Sunitinib in Patients with Metastatic Breast Cancer with *FGFR1* mutations or amplifications: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Carmen Calfa, MD[1], Michael Rothe, MS[2], Pam K. Mangat, MS[2], Elizabeth Garrett-Mayer, PhD[2], Eugene Ahn, MD[3], Keerthi Gogineni, MD, MSHP[4], Nitin Rohatgi, MD[5], Monika L. Burness, MD[6], Anu Gaba, MD[7], Omid Hamid, MD[8], Tareq Al-Baghdadi, MD[9], Alison Conlin, MD[10], Philip Gold, MD[11], Jordi Rodon, MD[12], Ramya Thota, MD[13], Richard L. Schilsky, MD, FACP, FSCT, FASCO[2]

[1]University of Miami Sylvester Cancer Center, Miami, FL; [2]American Society of Clinical Oncology, Alexandria, VA; [3]Cancer Treatment Centers of America, Atlanta, GA; [4]Emory University Winship Cancer Institute, Atlanta, GA; [5]Sutter Cancer Research Consortium, Sacramento, CA; [6]University of Michigan, Ann Arbor, MI; [7]Sanford Health, Sioux Falls, SD; [8]The Angeles Clinic, Los Angeles, [9]Michigan Cancer Research Consortium, Ypsilanti, MI; [10]Providence Cancer Institute, Portland, OR; [11]Swedish Cancer Institute, Seattle, WA; [12]University of Texas MD Anderson, Houston, TX; [13]Intermountain Healthcare, Murray, UT

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 in a cohort of metastatic breast cancer (mBC) pts with *FGFR1* mutations (mut) or amplifications (amp) treated with sunitinib (S) are reported.

Methods

Study Design:

- Pts with advanced mBC with no remaining treatment options, PS 0-2, adequate organ function, and measurable disease were eligible. 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.
- Pts received S 50 mg orally daily for four weeks followed by two weeks off, until tumor 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, 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.

Results

- 30 pts with *FGFR1* mutation (1 pt), amplification (28 pts), or both (1 pt) were enrolled from Oct 2016 to June 2019. Three pts were not evaluable for efficacy as 1 pt did not meet eligibility criteria, 1 pt withdrew consent prior to any follow-up visits, and 1 pt stopped treatment due to a treatment-related AE. Baseline demographics and clinical characteristics are shown in Table 1.

Table 1: Demographics and Baseline Characteristics (N=30)

Characteristic		N (%)
Median Age	Years (range)	61 (28, 81)
Sex	Female	29 (97%)
Race	White	18 (60%)
	Black	8 (27%)
	Asian	2 (7%)
	American Indian/ Alaska Native	2 (7%)
ECOG Performance Status	0	14 (47%)
	1	11(37%)
	2	5 (17%)
Prior systemic regimens	1-2	3 (10%)
	≥3	27 (90%)
HR and HER2 Status	HR+ HER2-	23 (77%)
	TNBC	4 (13%)
	HR+ HER2+	2 (7%)
	Not Reported	1 (3%)
Genomic test performed	FoundationOne	21 (70%)
	Guardant Health	4 (13%)
	In house laboratory	3 (10%)
	Caris Life Sciences	2 (7%)

Clinical Outcomes:

- DC and OR were observed in 7 (29%) and 2 (7%) pts, respectively (Table 2) with *FGFR* amp. Median PFS (mPFS) and mOS are reported in Table 2 and Figure 1.
- Figure 2 shows % change from baseline in target lesions.
- Time on treatment among pts with SD16+ and OR is shown in Figure 3.
- Safety was consistent with product label for S except encephalopathy (Table 3).

Table 2: Clinical Outcomes of mBC Pts with *FGFR1* mutations or amplifications treated with S (N=27)

Clinical Outcomes	
DC rate (OR or SD 16+wks) [95% CI]	29% [13%, 42%]
OR rate, (CR or PR) [95% CI]	7% [1%, 24%]
mPFS, wks [95% CI]	8.7 [8.1, 15.7]
mOS, wks [95% CI]	33.9 [23.0, 49.0]

Table 3: SAE/AEs (maximum grade reported) at least possibly related to S experienced by 12 Pts

Grade	# Pts	AEs
2	1	skin infection (SAE)
3	9	cytopenia, encephalopathy (SAE), febrile neutropenia (SAE), increased alkaline phosphatase, Palmar-plantar erythrodysesthesia syndrome, vomiting
4	2	cytopenia, hypertension

Figure 1: OS and PFS in Pts with Advanced mBC with *FGFR1* mutations or amplifications treated with S (N=27)

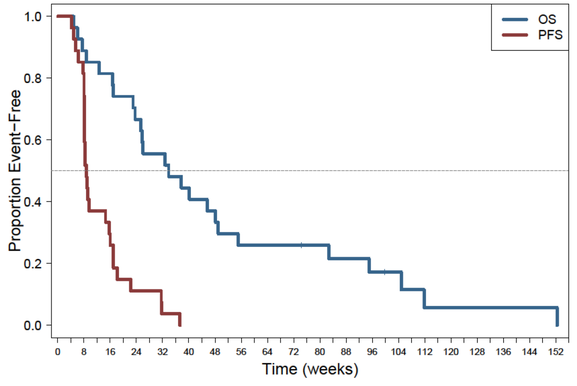


Figure 2: Best percent change from baseline in target lesion size (N=27)

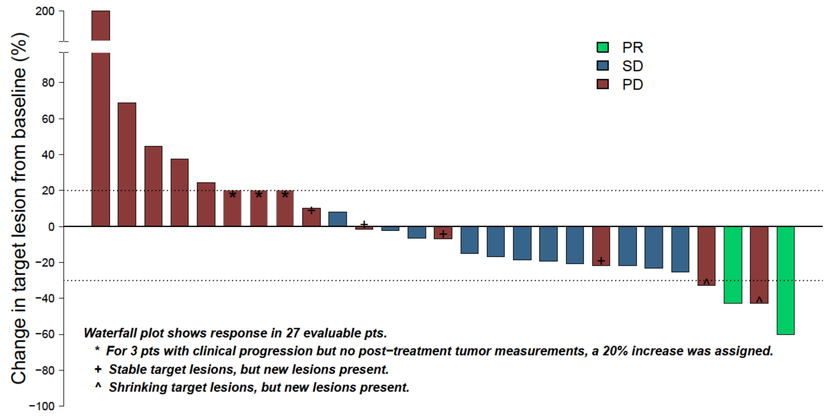
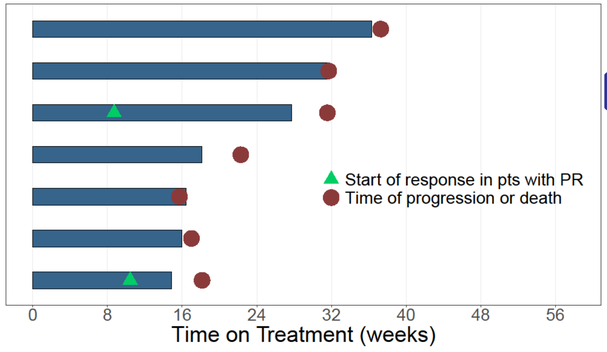


Figure 3: Time on Treatment in Pts with SD16+ or OR (N=7)



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Conclusions

Monotherapy S showed modest anti-tumor activity and clinically significant AEs in heavily pre-treated pts with mBC with *FGFR1* amplification.

ABSTRACT #CT173

CONTACT: TAPURPublications@asco.org