Temsirolimus in patients with solid tumors with *PTEN* mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Abstract #: CT231

K Wentzel[1], M Rothe[2], PK Mangat[2], E Garrett-Mayer[2], L Ding[3], E Pisick[4], M Krishnan[5], D Behl[6], OB Alese[7], CJ Calfa[8], KA Cooper[9], HL Duvivier[10], RR Induru[11], JC Ruzich[12], S Zhao[13], GN Grantham[2], A Gregory[2], DC Hinshaw[2], S Halabi[14], RL Schilsky[2]

[1]The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, CA; [2]American Society of Clinical Oncology, Alexandria, VA; [3]Trinity Health IHA Hematology/Oncology, Michigan Cancer Research Consortium, Ypsilanti, MI; [4]Cancer Treatment Centers of America - Chicago, part of City of Hope, Zion, IL; [5]University of Nebraska Medical Center, Omaha, NE; [6]Sutter Sacramento Medical Center, Sacramento, CA; [7]Winship Cancer Institute of Emory University, Atlanta, GA; [8]Sylvester Comprehensive Cancer Center, University Of Miami Miller School Of Medicine, Miami, FL; [9]Cancer Research Consortium of West Michigan, Grand Rapids, MI; [10]Cancer Treatment Centers of America - Atlanta, part of City of Hope, Newnan, GA; [11]Levine Cancer Institute, Atrium Health, Concord, NC; [12]Providence Cancer Institute, Portland, OR; [13]Swedish Cancer Institute, Seattle, WA; [14]Duke University Medical Center, Durham, NC

Background

- The TAPUR Study is a phase II basket study that evaluates the antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Results in a cohort of pts with advanced solid tumors with *PTEN* mutation (mut) treated with temsirolimus (T) are reported.

Methods

Study Design:

- **Eligible pts:** Advanced solid tumors, ECOG performance status (PS) 0-2, adequate organ function, measurable disease and no standard treatment (tx) options. Tx was assigned according to pre-specified protocol matching rules based on genomic testing selected by clinical sites.
- After antihistamine pre-tx, pts received 25 mg 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) defined 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 response was not required.
- **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response (DOR), duration of SD, and safety per CTCAE v4.0. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to T are reported. DOR is defined as time from pt's first documented OR to progressive disease (PD). Duration of SD is defined as time from tx start to PD.
- Low accruing histology-specific cohorts with the same genomic alteration were collapsed into one histology-pooled cohort for this analysis.

Statistical Methods:

- Inferences are based on a one-sided exact binomial test with a null hypothesis of DC rate ≤15%; power and alpha were 88% and 0.10, respectively. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results

- Thirty-four pts with solid tumors with *PTEN* mut were enrolled from March 2017 to January 2021.
- Seven of 34 pts were not evaluable for efficacy: two pts were ineligible because of no measurable disease; five pts were not evaluable due to lack of post-baseline tumor evaluation: three pts elected to receive hospice/palliative tx; one pt left due to an unrelated AE; one pt chose to discontinue in the study. 27 pts were evaluable for the efficacy analyses.
- Baseline clinical characteristics are shown in **Table 1.**

Table 1: Baseline Characteristics (N=34)

Characteristic		No. (%)
Median Age	Years (range)	65 (42-84)
Sex	Female	14 (41)
Race	Black/African American	5 (15)
	White	25 (74)
	More than one race	1 (3)
	Prefer not to answer	3 (9)
Ethnicity	Not Hispanic or Latino	32 (94)
	Prefer not to answer	2 (6)
ECOG PS	0	13 (38)
	1	18 (53)
	2	3 (9)
Prior systemic regimens	1-2	8 (24)
	≥3	26 (76)
Primary Tumor Origin	Prostate	10 (29)
	Breast	4 (12)
	NSCLC	3 (9)
	Salivary gland	3 (9)
	Leiomyosarcoma	2 (6)
	Liposarcoma	2 (6)
	Unknown primary	2 (6)
	SCLC	2 (6)
	Anal	1 (3)
	Head/Neck	1 (3)
	Rectal SCC	1 (3)
	Soft tissue sarcoma	1 (3)
	Stomach	1 (3)
	Uterus	1 (3)

Efficacy Outcomes (n=27):

- Two pts had PR and five pts had SD16+ (**Table 2**).

Table 2. Tumor Origin and Alteration of Pts with PR or SD16+ (n=7)

Response	Tumor Origin	Alteration	Comutations[a]
PR [b]	Prostate	*PTEN* Y76del	none
PR [c]	Leiomyosarcoma	*PTEN* E43fs*11, S170R	none
SD16+	Unknown primary	*PTEN* I168fs*11	none
SD16+	SCLC	*PTEN* N329fs*14	none
SD16+	Salivary gland	*PTEN* splice site 209+1G>A	none
SD16+	Breast (HR+ HER2-)	*PTEN* N323fs*2, S287fs*10	none
SD16+	Uterus	*PTEN* N212lfs*9	*PIK3CA* amp, E81K

[a] The following comutations were examined: *MTOR*, *PIK3CA* and *PIK3R1*, [b] Pt had a duration of response of 52 wks, [c] Pt had a duration of response of 11 wks.

- 2 PR pts had durations of response of 11 wks (1 prior systemic therapy) and 52 wks (4 prior systemic therapies). Median duration of SD was 27 wks (range: 24, 36) for pts with SD16+.
- DC and OR rates were 26% and 7%, respectively (**Table 3**). The null DC rate of 15% was rejected (p=0.099).

Safety Outcomes (N=34)

- 12 pts (35%) experienced ≥1 grade 3-4 AEs or SAEs at least possibly related to T. Safety was consistent with product label except acute kidney injury, chronic kidney disease, generalized muscle weakness, lung infection, and oral pain.

Table 3: Efficacy Outcomes (n=27)

DC rate, % (1-sided 90% CI)	26 (15.1, 100)
OR rate, % (95% CI)	7 (1, 24)
Median PFS, wks (95% CI)	10 (7, 17)
Median OS, wks (95% CI)	32 (13, 42)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=27)

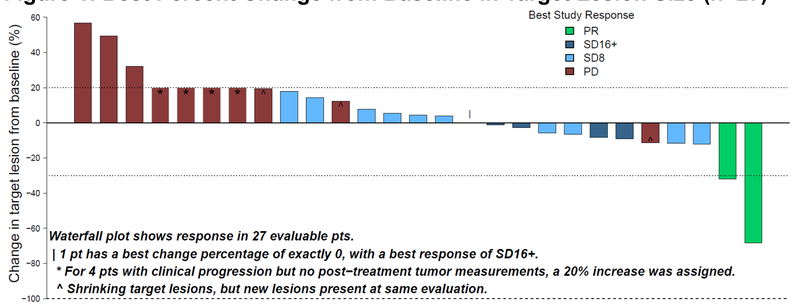


Figure 2: Time on Treatment in Pts with SD16+ or OR (n=7)

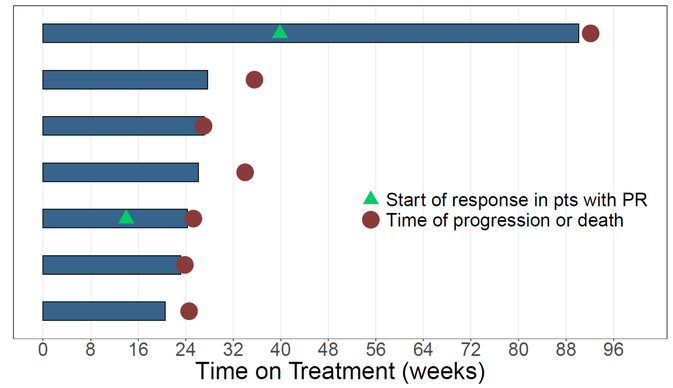
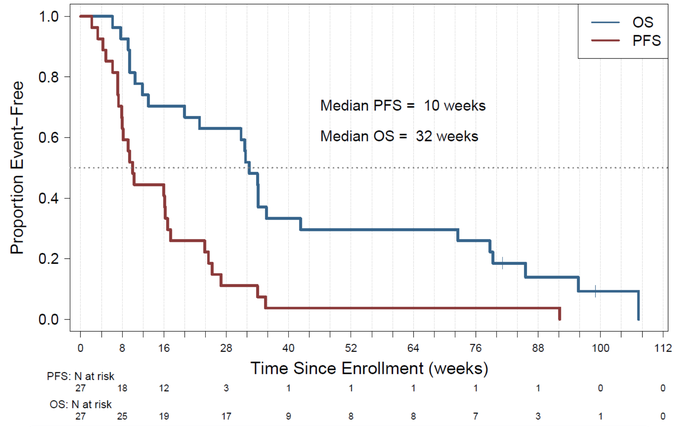


Figure 3: PFS and OS in Pts with Advanced Solid Tumors with *PTEN* Mut treated with T (n=27)



Conclusions

Temsirolimus met prespecified criteria to declare a signal of activity in pts with solid tumors with *PTEN* mut. Additional study is warranted to confirm the efficacy in this patient population.

Acknowledgements

The authors would like to thank the patients who participated in this cohort, the clinical centers and staff, as well as Betty "B" Thompson, clinical lead of Pfizer, a TAPUR supporting pharmaceutical company.

Contact: TAPURPublications@asco.org