Pertuzumab + Trastuzumab in Patients with Colorectal Cancer with *ERBB2* Amplification or Overexpression: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Ranju Gupta[1], Elizabeth Garrett-Mayer[2], Susan Halabi[3], Pam K. Mangat[2], Stacy D'Andre[4], Eyal Meiri[5], Sagun Shrestha[6], Sasha L. Warren[2], Shamika Ranasinghe[2], Richard L. Schilsky[2]

[1]Lehigh Valley Health Network, Allentown, PA; [2]American Society of Clinical Oncology, Alexandria, VA; [3]Duke University Medical Center, Durham, NC; [4]Sutter Medical Center, Sacramento, CA; [5]Cancer Treatment Centers of America, Atlanta, GA; [6]Cancer Treatment Centers of America, Tulsa, OK

Background

- The TAPUR Study is a phase II basket study that evaluates the anti-tumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Results of a cohort of metastatic colorectal cancer (mCRC) pts with *ERBB2* overexpression or amplification treated with pertuzumab plus trastuzumab (P+T) are reported.

Methods

Study Design:

- Eligible pts had advanced CRC with no remaining standard treatment options, PS 0-2, adequate organ function, and measurable disease. Treatment was assigned according to pre-specified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites.
- After standard loading dose, pts received P at 420 mg IV over 30-60 min every 3 weeks and T at 6 mg/kg over 30-60 min every 3 weeks until disease progression. Tumor evaluations were performed at 8 and 16 weeks (wks) then Q12 wks after treatment initiation.
- Primary endpoint is disease control (DC) defined as objective response (OR) or stable disease (SD) at 16+ wks per RECIST v1.1. Secondary endpoints are progression-free survival (PFS), overall survival (OS) and toxicity per CTCAE. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to drug are reported.

Statistical Methods:

- Simon's optimal two-stage design was used to test the null hypothesis of 15% DC rate versus the alternative of 35%. Power and one-sided type I error rate were set at 85% and 10%, respectively.
- Design requires 10 pts in stage I and if ≥2 pts have DC (OR or SD at 16+ wks), the cohort is expanded to stage II with 28 pts. If ≥7 of 28 pts have DC, the treatment is considered worthy of further study.

ABSTRACT #132

Results

- 28 pts were enrolled between November 2016 and September 2018. Baseline demographics and clinical characteristics are shown in Table 1.
- All pts had *ERBB2* amplification; one pt also had an *ERBB2* mutation.

Table 1: Demographics and Baseline Characteristics (N=28)

Characteristic	N (%)
Median Age, years (range)	54 (23, 77)
Sex	
Male	18 (64%)
Race	
White	22 (79%)
Black	3 (11%)
Asian	2 (7%)
Prefer not to answer	1 (3%)
ECOG Performance Status	
0	8 (29%)
1	19 (68%)
2	1 (3%)
Prior systemic regimens	
1	4 (14%)
2	2 (7%)
≥3	22 (79%)
Genomic test performed	
FoundationOne	18 (64%)
In house laboratory	3 (11%)
Other	7 (25%)

Clinical Outcomes:

- DC and OR were observed in 50% and 25%, respectively (Table 2). Median PFS (mPFS), 1 year OS and mOS are reported in Table 2 and shown in Figure 1.
- Figure 2 shows % change from baseline in target lesions.
- Time on treatment among pts with SD and OR is shown in Figure 3.
- Safety was consistent with product label for P+T (Table 3).

Table 2: Clinical Outcomes of mCRC Pts with *ERBB2* Amplifications treated with P+T (N=28)

Clinical Outcomes	
DC rate, % (OR or SD16+) N (%), [90% CI]	14 (50%), [36%, 60%]
OR rate, % (CR or PR) (95% CI)	7 (25%), [11%, 45%]
mPFS, wks (95% CI)	17.2 (11.1, 27.4)
mOS, wks (95% CI)	108.6 (26.3, inf)
1 year OS rate, % (95% CI)	58 (37, 75)

Table 3: SAE/AEs at least possibly related to P+T experienced by 2 Pts

Grade	SAE	AEs
3	N	anemia, infusion reaction
3	Y	left ventricular systolic dysfunction

Figure 1: OS and PFS in Advanced mCRC Pts with *ERBB2* Amplifications Treated with P+T (N=28)

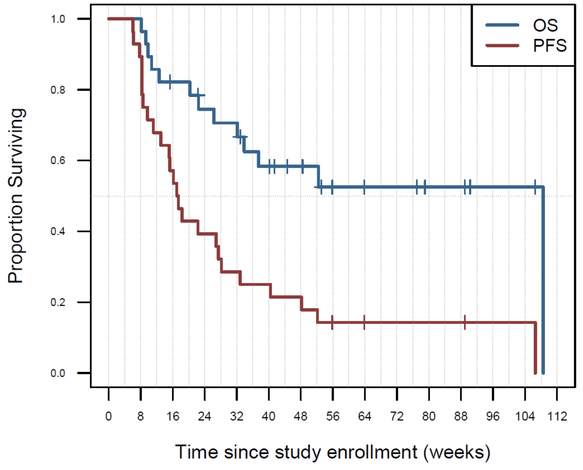


Figure 2: Best percent change from baseline in target lesion size (N=28)

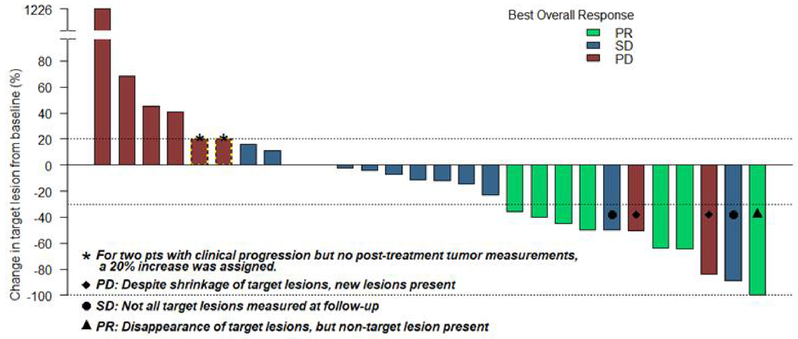
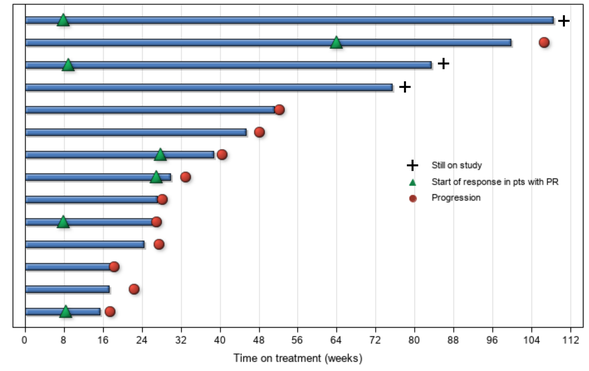


Figure 3: Time on Treatment in Pts with SD at 16 wks or OR (N=14)



Conclusions

The combination of P+T showed anti-tumor activity in heavily pre-treated mCRC patients with *ERBB2* amplification. Further study is warranted to confirm efficacy of P+T in this population.

Acknowledgements

The authors would like to acknowledge the pts who participated in this cohort as well as the following clinical leads of Genentech, Mary Beattie, MD and Vaikunth Cuchelkar, MBBS, PhD.

CONTACT: TAPURPublications@asco.org