Abstract 3117: Temsirolimus in Patients with Solid Tumors with *PIK3CA* Mutations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

CJ Calfa[1], M Rothe[2], PK Mangat[2], E Garrett-Mayer[2], G Srkalovic[3], HL Duvivier[4], D Behl[5], JM Straughn[6], KJ Yost[7], I Mehmi[8], E Pisick[9], B Sharma[10], R Thota[11], DS Veljovich[12], OB Alese[13], TL Cannon[14], A Gaba[15], WJ Urba[16], M von Mehren[17], GN Grantham[2], A Gregory[2], DC Hinshaw[2], S Halabi[18], RL Schilsky[2]

[1]Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL; [2]American Society of Clinical Oncology, Alexandria, VA; [3]Herbert-Herman Cancer Center, Lansing, MI, Michigan Cancer Research Consortium, Ypsilanti, MI; [4]Cancer Treatment Centers of America - Atlanta, part of City of Hope, Newnan, GA; [5]Sutter Sacramento Medical Center, Sacramento, CA; [6]Division of Gynecologic Oncology at the University of Alabama at Birmingham School of Medicine, Birmingham, AL; [7]Cancer Research Consortium of West Michigan, Grand Rapids, MI; [8]The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, CA; [9]Cancer Treatment Centers of America - Chicago, part of City of Hope, Zion, IL; [10]University of Nebraska Medical Center, Omaha, NE; [11]Intermountain Healthcare, Murray, UT; [12]Swedish Cancer Institute, Seattle, WA; [13]Winship Cancer Institute of Emory University, Atlanta, GA; [14]Inova Schar Cancer Institute, Fairfax, VA; [15]Sanford Health, Fargo, ND; [16]Providence Cancer Institute, Portland, OR; [17]Fox Chase Cancer Center, Philadelphia, PA; [18]Duke University Medical Center, Durham, NC

Background:

- TAPUR is a phase II basket study that evaluates antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- **Results of two cohorts of pts with breast cancer (BC) or other solid tumors with *PIK3CA* mutations (mut) treated with temsirolimus (T) are reported.**

Methods:

Study Design:

- **Eligible pts:** Advanced BC or other solid tumors, ECOG performance status (PS) 0-2, adequate organ function, measurable disease and no standard treatment (tx) options. Tx was assigned according to prespecified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites.
- After antihistamine pre-tx, pts received 25 mg of T infused over 30-60 minutes once weekly until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- **Primary endpoint:** Disease control (DC) determined by investigator assessment of objective response (OR) or stable disease (SD) of at least 16 weeks (wks) duration (SD16+) per RECIST v1.1. Confirmation of OR or SD was not required.
- **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response, duration of SD, and toxicity per CTCAE v4.0. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to tx are reported.

Statistical Methods:

- For the BC cohort, Simon's optimal two-stage design was used to test null hypothesis of 15% DC rate vs. alternative of 35%. Power = 85%; 1-sided α = 10%.
- For the histology-pooled (HP) cohort, inferences are based on a one-sided exact binomial test with a null hypothesis of DC rate ≤15%; power and alpha were 82% and 0.10, respectively.
- Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results:

- 12 pts with BC and 29 pts with other solid tumors were enrolled from January 2017 to December 2020. One pt from each cohort was found to be ineligible after receiving at least one dose of tx and are not included in efficacy analyses.
- Pt demographics and clinical characteristics are summarized in **Table 1.**
- Tumor Types (# pts): breast (12), ovary (8), cervix (6), anal (4), head and neck (4), small intestine (2), esophagus (2), kidney (1), liver (1), stomach (1).
- **Outcomes**: In the BC cohort, one pt had a PR for a DC rate of 9% (90% CI: 1 to 100). The null DC was not rejected (p=0.83). In the HP cohort, eight pts had DC [PR (3), SD16+ (5)] for a DC rate of 29% (90% CI: 17 to 100). The null DC rate of 15% was rejected (p=0.049). (**Table 2 and 3**)
- **Safety:** 11 pts (27%) had ≥1 SAE or grade 3-4 AE at least possibly related to tx. Events were consistent with the drug label except pneumonitis (grade 3 AE) and sepsis (grade 4 SAE).

Conclusion: Temsirolimus showed antitumor activity in patients with non-breast solid tumors with *PIK3CA* mutations.

Future Direction: Additional study is warranted to confirm the efficacy of temsirolimus in patients with non-breast cancer solid tumors with *PIK3CA* mutations.

Table 1. Clinical Characteristics (N=41)

Characteristic		BC Cohort No. (%) n=12	HP Cohort No. (%) n=29
Median Age	Years (range)	61 (48, 68)	59 (32, 78)
Sex	Female	12 (100)	20 (69)
Race	Asian/Asian American	2 (17)	3 (10)
	Black or African American	1 (8)	0 (0)
	White	9 (75)	22 (76)
	More than one race	--	1 (3)
	Other/prefer not to answer	--	3 (10)
Ethnicity	Hispanic or Latino	--	3 (10)
	Not Hispanic or Latino	12 (100)	25 (86)
	Prefer not to answer	--	1 (3)
ECOG PS	0-1	12 (100)	28 (97)
	2	--	1 (3)
Prior Systemic Regimens	1-2	1 (8)	6 (21)
	≥3	11 (92)	23 (79)

Table 2. Tumor Type and Mut of Pts Meeting Response Criteria (n=9)

Response	Duration of PR or SD	Primary Tumor Type	*PIK3CA* Mut
PR	13 wks	Breast	H1047R
PR	96+ wks (ongoing)*	Ovary	H1047R
PR	15 wks	SCC of tongue	D350N
PR	8 wks	Cervix	E545K
SD16+	63 wks	Salivary duct	E542K
SD16+	40 wks	Liver	H1047L
SD16+	27 wks	Ovary	Q546P
SD16+	23 wks	Cervix	E542K
SD16+	16 wks	Head and neck	E545K

*as of May 5, 2023

Table 3: Efficacy Outcomes (N=39)

	BC Cohort (n=11)	HP Cohort (n=28)
DC rate, % (90% CI)	9 (1, 100); p=0.83	29 (17, 100); p=0.049
OR rate, % (95% CI)	9 (0.2, 41)	11 (2, 28)
Median PFS, wks (95% CI)	8 (5, 12)	8 (8, 16)
Median OS, wks (95% CI)	36 (8, 82)	27 (20, 45)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=39)

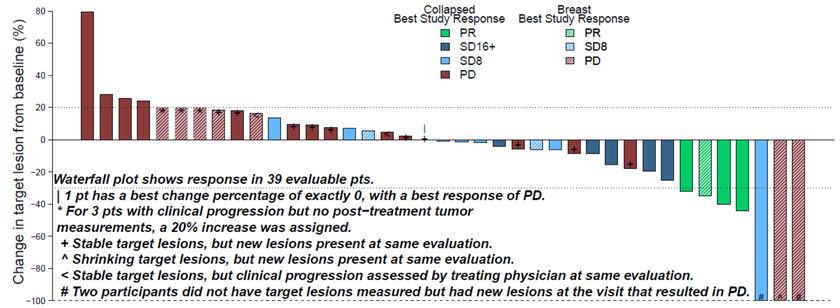
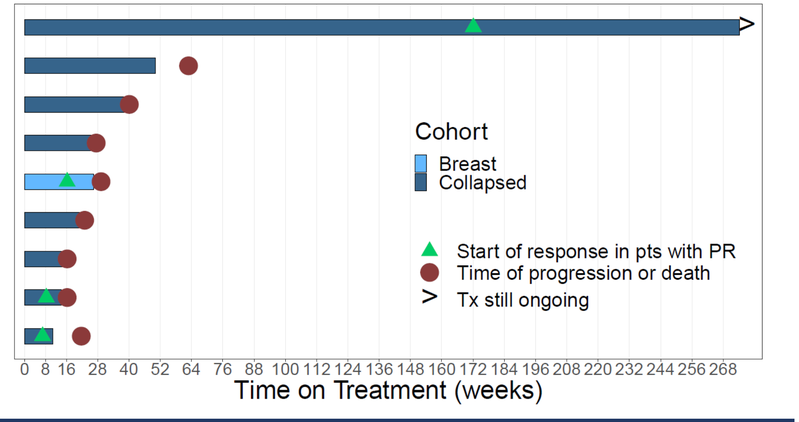


Figure 2: Time on Tx in Pts with OR or SD16+ (n=9)



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Contact: TAPURPublications@asco.org