AACR Annual Meeting

Abstract # 9563

北京大学肿瘤医院 BEIJING CANCER HOSPITAL

A Phase I Trial of Surufatinib plus Toripalimab in Patients with Advanced Solid Tumor

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Study Design

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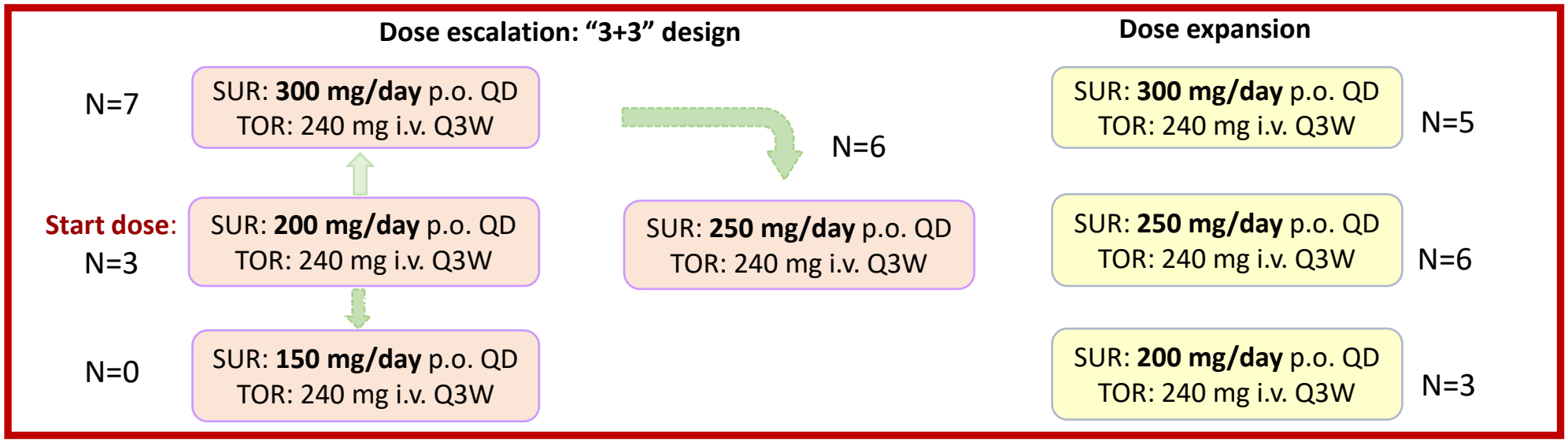
- **Surufatinib** (SUR/012): a TKi, targeting **VEGFR 1,2&3**, **FGFR 1**, and **CSF-1R** **(created by Hutchison Medipharma)**
- **Toripalimab** (TOR/JS001): a monoclonal humanized **IgG4 PD-1 antibody** **(created by JunShi Biology)**

Primary Objectives:

- To evaluate treatment-related dose-limiting toxicities (DLTs) of SUR in combination with TOR during 28 days post first dosing
- To investigate the maximum tolerated dose (MTD) and to establish a recommended phase 2 dose (RP2D)

Secondary Objectives:

- To evaluate objective response rate (ORR), progression-free survival (PFS), overall survival (OS), disease control rate (DCR)
- To determine the pharmacokinetics (PK) of SUR and TOR



Key eligibility criteria:
--ECOG PS of 0 or 1
--No prior SUR or immune checkpoint inhibitors
--Metastatic or locally advanced and unresectable cancer
--Progression on prior standard or no effective therapy

NCT03879057

- Tumor response assessed by RECIST v1.1 every 6 weeks(±7 days) for 24 weeks and every 12 weeks (±7 days) thereafter
- Patients treated until confirmed progressive disease or any other decision to discontinue

Patient Baseline Characteristics and Disease Diagnosis

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Parameter	200mg (N=6)	300mg (N=12)	250mg (N=12)	All (N=30)
Median age (range), years	57 (36, 74)	61.5 (45, 68)	61.5 (30, 71)	61 (30, 74)
Sex (Male / Female)	5/1	9/3	10/2	24/6
ECOG (0/1)	2/4	7/5	3/9	12/18
Diagnosis				
NET G1&G2	0	3	1	4
NET G3	3	0	1	4
NEC	3	5	5	13
CRC (with MSI-H)	0	1 (0)	3 (1)	4 (1)
GC	0	2	0	2
EC	0	1	1	2
Metastatic squamous cell carcinoma	0	0	1	1
PD-L1 expression (0%/<5%/≥5%/NE)	2/1/2/1	7/0/2/3	3/2/1/6	12/3/5/10
Prior line of therapy (1/2/≥3)	1/4/1	6/3/3	4/5/3	11/12/7
Previous received targeted therapy				
VEGFi/VEGFRi	2	5	0	7
M-TORi	1	0	0	1
EGFRi/HER2i	0	1	1	2

Summary of Treatment Emergent Adverse Events (TEAEs) (Data cut-off: Apr 10, 2020)

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Parameter, n (%)	200mg (N=6)	300mg (N=12)	250mg (N=12)	Total (N=30)
DLT Evaluable patients	3	7*	6	15
DLTs	0	1#	0	1
TEAEs	6 (100)	12 (100)	12 (100)	30 (100)
Treatment-related TEAEs	6 (100)	12 (100)	12 (100)	30 (100)
TEAEs ≥G3	2 (33.3)	8 (66.7)	3 (25.0)	13 (43.3)
Treatment-related TEAEs≥G3	1 (16.7)	7 (58.3)	3 (25.0)	11 (36.7)
SAEs	1 (16.7)	5 (41.7)	1 (8.3)	7 (23.3)
Fatal SAEs	0 (0)	1& (8.3)	0 (0)	1(3.3)
Dose modifications	5 (83.3)	7 (58.3)	4 (33.3)	16 (53.3)
SUR or TOR dose interruptions due to TEAEs	5 (83.3)	7 (58.3)	3 (25.0)	15 (50.0)
SUR dose reductions due to TEAEs	0 (0)	0 (0)	1 (8.3)	1 (3.3)
Discontinuation of SUR or TOR due to TEAEs	0 (0)	0 (0)	0 (0)	0 (0)

* One non-evaluable DLT patient was terminated treatment early for PD within DLT observation period. &: One fatal SAE is multi-organ failure due to disease progression.

 # DLT: G3 Hyperthyroidism

- SUR related TEAEs of ≥grade 3 (≥5%): transaminase elevation, bilirubin elevation, fatigue, blood pressure increased and vomit
- TOR related TEAEs of ≥grade 3 (≥5%): transaminase elevation, bilirubin elevation, creatine kinase increased
- Immune related TEAEs of all grade (>10%): transaminase elevation, bilirubin elevation, creatine kinase increased, thyroid function abnormal, blood amylase increased

Less severe and occurrence of TEAEs in 250 mg group than in 300 mg group

Summary of Efficacy Results (Data cut-off: Apr 10, 2020)

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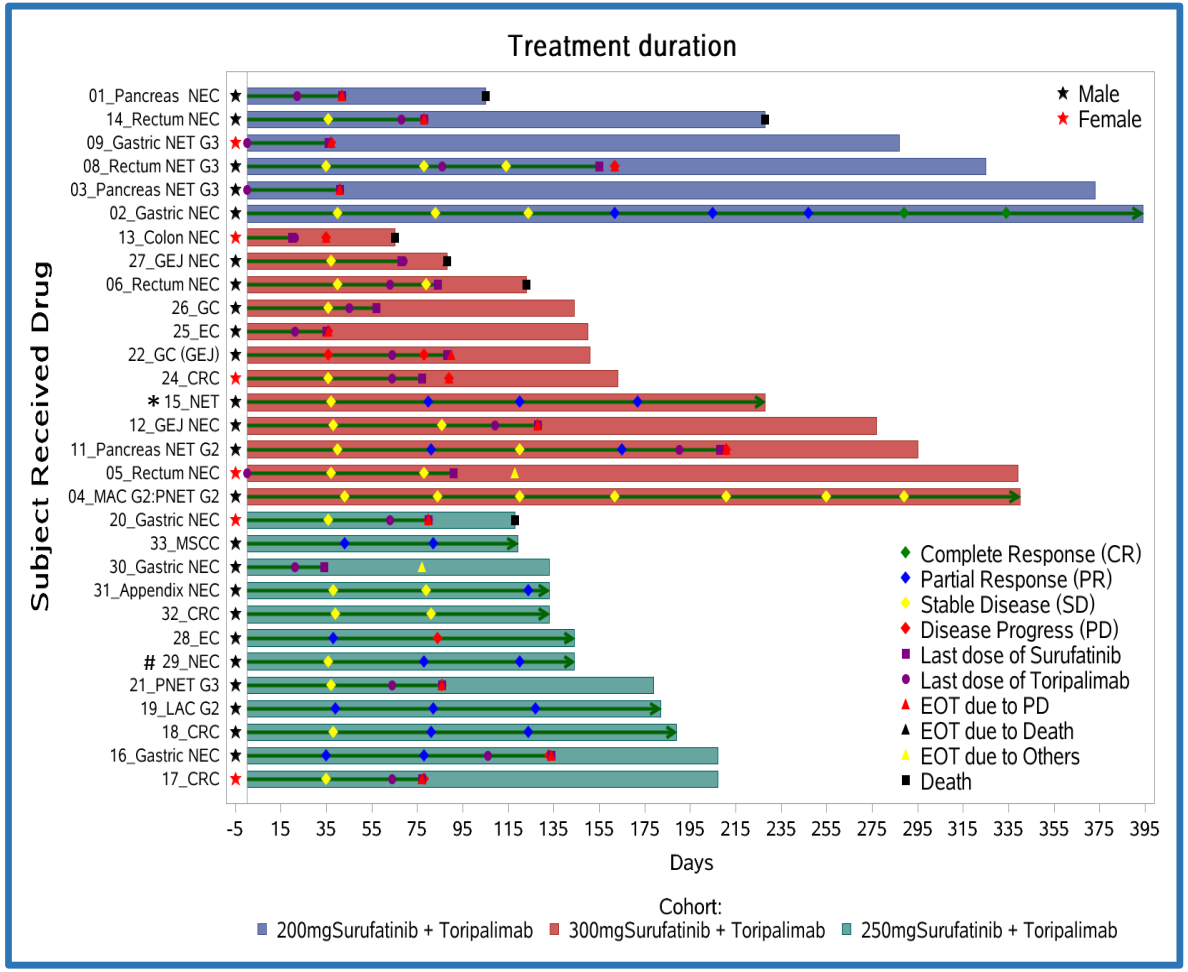

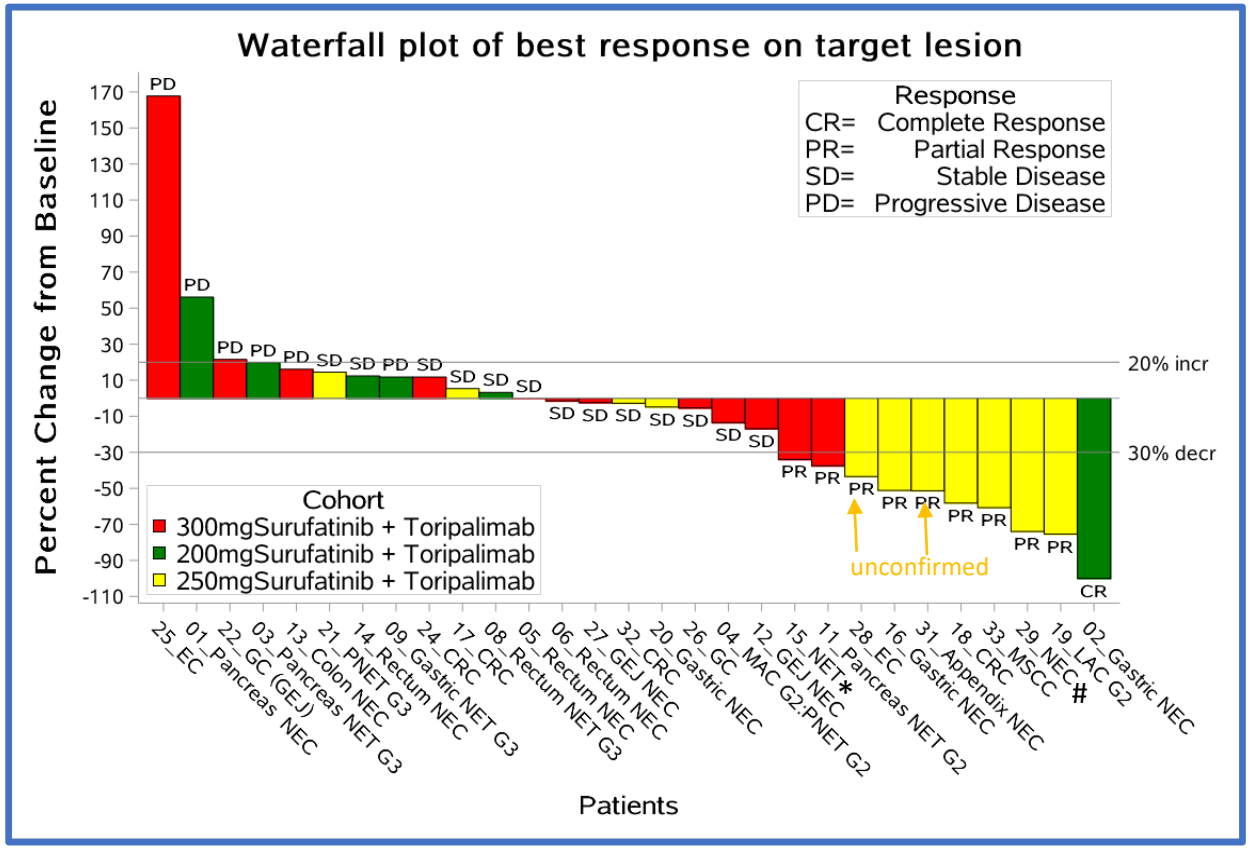

- 29 patients: DCR 79.3%, ORR: 34.5% (1 pt without tumor assessment)
  - 200 mg: DCR 50%, ORR 16.7%
  - 300 mg: DCR 75%, ORR 16.7%
  - 250 mg: DCR 100%, ORR: 63.6% (2 PR not confirmed: 1 missing medication due to COVID-19 followed by PD, 1 newly evaluated and waiting for confirmation)
- 30% (10/30) patients' treatment are ongoing

NET: neuroendocrine tumor; NEC: neuroendocrine carcinoma; CRC: colorectal carcinoma; GC: gastric adenocarcinoma; EC: esophageal squamous cell carcinoma; GEJ: gastroesophageal junction; MAC G2:PNET G2: mediastinal atypical carcinoid G2: Pancreas NET G2; MSCC: metastatic squamous cell carcinoma with unknown primary; LAC: Lung atypical carcinoid; *: Left supraclavicular lymph node neuroendocrine tumor; #: merkel cell carcinoma

Better clinical efficacies were achieved in 250 mg group than in other two groups, especially in neuroendocrine neoplasms

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Hutchison Medi Pharma

Key conclusions from this study:

- Surufatinib plus toripalimab were **well tolerated** with **no unexpected safety signals** observed
- **Surufatinib 250 mg/Day** is recommended for Phase II combination study
- Surufatinib plus toripalimab showed **encouraging antitumor activity** in patients with advanced solid tumor, especially in **NENs** patients. The phase II trial (NCT04169672) has been initiated

Many thanks to patients and their family!

Thanks to Hutchison MediPharma and JunShi Biology

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