Surufatinib in US Patients with Soft Tissue Sarcoma

Sujana Movva, MD[1]; Alexander I. Spira, MD, PhD[2]; Erika Hamilton, MD[3]; Judy S. Wang, MD[4]; Allen Cohn, MD5; James Strauss, MD[6]; Silvia Stacchiotti, MD[7]; Christopher Tucci, MBS, CCRP[8]; John S. Kauh, MD, FACP[8]; Shivani Nanda, MS[8]; Marek Kania, MD, MBA[8]; Shreyaskumar R. Patel, MD[9]

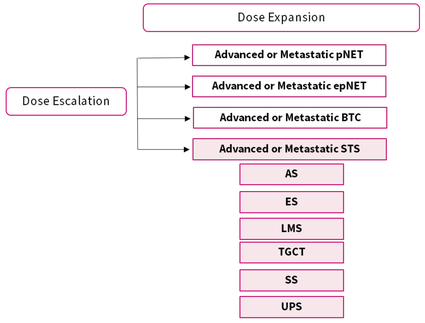
[1]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [2]Virginia Cancer Specialists, Fairfax VA, USA; [3]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA; [4]Florida Cancer Specialists/Sarah Canon Research Institute, Sarasota, FL, USA; [5]Rocky Mountain Cancer Centers, Denver, CO, USA; [6]Mary Crowley Cancer Research, Dallas TX, USA; [7]Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy; [8]HUTCHMED International Corporation, Florham Park, NJ, USA; [9]The University of Texas MD Anderson Cancer Center Houston, TX, USA

11557

INTRODUCTION

- Soft tissue sarcomas (STS) are rare and heterogenous; >13,000 new cases will be diagnosed in the US in 2022[1]; patients (pts) have a 5-year survival rate of between 55% and 70%[2]
- Current treatments include surgery, radiation, and chemotherapy
- Angiogenesis inhibitors and kinase inhibitors have shown some activity in STS[3]
- Surufatinib is a selective inhibitor of VEGFR1, 2, & 3, FGFR1, and CSF-1R that inhibits tumor angiogenesis
- In two phase 3 placebo-controlled studies, surufatinib has demonstrated a manageable safety profile and statistically significant improvement in progression-free survival (PFS) in pts treated with advanced, well differentiated neuroendocrine tumors (NETs) of extrapancreatic (epNET; SANET-ep: NCT02588170)[4] and pancreatic (pNET; SANET-p: NCT02589821)[5] origin conducted in China
- As previously reported, surufatinib has shown a consistent pharmacokinetic (PK) and safety profile, and efficacy benefit in patients with NETs compared with earlier studies conducted in China
- **Here we report findings with surufatinib in patients with STS (NCT02549937)**

Figure 1: Dose Expansion Study Schema



AS=angiosarcoma; ES=epithelioid sarcoma; LMS=leiomyosarcoma; TGCT=tenosynovial giant cell tumor; SS=synovial sarcoma; UPS=undifferentiated pleomorphic sarcoma

STUDY DESIGN

- This study is a phase 1, dose escalation (ESC)/expansion (EXP) study to evaluate the safety and efficacy of surufatinib in the US and Europe (EXP only)

Key Inclusion/Exclusion Criteria

- Inclusion criteria for the EXP STS cohort include ≥18 years; Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 or 1; locally advanced or metastatic advanced STS (angiosarcoma [AS], epithelioid sarcoma [ES], leiomyosarcoma [LMS], tenosynovial giant cell tumor [TGCT], synovial sarcoma [SS] and undifferentiated pleomorphic sarcoma [UPS]) that had progressed on at least 1 line of standard therapy (if available) or refused standard frontline cytotoxic chemotherapy
- Patients with squamous non-small cell lung cancer were ineligible

Recommended Phase 2 Dose

- ESC previously reported the recommended phase 2 dose (RP2D) as 300mg once daily.

Study Objectives

- The primary objective of EXP was to evaluate the anti-tumor activity of surufatinib at the RP2D from ESC in patients with advanced biliary tract cancer (BTC), pancreatic neuroendocrine tumors (pNET), extrapancreatic NETs (epNET), and patients with STS treated at a dose of 300 mg once daily (QD)
  - The primary endpoint for the STS EXP cohort was PFS rate at 4 months (mo) according to RECIST version 1.1
  - Tumor assessments were performed at screening, Cycle 2 Day 1 and every 8 ±1 weeks thereafter
- Secondary objectives of EXP included evaluation of the PK, safety, and anti-tumor activity of multiple dose surufatinib
  - Secondary endpoints of EXP include objective response rate (ORR), disease control rate (DCR), time to response (TTR), duration of response (DoR) and percentage change in tumor size from baseline

Statistical Analysis

- PFS was summarized using Kaplan-Meier method. TTR and DoR were analyzed in the same way. ORR and DCR were estimated, and 95% confidence interval (CI) were calculated based on the Clopper-Pearson method

RESULTS

Table 1: Demographics and Baseline Characteristics

	STS (N=32)
Age, years median (range)	56.5 (26-77)
Gender, n (%)	
Female	22 (68.8)
Male	10 (31.2)
Race, n (%)	
White	25 (78.1) (2 not reported)
Hispanic or Latino	7 (21.9) (2 not reported)
Baseline ECOG PS, n (%)	
0	15 (46.9)
1	17 (53.1)
Prior pazopanib, n (%)	13 (40.6)
Prior lines of therapy, n (%)	
≤ 2	12 (37.5)
3-4	10 (31.3)
5-6	10 (31.3)

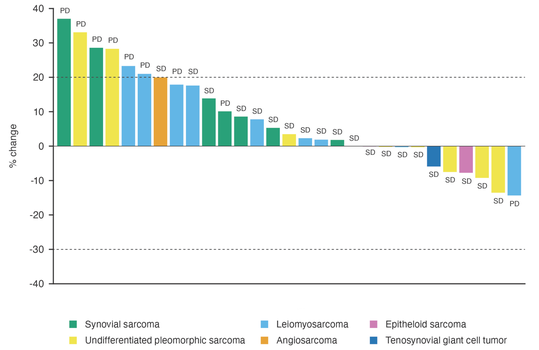
ECOG PS= Eastern Cooperative Oncology Group performance status; STS=soft tissue sarcoma

Table 2: Anti-tumor Efficacy

	STS (N=32)
PFS (all patients)	
Rate at 4 months, %	17.5
Median, months (95% CI)	2.56 (0.92-2.92)
PFS (by histology) months, median (95% C)⁺	
LMS (n=10)	2.76 (0.92, 3.06)
SS (n=9)	0.92 (0.16, -)
UPS (n=8)	2.04 (0.72, -)
mDoT, weeks (95% CI)⁺	
All tumor types (N=32)	11.2 (0.4-39.0)
LMS (n=10)	11.6 (3.1-36.0)
SS (n=9)	11.9 (0.4-27.9)
UPS (n=8)	8.2 (2.7-27.9)
ORR, n	0
SD, n (%)	6 (18.7)
PD, n (%)	18 (56.3)
NE, n (%)	8 (25.0)

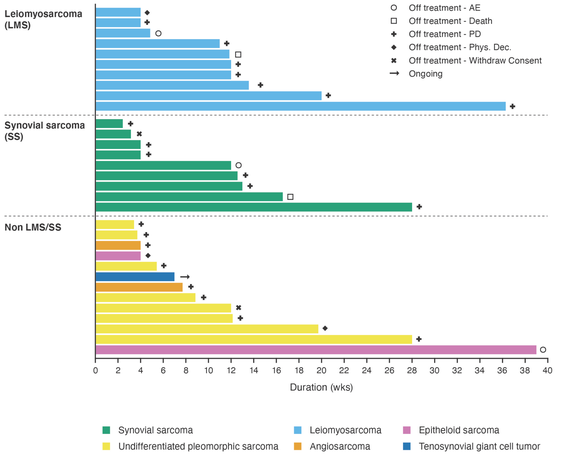
AE=angiosarcoma; ES=epithelioid sarcoma; CI=confidence interval; LMS=leiomyosarcoma; mDoT=median duration of treatment; NE=not evaluable; ORR=objective response rate; PD=progressive disease; PFS=progression-free survival; pt=patient; SD=stable disease; SS=synovial sarcoma; TGCT=tenosynovial giant cell tumor UPS= Undifferentiated pleomorphic sarcoma
⁺mDoT and PFS were not calculated for AS, ES, or TGCT due to low patient numbers

Figure 2: Best Percent Change in Target Lesion Measurements



PD=progressive disease; SD=stable disease

Figure 3: Duration of Response



AE=adverse event; PD=progressive disease; Phys. Dec.=physician's decision; wks=weeks

Table 3: TEAEs in >10% of the Patients

	All grade, n (%)	Grade ≥3, n (%)
Any TEAE	32 (100)	21 (65.6)
Fatigue	17 (53.1)	4 (12.5)
Hypertension	14 (43.8)	7 (21.9)
Diarrhea	13 (40.6)	0
Anemia	8 (25.0)	3 (9.4)
Blood bilirubin increase	8 (25.0)	0
Headache	7 (21.9)	0
Proteinuria	7 (21.9)	1 (3.1)
Back pain	6 (18.8)	0
Nausea	6 (18.8)	0
Edema peripheral	6 (18.8)	0
Cough	5 (15.6)	0
Arthralgia	4 (12.5)	0
Dyspnea	4 (12.5)	0
Urinary tract infection	4 (12.5)	0

TEAE=treatment emergent adverse event

- The safety profile of surufatinib in the STS cohorts remains consistent with previously completed trials. All pts (n=32) reported ≥1 adverse event (AE), and 21 pts (65.6%) reported AEs ≥ grade 3 (Table 3)
- The most common AEs of any grade were fatigue (53.1%), hypertension (43.8%), diarrhea (40.6%), anemia (25.0%), blood bilirubin increase (25.0%), headache (21.9%), and proteinuria (21.9%). The most commonly reported AEs ≥ grade 3 in >1 pt were hypertension (21.9%), fatigue (12.5%), and anemia (9.4%)
- AEs leading to treatment discontinuation occurred in 3 (9.4%) pts and included ejection fraction decrease (n=1) (related to study drug) and respiratory failure, spinal fracture, and subarachnoid hemorrhage (n=1 each) (not related to study drug)

CONCLUSIONS

- **Surufatinib demonstrated minimal anti-tumor activity as a single agent in heavily pretreated patients across various types of STS**
- **The safety profile in patients with STS remains consistent with previously reported and ongoing studies with surufatinib**
- **Clinical trials are ongoing with surufatinib globally, with active recruitment in programmed death-ligand 1 (PD-L1) combination studies**

ACKNOWLEDGMENTS
We would like to thank all patients and their families who participated in this trial. We would like to thank all investigators, study coordinators, and the entire project team.

REFERENCES
1. Siegel et al. CA:Cancer J Clin. 2022; 2:7-33
2. Liang et al. Frontiers in Oncology. 2020;10
3. van der Graaf et al. Lancet. 2012;379:1879-86
4. Xu et al. The Lancet Oncology. 2020;21:1500-12
5. Xu et al. The Lancet Oncology. 2020;21:1489-99

Copies of this poster obtained through Quick Response (QR) Code are for personal use only and may not be reproduced without permission from ASCO® or the author of this poster.