Abstract 3126: Pertuzumab plus trastuzumab in patients with bladder or ovarian cancer with *ERBB2* or *ERBB3* alterations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

ASCO TAPUR
Targeted Agent and Profiling Utilization Registry Study

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Background:

- TAPUR is a phase II basket study that evaluates the antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Pertuzumab and trastuzumab (P+T) are HER2/neu receptor antagonists that are primarily used to treat pts with HER2 positive breast cancer.
- **Results of two cohorts of pts with bladder (BC) or ovarian cancer (OC) with *ERBB2* or *ERBB3* amplification (amp) or mutation (mut) treated with (P+T) are reported.**

Methods:

Study Design:

- **Eligible pts:** Advanced BC or OC, ECOG performance status (PS) 0-2, adequate organ function, measurable disease, and no standard treatment (tx) options. Tx was assigned according to prespecified matching rules based on genomic tests performed in CLIA-certified, CAP-accredited labs selected by sites. Amp cut-offs were defined per test providers.
- Pts received P at an initial dose of 840 mg intravenously (IV) over 60 minutes (m), then 420 mg IV over 30-60 m every 3 weeks (wks) and T at an initial dose of 8 mg/kg IV over 90 m, then 6 mg/kg IV over 30-60 m every 3 wks until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- **Primary endpoint:** Disease control (DC) defined by investigator assessment of objective response (OR) or stable disease (SD) of at least 16+ wks duration (SD16+) per RECIST v1.1. Radiographic confirmation of response was not required.
- **Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response (DOR), and duration of SD are reported. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) per CTCAE at least possibly related to tx are reported.

Statistical Methods:

- Simon's optimal two-stage design was used to test the null hypothesis of 15% DC rate vs. alternative of 35% for each cohort. Power = 85%; 1-sided α = 10%.
- At least 7 of 28 pts must have achieved DC to reject null hypothesis and consider tx worthy of further study.

Results:

- **BC Cohort**
  - **Demographics:** 28 pts with BC were enrolled from March 2017 to April 2023. Median age was 68 years (range 44-89); 29% female; 4% Asian/Asian American, 11% Black/African American, 79% White, 4% other, and 4% preferred not to answer; 4% as Hispanic/Latino and 4% preferred not to answer.
  - **Clinical Characteristics:** 82% ECOG PS 0-1, 18% ECOG PS 2; 79% received ≥3 prior systemic regimens. 11 pts (39%) had *ERBB2* mut; 8 (29%) had *ERBB2* amp; 3 (11%) had both *ERBB2* amp and mut; 3 (11%) had *ERBB3* mut; 2 (7%) had *ERBB2* amp and *ERBB3* mut; and 1 (4%) had *ERBB2* mut and amp and *ERBB3* mut.
  - **BC Outcomes:** 2 pts had CR, 5 had PR, and 3 had SD16+ for a DC rate of 37% (1-sided 90% CI, 24 to 100). The null DC rate of ≤15% was rejected (p=0.005) (**Tables 1 and 2**).
- **OC Cohort**
  - **Demographics:** 27 pts with OC enrolled from November 2017 to June 2023. One patient with SD16+ was found to have ineligible histology after the abstract submission and was removed from the analysis. Median age was 62 years (range 23-82); 100% female; 19% Asian/Asian American, 11% Black/African American, 70% White; 100% not Hispanic/Latino.
  - **Clinical Characteristics:** 96% ECOG PS 0-1, 4% ECOG PS 2; 56% received ≥3 prior systemic regimens. 23 pts (85%) had *ERBB2* amp; 2 (7%) had *ERBB2* mut; 1 (4%) had *ERBB2* amp and mut; 1 (4%) had *ERBB2* and *ERBB3* mut.
  - **OC Outcomes:** 2 pts had PR and 2 had SD16+ for a DC rate of 23% (1-sided 90% CI, 8 to 100). The null DC rate of ≤15% was not rejected (p=0.37) (**Tables 1 and 2**).

Conclusion: Pertuzumab plus trastuzumab demonstrated sufficient activity for further study in patients with bladder cancer with *ERBB2/3* alterations, but not in patients with ovarian cancer with *ERBB2/3* alterations.

- **Safety:** Across both cohorts, 4 pts had 6 tx-related SAEs including: infusion-related reaction, confusion, diarrhea, and fever, and 2 pts had 1 grade 3 tx-related AE each including: GGT increase and lymphopenia. No pts had grade 5 SAEs.

Table 1. Response and Tumor Alterations in Pts with DC (n=14)

Pt	Response	Cohort	Time on Tx (wks)	*ERBB2/3* Alteration(s)	Co-alterations[a]
A	CR	BC	310	*ERBB2* amp	*CDKN2A* exons 1-3 loss *TP53* R248W
B	CR	BC	30	*ERBB2* amp, S310Y	*ARID1A* W337* *TP53* E336*, R337C
C	PR	BC	21	*ERBB2* amp, S9013I[b]	--
D	PR	BC	21	*ERBB2* amp	*AKT2* amp *ALK* R311H[b] *ARID1A* G87*, E1019D[b] *EGFR* R138*[b] *TP53* F113L
E	PR	BC	51	*ERBB2* amp	*CDKN2A* deletion *CDKN2B* deletion *TP53* E28Q *MAPK1* D20N[b]
F	PR	BC	9	*ERBB2* amp *ERBB3* E332K	*PIK3CA* E545K
G	PR	BC	27	*ERBB2* S310F	*TP53* P152L, D21fs
H	SD16+	BC	30	*ERBB2* S310F	*ARID1A* L1805fs*6, Q605*
I	SD16+	BC	25	*ERBB2* I767M	*CDKN2A* amp *EGFR* amp, fusion
J	SD16+	BC	49	*ERBB2* S310F	--
K	PR	OC	15	*ERBB2* amp	*TP53* C176S
L	PR	OC	64	*ERBB2* I655F[b]	*PIK3CA* E542K
M	SD16+	OC	33	*ERBB2* amp	*ARID1A* I1725fs*6
N	SD16+	OC	27	*ERBB2* amp, N124K[b]	*TP53* C141G

[a] Of the following genes examined: *AKT1, AKT2, AKT3, ALK, ARID1A, BRAF, CDKN2A, CDKN2B, EGFR, HRAS, KRAS, MAPK1, MET, MTOR, MYC, NRAS, PIK3CA, PIK3R1 , PTEN, RAF1, SMAD4,* and *TP53*
[b] Variant of unknown significance

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Table 2. Efficacy Outcomes

	BC Cohort (N=28)	OC Cohort (N=27)
DC rate, % (1-sided 90% CI) (p-value)	37 (24, 100) (p=0.005)	23 (8, 100) (p=0.37)
OR rate, % (95% CI)	25 (11, 45)	7 (1, 24)
Median PFS, wks (95% CI)	13 (7, 22)	8 (8, 16)
Median OS, wks (95% CI)	32 (17, 54)	37 (24, 89)
Duration of CR, wks (BC, n=2)	25 and 48	--
Median duration of PR (range), wks (BC, n=5) (OC, n=2)	17 (2, 44)	9 and 56
Median duration of OR (range), wks (BC, n=7) (OC, n=2)	20 (2, 295)	9 and 56
Duration of SD in pts with SD16+, wks (BC, n= 3) (OC, n=3)	28, 34, 52	28 and 30

Figure 1: Best Percent Change from Baseline in Target Lesion Size (N=55)

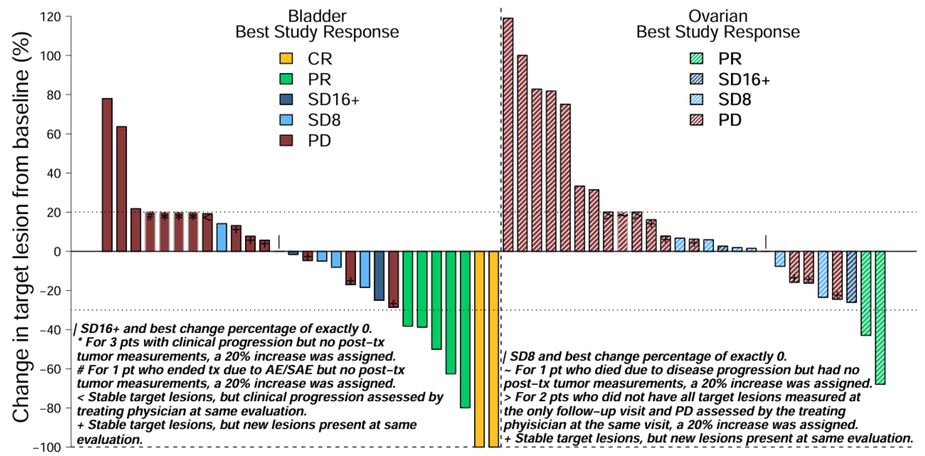
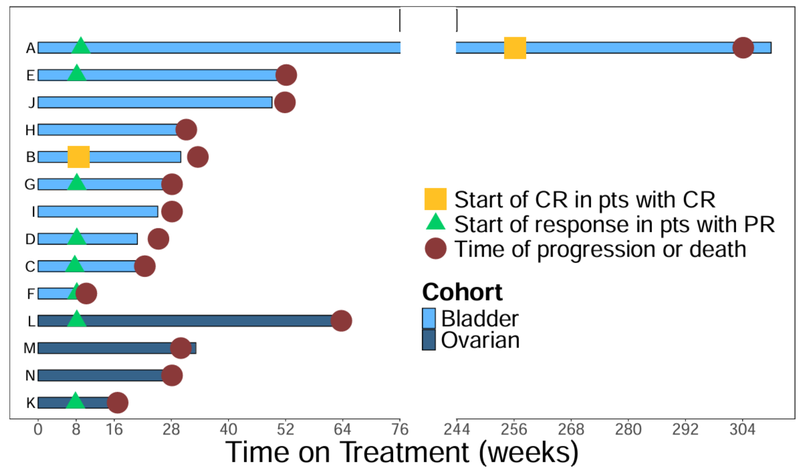


Figure 2: Time on Tx in Pts with OR or SD16+ (n=14)[a]



[a] Letters for each bar correspond to pt listed in Table 1.