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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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.

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.

Results:
- 10 pts enrolled November 2017 to May 2020. 5 pts had tumors with PIK3CA mutation: 1 with 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)

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<thead>
<tr>
<th>DC rate, % (95% CI)</th>
<th>10 (0, 45)</th>
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<tr>
<td>OR rate, % (95% CI)</td>
<td>0 (0, 31)</td>
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<tr>
<td>Median PFS, wks (95% CI)</td>
<td>8.1 (5.0, 15.7)</td>
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<tr>
<td>Median OS, wks (95% CI)</td>
<td>38.7 (24.3, 68.3)</td>
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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.

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

Waterfall plot shows change in target lesion size in 19 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.

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