Sunitinib in patients with solid tumors with *FGFR2* alterations: Results from the Targeted Agent and Profiling Utilization Registry (TAPUR) Study

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Abstract #: CT226

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.
- Sunitinib (S) is a multi-targeted tyrosine kinase inhibitor primarily used to treat RCC, GIST, and pNET.
- Results in a cohort of pts with solid tumors with *FGFR2* mutation (mut), amplification (amp), or fusion treated with S are reported.

Methods

Study Design:

- **Eligible pts:** Advanced solid tumors, Eastern Cooperative Oncology Group performance status (ECOG PS) 0-2, adequate organ function, measurable disease and no standard treatment (tx) options available. Tx was assigned according to prespecified 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 S at 50 mg orally once daily in cycles of 4 weeks (wks) on followed by 2 wks off, 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 wks duration (SD16+) per RECIST v1.1. Radiographic confirmation of response was not required.
- **Secondary endpoints:** OR, progression-free survival (PFS), overall survival (OS), duration of response (DOR), and duration of SD are reported. Grade 3-5 adverse events (AEs) or serious adverse events (SAEs) per CTCAE v4.0 at least possibly related to tx 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 82% and 0.10, respectively. Two-sided 95% CIs are used for other efficacy endpoint estimates.

Results

- 28 pts with *FGFR2* mut (n=19), amp (n=2), both amp and mut (n=4), *FGFR2* fusion (n=2), or *FGFR2* fusion, mut, and amp (n=1) were enrolled from April 2016 to March 2022.
- Baseline demographics and clinical characteristics are summarized in **Table 1.**
- 3 pts had PR and 8 pts had SD16+ (**Table 2**).
- The 3 pts with PR had DOR of 4, 20, and 46 wks. Median duration of SD was 27 wks (range, 18-42) for pts with SD16+.
- The DC rate was 39% (1-sided 90% CI, 27% to 100%); the null DC rate was rejected (p=0.0015). The OR rate was 11% (95% CI, 2 to 28; **Table 3**).

Safety:

- 10 pts (36%) experienced 11 tx-related grade 3 AEs or SAEs. All were consistent with the drug label except anemia, neutropenia, proteinuria, Stevens-Johnson syndrome, and leukopenia.

Table 1. Baseline Characteristics (N=28)

Characteristic		No. (%)[a]
Median Age	Years (range)	67 (30-78)
Sex	Female	17 (61)
Race	Black/African American	3 (11)
	Native Hawaiian/Pacific Islander	1 (4)
	White	22 (79)
	Prefer not to answer	1 (4)
	Other	1 (4)
Ethnicity	Hispanic or Latino	3 (11)
	Not Hispanic or Latino	24 (86)
	Prefer not to answer	1 (4)
ECOG Performance Status	0	7 (25)
	1	16 (57)
	2	5 (18)
Prior systemic regimens	0	1 (4)
	1	1 (4)
	2	4 (14)
	≥3	22 (79)
Primary Tumor Origin	Lung	8 (29)
	Uterus	6 (21)
	Ovary	5 (18)
	Esophagus	2 (7)
	Appendix	1 (4)
	Cholangiocarcinoma	1 (4)
	Colon	1 (4)
	Gallbladder	1 (4)
	Liver	1 (4)
	Osteosarcoma	1 (4)
	Unknown primary	1 (4)

[a] Percentages may not sum to 100% due to rounding.

Table 2. Tumor Origin and Alteration in Pts with DC (n=11)

Pt	Response	Tumor Origin	*FGFR2* Alteration	Co-alterations[a]
A	PR	NSCLC	C491F	--
B	PR	NSCLC	N549K[b]	*PTEN* T286fs*12 *RAF1* R143Q[c]
C	PR	Uterus	P253R[b]	*HRAS* A59T *PTEN* D92E *MAP3K1* C1430Y[c]
D	SD16+	Osteosarcoma	V395D	--
E	SD16+	NSCLC	K659E[b]	*ATM* K24M[c] *PALB2* C949fs*13
F	SD16+	SCLC	V69M[c]	*FGFR1* P25P
G	SD16+	Gallbladder	Amp, Y375C[b]	*BRAF* fusion *FGFR1* amp *MAP2K1* amp
H	SD16+	Cholangiocarcinoma	C382R[b]	--
I	SD16+	Ovary	*FGFR2-SORBS1* Fusion[b]	*PALB2* S951P[c]
J	SD16+	Ovary	S252W[b]	*ATM* splice site 2125-1G>C *PIK3CA* E542K *PTEN* C136fs, splice site 635-1G>A
K	SD16+	Uterus	Y375C[b]	*PIK3CA* R93W *PTEN* R233*

Abbreviations: NSCLC, non-small cell lung cancer; PR, partial response; SCLC, small cell lung cancer

[a] The following comutations were examined: *ATM, BARD1, BRAF, CHEK2, FGFR1, HRAS, KRAS, MAP2K1, MAP2K2, MAP3K1, MAPK1, MAPK3, MTOR, NRAS, PALB2, PIK3CA, PTEN, RAF1, RAD51C, RAD51D*

[b] Alteration likely activating

[c] Variant of unknown significance

Table 3. Efficacy Outcomes (N=28)

DC rate, % (1-sided, 90% CI), p-value	39 (27, 100), p=0.0015
OR rate, % (95% CI)	11 (2, 28)
Median PFS, wks (95% CI)	8 (6, 18)
Median OS, wks (95% CI)	31 (13, 54)

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

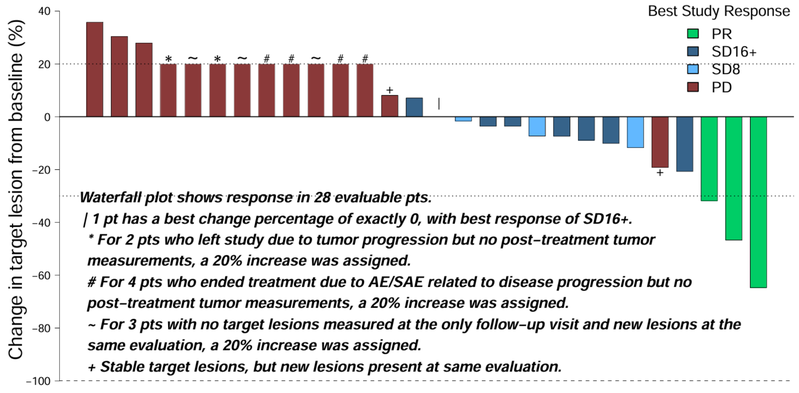
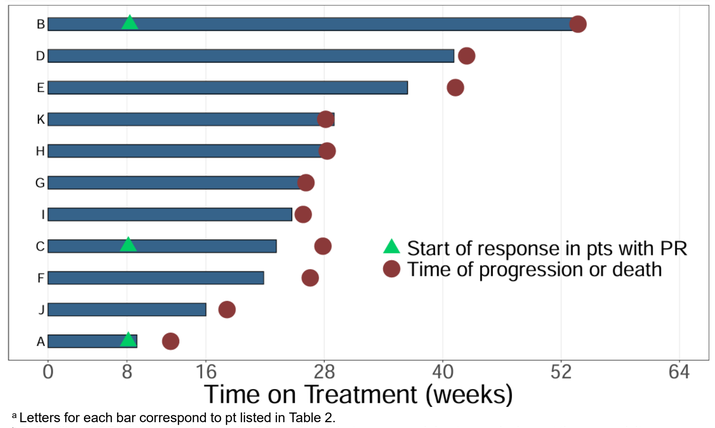


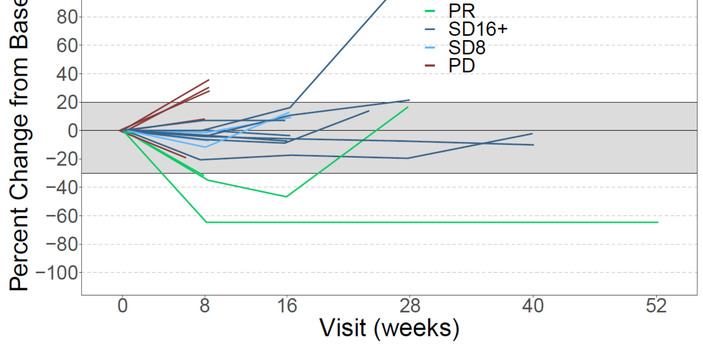
Figure 2: Time on Tx in Pts with SD16+ or OR (n=11)[a,b]



[a] Letters for each bar correspond to pt listed in Table 2.

[b] Pt B still had PR of target lesions at the 52-week visit but progressed due to new lesions at the same visit.

Figure 3: Percent Change from Baseline of Tumor Burden During Tx of S in Pts with Advanced Solid Tumors with *FGFR2* Alterations (N=28)



Conclusions

Sunitinib met prespecified criteria to declare clinical activity in patients with solid tumors with *FGFR2* alterations. Additional study is warranted to confirm the efficacy of sunitinib in this patient population.

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