Comparison of Pharmacokinetic Profiles and Safety of Surufatinib in Patients from China and the United States

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Presented by Arvind Dasari, MD

Dasari A,[1] Paulson S,[2] Hamilton E,[3] Wang J,[4] Sung M,[5] Falchook G,[6] Tucci C,[7] Li K,[7] Chien C,[7] Kauh J,[7] Kania M,[7] Li D[8]

[1] MD Anderson Cancer Center, Houston, TX, USA, [2] Baylor Sammons Cancer Center, Dallas, TX, MD Anderson Cancer Center, Houston, TX, USA, [3] Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN, USA, [4] Florida Cancer Specialists/Sarah Cannon Research Institute, Sarasota, FL, USA, [5] Mount Sinai Hospital, New York, NY, USA, [6] Sarah Cannon Research Institute at HealthONE, Denver, Co, USA,[7] Hutchison International Inc., Florham Park, NJ, USA, [8] City of Hope Cancer Center, Duarte, CA, USA.

Introduction

- Surufatinib is a novel, oral, targeted inhibitor of tyrosine kinases VEGFR1, 2, & 3, FGFR1, and CSF-1R.

- Two randomized placebo controlled phase 3 trials in advanced neuroendocrine tumor (NET) patients are complete. Both trials stopped per a pre-planned interim analysis showing superior efficacy of surufatinib over placebo.

  - ↗ **SANET-ep** (NCT02588170)
    demonstrated superior efficacy in patients with advanced extra-pancreatic neuroendocrine tumors.
    - ☐ Median progression free survival 9.2 vs. 3.8 months.

  - ↗ **SANET-p** (NCT02589821)
    demonstrated superior efficacy in patients with advanced pancreatic neuroendocrine tumors).
    - ☐ Results pending disclosure at upcoming scientific conference.
    - ☐ Overall safety and efficacy is consistent with previously disclosed surufatinib data

- Genetic differences leading to potential disparate metabolism in different patient populations are unknown.

- We report a comparison of pharmacokinetic (PK) and safety data across populations treated with surufatinib.

Methods

- **Two trials are compared to evaluate potential effects of race on surufatinib exposure.**
  - A phase I/II study of surufatinib (NCT02267967) conducted in China
  - A phase I/Ib study of surufatinib (NCT02549937) conducted in the United States (US)
- Both trials treated patients at the recommended phase 2 dose (RP2D) of 300 mg QD.
- Three tumor types including Pancreatic NET, extra-pancreatic NET, and Biliary Tract Cancer.

PK Collection Timepoints

- NCT02267967 (conducted in China): Dense PK samples obtained on days 1 and 14, (n=81 patients).
- NCT02549937 (conducted in US): Dense PK samples obtained on days 1, 8, 15, and 29, (n= 39 patients).
  - 29 (74.3%) Caucasian, 2 (5.1%) Asian, and 8 (20.5%) not reported.
- PK parameters were determined using non-compartmental analysis.

PK Results

PK Exposure of Surufatinib (following 300mg QD dosing) in Chinese Patients Compared to US Patients

	C_{max} geometric mean (%CV)		AUC_{tau} geometric mean (%CV)	
	Chinese patients (n=81)	US patients (n=39)	Chinese patients (n=81)	US patients (n=39)
Day 1	376 (70%) ng/mL	354 (61%) ng/mL	2770 (56%) hr*ng/mL	3050 (56%) hr*ng/mL
Day 14/15	487 (65%) ng/mL	471 (59%) ng/mL	4810 (58%) hr*ng/mL	5130 (50%) hr*ng/mL

%CV: percent coefficient of variation of geometric mean

- Following a single dose of surufatinib 300 mg on day 1 and steady state on day 14/15.
  - ↗ C_{max} and AUC_{tau}: less than 10% difference between Chinese and US populations.
- In US patients, surufatinib geometric mean C_{max} and AUC_{tau} on day 29 were 443 ng/mL and 4670 hr*ng/mL, respectively, and similar to those on days 14/15.

Safety Results

- **Treatment-related adverse events** (TRAE) observed in 100% of Chinese patients and 79.5% of US patients
  - ↗ Most common TRAE's reported
- **Serious adverse events** were reported in 27% of Chinese patients and 23.7% of US patients
- **Relative Mean Dose intensity:**
  - ↗ Chinese patients: 90%
  - ↗ US patients: 84%
- **Median Dose intensity:**
  - ↗ Chinese patients: 97%
  - ↗ US patients: 96%

Most Commonly Reported TRAE's in Chinese Patients Compared to US Patients

	Chinese Patients (n=81)		US Patients (n=39)	
	All Grade	≥ Grade 3	All Grade	≥ Grade 3
Proteinuria	81%	12%	12.8%	5.1%
Diarrhea	72%	6%	28.2%	7.7%
Hypertension	60%	33%	38.5%	23.1%
Nausea	17%	-	20.5%	2.6%
Fatigue	-	-	17.9%	5.1%

Conclusions

- Similar PK and toxicity profiles of surufatinib observed between Chinese and US patients
- Data suggest that race has no clinically meaningful impact on surufatinib PK exposure
- Further evaluations of safety and efficacy are being conducted in global studies

Thank you to all of our patients, their families and participating site staff
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For questions and comments please contact:

Arvind Dasari, MD - ADasari@mdanderson.org

John Kauh, MD – Johnk@hmpIglobal.com