2021 ASCO® ANNUAL MEETING

PERTUZUMAB PLUS TRASTUZUMAB IN PATIENTS WITH UTERINE CANCER WITH *ERBB2* OR *ERBB3* AMPLIFICATION, OVEREXPRESSION OR MUTATION: RESULTS FROM THE TARGETED AGENT PROFILING AND UTILIZATION REGISTRY (TAPUR™) STUDY

ASCO TAPUR™
Targeted Agent and Profiling Utilization Registry Study

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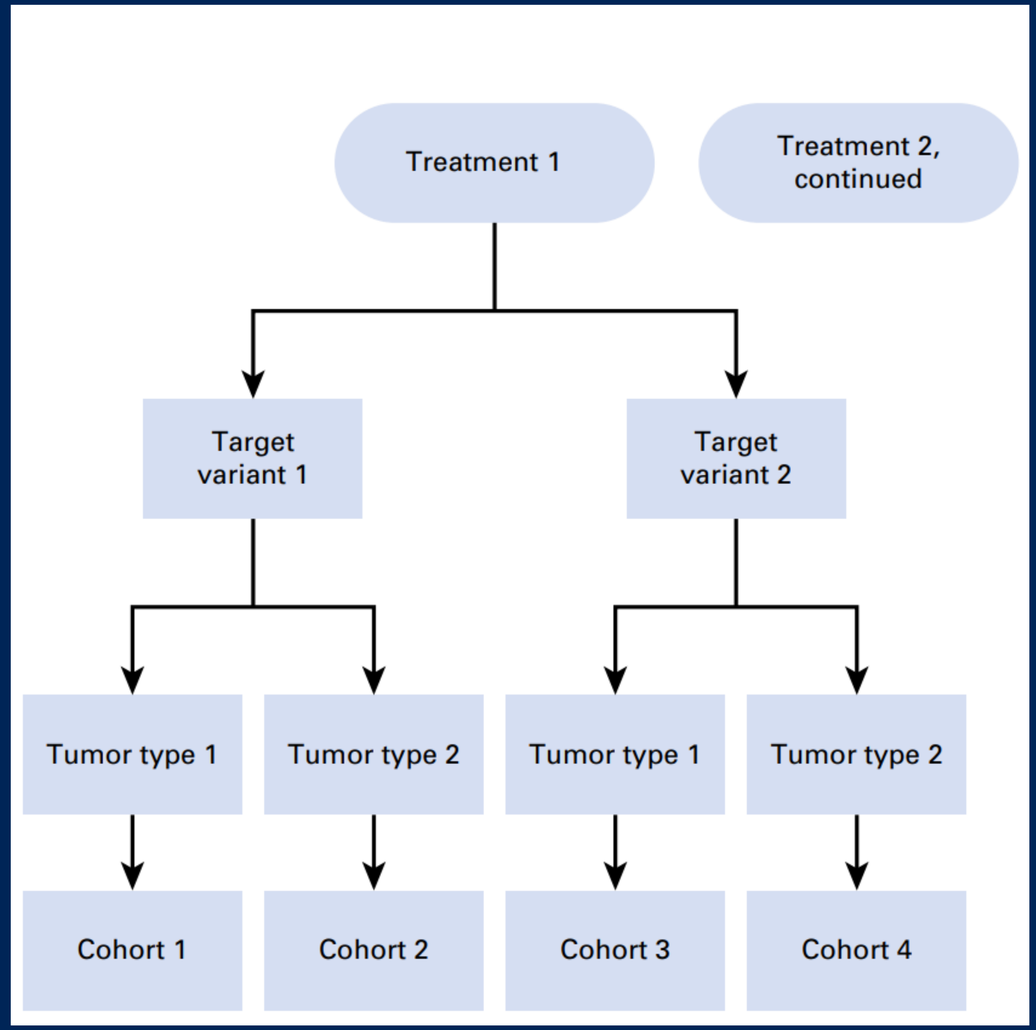
ERBB2/*ERBB3* Amplification/Overexpression in Uterine Cancer

- Clinical significance of *ERBB2* protein expression or gene amplification in endometrial cancer as a biomarker to identify patients likely to respond to anti-HER2 therapies is controversial
- High grade endometrial cancer has a 17-30% rate of *ERBB2* gene amplification with up to 80% exhibiting *ERBB2* protein overexpression[1]
- The most likely subtype to be *ERBB2*+ is uterine serous carcinoma, but only 9/20 *ERBB2*+ primary tumors had *ERBB2*+ metastatic lesions (45%) assessed by IHC or CISH[2]
- Single agent trastuzumab has little activity in *ERBB2*+ endometrial cancer
- We evaluated the combination of pertuzumab plus trastuzumab in this population

[1] Konecny et al Br J Cancer 2009
[2] Halle et al Br J Cancer 2017

TAPUR Study

- Non-randomized, phase II, basket trial
- 18 treatments
- 85+ genomic targets
- All solid tumors
- Pre-specified genomic matching rules and eligibility criteria
- Virtual Molecular Tumor Board



Primary Objective and Study Endpoints

- **Objective: Evaluate the anti-tumor activity of commercially available targeted agents in patients with advanced cancers with specific genomic alterations**
- **Primary Endpoint: Disease control (DC) defined as objective response (OR) or stable disease (SD) at 16+ weeks per RECIST v1.1**
- **Other Endpoints:**
  - Progression free survival (PFS)
  - Overall survival (OS)
  - Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to Pertuzumab + Trastuzumab are reported

Study Design

- Simon's optimal two-stage design
- Null Hypothesis: Disease control rate (DCR)<15%
- Alternative Hypothesis: DCR ≥ 35%
- Sample size (N=28) achieves 85% power and one-sided Type 1 error rate of 0.10

Key Eligibility Criteria and Treatment Administration

- Advanced uterine cancer
- ECOG Performance Status 0-2
- Adequate organ function
- Measurable disease
- Genomic test performed in CLIA-certified, CAP-accredited laboratory
- *ERBB2* or *ERBB3* amplification or overexpression or any of 13 pre-specified *ERBB2* mutations
- Dose administration per package insert (until disease progression)
    - Pertuzumab initial dose of 840 mg IV over 60 min, followed by 420 mg IV over 30-60 min every 3 weeks and Trastuzumab initial dose of 8mg/kg IV over 90 min, then 6mg/kg over 30-60 min every 3 weeks

Demographics and Clinical Characteristics (N=28)

Characteristic[1]		
Age, years	Median (range)	69 (44, 90+)
Sex, N (%)	Male	0 (0)
	Female	28 (100)
Race, N (%)	White	21 (75)
	Black	2 (7)
	Asian	1 (4)
	More than one race	1 (4)
	Other	2 (7)
	Prefer not to answer	1 (4)
Ethnicity, N (%)	Hispanic or Latino	2 (7)
	Not Hispanic or Latino	25 (89)
	Prefer not to answer	1 (4)
ECOG, PS, N (%)	0	9 (32)
	1	16 (57)
	2	3 (11)
Number of prior systemic treatments, N(%)	1-2	12 (43)
	≥3	16 (57)

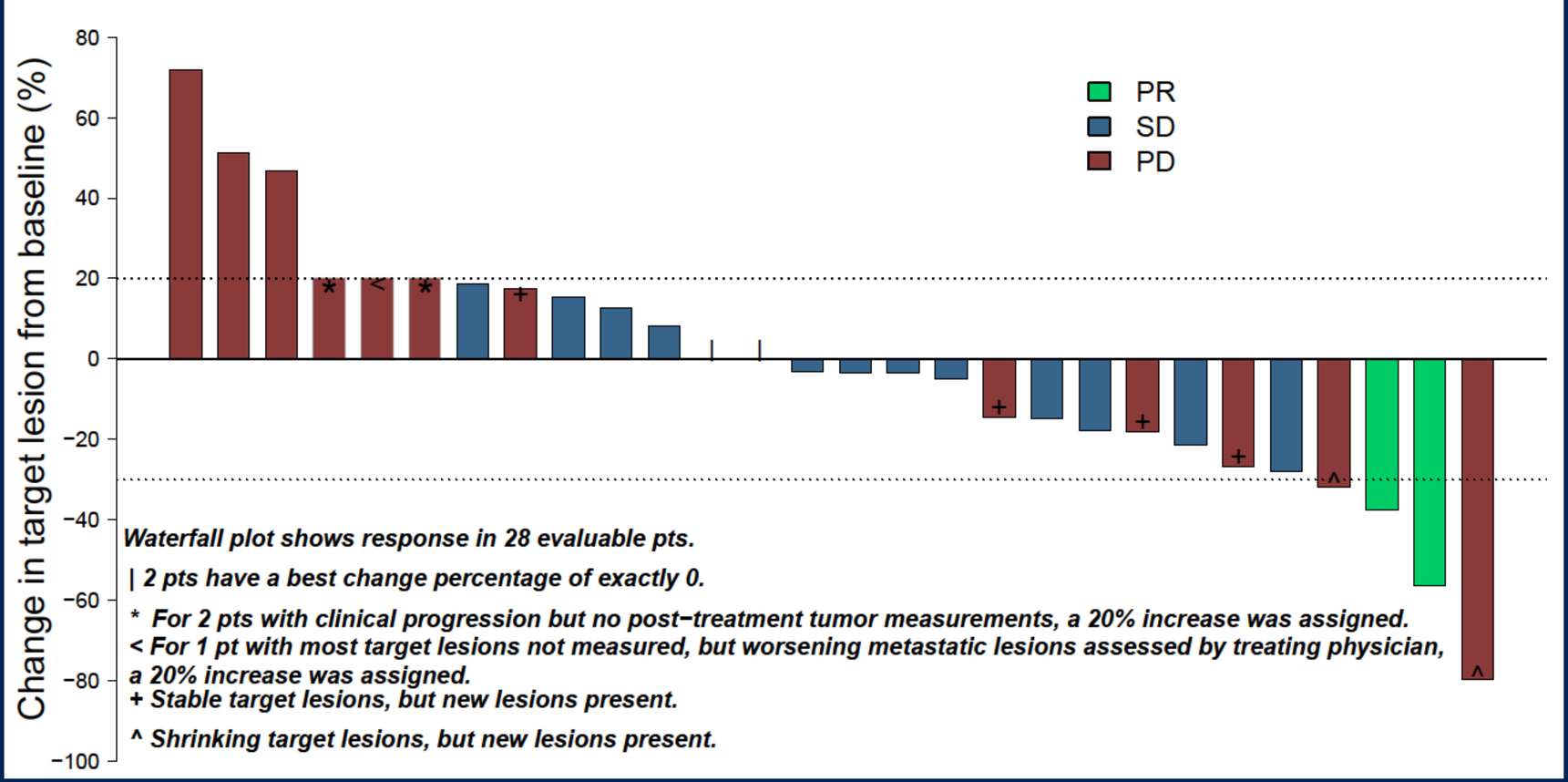
Characteristic[1,2]	
Genomic alteration, N (%)	
ERBB2 amplification	21 (75)
ERBB2 overexpression	1 (4)
ERBB2 mutations	4 (14)
ERBB3 amplification	1 (4)
ERBB2 amplification and mutation	1 (4)

[1]Percentages may not add up to 100% due to rounding.
[2]Of 5 patients with tumors with *ERBB2* mutations, there were 2 tumors with V842I, 2 tumors with S310F, and 1 tumor with R678Q

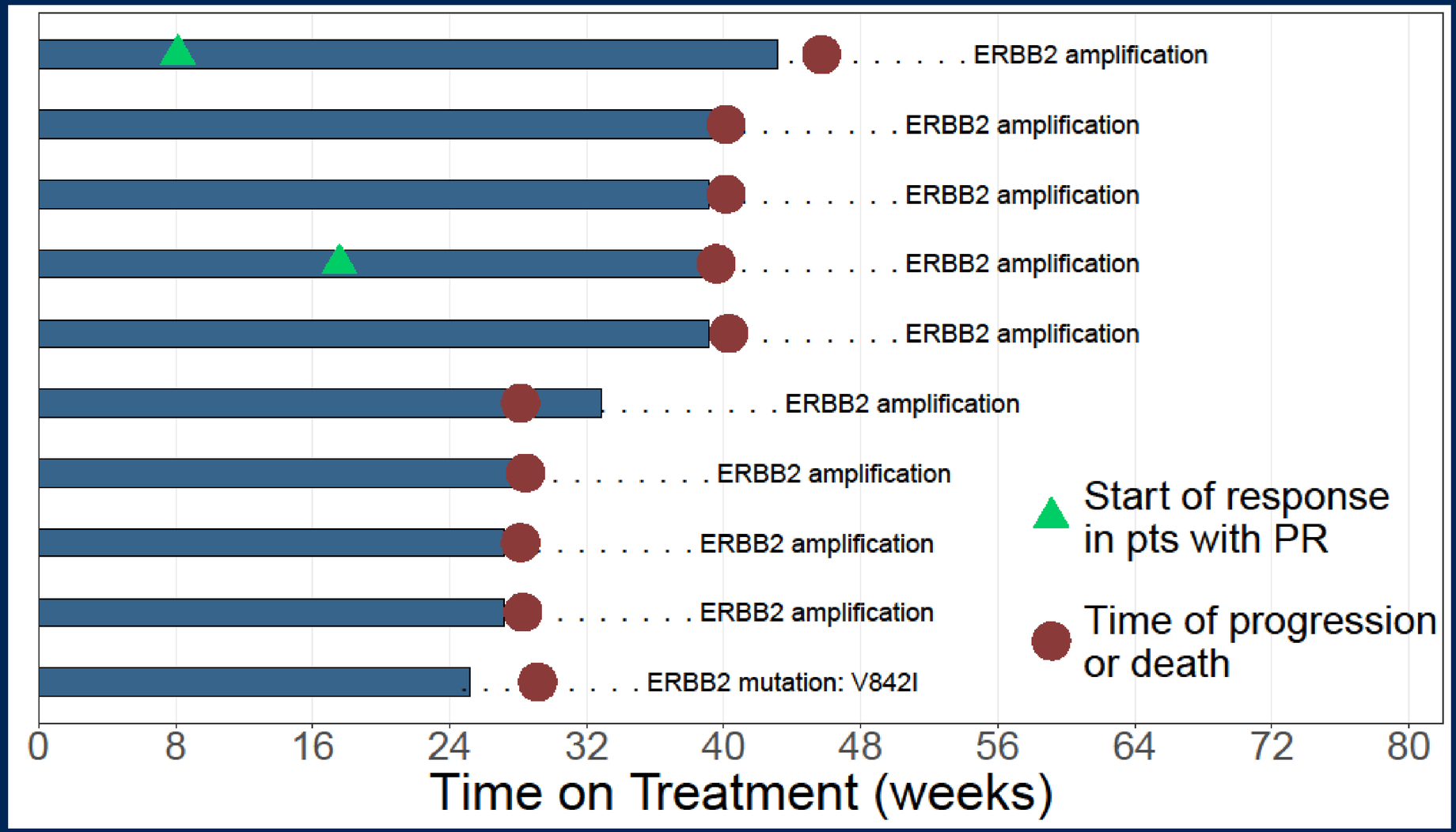
Efficacy Outcomes

Efficacy Outcomes (N=28)	
DC rate, % (95% CI)	37 (21, 50)
OR rate, % (95% CI)	7 (1, 24)

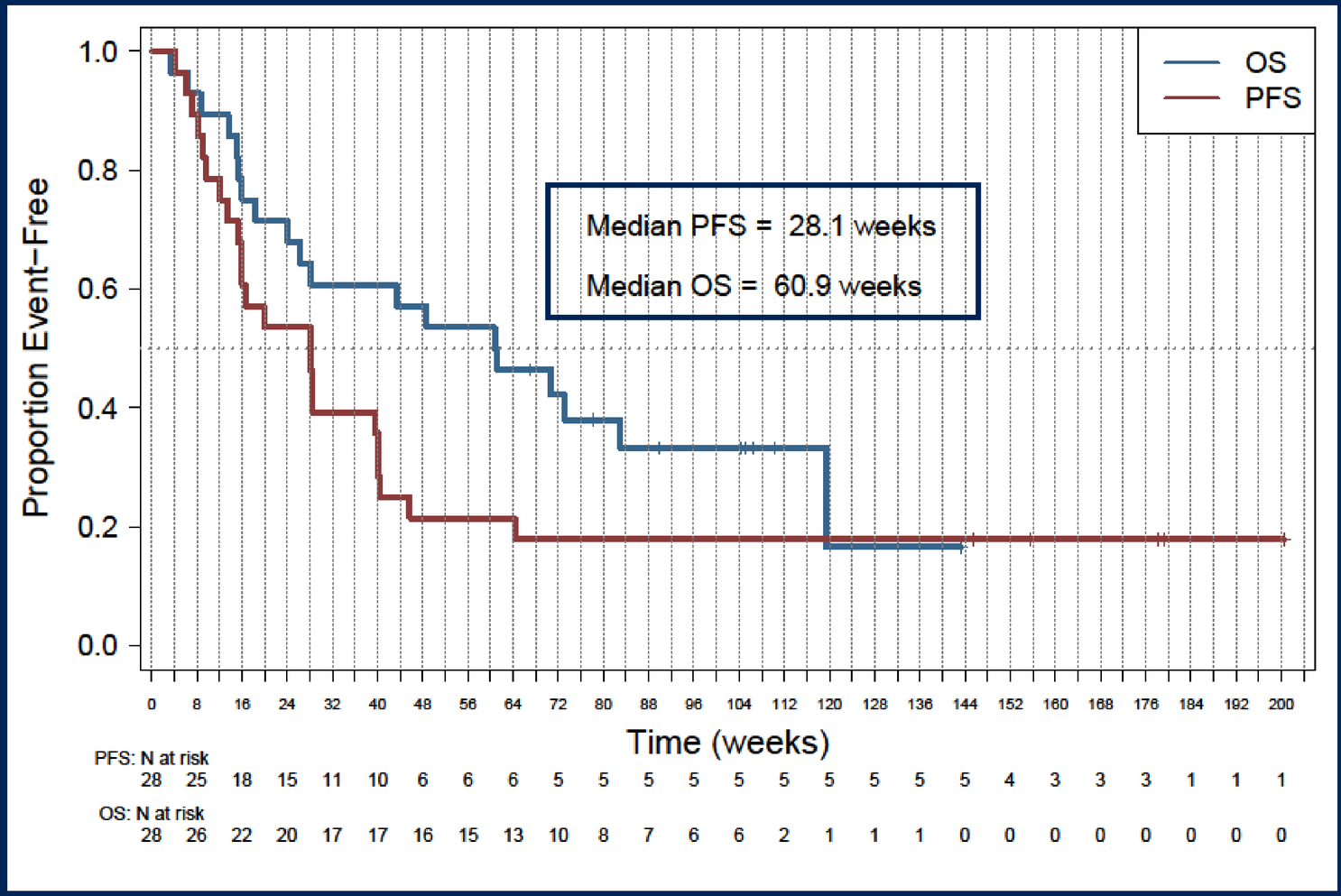
Best percent change from baseline target lesion size N=28



Time on Treatment in Pts with SD16+ or OR (n=10)



Progression Free Survival and Overall Survival (N=28)



Toxicity

- 1 patient experienced grade 3 muscle weakness at least possibly related to Pertuzumab + Trastuzumab
- No other treatment related Grade 3-4 AEs or SAEs reported

HER2-directed Therapies for *ERBB2* Amplified Uterine Cancer: Completed Trials

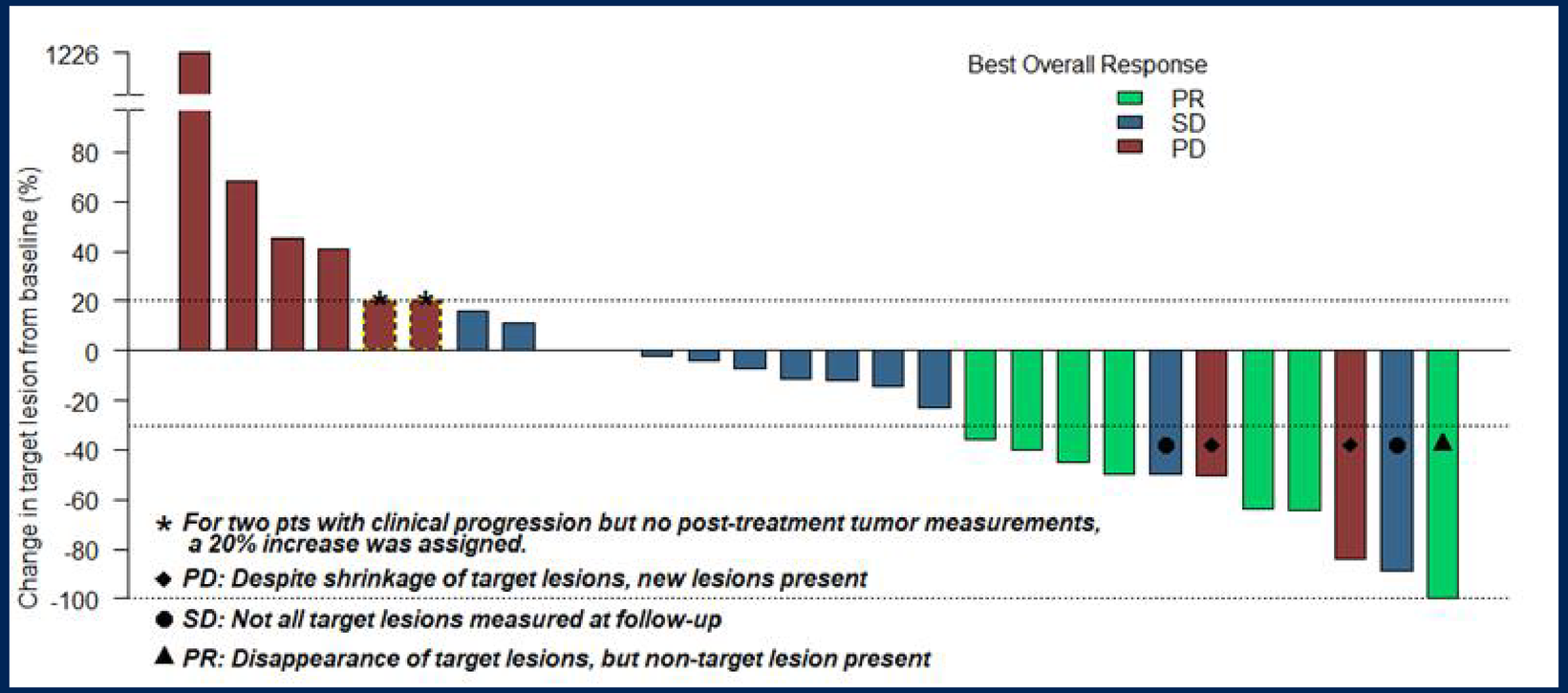
- **GOG181B phase II trial of trastuzumab for women with stage III/IV endometrial cancer with HER2+ (either by FISH or IHC (2-3+)[1]**
  - 33 women, no objective responses, closed early for low enrollment but had 86.5% power to confirm null hypothesis

- **NCT01367002: Randomized phase II trial of carboplatin/paclitaxel versus carboplatin-paclitaxel-trastuzumab…in uterine serous carcinomas that overexpress *ERBB2*[2]**
  - 58 women, PFS primary endpoint favoring T-arm 8.0 vs 12.9 months (HR 0.44 (90% CI, 0.26, 0.76), P=0.005)
  - OS analysis (secondary endpoint): 29.6 months vs 24.4 (HR 0.58 (90% CI, 0.34, 0.99), p=0.046)

[1] Fleming et al Gynecol Oncol 2010
[2] Fader et al Clin Cancer Res 2020

Pertuzumab + Trastuzumab in Patients with Colorectal Cancer with *ERBB2* Amplification or Overexpression: Results from the TAPUR Study

Efficacy Outcomes (N=28)	
DC rate, % (95% CI)	50 (36, 60)
OR rate, % (95% CI)	25 (11, 45)



Gupta et al Poster Presentation at ASCO GI Cancers Symposium 2020

Conclusions

- **Pertuzumab + Trastuzumab demonstrated anti-tumor activity in heavily pre-treated patients with uterine cancer with *ERBB2* amplification and/or certain mutations**
- **Additional study warranted to confirm the efficacy of Pertuzumab + Trastuzumab in this patient population**

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  - Sutter Cancer Research Consortium, San Francisco, CA
  - Inova Schar Cancer Institute, Fairfax, VA
  - The Angeles Clinic and Research Institute, Los Angeles, CA
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  - Intermountain Healthcare, St. George, UT
  - Swedish Cancer Institute, Seattle, WA
  - University of Alabama at Birmingham, Birmingham, AL
  - Providence Health and Services, Portland, OR
  - The University of Texas MD Anderson Cancer Center, Houston, TX
  - Coordinating Center: American Society of Clinical Oncology, Alexandria, VA
  - For a comprehensive list of all participating clinical sites, please see www.TAPUR.org