

Abstract 546: Pertuzumab plus Trastuzumab in patients with Biliary Tract Cancer with *ERBB2/3* amplification, overexpression, or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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Background:

- TAPUR is a phase II basket study that evaluates anti-tumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Results of a cohort of pts with biliary tract cancer (BTC) with *ERBB2/3* mutation (mut), amplification (amp) or overexpression (oe) treated with pertuzumab (P) plus trastuzumab (T) are reported.**

Methods:

Study Design:

- Eligible pts:** Advanced BTC, no standard treatment (tx) options, ECOG performance status (PS) 0-2, adequate organ function, measurable disease. Tx assigned according to pre-specified matching rules based on genomic tests selected by sites. Labs must be CLIA-certified and CAP-accredited. Amp and oe cut-offs were defined per local NGS or IHC assays.
- Pts received P at an initial dose of 840 mg IV over 60 minutes (m), then 420 mg IV over 30-60 m once every 3 weeks (wks), followed by T at an initial dose of 8 mg/kg IV over 90 m, then 6 mg/kg IV over 30-60 m once every 3 wks until disease progression, pt or physician recommendation or unacceptable toxicity.
- Primary endpoint:** Disease control (DC) defined as complete response (CR), partial response (PR), or stable disease (SD) of 16+ (SD16+) wks duration per RECIST v1.1 based on investigator assessment. Confirmation of response is not required.
- Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response, duration of SD and toxicity per CTCAE v4.0. Grade 3 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to P+T 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%. Power = 85%; 1-sided α = 10%.
- At least 7 of 28 pts must achieve DC to reject the null hypothesis and consider tx worthy of further study.

Results:

- 29 pts enrolled from February 2017 to January 2022. 1 pt was not evaluable for efficacy due to having no post-baseline tumor evaluation prior to choosing to discontinue in the study.
- Demographics:** Median age 66 y (range 34-83); 66% female; 52% self-identified as White, 21% as Black/African American, 10% as Asian/Asian American; 83% as not Hispanic or Latino.
- Clinical characteristics:** 83% PS 0-1, 17% PS 2; 48% received ≥ 3 prior systemic regimens. 15 pts (52%) had gallbladder cancer; 11 pts (38%) had bile duct cancer, and 3 pts (10%) had ampulla of Vater cancer.
- Alterations:** 16 pts (55%) had *ERBB2* amp, oe or both; 7 pts (24%) had *ERBB2* mut only; 3 pts (10%) had *ERBB2* amp + *ERBB2* mut; 1 pt (3%) each had *ERBB2* amp + *ERBB3* mut; *ERBB2* amp + *ERBB3* amp; or *ERBB2* amp, *ERBB2* mut + *ERBB3* mut.

Conclusion: Pertuzumab plus trastuzumab shows antitumor activity in heavily pre-treated patients with biliary tract cancer with *ERBB2/3* alterations.

Future Direction: Additional study is warranted to confirm the efficacy of pertuzumab plus trastuzumab in this patient population.

- Outcomes:** 1 pt had CR, 8 pts had PR and 2 pts had SD16+ for a DC rate of 40% (95% CI: 29, 53) (Table 1, 2, and Figure 1). The null hypothesis was rejected. Time on tx among pts with OR or SD16+ is shown in Figure 2.
- Safety:** 4 pts (14%) had ≥ 1 SAE or grade 3 AE at least possibly related to P+T, including: anemia, diarrhea, infusion related reaction (SAE), and fatigue.

Table 1. Tumor Origin and Alteration of Pts With OR or SD16+ (n=11)

Response	Primary Tumor Origin	Alteration
CR	Gallbladder	<i>ERBB2</i> amp
PR	Gallbladder	<i>ERBB2</i> amp
PR	Gallbladder	<i>ERBB2</i> amp
PR	Gallbladder	<i>ERBB2</i> amp
PR	Bile duct	<i>ERBB2</i> amp
PR	Bile duct	<i>ERBB2</i> mut (S310Y)
PR	Gallbladder	<i>ERBB2</i> amp
PR	Gallbladder	<i>ERBB2</i> mut (S310F)
PR	Gallbladder	<i>ERBB2</i> amp and <i>ERBB3</i> mut (R170 ^a)
SD16+	Ampulla of Vater	<i>ERBB2</i> mut (V842I), <i>ERBB2</i> amp, <i>ERBB3</i> mut (D297Y), <i>ERBB2</i> mut (rearrangement ^a)
SD16+	Gallbladder	<i>ERBB2</i> amp

^a Variant of unknown significance

Funding supported by Genentech. The authors would like to acknowledge the patients who participated in this cohort, the clinical centers and staff, as well as Tania Szado, PhD, clinical lead of Genentech, a TAPUR supporting pharmaceutical company.

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Table 2: Efficacy Outcomes (n=28)

DC rate, % (95% CI)	40 (29, 53), p=0.0015
OR rate, % (95% CI)	32 (16, 52)
Median PFS, wks (95% CI)	11 (8, 16)
Median OS, wks (95% CI)	30 (17, 49)
Duration of CR, wks (n=1)	71
Median duration of PR (range), wks (n=8)	30 (4, 69)
Duration of SD in pts with SD16+, wks (n=2)	24 and 60

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=28)

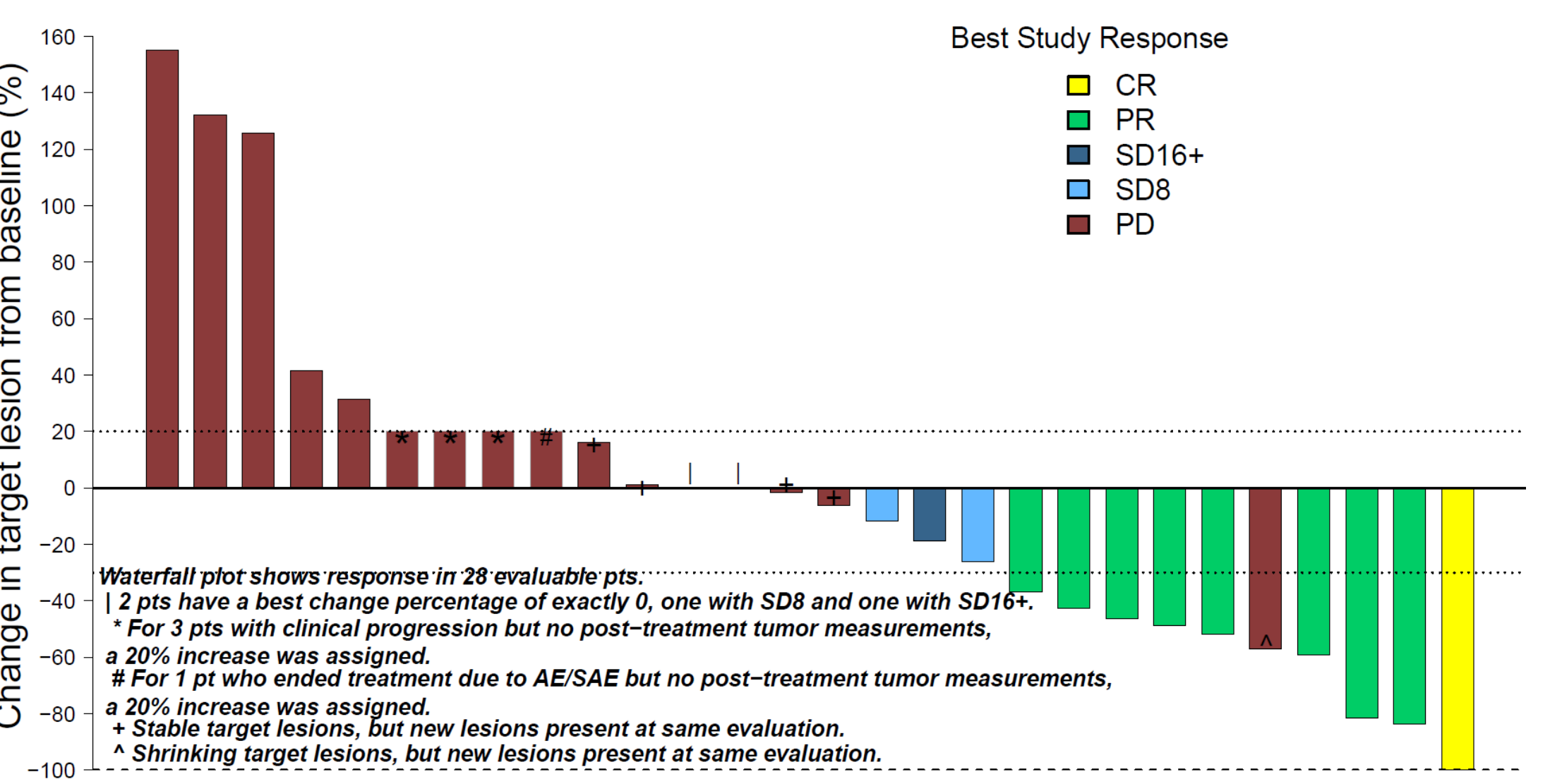


Figure 2: Time on Tx in Pts with OR or SD16+ (n=11)

