Crizotinib in patients with solid tumors with *MET* mutation or amplification: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

Abstract #: CT226

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Background

- The TAPUR Study 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 in a cohort of pts with advanced solid tumors with *MET* mutation (mut) or amplification (amp) treated with crizotinib (CRZ) are reported.

Methods

Study Design:

- **Eligible pts:** Advanced solid tumors, ECOG performance status (PS) 0-2, adequate organ function, measurable disease and no standard treatment (tx) options. Pts with non-small cell lung cancer were excluded. Tx was assigned according to pre-specified protocol matching rules based on genomic testing performed in CLIA-certified, CAP-accredited labs selected by clinical sites. Amp cutoffs were defined per NGS providers.
- Pts received CRZ at 250 mg orally BID until disease progression, unacceptable toxicity or pt or physician choice to discontinue.
- **Primary endpoint:** Disease control (DC) determined by investigator assessment of objective response (OR) or stable disease (SD) of at least 16 weeks (wks) duration (SD16+) per RECIST v1.1. Confirmation of response was not required.
- **Secondary endpoints:** Progression-free survival (PFS), overall survival (OS), duration of response (DOR), duration of SD, and safety per CTCAE v4.0. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) at least possibly related to CRZ are reported. DOR is defined as time from pt's first documented OR to progressive disease (PD). Duration of SD is defined as time from tx start to PD.
- Low accruing histology-specific cohorts with the same genomic alteration were collapsed into one histology-pooled cohort for this analysis.

Statistical Methods:

- Inferences are based on a one-sided exact binomial test with a null hypothesis of DC rate ≤15%; power and alpha were 88% and 0.10, respectively. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results

- Thirty-one pts with solid tumors with *MET* mut (n=10; two were exon 14 skipping), amp (n=19), or both (n=1) were enrolled from May 2016 to October 2020. One other pt with overexpression was enrolled and found ineligible after receiving ≥1 dose of tx.
- Four of 31 pts were not included in efficacy analyses: one ineligible, three not evaluable due to lack of post-baseline tumor evaluation (two pts elected hospice care after 1-2 weeks on study; one pt left study due to an unrelated SAE). 27 pts were evaluable for the efficacy analyses.
- Baseline characteristics are shown in **Table 1**.

Table 1: Baseline Characteristics (N=31)

Characteristic		No. (%)
Median Age	Years (range)	61 (30-82)
Sex	Female	16 (52)
Race	Black/African American	6 (19)
	White	22 (71)
	Other	2 (7)
	Prefer not to answer	1 (3)
Ethnicity	Hispanic or Latino	3 (10)
	Not Hispanic or Latino	27 (87)
	Prefer not to answer	1 (3)
ECOG PS	0	15 (48)
	1	12 (39)
	2	4 (13)
Prior systemic regimens	1-2	8 (26)
	≥3	23 (74)
Primary Tumor Origin	Colon	7 (23)
	Breast	6 (19)
	Pancreas	5 (16)
	Esophagus	2 (6)
	RCC	2 (6)
	Cervix	1 (3)
	HCC	1 (3)
	Head/Neck	1 (3)
	Phyllodes tumor	1 (3)
	Prostate	1 (3)
	Rectal	1 (3)
	Small bowel	1 (3)
	Thyroid	1 (3)
	Tongue	1 (3)

Efficacy Outcomes (n=27):

- Two pts had PR and four had SD16+ (**Table 2**). Both pts with *MET* exon 14 skipping mut had PD.

Table 2. Tumor Origin and Alteration of Pts with PR or SD16+ (n=6)

Response	Tumor Origin	Alteration	Comutations[a]
PR [b]	Esophagus	*MET* amp	none
PR [c]	Esophagus	*MET* amp	none
SD16+	RCC	*MET* mut [d]	*ROS1* D839E (VUS)
SD16+	RCC	*MET* amp	none
SD16+	Colon	*MET* amp	none
SD16+	Small bowel	*MET* amp	*PIK3R1* Q221*

[a] The following comutations were examined: *AKT1*, *AKT2*, *ALK*, *MAPK*, *PIK3CA*, *PIK3R1*, and *ROS1*. [b] Pt had 1 prior systemic therapy, [c] Pt had 3 prior systemic therapies, [d] cMET, Exon 2 S323G (VUS), cMET, Exon 14 V1014L (VUS). Variant of unknown significance (VUS).

- Durations of response were 20 wks and 14 wks for pts with PR, and the median duration of SD was 27 wks (range: 26, 28) for pts with SD16+.
- DC and OR rates were 22% and 7%, respectively (**Table 3**). The null DC rate of 15% was not rejected (p=0.210).

Safety Outcomes (N=31):

- Five pts (16%) experienced 14 grade 3 AEs or SAEs at least possibly related to CRZ. All were consistent with the drug label except acute kidney injury, dehydration, and GGT increase.

Table 3: Efficacy Outcomes (n=27)

DC rate, % (1-sided 90% CI)	22 (12, 100)
OR rate, % (95% CI)	7 (1, 24)
Median PFS, wks (95% CI)	8 (7, 15)
Median OS, wks (95% CI)	37 (26, 70)

Figure 1: Best Percent Change from Baseline in Target Lesion Size (n=27)

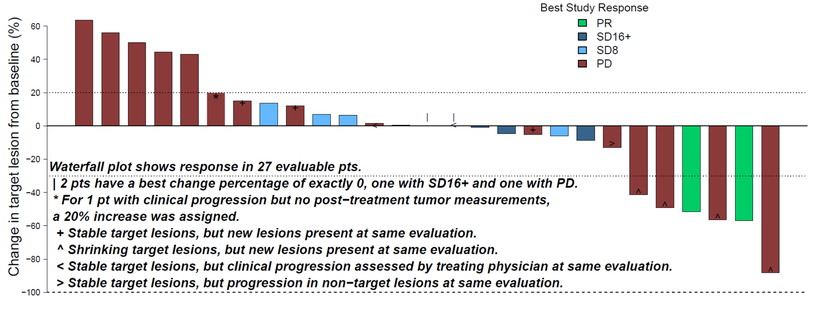


Figure 2: Time on Treatment in Pts with SD16+ or OR (n=6)

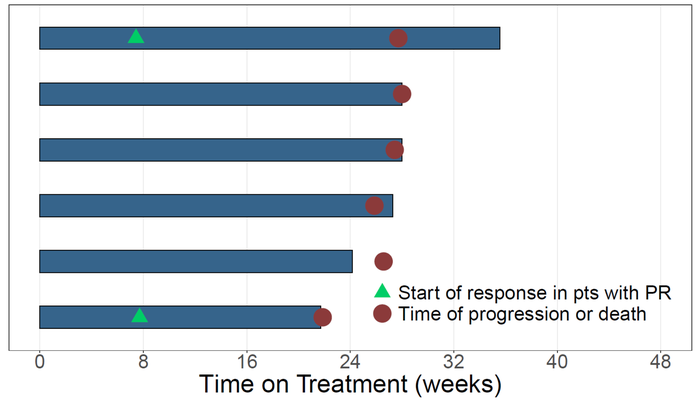
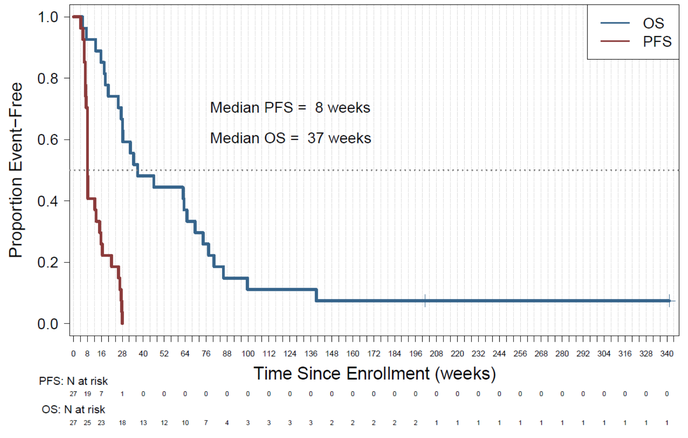


Figure 3: PFS and OS in Pts with Advanced Solid Tumors with *MET* Mut or Amp treated with CRZ (n=27)



Conclusions

Crizotinib did not meet prespecified criteria to declare a signal of activity in pts with solid tumors with *MET* mut or amp.

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