IRC-assessed PFS (non-inferiority margin HR≤1.09); secondary endpoints included investigator-assessed PFS, ORR, DCR, DoR, OS, liver metastases resection rate, and quality of life. With one-sided α=0.025 and 81.2% of power, 524 PFS events were required. **Results:** Between May 25th, 2021 to August 30th, 2023, 748 patients were randomly assigned and included in the intention-to-treat population, with 373 in anlotinib group and 375 in bevacizumab group. Patients had a median age of 59.0 years (IQR, 53.0-67.0) and 227 (30.35%) of all 748 patients were female. The median follow-up was 25.10 months (95% CI, 23.82-26.25). The median IRC-assessed PFS in anlotinib and bevacizumab group were 11.04 months (95% CI, 9.82-11.17) and 11.04 months (9.69-11.17), respectively, with HR 1.00 (0.84-1.18). Serious adverse events occurred in 143 (38.34%) of 373 patients in anlotinib group, and in 129 of 375 (34.40%) patients in bevacizumab group. **Conclusions:** In unresectable RAS/BRAF wild-type mCRC patients, anlotinib plus CapeOX showed comparable PFS time and safety compared with bevacizumab plus CapeOX. The results provide a new treatment option for unresectable RAS/BRAF wild-type mCRC patients. Clinical trial information: NCT04854668. Research Sponsor: Chia Tai Tianqing Pharmaceutical Group Co., Ltd.

	Anlotinib plus CapeOX (n=373)	Bevacizumab plus CapeOX (n=375)	HR (95% CI)
ORR (95% CI), %	61.93% (56.79-66.88)	62.13% (57.01-67.06)	
DCR (95% CI), %	92.76% (89.64-95.18)	93.07% (90.01-95.42)	
Median DoR (95% CI), months	9.66 (8.31-9.99)	9.69 (8.48-11.01)	1.04 (0.84-1.27)
Resection rate of liver metastases, %	3.75%	2.93%	
Grade ≥3 TEAE, n (%)	276 (73.99)	222 (59.20)	
TEAE leading to treatment discontinuation, n (%)	30 (8.04)	34 (9.07)	
TEAE leading to death, n (%)	16 (4.29)	17 (4.53)	

LBA3509 Clinical Science Symposium

Association between empirical dietary inflammatory pattern (EDIP) and survival in patients with stage III colon cancer: Findings from CALGB/SWOG 80702 (Alliance).

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Background: Systemic inflammation has been implicated in colon cancer progression. We examined whether intake of a proinflammatory diet is associated with survival among patients (pts) with stage III colon cancer. **Methods:** This prospective cohort study was nested within a randomized phase III trial of adjuvant therapy in pts with stage III colon cancer who had undergone curative-intent resection. EDIP score – a validated tool to classify the inflammatory nature of diets – was derived as a cumulative exposure using data from food-frequency questionnaires completed within 6 weeks of randomization and 14-16 months (mo) after randomization. Cox proportional hazards regression was used to assess the associations of EDIP with disease-free survival (DFS) and overall survival (OS). **Results:** Of 1625 included pts, the mean (SD) age was 60.9 (10.5) years (yrs). Compared to pts in the lowest EDIP quintile, pts in the highest quintile (a more inflammatory diet) were younger (58.7 ± 10.8 vs 61.3 ± 9.5 yrs old) and more likely to be female (64.0% vs 48.9%) and have worse performance status (ECOG 1-2: 35.7% vs 19.4%). Pts in the highest quintile were less likely to be White (76.6% vs 92.0 %) and more likely to be Black (15.4% vs 3.7%). Baseline aspirin use, assigned chemotherapy (3 mo vs 6 mo), and assigned pharmacotherapy (celecoxib vs placebo) were not significantly different across EDIP quintiles. Compared with pts in the lowest EDIP quintile, pts in the highest quintile had significantly worse OS (multivariable hazard ratio [HR] 1.87, 95% confidence interval [CI] 1.26-2.77, P_{trend}=0.01), but not DFS (HR 1.36, 95% CI 0.99-1.86, P_{trend}=0.22). Diet and physical activity jointly influenced OS. Those with lower EDIP scores (quintiles 1-4, 80% of the study population) and higher physical activity (≥9 MET-h/wk) had the best OS (HR 0.37, 95% CI 0.25-0.53) compared with pts in the highest EDIP quintile (20% of the study population) and lower physical activity (<9 MET-h/wk) ($P_{interaction}$ <0.001). The association between higher EDIP and OS was consistent when analyzed by celecoxib and placebo treatment arms ($P_{interaction}$ 0.54). The relationship between EDIP and OS did not differ significantly according to aspirin use, with HR 1.60 (95% CI 0.71-3.60) among aspirin users and HR 2.01 (95% CI 1.27-3.16) among aspirin non-users ($P_{interaction}$ 0.06). **Conclusions:** Our findings suggest that greater intake of a proinflammatory dietary pattern is associated with worse OS in pts with stage III colon cancer. Regular physical activity may attenuate the association, and further investigation of diet and physical activity intervention is warranted. Support: U10CA180821, U10CA180882, U24CA196171, U10CA180863, CCS 707213, UG1CA233234, U10CA180820, U10CA180868, U10CA180888; https://acknowledgments.alliancefound.org. Pfizer; ClinicalTrials.gov Identifier: NCT01150045. Research Sponsor: None.

LBA3510 Clinical Science Symposium

A randomized phase III trial of the impact of a structured exercise program on disease-free survival (DFS) in stage 3 or high-risk stage 2 colon cancer: Canadian Cancer Trials Group (CCTG) CO.21 (CHALLENGE).

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Background: Multiple observational studies have reported that post-diagnosis physical activity (PA) is associated with reduced recurrence rates in early-stage colon cancer but epidemiologic data is limited by confounding and reporting bias. CCTG CO.21 was designed to test the hypothesis that a meaningful increase in recreational PA after adjuvant therapy is achievable and will improve DFS in stage 3 or high-risk stage 2 colon cancer. **Methods:** CCTG CO.21 enrolled patients at 55 sites in 6 countries. Patients with resected stage 3 or high-risk stage 2 colon cancer who had received adjuvant chemotherapy were randomized to a structured exercise program (SEP) or health education materials (HEM). HEM participants received education materials promoting PA and healthy nutrition in addition to standard surveillance. SEP participants worked with a PA consultant who delivered an exercise intervention using behavior change methodology over 3 years. The SEP goal was to increase recreational PA by at least 10 MET-hours/week from baseline during the first 6 months and sustain this for 3 years. Participants chose the type, frequency, intensity and duration of aerobic exercise. The primary endpoint is DFS compared by a stratified log-rank test performed on an intention-to-treat basis. Secondary endpoints include overall survival (OS) and patient-reported outcomes (SF-36 physical function scale was primary PRO). **Results:** Between 2009 and 2024,889 participants were randomized to SEP (n=445) or HEM (n=444); 51% female, median age 61 years, 90% stage 3 disease. Compared to HEM, SEP resulted in statistically significant improvements in recreational PA, predicted VO2max, and 6-minute walk distance, all maintained over the 3-year intervention period. With a median follow-up of 7.9 years, 224 DFS events (93 in SEP and 131 in HEM) and 107 deaths (41 in SEP and 66 in HEM) were observed. 5-year DFS was 80% in SEP and 74% in HEM (HR 0.72; 95% CI 0.55-0.94; p=0.017). 8-year OS was 90% in SEP and 83% in HEM (HR=0.63; 95% CI=0.43-0.94; p=0.022). SF-36 physical function was substantially improved with SEP at 6 months (mean change scores 7.42 vs 1.10, $p<0.001$) and was sustained to 24 months. In the safety analysis, 19% (79/428) of patients on SEP reported any grade of musculoskeletal adverse event (MSK AE) over the course of the study, compared to 12% (50/433) on HEM. 10% (8/79) of MSK AE on SEP were considered to be related to participation in the PA program. **Conclusions:** Inpatients with stage 3 and high-risk stage 2 colon cancer, a 3-year structured exercise program initiated shortly after completion of adjuvant chemotherapy improves DFS, OS, patient-reported physical functioning, and health-related fitness. Health systems should incorporate structured exercise programs as standard of care for this patient population. Clinical trial information: NCT00819208. Research Sponsor: Canadian Cancer Society; National Health and Medical Research Council; Cancer Research UK; University of Sydney Cancer Research Fund.

LBA3511 **Clinical Science Symposium**

Aspirin as secondary prevention for colorectal cancer liver metastases (ASAC): A multicenter, randomized, double-blind, placebo-controlled, phase 3 trial.

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Background: Approximately 50% of patients with colorectal cancer develop liver metastases, and while surgical resection improves survival, over half experience recurrence. Evidence from laboratory and epidemiologic studies suggests that aspirin may have antineoplastic effects in colon cancer, but its role in the secondary prevention of colorectal cancer liver metastases remains unclear. **Methods:** This phase 3, randomized, double-blind, placebo-controlled trial was conducted across 14 centers in Norway, Sweden, and Denmark. Patients (aged ≥18 years old) radically treated for colorectal cancer liver metastases were randomly assigned in a 1:1 ratio using computer-generated blocks to receive aspirin 160 mg or placebo once daily for 3 years or until disease recurrence. Investigators and patients were masked to the treatment allocation. The primary endpoint was 3-year disease-free survival from the start of medication, with analyses performed on the full analysis set. The hazard ratio comparing the two treatment groups was estimated by Cox regression, and the 3-year disease-free survival in each group was estimated by the Kaplan-Meier method. **Results:** Between Dec 2017 and Jan 2022, 466 patients were randomly assigned to treatment (aspirin, n=234; placebo, n=232). There were 38 who did not start treatment (17/21 allocated to aspirin/placebo). All patients who started medication were included in the full analysis set (aspirin, n=217; placebo, n=211). Of these patients, the mean age was 62 years and 272 (64%) were males and 156 (36%) females. The primary tumor site was in right colon, left colon, or rectum in 98 (45.2%), 37 (17.1%), 82 (37.8%) in the aspirin group and 94 (44.5%), 54 (25.6%), 63 (29.9%) in the placebo group, respectively. Synchronous liver metastasis was present in 98 (45.2%) and 88 (41.7%) in the aspirin and placebo groups, respectively. The 3-year disease-free survival showed a hazard-ratio (HR) estimate of 1.06 (95% confidence interval (CI) 0.77–1.45, p-value 0.64) in disfavor of aspirin. The probability of surviving past 36 months was 76.1% in the aspirin group and 84.9% in the placebo group, with an overall survival HR of 1.60 (95% CI 0.99–2.61, p=0.057) in favor of the placebo. Adverse events were reported in 53 patients in the aspirin group (24.4%) and 42 patients in the placebo 19.9%). Among these, 17 participants in the aspirin group and 4 in the placebo group (7.8% vs 1.9%) had at least one serious adverse event. There were no treatment-related deaths in either group. **Conclusions:** This phase 3 trial showed that in patients with colorectal cancer liver metastasis, daily aspirin 160 mg after complete tumor removal did not improve disease-free or overall survival. Additionally, aspirin was associated with an increased incidence of serious adverse events. Clinical trial information: NCT03326791. Research Sponsor: Norwegian Cancer Society; Research Council of Norway; Therapy Research in the Specialist Health Services Norway (KLINBEFORSK); Oslo University Hospital.

LBA3515 Rapid Oral Abstract Session

Panitumumab retreatment followed by regorafenib versus the reverse sequence in chemorefractory metastatic colorectal cancer patients with *RAS* and *BRAF* wild-type circulating tumor DNA (ctDNA): Results of the phase II randomized PARERE trial by GONO.

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Background: Retreatment (re-tx) with anti-EGFR monoclonal antibodies offers a promising approach to extend the *continuum of care* of patients (pts) with *RAS* and *BRAF* wild-type (wt) metastatic colorectal cancer (mCRC) with no mutations of resistance in their ctDNA at the time of treatment re-exposure. **Methods:** PARERE (NCT04787341) is an open-label, multicenter, randomized phase II trial investigating the optimal sequencing of panitumumab (pani) and regorafenib (rego) in the chemorefractory setting of *RAS* and *BRAF* wt mCRC pts, who previously derived benefit from first-line anti-EGFR-containing regimens, then received at least one intervening anti-EGFR-free line of treatment, and were prospectively selected for the absence of *RAS* and *BRAF* mutations in their ctDNA. Eligible pts were randomized 1:1 to receive pani followed by rego after progression (arm A) *versus* the reverse sequence (arm B). Primary endpoint was overall survival (OS). 155 events were required to detect a hazard ratio (HR) of 0.69 in favor of arm B, using a two-sided unstratified log-rank test, with type I error of 0.15 and 80% power. Secondary endpoints included 1st and 2nd objective response rate (ORR), disease control rate (DCR), progression-free survival (PFS), and safety. **Results:** From December 2020 to December 2024, 428 pts from 37 Italian centers underwent molecular screening, and 213 with *RAS* and *BRAF* wt ctDNA were randomized (arm A/B = 106/107). Median age was 61 and 64 years (A/B), most pts had left-sided primary tumors (92/88%, A/B), and had received a median of 2 prior lines of therapy in both tx arms. After a median follow-up of 23.5 months (mos), 194 and 135 1st and 2nd disease progression events were recorded, while OS data were not mature yet. Key efficacy outcomes are summarized in the table. Adverse events occurred with the expected frequency and grade in both treatment arms. **Conclusions:** PARERE is the largest randomized trial demonstrating an ORR and PFS advantage in favor of liquid biopsy-guided anti-EGFR re-tx, compared to regorafenib, in the late-line setting of *RAS*/*BRAF* wt mCRC. Clinical trial information: NCT04787341. Research Sponsor: GONO Foundation; Amgen; Bayer.

	ARM A[a] pani, N = 106	ARM B rego, N = 107		p*	p**
1st PFS, median mos	4.1	2.4	HR: 1.23 (95% CI: 0.93 – 1.64)	0.15	0.12
1st ORR, %	16.0	1.9	OR: 0.1 (95% CI: 0.01 – 0.44); p < 0.01		
1st DCR, %	59.4	31.8	OR: 0.32 (95% CI: 0.18 – 0.56); p < 0.01		
	ARM A[a] rego, N = 75	**ARM B pani, N = 70**			
2nd PFS, median mos	2.7	3.7	HR: 0.76 (95%CI: 0.54 – 1.07)	0.12	0.07
2nd ORR, %	0	17.4	OR: NA (95% CI: 3.44 - NA); p < 0.01		
2nd DCR, %	37.3	55.7	OR: 2.17 (95% CI: 1.11 – 4.27); p = 0.02		
Per protocol population[b]					
2nd PFS, median mos	2.7	3.9	HR: 0.71 (95%CI: 0.5 – 1.01)	0.06	0.03

OR, Odds Ratio; CI, confidence interval; NA, not assessable; *Cox proportional hazards model; **stratified log-rank test according to ECOG PS; [a]reference; [b]pts actually treated with rego and pani (A/B, N = 68/69).

LBA3516 Rapid Oral Abstract Session

JMT101 in combination with irinotecan and SG001 versus regorafenib in patients with metastatic colorectal adenocarcinoma (mCRC): Results of a randomized, controlled, open-label, phase II study.

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Background: Both Becotatug (JMT101, humanized IgG1 anti-EGFR monoclonal antibody [mAb]) ± chemotherapy, and Enlonstobart (SG001, humanized IgG4 anti-PD-1 mAb), demonstrated promising antitumor activity with favorable safety in advanced solid tumors. This study evaluates the safety and preliminary efficacy of JMT101 + SG001 + irinotecan in patients (pts) with metastatic colorectal adenocarcinoma (mCRC). **Methods:** This multicenter, randomized, open-label phase II study enrolled pts with histologically or cytologically confirmed RAS/BRAF wild-type mCRC without MSI-H/dMMR, who had progressed after ≥ 2 prior systemic therapies. Upon dose confirmation in safety run-in part (SRI, 3-6 pts, JMT101 6 mg/kg + irinotecan 180 mg/m^2 + SG001 240 mg Q2W), eligible pts, stratified by PD-L1 expression (+/-), were randomized 1:1:1 to receive either JMT101 + irinotecan + SG001 (Arm A), JMT101 + irinotecan (Arm B), or regorafenib 160mg QD, days 1-21 of 28-day cycles (Arm C). The primary endpoint is the ORR per RECIST v1.1 by investigator. **Results:** After the SRI in 3 pts, 106 additional pts (median age 58 yrs [25-74], 62.3% male) were randomized (36/35/35 in Arm A/B/C). As of Jan 24, 2025, all SRI pts and 69/106 (65.1%) randomized pts (18/21/30 in Arm A/B/C) completed treatment. The median follow-up was 7.4 months, with 34, 35, 34 efficacy-evaluable pts in Arm A, B, and C, respectively. Detailed efficacy data are shown in the table. Arm A and B had comparable ORR, DCR, and PFS, all statistically superior to Arm C. The median OS was not reached. Grade ≥ 3 treatment-related adverse events (TRAEs) occurred in 38.9% (14/36), 54.3% (19/35), and 48.6% (17/35) pts in Arm A, B, and C, respectively. No TRAEs led to discontinuation in Arm A/B, compared to 2/35 (5.7%) in Arm C. No TRAEs leading to death occurred. **Conclusions:** Our results demonstrated a promising response rate and a tolerable safety profile of JMT101 + irinotecan +/- SG001 in pts with mCRC. Preliminary data support continued investigation, with updated results to follow. Clinical trial information: NCT06089330. Research Sponsor: Shanghai JMT-Bio Technology Co., Ltd.

	CR	PR	SD	PD	NE	ORR	RD*	DCR	RD*	6 mo-DoR	mPFS mo (95% CI)	P value#
SRI	0	1 (33.3)	0	2 (66.7)	0	33.3 (0.84, 90.6)	/	33.3 (0.84, 90.6)	/	/	2.0 (0.92, NR)	/
Arm A	0	15 (44.1)	13 (38.2)	4 (11.8)	2 (5.90)	44.1 (27.2, 62.1)	41.2 (23.7, 58.6)	82.4 (65.5, 93.2)	20.6 (0.06, 41.1)	48.0 (12.7, 77.0)	5.7 (3.75, NR)	0.003
Arm B	0	12 (34.3)	18 (51.4)	5 (14.3)	0	34.3 (19.1, 52.2)	31.1 (14.6, 47.5)	85.7 (69.7, 95.2)	23.9 (3.85, 43.9)	71.4 (25.8, 92.0)	7.4 (3.91, NR)	<0.001
Arm C	0	1 (2.90)	20 (58.8)	13 (38.2)	0	2.9 (0.07, 15.3)	Ref.	61.8 (43.6, 77.8)	Ref.	/	2.9 (2.14, 3.71)	1.000

Data are n (%) or % (95% CI), unless noted.
*Rate difference, analyzed by Cochran-Mantel-Haenszel test.
#Estimated via stratified log - rank test, stratifying by PD-L1 expression (+/-).

LBA3555 Poster Session

Safety and efficacy of reduced-port laparoscopic surgery for patients with colon and upper rectal cancer.

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Background: Radical laparoscopic resection is the mainstay of treatments for non-metastatic colorectal cancer (CRC). Reduced-port laparoscopic surgery (RPLS) has emerged with the concept of more minimal invasion on the basis of conventional laparoscopic surgery (CLS). RPLS has only 3 or 4 ports for surgeon and observer, which might increase the difficulty of the operation. The efficacy and safety of RPLS for CRC remains unclear. This study aims to evaluate the curative effect and safety of RPLS versus CLS for resectable CRC, which is registered with ClinicalTrials.gov (NCT05953662). **Methods:** From July 2023 to December 2024, a total of 500 patients with CRC received surgical treatment in the Sixth Affiliated Hospital of Sun Yat-sen University, Nanfang Hospital of Southern Medical University and Ruijin Hospital of Shanghai Jiao Tong University School of Medicine were enrolled in this prospective cohort study. The primary outcome measure is 1 year disease free survival (DFS). The secondary outcome measures are total operation time, intraoperative blood loss, postoperative hospital stays, complication rate, mortality, 3 years DFS and OS. Patients were randomized divided into RPLS group (n=250) and CLS group (n=250). The study has completed recruitment. **Results:** There were no significant differences of the clinical characteristics between the two groups. The RPLS group had significantly less intraoperative blood loss (26.23±22.33 ml vs 50.72±80.10 ml, $P<0.001$). The total operation time was also shorter for the RPLS group (147.89±52.40 min vs 189.77±67.79 min, $P<0.001$). The postoperative hospital stay was shorter for the RPLS group (7.63±4.45 days vs 8.22±3.61 days, $P<0.001$). Regarding postoperative complications, the RPLS group is comparable with CLS group in a total of grade I/II/III complication rate (6% vs 3.2%, $P=0.154$). Grade III complications were few in both groups, presenting in 0.4% of the RPLS group and 0.8% of the CLS group. The pTNM stage distribution was similar between the groups, with no significant differences ($P=0.59$). The mean number of harvested lymph nodes was similar (22.25±13.72 vs 23.55±18.22, $P=0.413$), as well as the mean number of positive lymph nodes (1.04±2.54 vs 0.93±2.23, $P=0.556$). All of the participants were received a radical resection (R0 resection) with negative margin and circumferential resection margin. There was no mortality in 30 days postoperative. With a median follow-up of 10 months, 2 cases experienced metastasis in the RPLS group and 4 cases in the CLS group experienced postoperative recurrence and metastasis. **Conclusion:** RPLS demonstrated non-inferiority in surgical safety compared to CLS, with significantly less intraoperative blood loss, shorter operation time. Additionally, RPLS showed superior postoperative recovery, with a shorter hospital stay. We need a long-term follow-up to validate the oncology safety of the reduced-port approach. Clinical trial information: NCT05953662. Research Sponsor: National Natural Science Foundation of China.

LBA4002 **Oral Abstract Session**

Trastuzumab deruxtecan (T-DXd) vs ramucirumab (RAM) + paclitaxel (PTX) in second-line treatment of patients (pts) with human epidermal growth factor receptor 2-positive (HER2+) unresectable/metastatic gastric cancer (GC) or gastroesophageal junction adenocarcinoma (GEJA): Primary analysis of the randomized, phase 3 DESTINY-Gastric04 study.

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Background: T-DXd 6.4 mg/kg is approved for pts with metastatic HER2+ GC/GEJA who received a prior trastuzumab-based regimen based on prior phase 2 studies. This is the primary efficacy analysis from a planned interim analysis of DESTINY-Gastric04 (NCT04704934), a global, randomized, multicenter, open-label, phase 3 study evaluating the efficacy and safety of T-DXd vs RAM + PTX in pts with HER2+ unresectable/metastatic GC/GEJA in this second-line setting. **Methods:** After biopsy-confirmed HER2+ status (IHC 3+ or IHC 2+/ISH+), pts were randomized 1:1 to T-DXd 6.4 mg/kg or RAM + PTX. The primary endpoint was overall survival (OS). OS between the 2 arms was compared by a log-rank test stratified using randomization factors. Secondary endpoints by investigator assessment include progression-free survival (PFS), confirmed objective response rate (cORR), disease control rate (DCR), and safety. **Results:** At data cutoff (October 24, 2024), 494 pts were assigned (T-DXd, n = 246; RAM + PTX, n = 248). Based on 266 OS events observed (information fraction = 78.5%), efficacy superiority was achieved (2-sided $P < 0.0228$). Median (m) (95% CI) OS follow-up was 16.8 mo (14.0-20.0) for T-DXd and 14.4 mo (13.1-19.7) for RAM + PTX. mOS (95% CI) was 14.7 mo (12.1-16.6) for T-DXd vs 11.4 mo (9.9-15.5) for RAM + PTX (hazard ratio [HR], 0.70; $P = 0.0044$). Additional efficacy data are in the Table. Median (range) treatment duration was 5.4 mo (0.7-30.3) with T-DXd and 4.6 mo (0.9-34.9) with RAM + PTX. Treatment-emergent adverse events (TEAEs) were reported in 244/244 (100%) vs 228/233 pts (97.9%) with T-DXd vs RAM + PTX, respectively; 68.0% vs 73.8% were grade (G) ≥3. Serious TEAEs with T-DXd vs RAM + PTX occurred in 41.0% vs 43.3% of pts; TEAEs associated with drug discontinuation occurred in 14.3% vs 17.2% of pts. Independently adjudicated drug-related interstitial lung disease/pneumonitis occurred in 34 pts (13.9%) with T-DXd (1 G3, 0 G4/5) vs 3 pts (1.3%) with RAM + PTX (2 G3, 1 G5). **Conclusions:** T-DXd showed statistically significant and clinically meaningful improvement in OS over RAM + PTX in pts with HER2+ unresectable/metastatic GC/GEJA, reinforcing its use as a second-line standard of care. The safety profile of T-DXd 6.4 mg/kg was consistent with the known safety profile of T-DXd in GC/GEJA, with no new safety signals. Clinical trial information: NCT04704934. Research Sponsor: Daiichi Sankyo, Inc.

Efficacy	T-DXd n = 246	RAM + PTX n = 248	HR (95% CI) *P* value
mOS (95% CI), mo	14.7 (12.1-16.6)	11.4 (9.9-15.5)	0.70 (0.55-0.90) *P*= 0.0044
mPFS (95% CI), mo	6.7 (5.6-7.1)	5.6 (4.9-5.8)	0.74 (0.59-0.92) *P*= 0.0074
cORR (95% CI), %	44.3 (37.8-50.9)	29.1 (23.4-35.3)	*P* = 0.0006
DCR (95% CI), %	91.9 (87.7-95.1)	75.9 (70.0-81.2)	

LBA4004 **Oral Abstract Session**

Results of a randomized phase III trial of pre-operative chemotherapy with mFOLFIRINOX or PAXG regimen for stage I-III pancreatic ductal adenocarcinoma.

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Background: Preoperative mFOLFIRINOX is a treatment option for patients (pts) with resectable/borderline resectable (R/BR) pancreatic ductal adenocarcinoma (PDAC). **Methods:** CASSANDRA (NCT04793932) is a multicenter phase 3 superiority trial randomizing pts ≤75y with R/BR PDAC, stratified by site and CA19.9, in a 2 by 2 factorial design to receive either PAXG (oral daily capecitabine 1250 mg/m^2 with biweekly cisplatin 30 mg/m^2, nab-paclitaxel 150 mg/m^2, gemcitabine 800 mg/m^2; arm A) or mFOLFIRINOX (biweekly 5-fluorouracil 2400 mg/m^2, irinotecan 150 mg/m^2, oxaliplatin 85 mg/m^2; arm B; 1st random) for either 6 months before or 4 months before and 2 months after surgery (2nd random). The results of 1st random are presented. The primary endpoint is event-free survival (EFS = absence of progression, recurrence, 2 consecutive CA19.9 increases ≥20% separated by ≥ 4 weeks, unresectability, intraoperative metastasis, death) in the intention-to-treat population (ITT). Secondary endpoints are overall survival (OS), radiological, CA19.9, and pathological response rate, resection rate, toxicity, QoL in the ITT. With 173 events (260 pts) the study has a power of 80% to demonstrate a statistically significant difference at 5% two sided stratified logrank test under the alternative hypothesis of HR=0.65. EFS and OS were analyzed by Kaplan-Meier and log-rank test, HR estimated by Cox proportional hazard model. **Results:** Between Nov 2020 and Apr 2024, 260 eligible pts (tab 1) were randomly assigned to either arm A (N=132) or B (N=128). At data cutoff on March 1, 2025, with a median follow-up of 23.9 mos, 3y EFS was 30% (CI 20% – 40%) in arm A and 14% (CI 5% – 23%) in arm B with HR 0.66 (CI 0.49-0.89, p=0.005). In A/B, disease control rate was 98%/91% (p=0.009); CA19.9 reduction>50% 88/64% (p=<0.001); resection rate 75/67% (p=0.165); pathologic stage < II 35/23% (p=0.03); main G3-4 toxicity was: neutropenia 44/30%; fatigue 8/8%; diarrhea 2/5%; nausea/vomiting 7/10%; neuropathy 7/4%; AST/ALT 3/8%; infections 6/9%. **Conclusions:** Neoadjuvant PAXG significantly improved EFS compared to mFOLFIRINOX in pts with R/BR PDAC. Clinical trial information: NCT04793932. Research Sponsor: Non-Profit Patient Associations: MyEverest; Codice Viola; Per la Vita; Oltre la Ricerca; Associazione Pierluigi Natalucci.

	A	B
Age	65 (42-76)	63 (41-76)
Females	68 (52%)	62 (48%)
KPS 90-100	123 (93%)	117 (91%)
cStage I-II	119 (90%)	115 (90%)
III	13 (10%)	13 (10%)
R	63 (48%)	63 (49%)
BR	69 (52%)	65 (51%)
CA19.9 Normal	32 (24%)	43 (34%)
Increased Median	261	226

LBA4005 Oral Abstract Session

PANOVA-3: Phase 3 study of tumor treating fields (TTFields) with gemcitabine and nab-paclitaxel for locally advanced pancreatic ductal adenocarcinoma (LA-PAC).

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Background: To date, no phase 3 clinical trial has demonstrated an overall survival (OS) benefit in patients with locally advanced pancreatic adenocarcinoma (LA-PAC). TTFields are electric fields that disrupt cancer cell division. TTFields therapy is approved for glioblastoma, pleural mesothelioma, and metastatic non-small cell lung cancer. A phase 2 trial in PAC demonstrated the safety and preliminary efficacy of TTFields therapy with gemcitabine with or without nab-paclitaxel. We report final data from PANOVA-3 (NCT03377491), the largest global, phase 3, randomized, open-label trial in LA-PAC to date. **Methods:** Adult patients with newly diagnosed unresectable LA-PAC were randomized 1:1 to receive TTFields therapy (150 kHz) with gemcitabine/nab-paclitaxel (GnP) or GnP. The primary endpoint was OS. Secondary endpoints included progression-free survival (PFS), local PFS, objective response rate (ORR), and pain-free survival. Distant PFS (metastases beyond the pancreas and regional lymph nodes) was assessed post hoc. Survival data were compared using the Kaplan-Meier method and a log-rank test. **Results:** 571 patients were randomized. Baseline characteristics were generally well balanced between the study arms. OS was significantly longer with TTFields/GnP than with GnP (median 16.2 [95% CI: 15.0, 18.0] vs 14.2 months [95% CI: 12.8, 15.4]; HR 0.82 [95% CI: 0.68, 0.99], p=0.039). One-year survival rate was also significantly improved with TTFields/GnP vs GnP (68.1% [95% CI: 62.0-73.5] vs 60.2% [95% CI: 54.2-65.7], p=0.029). There was no significant difference in PFS or local PFS between arms. Pain-free survival was significantly longer with TTFields/GnP vs GnP (median 15.2 [95% CI: 10.3, 22.8] vs 9.1 months [95% CI: 7.4, 12.7]; HR 0.74 [95% CI: 0.56, 0.97], p=0.027). Post-hoc analysis showed significant distant PFS benefit (median 13.9 [95% CI: 12.2, 16.8] vs 11.5 months [95% CI: 10.4, 12.9], HR 0.74 [95% CI: 0.57, 0.96], p=0.022) with TTFields/GnP vs GnP. ORR was similar between arms (36.1% [95% CI: 30.0, 42.4] vs 30.0% [95% CI: 24.3, 36.2], p=0.094). 97.8% and 98.9% of patients who received TTFields/GnP and GnP, respectively, had adverse events (AEs) and 88.6% and 84.3% had grade ≥3 AEs. The most frequent grade ≥3 AEs were neutropenia (47.8% and 47.6%) and anemia (21.9% and 22.3). 81% of patients receiving TTFields/GnP had device-related AEs, mostly grade 1/2 skin AEs, e.g., dermatitis (27.7%), rash (17.5%), and pruritus (15.0%); grade 3 and grade 4 device-related AEs occurred in 9.1% and 0.4% of patients, respectively. **Conclusions:** PANOVA-3 is the largest phase 3 trial exclusively performed in patients with LA-PAC and the first to show a statistically significant OS benefit. With no additive systemic toxicity and a statistically significant pain-free survival benefit, TTFields therapy is a potential new standard treatment for LA-PAC. Clinical trial information: NCT03377491. Research Sponsor: Novocure GmbH.

LBA4012 **Rapid Oral Abstract Session**

Disitamab vedotin (DV) plus toripalimab (Tor) and chemotherapy (C)/trastuzumab (Tra) as first-line (1L) treatment of patients (pts) with HER2-expressing locally advanced or metastatic (la/m) gastric cancer.

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Background: DV+T showed encouraging efficacy with manageable safety for pts with HER2-expressing gastric or gastroesophageal junction (G/GEJ) cancer in the second- and later-line setting in a phase 1 trial (Wang et al, eClinicalMedicine, 2024). Here, we first report the efficacy and safety of 1L DV+Tor+C/Tra in pts with HER2-postive or HER2-low la/m G/GEJ cancer from the randomized phase 2 part of a seamless phase 2/3 trial. **Methods:** Pts with previously untreated HER2-positive (IHC 3+, or IHC 2+/FISH+) la/m G/GEJ cancer were randomized (1:1:1) to receive DV (2.5 mg/kg, Q2W) + Tor (3.0 mg/kg, Q2W) + CAPOX (oxaliplatin [OX]: 130 mg/m^2, day 1; capecitabine [CAP]: 1000 mg/m^2, days 1-14; Q3W) (experimental group [EG] 1), or DV + Tor +Tra (staring dose of 8 mg/kg followed by 6 mg/kg, Q3W) (EG2), or Tor + Tra + CAPOX (control group [CG] 1). For pts with HER2-low (IHC 1+, or IHC 2+/FISH-) la/m G/GEJ cancer, they were initially randomized (1:1) to receive DV (2.5 mg/kg) + Tor + CAPOX (EG1), or Tor + CAPOX (CG1) in stage 1; based on the safety data from stage 1, stage 2 was designed to randomize pts (1:1:1) to receive DV (2.5 mg/kg) + Tor + CAPOX (reduced dose: OX 100 mg/m^2; CAP 750 mg/m^2) (EG2), or DV (2.0 mg/kg) + Tor + CAPOX (reduced dose) (EG3), or Tor + CAPOX (CG2). The primary endpoint was objective response rate (ORR). **Results:** By date cutoff (Feb 7, 2025), 51 HER2-positive pts (mostly being HER2 IHC 3+) and 93 HER2-low pts (mostly being HER2 IHC 1+) were enrolled. In HER2-positive pts, superior ORR of 82.4% was observed in EG2. In HER2-low pts, the ORR was 70.8% in EG1 and the hazard ratio (HR) for PFS was 0.67 compared to CG1 in stage 1, which favored the experimental group; the highest ORR was 76.9% in EG2 in stage 2. Main outcomes are listed in the Table. Data will be updated during presentation. **Conclusions:** In pts with HER2-positive la/m G/GEJ cancer, DV + Tor + Tra demonstrated a superior ORR, offering a potential chemo-free treatment option. In pts with HER2-low la/m G/GEJ cancer, DV + Tor + CAPOX showed superior ORR and PFS with a manageable safety profile; lowering the CAPOX dose improved tolerability of the combination therapy while maintaining high efficacy. Clinical trial information: NCT05980481. Research Sponsor: RemeGen Co., Ltd.

	HER2-positive pts			HER2-low pts				
	/			Stage 1		Stage 2 (dose optimization)		
	EG1 (n=18)	EG2 (n=17)	CG1 (n=16)	EG1 (n=25)	CG1 (n=23)	EG2 (n=14)	EG3 (n=15)	CG2 (n=16)
Confirmed ORR*, % (95% CI)	66.7 (41.0-86.7)	82.4 (56.6-96.2)	68.8 (41.3-89.0)	70.8 (48.9-87.4)	47.8 (26.8-69.4)	76.9 (46.2-95.0)	60.0 (32.3-83.7)	46.7 (21.3-73.4)
Median PFS follow-up, months	11.2	12.2	12.2	9.7			5.6	
Median PFS (95% CI), months		Immature		9.7 (5.8-NE)	7.2 (5.4-11.3)		Immature	
HR		/		0.67			/	
Any-G/G ≥3 TRAEs, %	100/ 94.4	100/ 82.4	100/ 75.0	100/ 100	100/ 87.0	100/ 85.7	100/ 73.3	100/ 75.0

*In pts with ≥1 post-baseline tumor assessment. PFS, progression-free survival; NE, not estimable; G, grade; TRAE, treatment-related adverse event.

LBA4175 Poster Session

NAPOLI 3, a phase 3 study of NALIRIFOX in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC): Final overall survival (OS) analysis and characteristics of the long-term survivors.

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Background: Metastatic pancreatic ductal adenocarcinoma (mPDAC) is an aggressive malignancy with a median overall survival (mOS) of between 8 and 11 months. With the use of modern chemotherapy regimens, some patients with mPDAC have been shown to achieve long-term survival of 18 months or longer (Rochefort *et al. Oncol.* 2019;24:1543–8). The aim of this analysis was to describe long-term survivors among the North American population treated with liposomal irinotecan plus 5-fluorouracil/leucovorin and oxaliplatin (NALIRIFOX) in the NAPOLI 3 trial and to explore clinical and pathological factors that might be associated with prolonged survival. **Methods:** Patients with confirmed untreated mPDAC randomized to receive NALIRIFOX in NAPOLI 3 were treatment on days 1 and 15 of a 28-day cycle. In this *post hoc* analysis of patients enrolled from centers in North America (n = 120), baseline characteristics and NALIRIFOX dosing patterns were evaluated for individuals who survived for 18 months of longer (long-term survivors; n = 15). The analysis was descriptive; no statistical tests were performed. Kaplan–Meier methods were used to estimate mOS (interquartile range [IQR]). **Results:** Among the long-term survivors, the mOS was 19.5 (IQR: 18.8–22.6) months and 53.3% were male. At baseline, long-term survivors had a median age of 61.0 (IQR: 49.0–70.5) years, had a median CA 19-9 level of 166.8 U/ml (IQR: 32.7–1728.4), 53.3% had Eastern Cooperative Oncology Group Performance Score (ECOG PS) 0, 53.3% had the main pancreatic tumor located in the body of the pancreas, 66.7% had liver metastasis, and 53.3% had ≥ 3 metastatic sites. Liposomal irinotecan and oxaliplatin dose reductions were experienced by 66.7% and 80.0% of long-term survivors, respectively, and dose delays by 86.7% and 80.0%, respectively. Median cumulative dose of liposomal irinotecan was 1229.4 (IQR: 821.9–1513.9) mg/m^2 for long-term survivors and median cumulative dose of oxaliplatin was 962.3 (655.0–1470.3) mg/ml. Median duration of exposure was 65.1 (IQR: 40.1–89.0) weeks for liposomal irinotecan and 39.9 (26.6–76.4) weeks for oxaliplatin. **Conclusions:** This *post hoc* analysis investigated characteristics and dosing patterns of long-term survivors from NAPOLI 3 treated with NALIRIFOX in North America. Patients with prolonged OS were generally younger (vs typical mPDAC diagnosis), few had tumors in the head or tail of the pancreas and, overall, CA19-9 levels and ECOG PS were low. A large proportion of long-term survivors experienced liposomal irinotecan and/or oxaliplatin dose reductions or treatment delays, but had prolonged exposure and high cumulative doses of both drugs. Despite liver metastasis and ≥ 3 metastatic sites in a substantial proportion of long-term survivors, dose modifications and an otherwise good clinical profile enabled attainment of a long mOS. Small sample size limits the generalizability of these results. Clinical trial information: NCT04083235. Research Sponsor: Ipsen.

LBA4504 Oral Abstract Session

Mitomycin plus BCG as adjuvant intravesical therapy for high-risk, non–muscle-invasive bladder cancer: A randomized phase 3 trial (ANZUP 1301).

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Background: Intravesical BCG is the standard of care for high-risk non-muscle invasive bladder (NMIBC) after maximal transurethral resection. Availability and access to BCG have been a global challenge since 2013. We sought to determine the efficacy and safety of intravesical treatment with BCG plus mitomycin (BCG+MM) compared with BCG-alone for high-risk, BCG-naïve NMIBC. **Methods:** This was an open-label, randomized, phase 3 trial. Eligible participants (pts) had high-grade papillary urothelial cancer stages pTa/pT1; concurrent CIS was allowed. Pts were randomly assigned BCG+MM vs BCG-alone. The BCG+MM regimen was weekly induction x 9 (BCG wks 1, 2, 4, 5, 7, and 8; MM wks 3, 6, and 9) followed by 4-weekly maintenance x 9 (MM wks 13, 17, 25, 29, 37, and 41; BCG wks 21, 33, and 45: total of 9 BCG doses). The BCG-alone regimen was weekly induction x 6, then 4-weekly maintenance x 10: total of 16 BCG doses. The primary endpoint was disease-free survival (DFS) at 2 years; secondary outcomes included complete response on cystoscopy at 3 months (CR3mos), time-to-recurrence (TTR), time-to-progression (TTP), overall survival (OS) and adverse events (AE). The target sample size of 500 provided 85% power to detect an absolute improvement of 10% in DFS at 2 years with a type-1 error rate of 0.05. Cox regression was used to calculate hazard ratios (HR), confidence intervals (CI), and account for competing risks. P-values are 2-sided and not adjusted for multiple comparisons. Clinicaltrials.gov NCT02948543. **Results:** We enrolled 501 pts from DEC2013 to MAY2023: median age 70 years (IQR 63-77); pTa 53%, pT1 47%, concurrent CIS 28%. In this primary analysis, the median follow-up was 47 months (IQR 31-64) at the data cut-off of 06DEC2024. Analyses of all key endpoints (DFS, CR3mos, TTR, TTP and OS) supported similar efficacy in the 2 treatment groups (see table), but none with $p<0.05$. The total numbers of instillations were higher for BCG+MM than BCG-alone (4,034 vs 3,383), whereas the total doses of BCG (2,056 vs 3,383), and median doses of BCG per pt (9 vs 16) were lower for BCG+MM than BCG-alone. The numbers of pts with grade 3-5 AEs were 43 in BCG-MM vs 37 in BCG-alone. The AE (of any grade) reported by the highest numbers of pts (BCG+MM vs BCG-alone) were fatigue (109 vs 110), renal/urinary (78 vs 83), and flu-like symptoms (34 vs 60). More pts had ≥75% of their planned doses with BCG+MM than BCG-alone (78% vs 68%; p=0.02). **Conclusions:** BCG+MM had similar efficacy and safety, but with fewer treatment discontinuations and fewer doses of BCG than BCG-alone. BCG+MM is a good alternative to BCG-alone. Clinical trial information: NCT02948543. Research Sponsor: Cancer Australia; National Health and Medical Research Council; The Australian and New Zealand Urogenital and Prostate Cancer Trials Group (ANZUP).

	BCG+MM N=248	BCG-alone N=252	HR (95% CI)	p-value
DFS at 2 years	76%	71%	0.86 (0.64-1.14)	0.30
CR at 3 months	90%	86%	1.05 (0.98-1.12)	0.22
Recurrence-free at 2 years	81%	75%	0.84 (0.61-1.18)	0.31
Progression-free at 5 years	87%	81%	0.74 (0.45-1.21)	0.23
OS at 5 years	87%	87%	1.07 (0.61-1.88)	0.81

LBA4513 Rapid Oral Abstract Session

ENLIGHTED phase 3 study: Interim results of efficacy and safety of padeliporfin vascular targeted photodynamic therapy (VTP) in the treatment of low-grade upper tract urothelial cancer (LG UTUC).

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Background: Padeliporfin VTP has demonstrated safety and efficacy for UTUC treatment in a Phase 1 study (NCT03617003). Padeliporfin VTP is a combination product of a drug, padeliporfin administered IV and a optical fiber coupled laser emitting near-infrared light endoluminally to UTUC tumors. We report the interim analysis of efficacy and safety outcomes of Padeliporfin VTP for treatment of LG UTUC in ENLIGHTED, a Phase 3 trial (NCT04620239). **Methods:** This is an open-label phase 3 study conducted in USA, EU, and Israel. Key inclusion criteria are: up to 2 biopsy-proven LG UTUC with index tumor ≤15mm in the kidney (≤20mm in the ureter) and absence of high-grade cytology. VTP is performed via retrograde upper tract endoscopy under anesthetic and low light conditions, Padeliporfin is injected IV and an optical fiber, 20-40 mm diffuser, is positioned in proximity of the tumor through the scope. After Padeliporfin injection, the laser is activated for 10 min. Patients (Pts) are treated in two phases: Induction (ITP) and Maintenance Treatment Phases (MTP). ITP consists of 1-3 VTPs provided at 4-week intervals until achieving complete response (CR) or treatment failure on Primary Response Evaluation (PRE) visit. Primary endpoint is CR on endoscopic evaluation and negative instrumental cytology at the time of PRE (28 ± 3 days post last treatment) during ITP. Pts achieving CR will proceed to MTP and be followed with endoscopic evaluation every 3 months (mos) with VTP provided for recurrent tumors in the period up to 12 mos. Pts completing MTP, will be followed for additional 48 mos for long-term outcomes. A total of 100 pts are to be enrolled. **Results:** Interim analysis is defined in the study protocol and conducted mid-way (50% of evaluable pts) into the study with the cut-off date 5 November 2024. CR rate 73%, Partial Response rate 13.5%, Disease Recurrency rate 10.8%, Disease progression rate 2.7%, Overall Response Rate 86.5%. The most frequent TEAEs (Grade 1-2, resolved within few days) were: hematuria 14%, flank pain 10%, procedural pain 6.4%, dysuria 5.2%, UTI 5.2%, abdominal pain 4.7%, vomiting 4.7%, fatigue 4%, nausea 3.5%. Sixteen (9.2%) Grade 3 serious adverse events (SAE) were reported. Grade 3 SAEs related to the VTP treatment were renal colic and flank pain, and resolved within 2 days. **Conclusions:** Padeliporfin VTP has demonstrated efficacy and safety aligned with previous findings. Recruitment in ENLIGHTED trial is ongoing, with results anticipated to support the approval of a new therapy offering clinical benefits and organ-sparing alternative for pts. Clinical trial information: NCT04620239. Research Sponsor: Steba/Impact Biotech.

LBA5006 Oral Abstract Session

Phase 3 AMPLITUDE trial: Niraparib (NIRA) and abiraterone acetate plus prednisone (AAP) for metastatic castration-sensitive prostate cancer (mCSPC) patients (pts) with alterations in homologous recombination repair (HRR) genes.

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Background: NIRA is a highly selective and potent inhibitor of poly (ADP-ribose) polymerase (PARP)-1/2. In the MAGNITUDE trial, NIRA + AAP significantly improved radiographic progression-free survival (rPFS) in HRR gene–altered metastatic castration-resistant prostate cancer. The double-blind, placebo (PBO)-controlled AMPLITUDE trial (NCT04497844) evaluated the efficacy and safety of NIRA + AAP in HRR gene–altered mCSPC. **Methods:** Pts with germline or somatic HRR gene alterations (*BRCA1*, *BRCA2*, *BRIP1*, *CDK12*, *CHEK2*, *FANCA*, *PALB2*, *RAD51B*, *RAD54L*) were randomized 1:1 to a dual-action tablet (NIRA 200 mg + abiraterone acetate 1000 mg) plus prednisone 5 mg, or PBO + AAP (hereafter AAP). Eligible pts had received ≤6 mo of androgen deprivation therapy (ADT) ± ≤6 cycles of docetaxel (DOC) ± ≤45 d of AAP with metastatic disease extended beyond lymph nodes. The primary end point is investigator-assessed rPFS (time from randomization to radiographic progression or death). Secondary end points include time to symptomatic progression (TSP), overall survival (OS), and safety. The Kaplan-Meier product limit method and a stratified Cox model were used for time-to-event variables and the hazard ratio (HR) and stratified log-rank test for estimating treatment effect. This is the first and final analysis for rPFS and the first interim analysis (of 3) for OS (data cutoff, 7 Jan 2025). Approximately 261 rPFS events were required (2-sided α, 0.025; power, 91%) for an HR ≤0.64 to demonstrate efficacy. **Results:** 696 pts were randomized to NIRA + AAP (n=348) or AAP (n=348). Median age was 68 y (IQR, 61–74); 55.6% had *BRCA1/2* alterations, 78% were high-volume metastatic (M1), 87% were de novo M1, and 16% had prior DOC. Median follow-up is 30.8 mo. The primary end point was met, with rPFS significantly longer with NIRA + AAP (median, not reached [NR]) vs AAP (29.5 mo [95% CI, 25.8–NR]; HR, 0.63 [95% CI, 0.49–0.80], p=0.0001), including in the prespecified *BRCA1/2* subgroup (HR, 0.52 [95% CI, 0.37–0.72], p<0.0001). TSP was significantly improved with NIRA + AAP vs AAP (HR, 0.50 [95% CI, 0.36–0.69], p<0.0001; *BRCA1/2*: HR, 0.44 [95% CI, 0.29–0.68], p=0.0001). A trend in OS was seen at this first interim analysis (193/389 events) favoring NIRA + AAP (HR, 0.79 [95% CI, 0.59–1.04], p=0.10; *BRCA1/2*: HR, 0.75 [95% CI, 0.51–1.11], p=0.15). Grade 3/4 adverse events (AEs) occurred in 75.2% with NIRA + AAP and 58.9% with AAP, most commonly anemia (29.1% vs 4.6%) and hypertension (26.5% vs 18.4%). Treatment discontinuations due to AEs were low: NIRA + AAP: 11.0%; AAP: 6.9%. **Conclusions:** NIRA + AAP significantly improved rPFS and TSP vs AAP in pts receiving ADT +/- prior DOC and had a favorable effect on OS. There were no new safety signals. AMPLITUDE supports NIRA + AAP as a potential new standard of care for pts with HRR gene–altered mCSPC. Clinical trial information: NCT04497844. Research Sponsor: Janssen Research & Development, LLC, a Johnson & Johnson company.

LBA5012 Rapid Oral Abstract Session

An open label randomized non-inferiority trial comparing adjuvant platinum plus paclitaxel to platinum plus 5-FU after curative resection in high-risk penile carcinoma.

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Background: There is limited evidence to guide adjuvant therapy in high-risk penile cancer. **Methods:** Patients with high-risk penile cancer [> 1 inguinal lymph node (LN), perinodal extension, pelvic LN, or LN > 4 cm] who underwent curative resection were randomized 1:1 to receive 4 cycles of platinum plus 5-FU (PF arm) or platinum plus paclitaxel (PP arm), followed by concurrent chemoradiotherapy. Primary endpoint was progression-free survival (PFS); secondary endpoints were overall survival (OS), toxicities and quality of life (QoL). The study was approved by IEC and registered with CTRI. Recruitment began in March 2017 but closed prematurely due to slow accrual. **Results:** Between March 2017 and October 2024, 49 patients were randomized (Table 1). Median follow-up was 60.1 months. There was no significant difference in median PFS (12.5 vs 35.9 months, p=0.460), 5-year PFS (36.1% vs 38.5%), median OS (21.6 vs 37.2 months, p=0.530) and 5-year OS (45.3% vs 41.1%) between PF and PP arm, respectively. Dose reductions were higher (33.3% vs 4.5%, p=0.015), similar dose delays (33.3% vs 31.8%, p=0.916) and a non-significant increase in drug discontinuation (42.9% vs 18.2%, p=0.078) in the PF arm. Grade 3/4 hematological (28.6% vs 4.5%, p=0.033) and gastrointestinal (33.3% vs 4.5%, p=0.015) toxicities were higher in PF arm. Infections (9.5% vs 13.6%, p=0.674) and hospitalizations (38.1% vs 18.2%, p=0.146) were similar. QoL (EORTC QLQ-C30 and MSHQ) analysis showed no difference in global health status (p=0.094), functional and symptom scales. Patients in PF arm reported more erectile dysfunction-related bother (p=0.018) while other MSHQ domains were similar. **Conclusion:** Adjuvant platinum plus 5-FU showed similar efficacy to platinum plus paclitaxel in high-risk penile carcinoma after curative resection, albeit with higher hematological and gastrointestinal toxicities, as well as erectile dysfunction-related bother. Clinical trial information: CTRI/2016/12/007567. Research Sponsor: Tata Memorial Hospital.

Baseline and treatment details.

Characteristics	5-FU + Platinum (N = 25)	Paclitaxel + Platinum (N = 24)	p-value
Age (years)			
Median (Range)	49 (29-70)	51 (26-70)	
Co-morbidities			
Hypertension	5 (20%)	5 (20.8%)	0.942
Diabetes Mellitus	5 (20%)	4 (16.7%)	0.763
Coronary Artery Disease	3 (12%)	1 (4.2%)	0.317
Prior phimosis	3 (12%)	1 (4.2%)	0.317
Smoker or smokeless tobacco	9 (36%)	10 (41.7%)	0.773
ECOG PS			0.715
0	2 (8%)	1 (4.2%)	
1	21 (84%)	22 (91.6%)	
2	2 (8%)	1 (4.2%)	
Surgery			0.995
Glansectomy	4 (16%)	4 (16.7%)	
Partial penectomy	17 (68%)	16 (66.6%)	
Total penectomy	4 (16%)	4 (16.7%)	
Degree of differentiation			0.566
Grade 1	2 (8%)	2 (8.3%)	
Grade 2	12 (48%)	8 (33.3%)	
Grade 3	11 (44%)	14 (58.3%)	
Pathological T stage			0.525
T1	10 (40%)	6 (25%)	
T2	8 (32%)	9 (37.5%)	
T3	7 (28%)	9 (37.5%)	
Pathological N stage			0.950
N2	4 (16%)	4 (16.7%)	
N3	21 (84%)	20 (8.3%)	
LVI or PNI	11 (44%)	9 (37.5%)	0.644
> 3 adjuvant cycles	15 (60%)	22 (91.6%)	**0.010**
Completed CTRT	12 (48%)	14 (58.3%)	0.469

LBA5078 Poster Session

Lower-dose versus standard-dose abiraterone in patients with metastatic castration resistant prostate cancer: A multicentric randomized phase III non-inferiority trial.

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Background: Abiraterone Acetate (AbA), a novel hormonal agent, is commonly used in patients with metastatic prostate cancer. However, the standard 1000 mg dose administered in the fasting state often results in poor patient compliance. Its high cost further limits access in resource-limited settings. Recently, lower-dose AbA (250 mg with a low-fat meal) has been included in the National Comprehensive Cancer Network guidelines, however, clinical efficacy data remain limited. This study evaluates the efficacy of lower-dose AbA in our patient cohort. **Methods:** This randomized, open-label, multicenter, phase III non-inferiority trial enrolled patients with metastatic castration-resistant prostate cancer (mCRPC). Patients were randomized 1:1 to receive either lower-dose AbA (250 mg with a low-fat meal, Arm-A) or the standard-dose (1000 mg fasting, Arm-B). The planned sample size was 314 (80% power, 5% alpha error, 1.37 non-inferiority margin), but slow accrual led to early trial closure. The primary endpoint was PSA Progression Free Survival (PSA-PFS). Secondary endpoints were PSA response rates [PSA_{30}, PSA_{50} (% of patients with >30% and >50% reduction in PSA level from baseline)], radiographic PFS, overall survival (OS), QOL, cost, and pharmacokinetic (pK) analysis (Pumas v2.6). **Results:** The study recruited 164 patients between September 2020 and January 2025. The median age was 65 years (IQR 60.0-71.6), with 31.7% (n = 52) patients aged >70 years. The ECOG-PS was 1 in 68.3% (n = 112) of patients. A total of 92.1% (n = 151) patients had a monthly income below the national average (~₹17,000). The median number of prior treatment lines was 1 (IQR, 1), with 64.0% (n = 105) receiving prior docetaxel. Arm-A included 86 (52.4%) patients, and Arm-B had 78 (47.6%). The PSA_{30} and PSA_{50} response rates in Arm-A were 49.4% (n = 40/81) and 38.3% (n = 31/81), compared to 55.7% (n = 39/70, p = 0.437) and 45.7% (n = 32/70, p = 0.355) in Arm-B. The median follow-up was 18.1 months (95% CI, 16.0-20.2). The median PSA-PFS was 5.7 months (95%CI, 3.9-7.4) in Arm-A vs. 3.8 months (95%CI, 2.0-5.6) in Arm-B [p = 0.792, HR 0.953 (95%CI, 0.663-1.369)]. The median OS was 18.1 months (95%CI, 10.0-26.2) vs. 15.1 months [95%CI, 9.3-20.9; p = 0.969; HR 0.991 (95%CI, 0.638-1.539)]. Grade >3 toxicities occurred in 36.6% (n = 30/82) patients in Arm-A and 31.6% (n = 24/76) patients in Arm-B (p = 0.507). pK analysis (n = 27 Arm-A, n = 31 Arm-B) showed an 8-fold higher AbA blood concentration in Arm-B [median C_{max} 80.5 ng/ml (range, 7.94-648), AUC 226 ng/ml*h (range, 27.2-1580)], vs. Arm-A [median C_{max} 10 ng/ml (range, 0.44-134.0), AUC 28.7 ng/ml*h (range, 0.22-158)]. **Conclusion:** Lower-dose AbA shows comparable efficacy to the standard-dose despite significantly lower blood levels, making it a viable alternative. This challenges the traditional MTD-based dose determination of anti-cancer drugs. Clinical trial information: CTRI/2020/08/026967. Research Sponsor: None.

LBA5500 Oral Abstract Session

TRUST: Trial of radical upfront surgical therapy in advanced ovarian cancer (ENGOT ov33/AGO-OVAR OP7).

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Background: Optimal timing of cytoreduction in non-frail patients (pts) with seemingly resectable stage IIIB-IVB ovarian, tubal, and peritoneal carcinoma (OC) remains controversial. **Methods:** TRUST is an international randomized multicenter phase III trial in pts with stage IIIB-IVB OC and good performance status (ECOG 0/1) comparing primary cytoreductive surgery (PCS) followed by 6 cycles of intravenous (iv) chemotherapy to 3 cycles of neoadjuvant iv chemotherapy (NACT) followed by interval cytoreductive surgery (ICS) and 3 further iv cycles. Maintenance treatment with bevacizumab and/or PARP inhibitors was allowed if selection criteria was similar for both arms. Pts were eligible for the study if preoperative clinical and radiologic assessment identified them as potential candidates for PCS. To ensure surgical quality, participating centers complied with an onsite surgery quality assurance audit, had adequate infrastructure, surgical proficiency (complete resection rates ≥50% in PCS) and sufficient volume (≥36 PCS/year). The intent to treat analysis population included all eligible pts with confirmed stage IIIB-IVB disease. The primary endpoint was overall survival (OS). Superiority was tested using a two-sided stratified log-rank test with significance level 0.05. Secondary endpoints were progression-free survival (PFS) and surgical complications. **Results:** A total of 688 eligible pts (median age: 63y; range: 32-83) underwent randomization: 345 were assigned to PCS and 343 to NACT/ICS. 91% had high-grade serous histology. Complete resection was achieved in 61.7%/62.9% of all randomized/all operated pts in the PCS group and 72%/76.6% in the ICS group. Median PFS was 22.2 months in the PCS group, and 19.7 months in the ICS group (HR 0.80 95%CI: 0.66-0.96; p=0.02). Median OS was 54.3 months in the PCS group and 48.3 months in the ICS group (HR 0.89 95%CI: 0.74-1.08; p=0.24). Pts with complete cytoreduction after PCS had the most favorable outcome, with a median PFS and OS of 27.9 and 67.0 months, respectively. A long-term benefit from PCS was seen in all analyzed subgroups. The benefit of PCS was most prominent in stage III pts (n=468): median PFS for PCS vs ICS, 26.3 vs 21.4 mos; median OS for PCS vs ICS, 63.7 vs 53.2 months. Major postoperative complication rates were acceptable, with a 30-day postoperative mortality rate of < 1% in both groups. **Conclusions:** In expert centers with proven surgical quality, PCS followed by iv chemotherapy resulted in a significantly longer median PFS and a numerically longer OS compared to NACT/ICS in non-frail OC pts. Although statistical significance in the primary endpoint was not reached, this is the first randomized trial to show a benefit of PCS over ICS. This benefit is likely to be associated with the high complete resection rate, reinforcing PCS as a standard of care in non-frail pts with seemingly resectable advanced OC. Clinical trial information: NCT02828618.
Research Sponsor: None.

LBA5501 Oral Abstract Session

Sentinel lymph node biopsy versus pelvic lymphadenectomy in cervical cancer: The PHENIX trial.

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Background: Limited data is available on survival outcomes following sentinel lymph node biopsy (SLNB) as a substitute for pelvic lymphadenectomy (PL) in cervical cancer. We aimed to prospectively compare survival outcomes between the two approaches for lym*ph* nod*e* dissectio*n* in cerv*ix* cancer. **Methods:** This multicenter, non-inferiority, randomized controlled trial involves patients with FIGO 2009 stage IA1 (lymphovascular invasion), IA2, IB1, or IIA1 cervical cancer, including squamous-cell carcinoma, adenocarcinoma, or adenosquamous carcinoma. Patients with radiological nodal metastases were excluded. All patients underwent SLNB first and all sentinel lymph nodes (SLNs) were examined by frozen section. Based on SLN status, patients were intraoperatively assigned to PHENIX-I (SLN-negative) or PHENIX-II (SLN-positive) cohorts and then randomized 1:1 to undergo PL or not. Side-specific PLs were performed in cases of unilateral detection and radical hysterectomies were performed for all patients. The primary endpoint was disease-free survival. **Results:** Between December 2015 and December 2023, 908 patients with at least one SLN detected were enrolled and randomized intraoperatively, including 838 SLN-negative patients in PHENIX-I and 70 SLN-positive patients in PHENIX-II (early terminated). Patients were assigned to undergo SLNB alone (455 cases: 420 in PHENIX-I, 35 in II) or PL (453 cases: 418 in PHENIX-I; 35 in II). The median age was 48 years (23 to 65) and the bilateral SLN detection rate was 82.6%. The clinicopathological characteristics, surgical approaches, and postoperative therapies were well-balanced between the SLNB and PL groups. SLNB demonstrated significantly shorter operative duration ($P < 0.0001$), less blood loss ($P < 0.001$), and lower morbidities ($P < 0.001$) compared to PL. The median follow-up time reached 52 months (1 to 104). In PHENIX-I, recurrences were observed in 16 patients in the SLNB group and 26 in the PL group. Retroperitoneal nodal recurrences were observed in 9 patients in the PL group, whereas no such recurrence was detected in the SLNB group ($P < 0.05$). There were 3 cancer-specific deaths in the SLNB group and 14 in the PL group. The 3-year disease-free survival rates were 96.8% for the SLNB group and 94.5% for the PL group (HR = 0.61, 95% confidence interval [CI] 0.33-1.14, P = 0.12); the 3-year cancer-specific survival rates were 100.0% for the SLNB group and 97.8% for the PL group (HR = 0.21, 95%CI 0.06-0.74, P = 0.007). Similar comparative trend was observed in PHENIX-II despite its early termination (HR = 0.47, 95%CI 0.14-1.58, P = 0.21 for disease-free survival; HR = 0.23, 95%CI 0.05-1.08, P = 0.061 for cancer-specific survival). **Conclusion:** When SLNB succeeds in cervical cancer, PL should be abandoned as it provides no survival benefit and increases surgical morbidity, yet may unexpectedly correlate with elevated risks of nodal recurrence and cancer-specific mortality. Clinical trial information: NCT02642471. Research Sponsor: The Health and Medical Cooperation Innovation Special Program of Guangzhou Municipal Science and Technology.

LBA5504 Oral Abstract Session

Pembrolizumab with chemoradiotherapy in patients with high-risk locally advanced cervical cancer: Final analysis results of the phase 3, randomized, double-blind ENGOT-cx11/GOG-3047/KEYNOTE-A18 study.

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Background: Prior results from ENGOT-cx11/GOG-3047/KEYNOTE-A18 (NCT04221945) showed that pembro + CCRT and then continued after CCRT provided statistically significant and clinically meaningful improvements in OS and PFS vs CCRT alone in pts with newly diagnosed, previously untreated, high-risk LACC. We present the final analysis (FA) results from this study. **Methods:** Eligible pts with newly diagnosed, previously untreated, high-risk LACC (FIGO 2014 stage IB2-IIB with node-positive disease or stage III-IVA regardless of lymph node status) were randomized 1:1 to 5 cycles of pembro 200 mg or placebo (pbo) Q3W + CCRT, then 15 cycles of pembro 400 mg or pbo Q6W. The CCRT regimen included 5 cycles (with optional 6th dose) of cisplatin 40 mg/m^2 Q1W + EBRT then brachytherapy. Pts were stratified by planned EBRT type (intensity-modulated radiotherapy [IMRT] or volumetric-modulated arc therapy [VMAT] vs non-IMRT or non-VMAT), stage at screening (stage IB2-IIB vs III-IVA) and planned total radiotherapy dose ($<$70 Gy vs $\geq$70 Gy equivalent dose). Primary endpoints are PFS per RECIST version 1.1 by investigator and OS. **Results:** 1060 pts were randomized to pembro + CCRT (n=529) or pbo + CCRT (n=531). At the protocol-specified FA (Jan 7, 2025, data cutoff), median follow-up was 41.9 mo (range, 24.8-55.0). 86 pts had received post-progression immunotherapy; of those, 64 had received pembro. Pembro + CCRT continued to show clinically meaningful improvements in OS and PFS vs pbo + CCRT (Table). The benefit of pembro + CCRT was generally consistent in prespecified subgroups, including pts with stage IB2-IIB node-positive disease (OS HR=0.92 [95% CI, 0.62-1.38]; PFS HR=0.84 [95% CI, 0.63-1.14]). The grade $\geq$3 TRAE incidence was 69.5% in the pembro + CCRT group and 61.5% in the pbo + CCRT group. **Conclusion:** With an additional 12 mo median follow-up, pembro + CCRT continued to show clinically meaningful improvements in OS and PFS vs pbo + CCRT in pts with high-risk LACC and had a manageable safety profile. These data are consistent with the prior interim analysis and provide further support for pembro + CCRT as the new standard of care for this population. Clinical trial information: NCT04221945. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Summary of PFS and OS in ENGOT-cx11/GOG-3047/KEYNOTE-A18.

	Final Analysis 07JAN25		Interim Analysis 2 08JAN24		Interim Analysis 1 09JAN23	
	Pembro + CCRT	Pbo + CCRT	Pembro + CCRT	Pbo + CCRT	Pembro + CCRT	Pbo + CCRT
OS, median (95% CI)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)	NR (NR-NR)
36-mo OS	81.8%	74.4%	82.6%	74.8%	NR (NR-NR)	NR (NR-NR)
HR (95% CI)	0.73 (0.57-0.94)		0.67 (0.50-0.90); *P*=0.0040		0.73 (0.49-1.07); *P*=0.0541	
PFS, median (95% CI)	47.6 (47.6-NR)	47.5 (41.0-NR)	NR (NR-NR)	NR (32.0-NR)	NR (NR-NR)	NR (NR-NR)
24-mo PFS	70.6%	59.7%	70.6%	58.6%	67.8%	57.3%
HR (95% CI)	0.72 (0.59-0.87)		0.68 (0.56-0.84)		0.70 (0.55-0.89); *P*=0.0020	

NR=not reached.

LBA5506 **Oral Abstract Session**

FIRST/ENGOT-OV44: A phase 3 clinical trial of dostarlimab (dost) and niraparib (nira) in first-line (1L) advanced ovarian cancer (aOC).

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Background: The FIRST/ENGOT-OV44 trial evaluated adding dost, a programmed cell death protein-1 inhibitor, to 1L platinum-based chemotherapy (PBCT) and nira maintenance (MT) ± bevacizumab (bev) in patients (pts) with aOC. **Methods:** In this randomized, double-blind, phase 3 trial, pts with newly diagnosed stage III–IV, high-grade nonmucinous epithelial OC received 1-cycle run-in of PBCT ± bev and were randomized (1:1:2) to arm 1 (PBCT+placebo [PBO] with PBO MT), arm 2 (PBCT+PBO with nira+PBO MT), or arm 3 (PBCT+dost with dost+nira MT). Stratification factors included intended bev use (yes/no), homologous recombination repair (HRR) mutation status (*BRCA*-mutated; *BRCA* wild-type HRR-positive; *BRCA* wild-type HRR-negative/not determined), and stage III disease with postoperative residual disease <1 cm (yes/no). After approvals for 1L MT poly(ADP-ribose) polymerase inhibitors, arm 1 enrollment closed, and pts were randomized (1:2) to arms 2 or 3. The primary endpoint was investigator-assessed progression-free survival (PFS) per RECIST v1.1, assessed in arms 2 and 3, and analyzed per randomized treatment. Safety was assessed among pts who received ≥1 dose of study treatment and analyzed per treatment received. The data cutoff was October 31, 2024. **Results:** Randomization was from 14Nov2018 to 05Jan2021. Efficacy analyses included 1138 randomized pts (arm 2, n=385; arm 3, n=753; stage IV disease at diagnosis, 37.3%; planned interval surgery, 54.6%; inoperable, 9.8%; homologous recombination-deficient [HRd] disease, 39.0%; programmed cell death ligand 1 [PD-L1]–positive tumors, 33.4% [of n=951 with nonmissing PD-L1 status]; median follow-up, 45.9 mo [IQR, 24.2–54.1]). Patient characteristics were balanced between arms. PFS was statistically significantly longer in arm 3 vs arm 2 (median PFS, 20.63 vs 19.19 mo, respectively; hazard ratio [HR], 0.85; 95% CI, 0.73–0.99; *P*=0.0351). PFS was reported in subgroups with PD-L1–positive tumors (HR, 0.84; 95% CI, 0.61–1.17), HRd tumors (HR, 0.95; 95% CI, 0.72–1.24), and concurrent bev use (yes: HR, 0.84; 95% CI, 0.68–1.03; no: HR, 0.86; 95% CI, 0.69–1.08).There was no statistically significant difference in overall survival (OS), a key secondary endpoint, between arms 3 and 2 (median OS, 44.39 vs 45.37 mo, respectively; HR, 1.01; 95% CI, 0.86–1.19; *P*=0.9060). The safety population (N=1321; arms 1–3) included 34 pts randomized to arm 1 who, upon unblinding, received arm 2 treatment; 10 randomized pts did not receive study treatment and were excluded from safety analyses. Median duration of exposure was 11.3, 15.2, and 15.2 mo in arms 1, 2, and 3, respectively. Safety results were generally consistent with the known profiles of each agent of the study. **Conclusion:** Adding dost to 1L PBCT and nira MT ± bev improved PFS in pts with aOC. No OS difference was observed. Clinical trial information: NCT03602859. Research Sponsor: This study (NCT03602859) was sponsored by GSK.

LBA5507 Oral Abstract Session

ROSELLA: A phase 3 study of relacorilant in combination with nab-paclitaxel versus nab-paclitaxel monotherapy in patients with platinum-resistant ovarian cancer (GOG-3073, ENGOT-ov72).

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Background: Relacorilant is an investigational, oral, selective glucocorticoid receptor antagonist (SGRA) that increases tumor sensitivity to chemotherapy-induced apoptosis. In a phase 2 study, the addition of relacorilant to nab-paclitaxel improved progression-free survival (PFS) and showed a trend towards improved overall survival (OS), with a comparable safety profile to nab-paclitaxel monotherapy, in patients with platinum-resistant ovarian cancer (PROC). The aim of this phase 3 study is to confirm the efficacy and safety of relacorilant + nab-paclitaxel in a larger population. **Methods:** ROSELLA (NCT05257408) is a randomized, controlled, open-label, global study of relacorilant + nab-paclitaxel compared to nab-paclitaxel monotherapy in patients with PROC. Patients were randomized 1:1 to either relacorilant (150 mg the day before, day of, and day after nab-paclitaxel) + nab-paclitaxel (80 mg/m^2 on days 1, 8, and 15 of each 28-day cycle) or nab-paclitaxel alone (100 mg/m^2 on the aforementioned schedule). Randomization was stratified by prior lines of therapy and region. Key eligibility criteria included 1–3 prior lines of anticancer therapy and prior bevacizumab. The dual primary endpoints are PFS by blinded independent central review (BICR) and OS. Secondary endpoints include PFS by investigator, objective response rate, best overall response, duration of response, and safety. PFS and OS endpoints were analyzed using Kaplan-Meier methods. A 2-sided stratified log-rank test was used to compare treatment groups. Hazard ratios (HR) were estimated with a Cox regression model. **Results:** A total of 381 women were randomized, all baseline characteristics were well balanced and 39% had received prior therapy in the PROC setting. ROSELLA met its primary endpoint: Patients receiving relacorilant + nab-paclitaxel had a statistically significant improvement in PFS by BICR compared to nab-paclitaxel monotherapy (HR 0.70, 95% CI 0.54-0.91, median 6.5 v 5.5 months, P=0.008); PFS by investigator showed a consistent benefit (HR 0.71, P=0.003). At an interim analysis, there was a clinically significant improvement in OS with the addition of relacorilant to nab-paclitaxel (HR 0.69, 95% CI 0.52-0.92, median 16.0 v 11.5 months, P=0.01). Adverse events (AEs) were comparable across study arms, relacorilant + nab-paclitaxel was well tolerated with no new safety signals. The most frequently reported AEs were known toxicities of nab-paclitaxel: anemia (58%), neutropenia (56%), and nausea (39%). **Conclusion:** Relacorilant + nab-paclitaxel is the first treatment regimen to demonstrate a PFS and OS benefit in patients with PROC compared to a weekly taxane, the most efficacious comparator. These positive efficacy data and a favorable safety profile position relacorilant + nab-paclitaxel as a new standard for patients with PROC, without the need for biomarker selection. Clinical trial information: NCT05257408. Research Sponsor: None.

LBA6003 Oral Abstract Session

PD-1 blockade with toripalimab incorporated into induction chemotherapy and radiotherapy with or without concurrent cisplatin in locoregionally advanced nasopharyngeal carcinoma (DIAMOND): A multicenter, non-inferiority, phase 3, randomized controlled trial.

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Background: This study aimed to assess the efficacy and safety of toripalimab combined with induction chemotherapy and radiotherapy alone in locoregionally advanced nasopharyngeal carcinoma (LANPC). **Methods:** Patients with non-metastatic T4N1 or N2–3 (AJCC 8th edition) NPC were recruited from 13 centers in China from Aug 2021 to Jul 2022 and randomly assigned (1:1) to receive either toripalimab plus gemcitabine-cisplatin induction chemotherapy and concurrent cisplatin-radiotherapy (*standard* arm) or standard therapy sparing concurrent cisplatin (*cisplatin-free* arm). Toripalimab was administered at a dosage of 240 mg once every 3 wks for up to 17 cycles (1.06 year), covering the induction ($\times$3 cycles), radiotherapy ($\times$3), and adjuvant ($\times$11) phases. The trial would be considered positive if both coprimary endpoints, failure-free survival (FFS; non-inferiority) and the incidence of all-grade vomiting (superiority), were significantly met, maintaining a 1-sided type I error of 5% without α splitting. A total of 532 patients were needed to achieve 80% power to detect a HR of 1.74, with non-inferiority defined as the lower limit of the 1-sided 95% CI for the difference in 3-year FFS greater than -8%. Quality of life (QoL) was assessed based on EORTC and FACT systems. Tolerability was measured by PRO-CTCAE questionnaires. **Results:** After a median follow-up of 36 mo, intention-to-treat analysis in 532 patients (266 *vs* 266) showed that the estimated 3-year FFS was 88.3% in the *cisplatin-free* arm and 87.6% in the *standard* arm, with a difference of 0.7% (1-sided 95% CI, -4.8% to ∞; $p_{non-inferiority}$ = 0.002); the stratified HR was 0.92 (95% CI, 0.66 to 1.79; log-rank p = 0.731). The incidence of all-grade vomiting in safety dataset was 25.6% (68/260) in *cisplatin-free* arm and 69.0% (156/261) in *standard* arm (χ^2 $p < 0.001$); the incidence of grade 3–4 vomiting, 3.8% *vs* 10.3%. Acute grade 3–4 adverse events (AEs) occurred in 136 (52.3%) and 166 (63.6%) patients, including immune-related AEs in 13 (5.0%) and 22 (8.4%) patients, in the *cisplatin-free* and *standard* arms, respectively. No treatment-related death was observed. Compared to *standard* arm, *cisplatin-free* arm had significantly better QoL in global health status, physical function, role function, nausea/vomiting, constipation, swallowing, sexuality, and H&N total score, as well as higher tolerability to nausea, vomiting, constipation, and fatigue during radiotherapy. **Conclusions:** Removing concurrent cisplatin from toripalimab plus chemoradiotherapy provides comparable survival, lower toxicity, and better QoL and tolerability for patients with LANPC. Clinical trial information: NCT04907370. Research Sponsor: Shanghai Junshi Biosciences Co., Ltd.

3-yr survival (%)	*Cisplatin-free* arm (n = 266)	*Standard* arm (n = 266)	$p_{non-inferiority}$
OS	96.1	96.5	< 0.001
LRRFS	92.9	93.6	0.001
DMFS	93.2	91.6	< 0.001

LBA6005 **Oral Abstract Session**

Becotatug vedotin vs. chemotherapy in pre-heavily treated advanced nasopharyngeal carcinoma: A randomized, controlled, multicenter, open-label study.

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Background: Becotatug vedotin (MRG003) is a novel EGFR-targeted antibody-drug conjugate. Previous Phase I/II studies have demonstrated optimistic efficacy in R/M NPC pts who had failed platinum chemotherapy and PD-(L)1 inhibitor. This study aimed to assess clinical efficacy and safety of MRG003 in pts compared with chemotherapy. **Method:** Eligible pts with R/M NPC had failed ≥2 lines of systemic chemotherapy and PD-(L)1 inhibitor, and were randomized to receive MRG003 (2.3 mg/kg, d1, iv, Q3W) or chemotherapy (capecitabine 1000 mg/m^2, po, twice daily, d1-14, Q3W; or docetaxel 75 mg/m^2, iv, d1, Q3W). Randomization was stratified according to liver metastasis (yes or no) and ECOG PS (0 or 1). The primary endpoints were ORR and PFS assessed by BICR, and OS. Pts in the chemotherapy arm were allowed to cross over to receive MRG003 after disease progression. **Result:** A total of 173 R/M NPC pts were randomly assigned to MRG003 (n=86) or capecitabine(n=36)/docetaxel (n=51). The median prior treatment lines (range) were 3 (2-10) vs. 3 (2-11), and the ECOG score 0 was 17.4% vs. 17.2% for two arms. 40 pts (46.5%) vs. 41 pts (47.1%) of two arms had liver metastasis. By 30 June 2024, the study reached the significantly improved BICR-assessed ORR with MRG003 compared to chemotherapy (30.2% vs. 11.5%, difference: 18.7%, 95%CI: 7.0%, 30.5%, P=0.0025). Also, PFS was significantly improved in the MRG003 arm (HR=0.63, 95% CI: 0.43, 0.91, P=0.0146). Median PFS (95%CI) by BICR were 5.8m (4.2, 6.2) vs. 2.8m (2.0, 5.5). As of 30 December 2024, the updated mOS (95%CI) were 17.1m (11.4, NE) vs. 12.0m (9.7, 15.4) of two arms (HR=0.73, 95%CI: 0.48, 1.12). By supplementary analysis excluding the impact of crossover treatment, the HR of OS was 0.59 (95%CI: 0.37, 0.93). MRG003 has shown a trend of survival benefits. The OS will be continually followed up. The incidence of adverse events in the two arms was similar. 39 pts (45.3%) vs.44 pts (50.6%) in two arms experienced grade ≥3 TRAEs. White blood cell count decreased was the most common grade ≥3 TRAE of two arms (9.3% vs. 35.6%). **Conclusions:** As the first ADC clinical study targeting heavily pretreated R/M NPC, becotatug vedotin demonstrated statistically and clinically meaningful benefits while maintaining a manageable safety profile in this population. This study will lead to a paradigm shift in the treatment of R/M NPC. Sponsor: Lepu Biopharma Co., Ltd. Clinical trial information: NCT05126719. Research Sponsor: None.

	MRG003 (N=86)	Chemotherapy (N=87)	HR (95% CI)
ITT analysis			
Information fraction (n, %)	87, 71.3		-
Median follow-up (m)	13.5	13.6	-
mOS (m, 95% CI)	17.1 (11.4, NE)	12.0 (9.7, 15.4)	0.73 (0.48, 1.12)
12-m rate (%, 95% CI)	55.9 (44.2, 66.0)	48.9 (37.7, 59.2)	-
Supplementary analysis*			
mOS (m, 95% CI)	17.1 (11.4, NA)	11.1 (8.5, NA)	0.59 (0.37, 0.93)

*Using hypothetical strategy to exclude the impact of crossover treatment.

LBA8000 **Oral Abstract Session**

Overall survival with neoadjuvant nivolumab (NIVO) + chemotherapy (chemo) in patients with resectable NSCLC in CheckMate 816.

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Background: NIVO + chemo is an established standard of care neoadjuvant treatment (tx) for eligible patients (pts) with resectable NSCLC and has shown statistically significant and clinically meaningful improvements in EFS and pCR in the phase 3 CheckMate 816 study. Here, we report the planned final analysis of OS from CheckMate 816 at 5-y follow-up (f/u). **Methods:** Adults with stage IB (≥ 4 cm)–IIIA (per AJCC v7) resectable NSCLC, ECOG PS ≤ 1, and no known *EGFR*/*ALK* alterations were randomized 1:1 to receive neoadjuvant NIVO + chemo Q3W or chemo alone Q3W for 3 cycles, followed by surgery. Primary endpoints were EFS and pCR (both by blinded independent review). OS was a key prespecified, statistically powered secondary endpoint that was tested hierarchically. Exploratory analyses included OS by ctDNA clearance and pCR status. **Results:** At a median f/u of 68 mo (range, 60–85; database lock, 23 Jan 2025), neoadjuvant NIVO + chemo demonstrated a statistically significant OS benefit vs chemo alone (median [95% CI], not reached [NR] vs 73.7 mo [47.3–NR]; HR [95% CI], 0.72 [0.523–0.998]; *P* = 0.0479); 5-y OS rates were 65% vs 55%. OS favored NIVO + chemo in the subgroups defined by tumor PD-L1 expression, baseline disease stage, and histology (Table). In an exploratory analysis in pts with ctDNA+ at baseline (NIVO + chemo, n = 43; chemo, n = 43), pts with presurgical ctDNA clearance (56% vs 35%) had continued OS improvement vs those without across both tx arms (HR [95% CI]: NIVO + chemo, 0.38 [0.15–1.00]; chemo, 0.39 [0.14–1.11]). Furthermore, pts who had pCR with NIVO + chemo had sustained OS improvement vs those without (HR [95% CI], 0.11 [0.04–0.36]; 5-y OS rates, 95% vs 56%). Neoadjuvant NIVO + chemo continued to improve EFS vs chemo (median [95% CI], 59.6 [31.6–NR] vs 21.1 mo [16.5–36.8]; HR [95% CI], 0.68 [0.51–0.91]); 5-y EFS rates were 49% vs 34%. No new safety signals were observed at this long-term f/u. **Conclusions:** CheckMate 816 is the only neoadjuvant-only immunotherapy phase 3 trial to demonstrate a statistically and clinically significant OS benefit at 5 y for a resectable solid tumor. Pts with pCR with neoadjuvant NIVO + chemo had a ~90% reduction in their risk of death by 5 y compared with those without pCR. The findings show long-term survival benefit from a short course of neoadjuvant NIVO + chemo and affirm a paradigm shift in the tx of resectable NSCLC without actionable genomic alterations. Clinical trial information: NCT02998528. Research Sponsor: Bristol Myers Squibb.

	All pts NIVO + chemo (N = 179) vs chemo (N = 179)	PD-L1 < 1% NIVO + chemo (n = 78) vs chemo (n = 77)	PD-L1 ≥ 1% NIVO + chemo (n = 89) vs chemo (n = 89)	Stage IB/II NIVO + chemo (n = 65) vs chemo (n = 61)	Stage IIIA NIVO + chemo (n = 113) vs chemo (n = 116)	Squamous NIVO + chemo (n = 87) vs chemo (n = 95)	Non-squamous NIVO + chemo (n = 92) vs chemo (n = 84)
Median OS, mo	NR vs 73.7	NR vs 61.8	NR vs 73.7	NR vs 76.8	NR vs 73.7	NR vs 73.7	NR vs NR
HR (95% CI)	0.72 (0.523–0.998)	0.89 (0.57–1.41)	0.51 (0.31–0.84)	0.77 (0.44–1.35)	0.70 (0.47–1.05)	0.71 (0.46–1.11)	0.72 (0.45–1.16)

LBA8004 **Oral Abstract Session**

R-ALPS: A randomized, double-blind, placebo-controlled, multicenter phase III clinical trial of TQB2450 with or without anlotinib as maintenance treatment in patients with locally advanced and unresectable (stage III) NSCLC without progression following concurrent or sequential chemoradiotherapy.

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Background: Benmelstobart (TQB2450) is a novel humanized IgG1 monoclonal antibody targeting programmed death-ligand 1 (PD-L1). Anlotinib, a multi-target antiangiogenic TKI, synergizes with PD-(L)1 inhibitors by normalizing tumor vasculature to enhance T-cell infiltration and augmenting antitumor immunity in advanced NSCLC. **Methods:** The phase III R-ALPS trial (NCT04325763) randomized 553 patients with locally advanced, unresectable stage III NSCLC and non-progression after concurrent/cequential chemoradiotherapy (60 Gy ± 10%) to three arms: 1) benmelstobart (1200 mg IV q3w) + anlotinib (8 mg po d1-14/q3w); 2) benmelstobart monotherapy; 3) placebo. Sample size: Phase I 1:1:1; Phase II 1:1. Stratification factors: Smoking:Yes/No; Prior treatment: Sequential/Concurrent. Primary endpoint: IRC-assessed PFS (RECIST 1.1). **Results:** At data cutoff (November 30, 2023): IRC-assessed mPFS: Combination arm: 15.15 months (95% CI 9.40-21.65) vs 4.17 months with placebo (HR 0.49 (95% CI 0.36-0.66), Log-rank p<0.0001; Monotherapy: 9.69 months (95% CI 5.98-34.43) vs 4.17 months with placebo (HR 0.53, 95% CI 0.39-0.72),Log-rank p<0.0001; 12-month PFS rates: 54.9% (combination) vs 45.7% (monotherapy) vs 26.4% (placebo). OS: OS data has not reached median time, pending updates. Grade ≥ 3 TEAEs: 8% (combination) vs 31.8% (monotherapy) vs 21.2% (placebo). Most frequent: Hypertension (8.6% vs 1.0% vs 1.5%), hypertriglyceridemia (9.6% vs 2.8% vs 1.5%). Treatment discontinuation due to TEAEs: 5% (combination) vs 14.2% (monotherapy) vs 9.1% (placebo). Treatment-related fatal due to TEAEs: 2%(combination) vs 1%(monotherapy) vs and 0.8%(placebo). At data cutoff (July 8,2024): IRC-assessed mPFS: Combination arm: 17.38 months (95% CI 12.45-24.77) vs 11.20 months (95% CI 7.00-20.73) with monotherapy (HR 0.82, 95% CI 0.63-1.08) , Log-rank p=0.1218. **Conclusions:** Benmelstobart, both as monotherapy and in combination with anlotinib, significantly prolonged PFS compared to placebo. Secondary endpoints also showed superiority, and the safety profile of the treatment group remained within acceptable parameters. (Funded by Chia Tai Tianqing Pharmaceutical Group Co., Ltd.; ClinicalTrials.gov number, NCT04325763). Clinical trial information: NCT04325763. Research Sponsor: None.

LBA8005 **Oral Abstract Session**

Randomized phase II trial investigating whether atezolizumab after chemo-radiotherapy (CRT) prolongs survival in limited stage (LS) small cell lung cancer (SCLC).

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Background: A majority of patients with LS SCLC relapse after potentially curative CRT and better treatment is needed. Immunotherapy prolongs survival in extensive stage SCLC and after CRT in non-small cell lung cancer. We investigated whether atezolizumab ("atezo") after CRT prolongs survival in LS SCLC. **Methods:** Patients with PS 0-2 and non-progression (PD) after platinum/etoposide chemotherapy and concurrent twice-daily thoracic radiotherapy (TRT) of 45 Gy/30 or 60 Gy/40 fractions were randomized 1:1 to observation or atezo 1200 mg Q3W for 1 year, until PD or unacceptable toxicity. Atezo commenced 3-7 weeks after CRT. Randomization was stratified by performance status (PS) (0-1 vs. 2), CRT-response (stable disease [SD] vs. complete/partial response [CR/PR]) and TRT-dose (45 Gy vs. 60 Gy). CRT-responders were offered prophylactic cranial irradiation (PCI) of 25-30 Gy. PCI was allowed after start of atezo. Primary endpoint: Overall survival (OS). Secondary endpoints: Response rate (ORR), progression-free survival (PFS) and toxicity. To detect an increase in 2-year survival from 53% to 66% with a 1-sided a=0.1 and b=0.2, 75 patients were required in each group. **Results:** From July 2018-April 2022, 216 patients were included at 37 European hospitals. 170 (78.7%) were randomized (atezo: n=85, observation: n=85). Median age was 66 years, 46% were women, 92% had PS 0-1 and 82% stage III disease. ORR to CRT was similar in the atezo (95%) and observation (94%) groups. 67% in both groups received PCI. Median number of atezo-cycles was 8 (range 0-18), 2% of patients received 0 cycles and 34% completed 1 year of treatment. Atezo was discontinued due to PD (n=18), pneumonitis (n=8), endocrinopathy (n=3), neurotoxicity (n=2), myositis (n=2), other toxicity (n=9), patients' wish (n=5), death from other disease (n=2) and other (n=5). Median time until discontinuation of atezo due to toxicity was 2.8 (range 0.1-12.1) months. After randomization (i.e. post CRT), G3-4 toxicity was reported for 34% in the atezo group (dyspnea [n=6], fatigue [n=5], endocrinopathies [n=5], cardiac disorder [n=4], other [n=36]), and 20% in the control group (anorexia [n=6], neuropathy [n=5], dyspnea [n=4], and other [n=24]). G3-4 pneumonitis occurred in 4 patients, 2 in each group. There were 3 treatment-related deaths (neurotoxicity, pneumonitis and pneumonia), all in the atezo group. After 99 events and median follow-up 45.1 months (95% CI 40.7-47.3), median OS from randomization was 43.3 months (95% CI 25.1-51.2) in the atezo and 38.8 months (95% CI 25.8-NR) in the observation group (HR 1.14, 95% CI 0.76-1.72; p=0.5). Median PFS was 21.1 months (95% CI 9.5-43.4) in the atezo and 15.9 (95% CI 10.6-23.2) in the observation group (HR 0.88, 95% CI 0.60-1.28, p=0.5). **Conclusion:** Atezolizumab therapy after CRT did not improve progression free or overall survival in patients with LS SCLC. Clinical trial information: NCT03540420. Research Sponsor: Roche; The Norwegian Cancer Society; Central Norwegian Health Authority.

LBA8008 **Oral Abstract Session**

Tarlatamab versus chemotherapy (CTx) as second-line (2L) treatment for small cell lung cancer (SCLC): Primary analysis of Ph3 DeLLphi-304.

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Background: Tarlatamab, a bispecific T-cell engager (BiTE) immunotherapy, demonstrated promising activity in patients (pts) with previously treated SCLC in phase 1/2 trials. We report results from the primary analysis of the randomized controlled, phase 3 DeLLphi-304 study, evaluating tarlatamab vs CTx in pts with SCLC following progression on or after platinum-based chemotherapy. **Methods:** Pts were randomized 1:1 to tarlatamab or CTx (topotecan, lurbinectedin or amrubicin), stratified by prior treatment with a PD-(L)1 inhibitor, chemotherapy-free interval, brain metastases, and intended CTx. Primary endpoint was overall survival (OS). Key secondary endpoints were progression-free survival (PFS) and patient-reported outcomes (PRO). Other secondary endpoints included objective response rate (ORR), duration of response (DOR), disease control rate (DCR), and safety. **Results:** 509 pts were randomized (254, tarlatamab; 255, CTx). At median follow-up of 11.2 months (mo) for tarlatamab and 11.7 mo for CTx, pts in the tarlatamab arm had significantly longer OS (median OS: 13.6 vs 8.3 mo; hazard ratio [HR], 0.60 [95% CI: 0.47, 0.77]; $P < 0.001$) and PFS (median PFS: 4.2 vs 3.2 mo; HR, 0.72 [95% CI: 0.59, 0.88]; $P < 0.001$) vs pts in the CTx arm. Tarlatamab improved cancer-related symptoms of dyspnea and cough compared to CTx (Table). Lower rates of grade (Gr) ≥3 treatment-related adverse events (TRAEs) occurred with tarlatamab vs CTx (27% vs 62%); discontinuations due to TRAEs were lower with tarlatamab (3% vs 6%). The most common Gr ≥3 TRAEs were neutropenia (4%) and lymphopenia (4%) with tarlatamab and anemia (28%) and neutropenia (22%) with CTx. Cytokine release syndrome with tarlatamab was primarily low grade (42% Gr1; 13% Gr2; 1% Gr3) and manageable. **Conclusions:** The DeLLphi-304 trial showed tarlatamab significantly improved OS, PFS, and PROs, with a favorable safety and tolerability profile compared to CTx in pts with SCLC that progressed on or after initial platinum-based CTx, defining a new standard of care for these patients. Clinical Trial Information: NCT05740566; Legal entity responsible: Amgen Inc.; Funding: Amgen Inc.; Editorial acknowledgement: Medical writing support for the development of this abstract was provided by Sukanya Raghuraman, PhD, of Cactus Life Sciences, part of Cactus Communications, and was funded by Amgen Inc. Clinical trial information: NCT05740566. Research Sponsor: Amgen Inc.

	Tarlatamab (n=254)	CTx* (n=255)	Tarlatamab treatment effect (*P*-value)
Median OS, mo (95% CI)	13.6 (11.1-NE)	8.3 (7.0-10.2)	HR = 0.60 ($P < 0.001$)
Median PFS, mo (95% CI)	4.2 (3.0-4.4)	3.2 (2.9-4.2)	HR = 0.72 ($P < 0.001$)
ORR, % (95% CI)	35 (29-41)	20 (16-26)	Odds ratio = 2.13
Median DOR, mo (95% CI)	6.9 (4.5-12.4)	5.5 (4.2-5.7)	—
DCR, % (95% CI)	68 (62-74)	64 (58-70)	—
Dyspnea score, change from baseline after18 wks†, mean (95% CI)	-1.94 (-4.32, 0.45)	7.20 (4.58-9.81)	MD = -9.14 ($P < 0.001$)
Cough score, pts with improvement 18 wks after baseline‡, n (%)	41 (16)	23 (9)	OR = 2.04 ($P = 0.012$)
Chest pain score, pts with improvement 18 wks after baseline‡, n (%)	22 (9)	9 (4)	OR = 1.84 ($P = 0.100$§)

MD: mean difference; NE: not estimable; wks, weeks.
*Topotecan (n=185), lurbinectedin (n=47), or amrubicin (n=23).
†EORTC QLQ-C30 scale.
‡EORTC QLQ-LC13 scale.
§Non-significant.

LBA8010 **Rapid Oral Abstract Session**

Perioperative nivolumab (NIVO) vs placebo (PBO) in patients (pts) with resectable NSCLC: Updated survival and biomarker analyses from CheckMate 77T.

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Background: The phase 3 CheckMate 77T study demonstrated statistically significant and clinically meaningful improvement in EFS with perioperative NIVO vs PBO in pts with resectable NSCLC. pCR rates were also improved. Here, we report updated EFS, OS from the first prespecified interim analysis, and exploratory biomarker analyses. **Methods:** Pts with resectable stage IIA–IIIB (N2; AJCC v8) NSCLC were randomized 1:1 to neoadjuvant (neoadj) NIVO + chemotherapy (chemo) Q3W (up to 4 cycles [cyc]) followed by adjuvant (adj) NIVO Q4W (up to 13 cyc) or neoadj PBO + chemo Q3W (up to 4 cyc) followed by adj PBO Q4W (up to 13 cyc). The primary endpoint was EFS per BICR. Secondary endpoints included pCR, OS, and safety. Exploratory analyses included efficacy by pCR status, presurgery ctDNA clearance (CL), and tumor genomic alterations. **Results:** At a median follow-up of 41.0 mo (database lock, 16 Dec 2024), NIVO continued to provide EFS benefit vs PBO (HR [95% CI], 0.61 [0.46–0.80]; 30-mo EFS rates, 61% vs 43%) in all randomized pts and regardless of disease stage, tumor histology, or PD-L1 expression (Table). EFS from surgery (HR [95% CI]) continued to favor NIVO vs PBO in pts with pCR (0.90 [0.19–4.15]) or without (w/o; 0.72 [0.50–1.05]). In biomarker-evaluable pts (NIVO, 98; PBO, 92), pts with ctDNA CL had greater EFS benefit (assessed from randomization) vs pts w/o (HR [95% CI]: NIVO, 0.41 [0.20–0.86]; PBO, 0.62 [0.31–1.22]); pts with ctDNA CL with or w/o pCR had improved EFS vs pts w/o ctDNA CL and pCR (data to be presented). EFS (HR [95% CI]) favored NIVO vs PBO in pts with tumor genomic alterations (*KRAS*, and/or *STK11*, and/or *KEAP1* mutations; 0.63 [0.32–1.23]) or w/o (0.65 [0.39–1.10]). Higher ctDNA CL and pCR rates were seen with NIVO vs PBO regardless of mutation status; additional efficacy and ctDNA outcomes will be presented. At the first prespecified interim OS analysis, NIVO showed a trend of OS improvement vs PBO in all randomized pts (HR [97.63% CI], 0.85 [0.58–1.25]; median OS, not reached in both tx arms; 30-mo OS rates, 78% vs 72%). Safety outcomes were consistent with previous reports. **Conclusions:** In this update, perioperative NIVO continued to show long-term EFS benefit and a favorable OS trend vs PBO in pts with resectable NSCLC; no new safety signals were observed. In exploratory analyses, presurgery ctDNA CL was associated with EFS benefit. EFS favored NIVO vs PBO regardless of *KRAS*, *STK11*, and *KEAP1* mutation status. Clinical trial information: NCT04025879. Research Sponsor: Bristol Myers Squibb.

	All pts NIVO (N = 229) vs PBO (N = 232)	Stage II NIVO (n = 80) vs PBO (n = 81)	Stage III NIVO (n = 149) vs PBO (n = 149)	Squamous NIVO (n = 116) vs PBO (n = 118)	Non-squamous NIVO (n = 113) vs PBO (n = 114)	PD-L1 < 1% NIVO (n = 93) vs PBO (n = 93)	PD-L1 ≥ 1% NIVO (n = 128) vs PBO (n = 128)
Median EFS, mo	46.6 vs 16.9	NR vs NR	42.1 vs 13.4	NR vs 16.4	40.1 vs 16.9	40.1 vs 19.8	46.6 vs 15.1
HR (95% CI)	0.61 (0.46–0.80)	0.77 (0.46–1.30)	0.54 (0.39–0.74)	0.53 (0.35–0.80)	0.69 (0.48–1.00)	0.79 (0.52–1.21)	0.53 (0.36–0.76)

LBA8027 **Poster Session**

An international, multicenter, prospective randomized trial of adjuvant chemotherapy for stage Ia-IIa non-small cell lung cancer identified as high-risk by a 14-gene molecular assay.

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Background: Despite advances in late-stage treatments, survival of early-stage non-small cell lung cancer (NSCLC) remains dismal, with 5-year disease free survival (DFS) of only 65% even in stage Ia. Preliminary, non-randomized clinical data suggest the predictive efficacy of RiskReveal, a 14-gene expression profile, in identifying stage Ia-IIa patients with non-squamous NSCLC who benefit from adjuvant therapy. We undertook an international, multicenter, randomized clinical trial to confirm these findings. Here, we report the results of an early interim analysis that was planned to detect a large discrepancy in outcomes between arms. **Methods:** 421 patients who underwent resection of stage pIa-IIa NSCLC were categorized as low-, intermediate-, or high-risk by the RiskReveal assay. Intermediate- and high-risk patients were randomized to observation or to 4 cycles of platinum-based adjuvant chemotherapy. The modified intent-to-treat (mITT) population was defined as randomized patients who continued to meet eligibility criteria either at the time of chemotherapy initiation or at randomization to observation. The primary endpoint was DFS in the mITT population, defined as the time from randomization to disease recurrence, exclusive of new primary lung cancer, or death from any cause. DFS was compared between arms using a log-rank test and Kaplan-Meier analysis. An early interim analysis was planned with a type I error rate of 0.02. **Results:** Of 194 evaluable patients at the time of the interim analysis, 87 had been randomized to adjuvant chemotherapy (55% stage Ia), and 107 to observation (55% stage Ia). There were no significant differences between the groups with respect to age, sex, or tumor size >4 cm; median follow-up was 19.5 months in the chemotherapy arm and 19.0 months in the observation arm. At 24 months, adjuvant chemotherapy significantly improved DFS compared to observation, with a HR of 0.22 (95% CI 0.06, 0.76; p=0.0087). DFS at 24 months was 96% with adjuvant chemotherapy (95% CI 0.92, 1.00) vs. 79% with observation (95% CI 0.70, 0.90). Median DFS was not reached in either group. **Conclusion:** A 14-gene molecular assay identified a high-risk population of stage Ia-IIa non-squamous NSCLC patients who benefited substantially from adjuvant chemotherapy. Improved survival in lung cancer is best achieved by optimizing outcomes in the earliest stages of disease. Identification of patients who benefit from adjuvant chemotherapy using this predictive test could result in a dramatic improvement in survival for the growing percentage of patients diagnosed in stages I-IIa. Although the study DSMB recommended a halt to enrollment, follow up continues and may provide further confirmation of this benefit. Clinical trial information: NCT01817192. Research Sponsor: Razor Genomics, Inc.

LBA8502 Oral Abstract Session

CAMPASS: Benmelstobart in combination with anlotinib vs pembrolizumab in the first-line treatment of advanced non-small cell lung cancer (aNSCLC)—A randomized, single-blind, multicenter phase 3 study.

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Background: Anti-PD-(L) 1 monotherapy has been the standard first-line treatment for PD-L1 positive NSCLC, but its clinical benefit remains unsatisfactory. Benmelstobart (TQB2450) is a humanized monoclonal antibody against PD-L1 and anlotinib is a multikinase inhibitor that has been approved as the standard of care in the third-line treatment of NSCLC in China. This phase 3 study aimed to compare the efficacy of benmelstobart in combination with anlotinib and pembrolizumab as first-line treatment of PD-L1 positive aNSCLC. **Methods:** This is a randomized, single-blind, multicenter phase III study (NCT04964479). Eligible patients (pts) were previous systemic treatment naïve, diagnosed with locally advanced or recurrent/metastatic NSCLC and had PD-L1 positive expression (defined as TPS ≥1%). Pts were randomized in a 2:1 ratio to receive either benmelstobart plus anlotinib (benmel+ anlo) or pembrolizumab plus placebo (pem+placebo). Anlotinib or placebo was administered orally at a dose of 12/0mg QD on days 1-14 of a 21-day cycle, while benmelstobart or pembrolizumab was given intravenously at a dose of 1200mg or 200mg on the first day of each cycle. The primary endpoint was progression-free survival (PFS) assessed by independent review committee (IRC). **Results:** Between August 2021 and December 2022, 531 pts were randomized (528 treated). At the data cutoff date of 20 May 2023, the median follow-up for PFS was 11.4 months for the benmel+anlo arm and 10.6 months for the pem+placebo arm. The study met its primary endpoint that the median PFS was significantly prolonged to 11.0 months (95% CI 9.2-12.6) in the benmel+anlo arm compared with 7.1 months (95% CI 5.8-9.5) in the pem+placebo arm (P = 0.007). The hazard ratio (HR) was 0.70 (95% CI 0.55-0.91). The HR for pts with squamous cell carcinoma and PD-L1 expression ≥50% was 0.63 (95% CI 0.46-0.86) and 0.60 (95% CI 0.41-0.88). The confirmed objective response rate was also obviously higher with combination therapy (57.3% vs. 39.6%; P < 0.001). The data for overall survival (OS) was immature. In total, 98.3% of pts in the benmel + anlo arm and 88.1% in the pem + placebo arm experienced at least one treatment-related adverse event (TRAE). The incidence of grade ≥3 TRAE was 58.5% and 29.0% in each group, respectively. Only 5.7%/3.7% of pts permanently discontinued benmelstobart/anlotinib since TRAE, while termination of pembrolizumab/placebo due to TRAE occurred in 8.0%/2.3% of pts. **Conclusions:** To our knowledge, this is the first phase III study to demonstrate the significant PFS benefit of a multikinase inhibitor plus an anti-PD-L1 mAb in the first-line treatment of PD-L1-positive aNSCLC compared to pembrolizumab. Tolerability is favourable with a lower incidence of treatment discontinuation due to TRAE. The data support this combination as a new option for these pts. Clinical trial information: NCT04964479. Research Sponsor: Chia Tai TianQing Pharmaceutical Group Co., Ltd.

LBA8505 Oral Abstract Session

Savolitinib (Savo) combined with osimertinib (osi) versus chemotherapy (chemo) in EGFR-mutant (EGFRm) and *MET*-amplification (*MET*amp) advanced NSCLC after disease progression (PD) on EGFR tyrosine kinase inhibitor (TKI): Results from a randomized phase 3 SACHI study.

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Background: Savo, a highly selective *MET*-TKI, combined with osi, may overcome acquired *MET*-driven resistance in EGFRm advanced NSCLC after PD on EGFR-TKIs. Here we report primary results of the prespecified interim analysis (IA) in SACHI study, comparing efficacy and safety of savo + osi with chemo in this disease setting. **Methods:** In this randomized, open-label, phase 3 study, 250 EGFRm and *MET*amp advanced NSCLC patients (pts) post PD on first-line EGFR-TKI were planned (*MET* copy number ≥5 or *MET*/CEP7 ratio of ≥2.0 by FISH for pts with prior $1^{st}/2^{nd}$ generation [G] EGFR-TKI; *MET* copy number ≥10 for pts with prior 3^{rd} G EGFR-TKI); T790M negative after PD on $1^{st}/2^{nd}$ G EGFR-TKI was required. Eligible pts were randomly assigned (1:1) to receive savo 400 or 600 mg QD (for body weight of < 50, or ≥ 50 kg respectively) + osi 80 mg QD, or chemo (pemetrexed + carboplatin/cisplatin), stratified by brain metastases, prior use of 3G EGFR-TKI, and type of EGFR mutations. Crossover to savo + osi after IRC-PD was permitted for chemo group. The primary endpoint, PFS by investigator (INV) per RECIST 1.1, was hierarchically tested via a stratified log-rank test in 3G EGFR-TKI treatment-naïve set firstly, then in ITT set. This is a prespecified IA conducted via an independent data monitoring committee to assess efficacy superiority or sample size re-estimation. **Results:** From 15 Oct 2021 to 30 Aug 2024 (DCO for IA), 211 pts were randomized to receive savo + osi or chemo (n=106 vs 105). Baseline characteristics were well balanced. mPFS by INV was significantly longer with savo + osi vs chemo in both 3G EGFR-TKI treatment-naïve set and ITT set ($p< 0.0001$ in both sets), which met prespecified IA efficacy boundary ($p<0.0099$ and 0.0228 in 2 sets, respectively); in 3G EGFR-TKI treated pts, mPFS was also significantly prolonged with savo + osi (6.9m vs 3.0m, HR=0.32, $p < 0.0001$). IRC-assessed PFS benefits were consistent (table). OS was immature at this DCO. Grade ≥3 TEAE occurred in 56.6% vs 57.3% of pts with savo + osi vs chemo; savo + osi had lower rates of hematologic events than chemo. **Conclusion:** Savo + osi significantly improved PFS versus chemo in *MET*amp NSCLC post EGFR-TKI, and the combination was safe and well tolerated. Savo + osi is a potential new treatment option for this genomically defined population. Clinical trial information: NCT05015608. Research Sponsor: This study is funded by HUTCHMED Limited and AstraZeneca.

ITT set	Savo + osi N=106	Chemo N=105	Hazard ratio/ Odds ratio	Two sided-*p* value
mPFS (95% CI) (INV), m	8.2 (6.9, 11.2)	4.5 (3.0, 5.4)	0.34	<0.0001
mPFS (95% CI) (IRC), m	7.2 (5.7, 11.1)	4.2 (4.0, 5.7)	0.40	< 0.0001
ORR (95% CI) (IRC), %	63.2 (53.3, 72.4)	36.2 (27.0, 46.1)	3.05	< 0.0001
mDoR (95% CI) (IRC), m	9.7 (5.8, 12.4)	4.3 (2.8, 5.1)	NA	NA
mOS (95%CI), m*	22.9 (16.8, NE)	17.7 (14.9, 26.3)	0.84	0.4191

*52.4% of pts in chemo group were crossover to receive savo + osi or other MET Inhibitors.

LBA8671 Rapid Oral Abstract Session

PRAGMATICA-LUNG (SWOG S2302): A prospective, randomized study of ramucirumab plus pembrolizumab versus standard of care for participants previously treated with immunotherapy for stage IV or recurrent non-small cell lung cancer.

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Background: Effective therapy after frontline immune checkpoint inhibitor (ICI)-based treatment for advanced NSCLC is needed as limited options are available. Lung-MAP S1800A was a phase II randomized study of RP versus SoC for pts with NSCLC previously treated with ICI that showed benefit in overall survival (OS) with an improved toxicity profile over SOC. S2302 Pragmatica-Lung was designed to evaluate the impact on OS while reducing the barriers and burdens of trial participation. **Methods:** S2302 is a registration-intent randomized phase III trial for pts with advanced NSCLC who previously received ICI for at least 84 days and platinum-based therapy, randomized to SOC or RP, stratified by immediate prior therapy including ICI (yes/no) and PS (0/1 v. 2). The pragmatic design led to eligibility focus on stage, prior therapy and safety to enroll pts. Laboratory assessment and imaging were not required. Data collection was developed to minimize the burden with fewer number of forms, data elements and time points for data submitted. Only related and unexpected grade 3/4 and all grade 5 adverse events were collected. Two interim analyses (at 40% and 60% of expected deaths) were planned. The criteria for early reporting were a fixed sample p-value from a stratified log-rank test ≥ 0.3156 for futility and ≤ 0.0054 for efficacy. **Results:** S2302 enrolled 838 pts in 21 months (mos) from March 2023 to December 2024 (419/arm), averaging >50 pts/month in the final 6 mos. Median age (range) was 68 (34-88), 22% non-white /13% Black, 15% rural, 29% squamous cell carcinoma (SCC), 63% adenocarcinoma, 81% had ICI as the most recent treatment, 13% had PS2. The study met futility criteria for early reporting at the second interim analysis (April 2025). With 370 deaths reported and median of follow-up for alive pts of 5.2 mos (0.2-22.1 mos), OS is not different between the arms: HR (95% CI): 0.99 (0.81-1.22), p=0.46; median OS of 10.1 mos for RP and 9.3 for SOC. Within histologic subgroups, the HR (95% CI) for 242 pts with SCC is 0.82 (0.56-1.22), p=0.17 and for 596 with non-SCC is 1.09 (0.85-1.39), p=0.75. **Conclusions:** Accrual was rapid, and participant representativeness enhanced in this study with pragmatic design features. Often understudied groups were better represented; the study represents a contrast with the usual better prognosis of trial populations. While RP did not improve OS, RP was not worse than SOC overall, may benefit some with SCC, and is chemotherapy-free. There is some evidence of subgroups benefiting with delayed curve separation. Longer follow-up and reported events will provide more clarity on these hypotheses. Support: NIH/NCI/NCTN grants U10CA180888 and U10CA180819; and in part by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA, and Eli Lilly and Company. Clinical trial information: NCT05633602. Research Sponsor: NIH/NCI/NCTN Grant; U10CA180888; NIH/NCI/NCTN Grant; U10CA180819; Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Eli Lilly and Company.

LBA9500 **Oral Abstract Session**

Nivolumab plus relatlimab vs nivolumab alone for the adjuvant treatment of completely resected stage III–IV melanoma: Primary results from RELATIVITY-098.

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Background: NIVO + RELA fixed-dose combination (FDC), compared with NIVO alone, demonstrated a clinically meaningful benefit to progression-free survival (HR 0.79, 95% CI 0.66–0.95) and overall survival (OS; 0.80, 95% CI 0.66–0.99) after a 3-y follow-up, with a manageable safety profile in patients (pts) with untreated advanced melanoma (RELATIVITY-047). To address a current unmet need for more efficacious adjuvant regimens for completely resected melanoma, RELATIVITY-098 was designed to evaluate adjuvant NIVO + RELA FDC vs NIVO alone in pts after complete resection of stage III–IV melanoma (NCT05002569). **Methods:** In this phase 3, randomized, double-blind study, pts aged ≥ 12 years were stratified by AJCC v8 stage at screening (stage IIIA/IIIB vs IIIC vs IIID/IV) and geographic region (USA/Canada/Australia vs Europe vs rest of the world). Pts were randomized 1:1 to receive NIVO 480 mg + RELA 160 mg FDC or NIVO 480 mg every 4 weeks for a maximum of 1 year or until first recurrence, unacceptable toxicity, or withdrawal of consent. The primary endpoint was recurrence-free survival (RFS) by investigator; secondary endpoints included OS (key), distant metastasis-free survival (DMFS), and safety. **Results:** Pts randomized to NIVO + RELA (n = 547) vs NIVO alone (n = 546) had stage IIIA/B (38% vs 36%) or IIIC (49% vs 50%) disease; 80% vs 83% had cutaneous nonacral melanoma, 11% vs 10% had cutaneous acral, and 2% vs 1% had mucosal. Median duration of therapy was 11.0 mo for each arm. At a minimum follow-up of 23.4 mo, there was no statistical difference in RFS for NIVO + RELA vs NIVO (Table). The RFS outcome was generally consistent across stratification factors and prespecified subgroups. OS was not tested per the hierarchical testing strategy. There were 148 OS events (48% data maturity). DMFS was similar in both treatment groups (Table). Grade 3/4 treatment-related adverse events (TRAEs) occurred in 19% of pts treated with NIVO + RELA vs 8% with NIVO alone (compared with 22% vs 12% in RELATIVITY-047); any-grade TRAEs led to discontinuation of therapy in 17% vs 9% of pts, respectively. There were 2 treatment-related deaths with NIVO + RELA and 1 with NIVO. **Conclusions:** NIVO + RELA did not result in significant RFS improvement vs NIVO alone as adjuvant treatment for pts after complete resection of stage III–IV melanoma. The safety profile of NIVO + RELA in this setting was generally consistent with results from RELATIVITY-047. A robust biomarker analysis for the study is currently underway. Clinical trial information: NCT05002569. Research Sponsor: Bristol Myers Squibb.

	NIVO + RELA	NIVO
RFS		
24-mo rate, %	62.0	63.6
(95% CI)	(57.7–66.0)	(59.4–67.6)
Median, mo (95% CI)	NR (30.8–NR)	33.1 (31.0–NR)
(events/pts)	(214/547)	(213/546)
HR	1.01 (95% CI, 0.83–1.22)	
DMFS		
24-mo rate, %	73.1	76.3
(95% CI)	(68.8–76.9)	(72.3–79.9)
Median, mo (95% CI)	NR (NR–NR)	33.1 (31.5–NR)
(events/pts)	(133/499)	(129/494)
HR	1.07 (95% CI 0.84–1.36)	

HR, hazard ratio; NR, not reached.

LBA9501 **Oral Abstract Session**

Primary analysis of the EORTC-2139-MG/Columbus-AD trial: A randomized trial of adjuvant encorafenib and binimetinib versus placebo in high-risk stage II melanoma with a BRAF-V600E/K mutation.

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Background: Resected stage IIB/IIC melanoma has a high risk of recurrence. While, for decades, surgery was the only option for high-risk stage II disease in most countries, adjuvant therapies now exist. Anti-PD-1 significantly improve recurrence-free survival (RFS) vs. placebo in patients with fully resected stage IIB/IIC melanoma. Combined BRAF&MEK inhibitor therapy showed benefit in high-risk stage III & advanced disease, but its role in patients with fully resected *BRAF*-mutated stage IIB/IIC melanoma is unknown. Encorafenib and binimetinib could be considered a valuable alternative with a lower risk of chronic toxicities. **Methods:** Adult patients with fully resected stage IIB or IIC cutaneous melanoma who harbored a BRAF mutation V600E or K were randomized 1:1 to receive encorafenib (enco) 450 mg QD + binimetinib (bini) 45 mg BID orally for one year or placebo. The study planned to randomize 815 patients. It was designed to demonstrate superiority regarding the primary endpoint RFS defined as time from randomization to the earliest of recurrence, new melanoma that was either ulcerated, thick or requiring a treatment other than surgery, or death with a power of 97% to detect a hazard ratio (HR) of 0.55 and 91% to detect a HR of 0.6 with a level of statistical significance of 0.025 for a one-sided log-rank test. Following a premature termination of accrual, the study was amended to become a randomized trial with safety as the primary and RFS a secondary endpoint. **Results:** Between June 9, 2022, and October 9, 2023, 339 patients were screened for a BRAF mutation and 110 were equally randomized between enco+bini and placebo arms. Median age was 59 yrs and 54% were male. Data cutoff was on 19 Nov. 2024, after the last patient was discontinued from the study. Among randomized patients, 87 (79%) had BRAF V600E and 23 (21%) V600K mutation, 71 (65%) AJCC8 stage IIB and 39 (35%) IIC. Median follow-up was 12 and 7 months for enco+bini and placebo arms. Among 54 patients who initiated enco+bini, grade ≥3 treatment-related adverse events (AE) occurred in 13 (24%) patients, and 18 (33%) patients had an AE leading to permanent treatment discontinuation. A serious treatment-related adverse event occurred in 1 patient. No patients died. In the enco+bini and placebo arm, respectively, 4 and 9 patients had an RFS event and 3 and 5 developed distant metastases. Descriptive RFS at 12 months was 86% (95% CI: 65-95%) in the enco+bini and 70% (95% CI: 46-85%) in the placebo arm, Distant Metastasis-Free Survival (DMFS) at 12 months was 92% (95% CI: 77-97%) for enco+bini and 82% (95% CI: 55-93%) for placebo arms. **Conclusion:** EORTC 2139 - Columbus-AD demonstrated a consistent safety profile for enco+bini. Descriptive analyses of efficacy show encouraging results of the combination of enco+bini for adjuvant treatment of stage IIB/C BRAF V600E/K cutaneous melanoma. Clinical trial information: NCT05270044. Research Sponsor: Pierre Fabre.

LBA9504 Oral Abstract Session

Randomized phase II study of neoadjuvant (neoadj) anti-PD-1 dostarlimab (D) vs. D + anti-TIM-3 cobolimab (C) in high-risk resectable melanoma (mel) (NEO-MEL-T): Primary analysis.

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Background: Neoadj immunotherapy improves outcomes in high-risk resectable mel, although novel combinations that enhance efficacy while minimizing toxicity are needed. TIM-3 is highly expressed on dysfunctional CD8T cells and APCs within TME. Dual PD-1 and TIM-3 blockade promotes expansion and function of antigen-specific T cells, resulting in potent antitumor immunity. D and C are monoclonal antibodies targeting PD-1 and TIM-3. D+C has efficacy in PD-1 relapsed/refractory mel (Ribas, ASCO 2022) and NSCLC (Davar, SITC 2023). NEO-MEL-T is a randomized phase II study of neoadj D vs. D+C in patients (pts) with clinical stage III (AJCC IIIB-D) cutaneous mel. **Methods:** Pts aged >18 yo with clinical stage III mel were randomized (1:1) to neoadj D (500mg Q3W; Arm A) or D+C (500mg Q3W D + 300mg Q3W C; Arm B) for 2 cycles prior to surgery. Post-surgery, pts received further D (500mg Q3W x4; then 1000mg Q6W x6). Primary endpoint was major pathologic response (MPR) rate assessed by blinded pathologist. Secondary endpoints included safety, radiographic response rate (ORR), event-free survival (EFS), distant metastasis free survival (DMFS), and overall survival (OS). Target enrollment of 28 evaluable pts per arm (56 total) provided 80% power (1-sided α 0.05) to distinguish between null hypothesis of 28% MPR rate (historical neoadj PD-1) and alternative hypothesis of >50% in either arm. Primary analysis was a 1-sided z test. **Results:** Between 6/ 2020-11/2024, 57 pts were enrolled and randomized to either Arm A with neoadj D (n=30, 52.6%) or Arm B with neoadj D+C (n=27, 47.4%). Majority of pts were either stage IIIB (n=25, 43.9%) or IIIC (n=25, 43.9%), balanced across both arms. Median time to surgery was 51 days (range: 38-82), and all pts underwent curative surgery. Median follow-up time was 22 mos (range: 2-55). MPR rate was 33.3% (Arm A) and 51.9% (Arm B). MPR rate in Arm B was significantly greater than historical control (p=0.0029,1-sided z-test). Across both arms, median EFS was superior in MPR (unreached) vs. non-MPR (48 mos) (p=0.0380, log-rank test) pts, while median DMFS and OS have not been reached. 1-year EFS estimates were greater in Arm B (92%) compared to Arm A (82%), although this was not significant. The 1-year EFS in Arm B was significantly greater than historical adjuvant anti-PD-1 (p=0.0365, 1-sided z test). The proportion of pts with grade 3+ irAEs was similar in Arms A (16.7%) and B (14.9%) (p=0.4273). **Conclusion:** Neoadj D+C was safe and efficacious. The 1-year EFS of 92% in Arm B was significantly improved relative to adjuvant anti-PD-1, and this combination warrants further investigation. Clinical trial information: NCT04139902. Research Sponsor: GlaxoSmithKline.

	Arm A (D) (N=30)	Arm B (D+C) (N=27)
MPR (%; 95% CI)	10 (33;17-53)	14 (52;33-71)
1-year EFS (95% CI)	82 (61-92)	92 (71-98)
1-year EFS in MPR (95% CI)	100 (54-100)	100 (74-100)
1-year EFS in non-MPR (95% CI)	73 (47-88)	82% (45-95)

LBA9505 **Oral Abstract Session**

A phase II randomized study of neoadjuvant pembrolizumab (P) alone or in combination with vidutolimod (V) in high-risk resectable melanoma: ECOG-ACRIN EA6194.

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Background: Advances in the neoadjuvant (neo) setting of locoregionally advanced melanoma have recently transformed practice. However, there continues to be a need to enhance efficacy while minimizing systemic toxicity. Preliminary data support an important role for vidutolimod (V), a CpG-A TLR9 agonist packaged within a virus-like particle given intratumorally (IT) in combination with IV anti-PD1. **Methods:** A U.S. intergroup randomized phase II trial of pembrolizumab (P) *vs* P + V in patients (pts) with resectable clinical AJCC8 stages IIIB-D. It planned to randomize ~60 pts (for 54 evaluable) 1:1 to Arm A (neo P 200 mg IV Q3W x3) or Arm B (neo P 200 mg IV Q3W x3 + V 5 mg SC x1 then 10 mg IT QW x6) followed by definitive surgery then adjuvant P 400 mg IV Q6W x8, stratified by stage (IIIB/C *vs* IIID). Primary endpoint was pathologic (path) complete response (pCR) on each arm. Secondary endpoints included path responses, recurrence, overall survival, event-free survival [EFS: disease progression (PD), recurrence or death] and safety. **Results:** EA6194 enrolled 57 pts March 2021-March 2024, 19 female, 38 male, all cutaneous primary (1 acral on Arm B), median age 64 (26-88), 29 on Arm A [10 IIIB (8N1b, 1N1c, 1N2b), 19 IIIC (3N1b, 1N1c, 3N2b, 3N2c, 7N3b, 2N3c)] and 28 on Arm B [13 IIIB (11 N1b, 2 N2b), 13 IIIC (5 N1b, 2N2b, 2N2c, 3N3b, 1N3c), 2 IIID (N3b)]. The median numbers of neo P/adjuvant P doses were similar for both arms at 2/7. Median number/total dose of V were 7/60 mg. Among pts who initiated treatment, highest grade related AEs (Gr 3/4) were 25% in Arm A (N=28) and 29% in Arm B (N=28) including in Arm B diarrhea (1), injection site reaction (1), cytokine release (1), wound dehiscence (1), lymphocytopenia (1), pain (1), headache (1), hypertension (1), hypotension (1), all Gr 3 and one Gr 4 hyperglycemia. Median time to surgery from randomization 2.5 months. Median follow up time from enrollment 19 months. There were 3 deaths on Arm A and 1 on Arm B. On Arm A 25 pts had surgery, 6 path non-response (pNR), 2 partial (pPR), 3 near-pCR, 14 pCR (56%; 95% CI, 35 - 76). MPR (pCR + near-pCR) was 17/25 (68%; 95% CI, 46 - 85). Among these, 3 had recurrence after surgery (1 pNR, 1 near-pCR, 1 pCR). On Arm B 27 pts had surgery, 3 pNR, 2 pPR, 2 near-pCR, 20 pCR (74%, 95%, CI 54 - 89). MPR 22/27 (79%; 95% CI 62 - 94). Among these, 2 had recurrence after surgery (1 pNR, 1 pPR). Table 1 summarizes efficacy data including all enrolled pts. **Conclusions:** Neoadjuvant P + Vdemonstrated acceptable safety and encouraging clinical activity in pts with resectable clinical stages IIIB/IIIC/IIID melanoma when considering Arm A and historical controls, warranting further investigation. Clinical trial information: NCT04708418. Research Sponsor: NCI, ECOG-ACRIN.

	Arm A: P (N=29*)	Arm B: P + V (N=28*)
pCR (%; 95% CI)	14 (48; 29 - 67)	20 (71; 51 - 87)
MPR (%; 95% CI)	17 (59; 39 - 76)	22 (79; 59 - 92)
1-year EFS (95% CI)	75% (59 – 91)	89% (78 - 100)

*4 on Arm A and 1 on Arm B did not have surgery due to PD.

LBA9507 Oral Abstract Session

A randomized phase 2 trial of encorafenib + binimetinib + nivolumab vs ipilimumab + nivolumab in BRAFV600-mutant melanoma brain metastases: SWOG S2000 (NCT04511013).

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Background: While anti-PD-1 and anti-CTLA4 immunotherapies have efficacy in the treatment of patients (pts) with asymptomatic melanoma brain metastases (MBM), their efficacy in pts with symptomatic MBM is very limited. In the Checkmate-204 trial of ipilimumab with nivolumab in MBM, 6-month progression-free survival (PFS) rate was 19% with a median PFS of only 1.2 months in symptomatic pts. In the COMBI-MB study of BRAF/MEK-inhibitors in MBM, median PFS was 5.5 months in symptomatic pts (n=17). A head-to-head approach of targeted and immunotherapy has not been tested; moreover, a combination of targeted and immunotherapy is feasible as demonstrated by prior studies. **Methods:** SWOG S2000 is a 1:1 randomized phase 2 trial exploring the efficacy of a front-line triplet regimen of BRAF/MEK inhibitors with anti-PD-1 monotherapy (encorafenib 450 mg qday + binimetinib 30 mg BID + nivolumab 480 mg IV q4w) versus ipilimumab 3 mg/kg + nivolumab 1 mg/kg q3w in pts with symptomatic BRAF-mutant MBM. Pts were ≥18 years old, ECOG 0-2, and prior neoadjuvant or adjuvant anti-PD-1, CTLA-4, or BRAF/MEK-inhibitors were permitted, but no systemic treatment in the metastatic setting. Steroids up to 8 mg of dexamethasone/day (or equivalent), leptomeningeal spread, and prior local therapy (radiation or surgery) for MBM were permitted, if there was at least one measurable, progressing MBM ≥ 0.5 cm. Disease assessments were performed at 6 and 12w, and then q12w from treatment start until progression. Primary objective was to compare PFS (intracranial + extracranial) per RECIST 1.1 between the arms. **Results:** Between September 2020 and June 2024, 30 pts with symptomatic MBM were enrolled; 1 pt was ineligible. Thirteen (45%) received prior corticosteroids and 14 pts (48%) received prior local therapy for MBM. Six-month PFS rate was 50% (95% CI 23-72%) with enco/bini/nivo, vs 29% (95% CI 9-52%) with ipi/nivo. The study met its primary endpoint with a hazard ratio (HR) of 0.51 (95% CI 0.0 – 0.92), with a statistically significant one-sided p-value of 0.07, less than 0.10 alpha pre-specified by study design. Median PFS was 6.2 months (3.0- 20.4) with enco/bini/nivo, vs 1.4 months (0.7 - 13.8) with ipi/nivo. Overall response rate (PR + CR) was 57% (31-83%) with enco/bini/nivo vs 15% (10-15%) with ipi/nivo . With enco/bini/nivo, 69% of pts had grade 3-4 toxicity, and with ipi/nivo, 75% had grade 3-5 toxicity, with one death due to cardiac arrest. **Conclusions:** S2000 is the first randomized trial in patients with symptomatic melanoma brain metastases. A first-line triplet regimen of enco/bini/nivo demonstrated a statistically significant improvement in PFS as compared to ipi/nivo, with a HR of 0.51. Both regimens also had toxicity rates consistent with their known profiles. In this difficult-to-treat pt population frequently requiring steroids, a triplet regimen may warrant further study. Clinical trial information: NCT04511013. Research Sponsor: National Cancer Institute - SWOG.

LBA9508 **Oral Abstract Session**

Comparison of 1 year versus minimum 2 years of anti-PD1-based immunotherapy as first-line treatment for metastatic melanoma: Results of the DANTE phase III trial.

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Background: Optimal first line therapy for patients with metastatic melanoma is an immunotherapy regimen containing an anti-PD1 antibody, regardless of tumour *BRAF* mutation status. Anti-PD1 antibodies are licensed for use until disease progression. Recurrence rarely occurs in responding patients after 2 years of treatment. Optimal duration of anti-PD1-based immunotherapy has not been established. Reduced treatment duration may reduce the risk of long-term side-effects and generate cost savings for healthcare systems. **Methods:** DANTE (ISRCTN15837212) was a UK academic multi-centre parallel group non inferiority trial. Adults with unresectable stage III/IV melanoma receiving first line anti-PD1 +/- anti-CTLA-4 antibody immunotherapy were eligible. Patients who were progression-free after 1 year of treatment were randomised (1:1) to stop treatment (with the option of restarting on progression) or to continue treatment to at least 2 years in the absence of disease progression / unacceptable toxicity (control). The primary endpoint was progression-free survival (PFS) at 1 year post-randomization. Secondary endpoints included quality of life, best objective response, overall survival, toxicity and cost-effectiveness. A qualitative study explored patient acceptance of randomization. Follow-up to 4-years was planned for PFS with secondary outcomes collected up to 18-months post-randomization. Assuming a 2-year PFS rate in the control arm of 86% and defining non-inferiority (NI) as a reduction in PFS of no more than 6%, a sample size of 1208 patients (604 per arm) was required (80% power, 5% significance, 5% drop-out). DANTE closed early due to slow patient enrolment. PFS was compared between arms using Cox's proportional hazards model, adjusting for stratification factors. **Results:** Between September 2018 and March 2023, 415 patients were registered from 36 UK hospitals and 166 patients (65.6% male, median age 74, *BRAF* mutant 25.9%) were randomised. Patient characteristics were broadly balanced. As of 27th January 2025, with a median follow-up of 29.1 (IQR 17.9-39.3) months, there were 53 PFS events in total: 18 in the control arm (15 progressions+3 deaths) versus 35 in the stop arm (29 progressions+6 deaths). PFS rates at 1-year were 87.6% in the control arm and 80.2% in the stop arm (HR 1.76; 90% CI 1.03-3.03), with an absolute difference of -7.4% and 90% two-sided CI -17.1-2.32, which is within the pre-defined NI margin of 6%. Analyses are ongoing, results for secondary endpoints will be presented. **Conclusions:** DANTE is the largest prospective melanoma trial evaluating immunotherapy duration completed to date. Although results suggest stopping immunotherapy at 1 year was non-inferior compared to at least 2 years of treatment, the trial was underpowered due to early closure. Continuing immunotherapy for at least 2 years should remain as standard treatment. Clinical trial information: 15837212. Research Sponsor: National Institute for Health Research (NIHR) Health Technology Assessment Programme; 15/57/66.

LBA10606 **Poster Session**

The Genetic Information and Family Testing (GIFT) trial.

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Background: Engaging patients with inherited cancer susceptibility is a potentially powerful strategy to reduce the gap in genetic risk evaluation for their families. The goal of the GIFT Trial is to engage patients to provide support to their relatives to initiate cancer genetic risk education and at-home germline genetic testing. **Methods:** GIFT is a 2x2 factorial cluster-randomized trial to implement and evaluate a direct-to-family, online education and communication tool including the offer of home genetic testing. We identified 4300 adult patients with any cancer type diagnosed in Georgia and California in 2018-19 who linked to a pathogenic variant (PV) in a clinically tested cancer susceptibility gene through a unique SEER-based data infrastructure, and surveyed those who were alive at time of selection four years after diagnosis (N=2285 completed surveys, response rate 55%). We invited all eligible respondents (recalled PV on germline genetic testing) to enroll in GIFT. Enrolled patients could invite their eligible first- and second-degree relatives to enroll. The index patient subject was randomized after consent, and relatives were then cluster-randomized by family. All participants received some level of intervention, including at least the online tool with information about genetic testing and an offer to relatives of home genetic testing through the tool. We examined the effects of two intervention features: 1) the level of family genetic risk navigation support: a technology-assisted, tailored patient and family member education and communication tool vs. the tool plus direct assistance from a lay human navigator; and 2) the cost of the genetic test offered to relatives (free vs $50, provided by Color Health). The primary endpoint is the Family Genetic Testing Fraction (the proportion of each patient's first and second-degree relatives who received testing through the tool). **Results:** 2,006 of 2285 patient respondents were eligible and invited to GIFT (87.8%) and 412 enrolled (20.5%). Enrolled patients had a total of 5016 first- and second-degree relatives, of whom 945 were invited (18.8%), 298 enrolled (5.9%), and 270 received genetic test results (5.4%). The Table shows differences in the outcome by trial arm adjusted by the number of family members and gender of the invited relative. **Conclusions:** Patient and relatives' engagement in GIFT was substantial but lower than anticipated. Free vs. low-cost had a modest effect on test rate, while there was no significant effect of the human navigator. GIFT demonstrates how an online genetic risk education and genetic testing tool can be delivered to families with hereditary cancer syndromes through a population-based approach. Trial Registration: NCT05552664 at Clincaltrials.gov September 20, 2022. Funding: NCI U01CA254822, P30CA046592, and ACS RSG-20-025-01. Clinical trial information: NCT05552664. Research Sponsor: National Cancer Institute; U01CA254822; American Cancer Society; RSG.

	Test Cost (0 vs $50)	Human Navigator (Yes vs No)
Family Test Fraction	4.5% (95% CI 1.9%, 7.4%)	1.4% (95% CI -0.9%, 3.3%)

LBA12000 Oral Abstract Session

PRO-ACTIVE: Results of a pragmatic phase IV randomized trial comparing the effectiveness of prophylactic swallow intervention for patients receiving radiotherapy for head and neck cancer.

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Background: Swallowing therapy during radiotherapy (RT) for head and neck cancer (HNC) has gained popularity as a dysphagia mitigation strategy, yet optimal timing and intensity of therapy remains uncertain. The PRO-ACTIVE trial compared the effectiveness of prophylactic and reactive swallowing therapies during RT. We hypothesized that PRO-ACTIVE therapies are more effective than RE-ACTIVE; and, that more intensive PRO-ACTIVE (EAT+EXERCISE) is superior to less intensive PRO-ACTIVE (EAT). **Methods:** PRO-ACTIVE was an international, multi-site pragmatic phase IV randomized clinical trial (NCT03455608). Eligible, adult patients had functional baseline swallowing and received RT ≥60-Gy for HNC with bilateral neck fields. Prior to RT, patients were randomized 1:2:2 to 1) RE-ACTIVE, 2) PRO-ACTIVE EAT, or 3) PRO-ACTIVE EAT+EXERCISE arms and followed for 1 year. RE-ACTIVE received weekly monitoring with therapy only if/when dysphagic, and PRO-ACTIVE arms received bi-weekly therapy pre- and during RT. The primary endpoint was feeding tube (FT) use in days from the end of RT to 1 year. Secondary endpoints were patient-reported and clinician-graded outcomes. Adjusted linear regression compared FT days per intention-to-treat with a gate-keeper approach to test hypotheses in hierarchical order with 80% power to detect a small effect size (≥.21 SD) with type 1 error probability of 0.5 (two-sided). **Results:** 952 patients from 13 institutions were randomized to RE-ACTIVE (n=196), PRO-ACTIVE-EAT (n=377) or PRO-ACTIVE-EAT+EXERCISE (n=379). 21 (2.2%) patients exited before intervention, thus, 931 were retained for analysis. The majority had stage I/II disease (552/931, 59.3%), oropharyngeal tumors (647/931, 69.5%), and p16+ and/or HPV+ disease (680/931, 73.0%). Baseline function was excellent (499/931 (53.5%) grade 0 dysphagia, mean [SD] MDADI 86 [14]). All patients received curative intent RT (median 70 Gy), 706/931 (75.8%) with chemotherapy, and 105/931 (11.3%) with primary site surgery. 364 of 931 (39.1%) required a FT with 34.4 (SD 75.9) mean days of use. Adjusted FT days at 12-months did not meaningfully differ by pro- and re-active timing (Δ5.4 days, 95% CI -6.5 to 17.2, p=0.37) or EAT versus EAT+exercise intensity (Δ5.9 days, 95% CI -3.8 to 17.6, p=0.21). Swallowing-related QOL, diet, weight/BMI, and dysphagia symptoms did not differ meaningfully by arm. **Conclusion:** FT utilization was lower than expected and secondary measures of swallowing outcomes were favorable across all arms of the PRO-ACTIVE trial reflecting relative effectiveness of EAT and exercise therapies regardless of timing or intensity of therapy delivery during RT for HNC. As a pragmatic trial, we are robustly powered to examine heterogeneous treatment effects in subgroup analyses and image-based swallowing metrics as critical next steps. Clinical trial information: NCT03455608. Research Sponsor: Patient Centered Outcomes Research Institute; 1609-36195.