Temsirolimus in patients with solid tumors with *AKT1/3* amplification or mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Abstract #: CT267

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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 solid tumors with *AKT1/3* amplification (amp) or mutation (mut) treated with temsirolimus (T) are reported.

Methods

Study Design:

- **Eligible pts:** Advanced solid tumors, Eastern Cooperative Oncology Group performance status (ECOG PS) 0-2, adequate organ function, measurable disease, and no standard treatment (tx) options available. Tx was assigned according to prespecified matching rules based on genomic tests performed in CLIA-certified, CAP-accredited labs selected by sites. Amp cut-offs were defined per test providers.
- 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. Radiographic confirmation of response was not required.
- **Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response, duration of SD are reported. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) per CTCAE v. 4.0 at least possibly related to tx-are reported.
- 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 82% and 0.10, respectively. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results

- 28 pts with *AKT1* mut (n=25), amp (n=1), both *AKT1* mut and amp (n=1), or *AKT3* amp (n=1) were enrolled from August 2016 to October 2021. 25 of 26 pts (96%) with an *AKT1* mut had an E17K mut. Baseline demographics and clinical characteristics are shown in **Table 1**.
- One pt was ineligible due to starting T while tapering off steroids for pain management. However, the pt showed clear progression at 8 wks and was therefore evaluable and included in efficacy outcomes.

Table 1. Baseline Characteristics (N=28)

Characteristic		No. (%)[a]
Median Age	Years (range)	66 (39-83)
Sex	Female	22 (79)
Race	Asian/Asian American	1 (4)
	Black/African American	2 (7)
	White	21 (75)
	Other	2 (7)
	Prefer not to answer	2 (7)
Ethnicity	Hispanic or Latino	3 (11)
	Not Hispanic or Latino	22 (79)
	Prefer not to answer	3 (11)
ECOG PS	0	12 (43)
	1	12 (43)
	2	4 (14)
Prior systemic regimens	1-2	8 (29)
	≥3	20 (71)
Primary Tumor Origin	Breast	5 (18)
	Endometrial	5 (18)
	NSCLC	4 (14)
	Ovary	3 (11)
	HNSCC	2 (7)
	Colon	1 (4)
	Duodenum	1 (4)
	Fallopian tube	1 (4)
	Fibromyxoid	1 (4)
	Pancreas	1 (4)
	Stomach	1 (4)
	Rectum	1 (4)
	SCLC	1 (4)
	Soft tissue sarcoma	1 (4)

[a] Percentages may not sum to 100 due to rounding

Outcomes:

- Four pts had SD16+ (**Table 2**).

Table 2. Tumor Origin and Genomic Alterations in Pts with DC (n=4)

Response	Tumor Origin	*AKT1* Alteration	Comutations[a]
SD16+	Breast	*AKT1* E17K	*ERBB2* V153F[b]
SD16+	Endometrial	*AKT1* E17K	--
SD16+	Fibromyxoid	*AKT1* E17K	--
SD16+	NSCLC	*AKT1* E17K *AKT1* T65M[b]	*MTOR* D138Y[b] *RICTOR* N947Y[b]

[a] Comutations in the following genes were examined: *AKT2, CCND1, CDH1, CDKN2A, EGFR, EPCAM, ERBB2, ERBB3, MLH1, MSH2, MSH6, MTOR, NOTCH1, PIK3CA, PIK3R1, PMS2, PTEN, RICTOR, SMAD4, TGFBR2, TP53, TSC1, TSC2, VHL.*
[b] Variant of Unknown Significance

- Median duration of SD was 26 wks (range, 18-40) for pts with SD16+.
- DC and OR rates were 14% and 0%, respectively (**Table 3**). The null DC rate was not rejected (p=0.62).

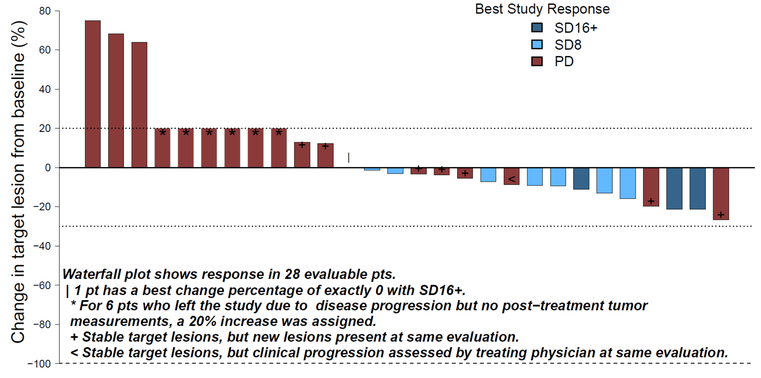
Safety:

- Five pts (18%) experienced six grade 3 AEs or SAEs at least possibly related to T. All were consistent with drug label except lymphopenia.

Table 3. Efficacy Outcomes (N=28)

DC rate, % (1-sided 90% CI) (p-value)	14 (6, 100) (p=0.62)
OR rate, % (95% CI)	0 (0, 12)
Median PFS, wks (95% CI)	8 (6, 8)
Median OS, wks (95% CI)	25 (14, 31)

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



Waterfall plot shows response in 28 evaluable pts.
| 1 pt has a best change percentage of exactly 0 with SD16+.
** For 6 pts who left the study due to disease progression but no post−treatment tumor measurements, a 20% increase was assigned.*
+ Stable target lesions, but new lesions present at same evaluation.
< Stable target lesions, but clinical progression assessed by treating physician at same evaluation.

Figure 2: Time on Tx-in Pts with SD16+ (n=4)

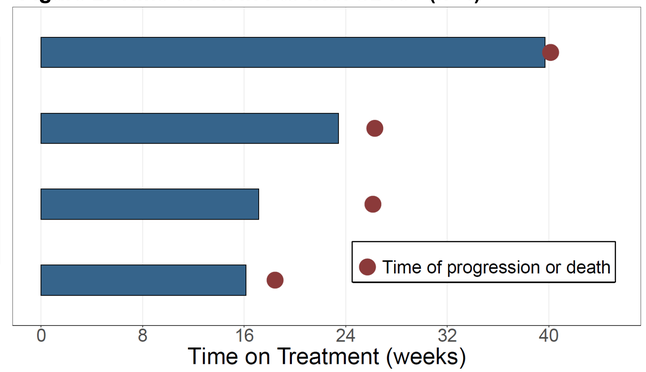
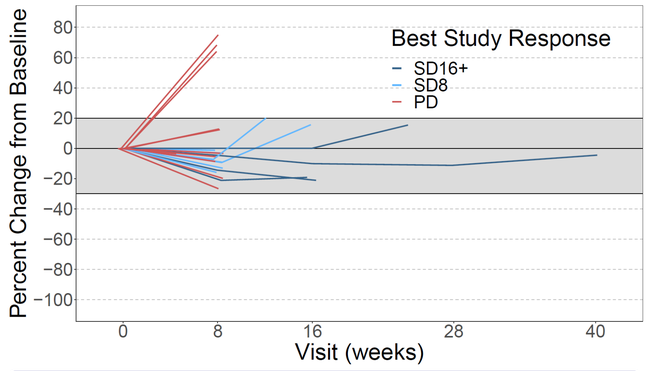


Figure 3: Percent Change from Baseline of Tumor Burden During Tx of T in Pts with Advanced Solid Tumors with *AKT1/3* Alterations (N=28)



Conclusions

T did not show evidence of antitumor activity in pts with solid tumors with *AKT1* alterations. Other tx should be considered for these pts, including tx offered in clinical trials.

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