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Background:

- TAPUR is a phase II basket study that evaluates the antitumor activity of commercially available targeted agents in patients (pts) with advanced cancers with specific genomic alterations.
- Results of a cohort of pts with esophageal cancer (EC) with *CDKN2A* loss or mutation (mut) treated with abemaciclib are reported.**

Methods:

Study Design:

- Eligible pts:** Advanced EC, ECOG performance status (PS) 0-2, adequate organ function, measurable disease, and no standard treatment options available. Treatment was assigned according to prespecified matching rules based on genomic tests performed in CLIA-certified, CAP-accredited labs selected by sites.
- Pts received abemaciclib at 200 mg (four 50 mg tablets) orally twice daily for a total daily dose of 400 mg until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- Primary endpoint:** Disease control (DC) defined by investigator assessment of objective response (OR) or stable disease (SD) of at least 16+ weeks (wks) duration per RECIST v1.1. Radiographic confirmation of response was not required.
- Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response, and toxicity per CTCAE v 4.0 are reported. For toxicity, grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to treatment are reported.

Statistical Methods:

- Simon's optimal two-stage design was used to test null hypothesis of 15% DC rate. Power of 85% and 1-sided α of 10% are based on alternative DC rate of 35%.
- If ≥ 2 of 10 pts in stage 1 have DC, 18 more pts are enrolled; otherwise, the cohort is closed. At least 7 of 28 pts at end of stage 2 must achieve DC to reject the null hypothesis and consider treatment worthy of further study.

Results:

- 10 pts with EC with *CDKN2A* loss (n=5) or mut (n=5) were enrolled to stage 1 between December 2019 to June 2022. Pt demographics and clinical characteristics are summarized in **Table 1**.
- Outcomes:** All pts were evaluable for efficacy. 1 pt achieved a partial response (PR) for a DC rate of 10% (1-sided 90% CI: 1 to 100). The null hypothesis was not rejected (p=0.80). The pt with PR had adenocarcinoma with *CDKN2A* loss, was HER2-negative and had comutations in *PIK3CA* and *TP53*. The duration of PR was 27 wks.

Conclusion: Abemaciclib did not demonstrate sufficient clinical activity in patients with esophageal cancer with *CDKN2A* loss or mutation for continued evaluation in this patient population.

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

- Safety:** 7 pts (70%) had ≥ 1 SAE or grade 3 AE at least possibly related to treatment, including: anemia, atrial fibrillation, increased blood bilirubin, increased creatinine, dehydration, dyspnea, generalized muscle weakness, heart failure, lung infection, pericardial effusion, and platelet count decreased. The lung infection led to the pt's death.

Table 1. Clinical Characteristics (N=10)

Characteristic		No. (%)
Age (Years)	Median (range)	68 (58-82)
Sex	Male	8 (80)
Race	Asian/Asian American	1 (10)
	Black/African American	1 (10)
	White	8 (80)
Ethnicity	Not Hispanic or Latino	10 (100)
ECOG PS	0	3 (30)
	1	7 (70)
Prior Systemic Regimens	2	4 (40)
	≥ 3	6 (60)
Histology	Adenocarcinoma	8 (80)
	Squamous cell carcinoma	2 (20)

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Table 2: Efficacy Outcomes (N=10)

DC rate, % (1-sided 90% CI) (p-value)	10 (1, 100) (p=0.80)
OR rate, % (95% CI)	10 (<1, 45)
Median PFS, wks (95% CI)	8 (2, 13)
Median OS, wks (95% CI)	17 (9, 35)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (N=10)

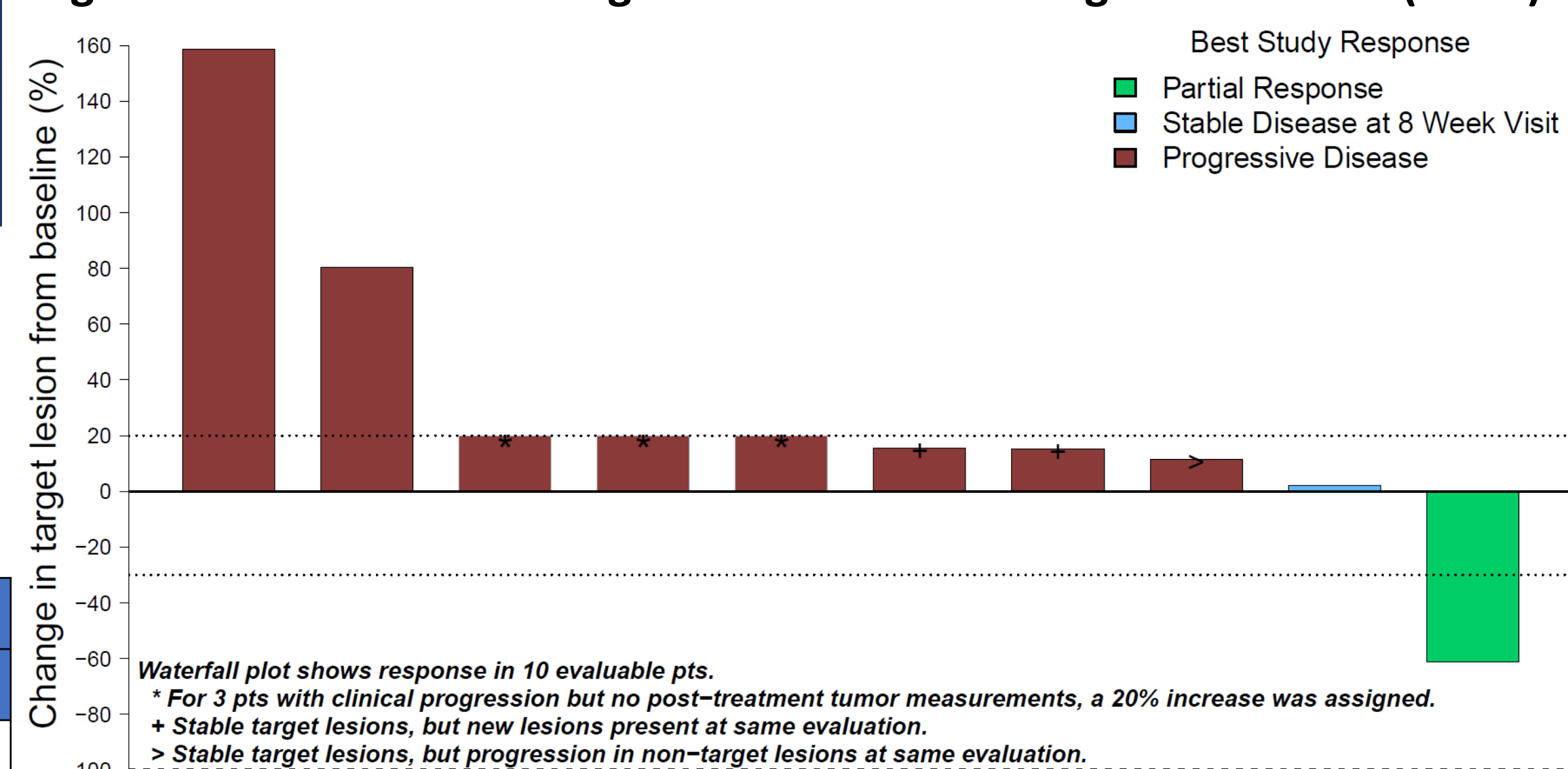
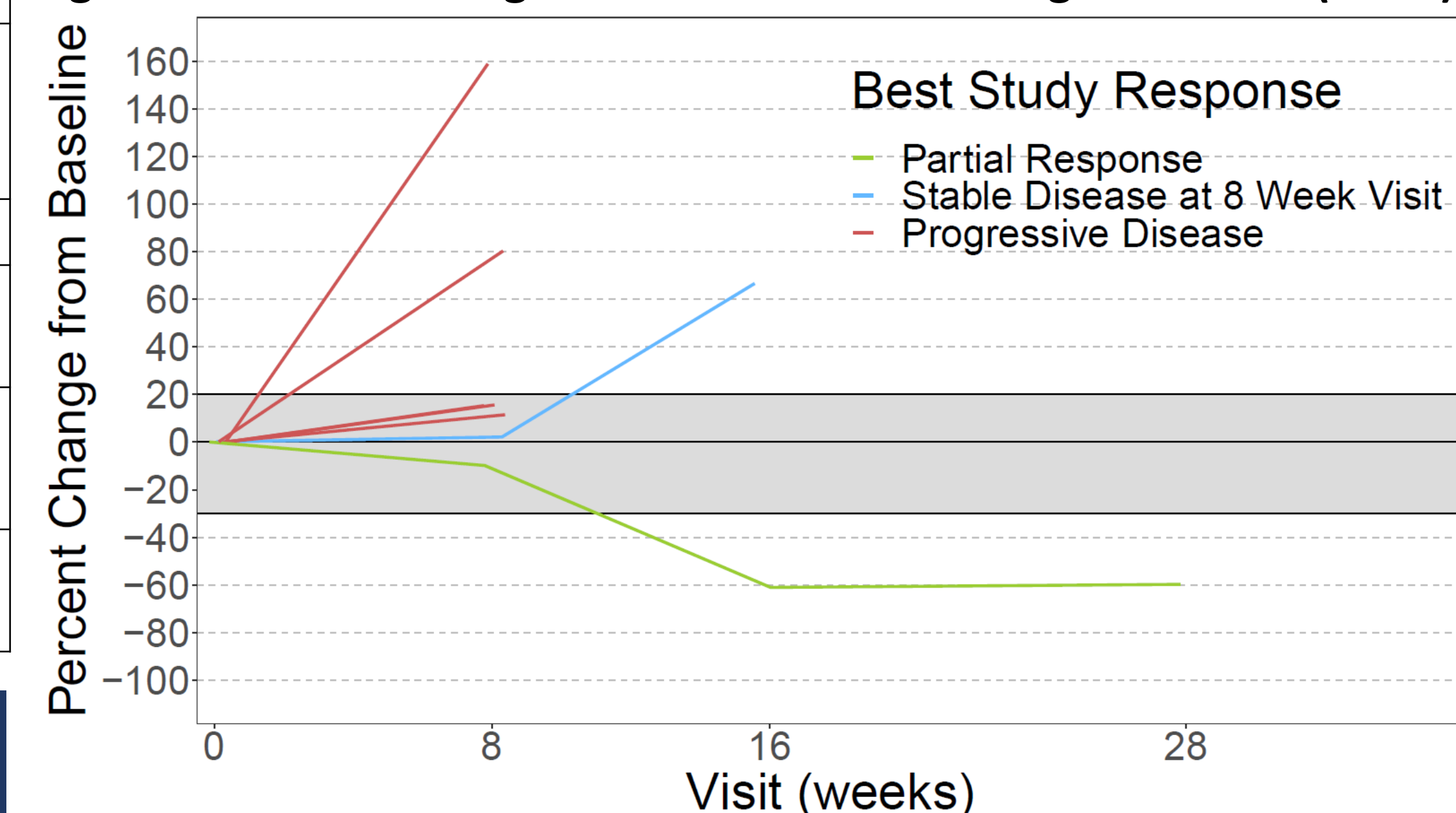


Figure 2: Percent Change of Tumor Burden During Treatment (N=10)



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