Abstract 3114: Temsirolimus in patients with solid tumors with *mTOR* mutation: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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Background:

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

Methods:

Study Design:

- **Eligible pts:** Advanced solid tumors, no standard treatment (tx) options, ECOG PS 0-2, adequate organ function, measurable disease. Tx assigned according to pre-specified matching rules based on genomic tests selected by clinical sites.
- After anti-histamine pre-tx, 25 mg T was infused over 30-60 minutes weekly until disease progression, unacceptable toxicity or pt choice to discontinue.
- **Primary endpoint:** Disease control (DC) defined as objective response (OR) or stable disease (SD) at 16+ wks per RECIST v1.1. **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response, and toxicity per CTCAE. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to T are reported.
- Duration of SD is also reported here and defined as time from initiation of study tx until disease progression.
- Low accruing histology-specific cohorts with the same genomic alteration were collapsed into one histology-pooled cohort for this analysis.

Statistical Methods:

- For histology-pooled cohorts with sample size <28, inferences are based on a one-sided exact binomial test with a null hypothesis of DC rate ≤15% and alpha of 0.10. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results:

- 29 pts were enrolled June 2016 to June 2020. During data validation and verification, 6 pts in this cohort were found to have tumors with mut other than *mTOR* and were removed from this analysis. The analysis presented here includes all 23 pts with *mTOR* mutated tumors.
- Of the remaining 23 pts, 3 pts were excluded from efficacy analysis; 1 pt was found ineligible due to lack of measurable disease and 2 pts had no post-baseline tumor evaluation.
- **Demographics**: Median age 62 y (range 36-78 y); 65% female.
- **Clinical characteristics:** 48% PS 0, 48% PS 1, 4% PS 2; 74% received ≥3 prior systemic regimens. Primary tumor origin (# of pts): breast (1), colon (7), endometrial (3), esophagus (1), gallbladder/bile duct (1), head and neck (2), hepatocellular (2), leiomyosarcoma (1), NSCLC (3), ovary (1), soft tissue sarcoma (1).

Temsirolimus shows anti-tumor activity in heavily pre-treated patients with solid tumors with *mTOR* mutation.

Future Direction: Additional study is warranted to confirm the efficacy of temsirolimus in this patient population.

- **Outcomes**: Among 20 pts included in efficacy analyses, 2 pts achieved PR and 7 pts had SD16+ (Table 1, Table 2, Figure 1, Figure 2), for a DC rate of 45% (one-sided 90% CI: 29%-100%). The null hypothesis was rejected (p=0.0013). Time on T among pts with OR or SD16+ is shown in Figure 2.
- **Safety:** Out of 23 pts included in safety analyses, 8 pts (35%) had ≥1 SAE or Grade 3-4 AE at least possibly related to T, including acute kidney injury, epistaxis, hyperglycemia, hypertension, hypertriglyceridemia, oral mucositis, leukopenia, thrombocytopenia, and pneumonitis.

Table 1. Tumor Origin and Mutation of Pts Meeting Response Criteria (N=9)

Response	Primary Tumor Origin	Mutation
PR	Head and neck	I1636V (VUS)/*PIK3CA* E542K
PR	Endometrial	T1977R/*AKT1* E17L
SD16+	Colon	T1834_T1837del
SD16+	Colon	T1834_T1837del, E1854K (VUS)
SD16+	Head and neck	C1483Y
SD16+	NSCLC	F1888L
SD16+	NSCLC	E866K
SD16+	Leiomyosarcoma	S2215T
SD16+	Endometrial	Cys1483_Leu1484del

Funding supported by Pfizer. 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.

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Table 2: Efficacy Outcomes (N=20)

DC rate, % (one-sided 90% CI)	45 (29, 100)
OR rate, % (95% CI)	10 (1, 32)
Median PFS, wks (95% CI)	16.1 (8.1, 32.3)
Median OS, wks (95% CI)	48.1 (27.4, 74.9)
Duration of PR, wks (N=2)	12.3 and 23.9
Median Duration of SD (range), wks (N=7)	36.7 (27.7, 63.9)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (N=20)

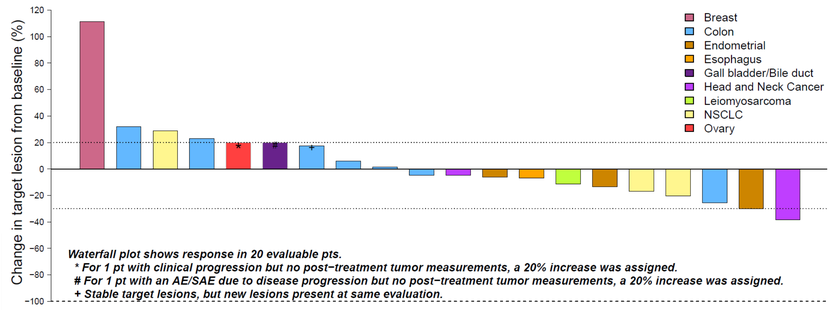

Figure 2: Time on Tx in Pts with OR or SD16+ (N=9)