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 lung cancer (LC) with ERBB2 mutation (mut) or amplification (amp) treated with pertuzumab plus trastuzumab (P+T) are reported.

Methods:
- **Study Design:**
  - Eligible pts: Advanced LC, 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.
  - Pts received P at an initial dose of 840 mg intravenously (IV) over 60 minutes (m), then 420 mg IV over 30-60 m every 3 weeks (wks) and T at an initial dose of 8 mg/kg IV over 90 m, then 6 mg/kg IV over 30-60 m every 3 wks 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+ (SD16+) wks per RECIST v1.1. Secondary endpoints: Progression-free survival (PFS), overall survival (OS), duration of response, duration of SD, and toxicity per CTCAE. Grade 3-5 adverse events (AEs) or serious AEs (SAEs) at least possibly related to P+T are reported.

Statistical Methods:
- Simon’s optimal two-stage design used to test null hypothesis of 15% response (OR) rate vs. alternative of 35%. Power = 85%; 1-sided α = 10%.
- On P+T among pts with OR or SD16+ is shown in Figure 2. The null hypothesis was rejected (p=0.005). Time on P+T among pts with OR or SD16+ is shown in Figure 2.

Safety:
- 5 pts (18%) had ≥1 SAE or Grade 3-5 adverse events (AEs) at least possibly related to P+T are reported.

Results:
- 28 pts enrolled November 2016 to July 2020. 15 pts (54%) had ERBB2 mut only; 12 (43%) had ERBB2 amp only, 1 pt (4%) had both ERBB2 mut and amp. All 28 pts were evaluable for efficacy and safety analyses.

Demographics:
- Median age 64 y (range 41-84); 54% female; 82% White, 7% Black of African American, 7% Asian/Asian American; 96% non-Hispanic or Latino.

Clinical characteristics:
- 32% PS 0, 61% PS 1, 7% PS 2; 46% female, 54% White, 7% Black of African American, 7% Asian/Asian American; 82% non-Hispanic or Latino.


Outcomes: 3 pts (11%) with PR and 7 pts (25%) with SD16+ (Table 1). The null hypothesis was rejected (p=0.005). Time on P+T among pts with OR or SD16+ is shown in Figure 2.

Safety:
- 5 pts (18%) had ≥1 SAE or Grade 4-5 AE at least possibly related to P+T including alanine aminotransferase increased, aspartate aminotransferase increased, dyspnea (SAE), fatigue, infusion related reaction (SAE), nausea, and vomiting.

Conclusion:
- Pertuzumab plus trastuzumab shows anti-tumor activity in heavily pre-treated patients with lung cancer with ERBB2 mutation or amplification.

Future Direction: Additional study is warranted to confirm the efficacy of pertuzumab plus trastuzumab in this population.

Table 1: Efficacy Outcomes (N=28)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Rate (%) (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>DC rate, % (95% CI)</td>
<td>37 (21, 50)</td>
</tr>
<tr>
<td>OR rate, % (95% CI)</td>
<td>11 (2, 28)</td>
</tr>
<tr>
<td>Median PFS, wks (95% CI)</td>
<td>16.1 (8.6, 23.4)</td>
</tr>
<tr>
<td>Median OS, wks (95% CI)</td>
<td>54.4 (36.6, 101.4)</td>
</tr>
</tbody>
</table>

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

![Figure 1](image1.png)

Figure 2: Time on Tx in Pts with OR or SD16+ (N=10)

![Figure 2](image2.png)

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References: