FPN 978P: Pertuzumab plus Trastuzumab in patients with lung cancer with *ERBB2* mutation or amplification: 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 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% 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 P+T worthy of further study.

A.K. Ganti: Advisory Board (self): AstraZeneca, Beigene Therapeutics, Cardinal Health, Flagship Biosciences, Mirati Therapeutics, Sanofi Genzyme; Invited Speaker (self): Plexus Communications; Other (self): YMAbs Therapeutics, American Society of Clinical Oncology, Hoosier Cancer Research Network; Royalties (self): Oxford University Press; Local PI (institution): Merck, Mirati Therapeutics, NEKTAR Therapeutics, TAB Biosciences. Non-financial: Leadership role (self): Academic and Community Cancer Research United; Other (self): Jazz Pharmaceuticals; Product Samples (self): Takeda Pharmaceuticals.

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 patient population.

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% received ≥3 prior systemic regimens. Histologies (# of pts): adenocarcinoma (23), adenosquamous (1), large cell neuroendocrine (1), squamous (1), small cell (1), non-small cell (NSCLC) not specified (1).
- **Outcomes**: 3 pts (11%) with PR and 7 pts (25%) with SD16+ (Table 1 and Figure 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 3-4 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.

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Table 1: Efficacy Outcomes (N=28)

DC rate, % (95% CI)	37 (21, 50)
OR rate, % (95% CI)	11 (2, 28)
Median PFS, wks (95% CI)	16.1 (8.6, 23.4)
Median OS, wks (95% CI)	54.4 (36.6, 101.4)
Duration of PR, wks (N=3)	13.1, 19.1, 56.3
Median duration of SD (range), wks (N=7)	28.1 (23.4, 99.7)

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

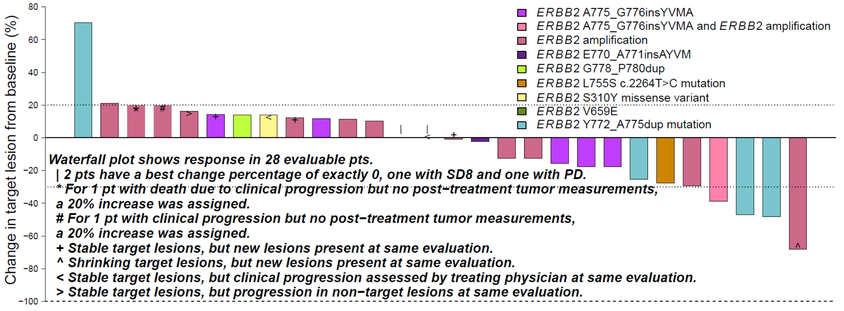

Figure 2: Time on Tx in Pts with OR or SD16+ (N=10)