Abstract 106: Temsirolimus in patients with colorectal cancer with *PIK3CA* 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 colorectal cancer (CRC) with *PIK3CA* mutation (mut) treated with temsirolimus (T) are reported.**

Methods:

Study Design:

- **Eligible pts:** Advanced CRC, 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 sites.
- Pts received T at 25 mg IV over 30-60 minutes weekly until disease progression.
- **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), and toxicity per CTCAE. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to T are reported.

Statistical Methods:

- Simon's optimal two-stage design used to test null hypothesis of 15% DC rate vs. alternative of 35%. Power = 85%; 1-sided α = 10%.
- At least 7 of 28 pts must achieve DC to reject null hypothesis and consider T worthy of further study.

Temsirolimus does not show anti-tumor activity in patients with colorectal cancer with *PIK3CA* mutation.

Other treatments should be considered for these patients, including treatments offered in clinical trials.

Results:

- 10 pts enrolled November 2017 to May 2020. 5 pts had tumors with *PIK3CA* E542K mut; 1 with K111del; 1 with M1040k mut; 1 with H1047R mut; 1 with H1047L mut; 1 with E542K, E545K – subclonal.
- **Demographics**: Median age 52 y (range 47, 64); 60% male.
- **Clinical characteristics:** 40% PS 0, 60% PS 1; 80% received ≥3 prior systemic regimens; 20% received 1-2 prior regimens.
- **Outcomes**: SD16+ in 1 pt (10%); no OR observed (Table 1 and Figure 1). OS and PFS are shown in Table 1 and Figure 2.
- **Safety:** 6 pts (60%) had ≥1 SAE or Grade 3-4 AE at least possibly related to T, including acute kidney injury, dehydration, decreased platelet count, hypertriglyceridemia, mucositis, neutropenia, and scrotal and penile edema.

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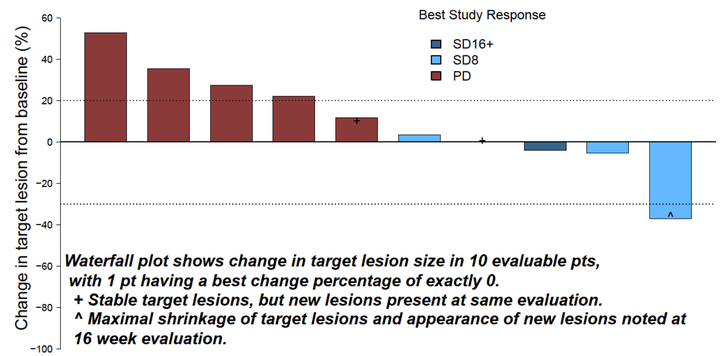
Table 1: Efficacy Outcomes (N=10)	
DC rate, % (95% CI)	10 (0, 45)
OR rate, % (95% CI)	0 (0, 31)
Median PFS, wks (95% CI)	8.1 (5.0, 15.7)
Median OS, wks (95% CI)	38.7 (24.3, 68.3)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (N=10) [SD16+, SD at 16+ wks; SD8*, SD at 8 wk follow-up visit; PD, progressive disease]

***Pts with SD<16 wks do not meet the study endpoint for response but SD8 is shown here for reference**



Waterfall plot shows change in target lesion size in 10 evaluable pts, with 1 pt having a best change percentage of exactly 0.
+ Stable target lesions, but new lesions present at same evaluation.
^ Maximal shrinkage of target lesions and appearance of new lesions noted at 16 week evaluation.

Figure 2: OS and PFS in pts with CRC with *PIK3CA* mut treated with T (N=10)