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WORLD CONGRESS ON Gastrointestinal Cancer

Safety and Efficacy Results from an Open-label, Multicentre, Phase I/II Study of Avapritinib in Chinese Patients with Gastrointestinal Stromal Tumor (GIST): A Bridging Study of NAVIGATOR

Prof. Jian Li, MD, PhD
Beijing Cancer Hospital, Beijing, China

Jian Li[1], Xinhua Zhang[2], Shirong Cai [2], Yanhong Deng[3], Xin Wu[4], Zhichao Zheng[5], Yongjian Zhou[6], Yanqiao Zhang[7], Jun Zhang[8], Kaixiong Tao[9], Yuehong Cui[10], Hui Cao[11], Kuntang Shen[12], Jiren Yu[13], Ye Zhou[14], Wenxiao Ren[15], Wanqi Zhao[15], Jin Hu[15], Didi Jin[15], Jianxin Yang[15], Lin Shen[1]

[1]Beijing Cancer Hospital, Beijing, China; [2]The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [3]The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; [4]Chinese PLA General Hospital, Beijing, China; [5]Liaoning Cancer Hospital & institute, Shenyang, China; [6]Fujian Medical University Union Hospital, Fuzhou, China; [7]Harbin Medical University Cancer Hospital, Harbin, China; [8]The First Affiliated Hospital of Chongqing Medical University; [9]Wuhan Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China; [10]Fudan University Zhongshan Hospital, Shanghai, China; [11]Renji Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China; [12]Fudan University Zhongshan Hospital, Shanghai, China; [13]The First Affiliated Hospital, ZheJiang University, Hangzhou, China; [14]Fudan University Shanghai Cancer Center, Shanghai, China; [15]CStone Pharmaceuticals (Suzhou), Suzhou, China

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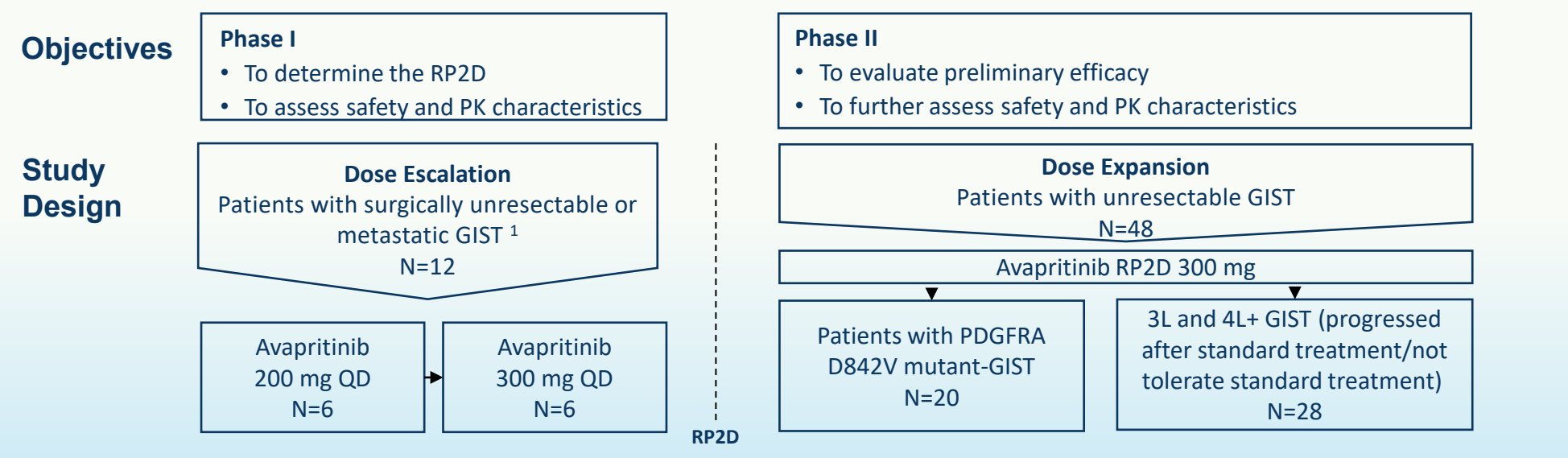
Disclosures

Prof. Jian Li:

- Honoraria as a speaker for Amoy Diagnositics, Boehringer Ingelheim, CStone Pharmaceuticals, Eli Lily China, Hengrui Medicine, Innovent Biologics, Luye Pharma, MSD, Qilu Pharmaceutical, Roche, Sanofi and TopAlliance Biosciences;
- Advisor role with Hengrui Medicine, Innovent Biologics, Qilu Pharmaceutical and TopAlliance Biosciences

Background and Study Design

- Avapritinib (BLU-285) is a potent and selective small-molecule inhibitor that targets KIT exon 17 and PDGFRA exon 18 mutations via a type 1 inhibition mechanism
- NAVIGATOR (BLU-285-1101) is an open-label, phase I study to evaluate avapritinib in the treatment of unresectable GIST
- This presentation will report data from CS3007-101/BLU-285-1105 study, which is a bridging study of NAVIGATOR in China, and these data are updated safety and efficacy results from a longer follow-up in Chinese GIST patients
- In March 2021, the China health authority has approved avapritinib for the treatment of adult patients with unresectable or metastatic GIST harbouring a PDGFRA exon 18 mutation, including PDGFRA D842V mutations, making it the first approved precision therapy for this population in China



GIST: gastrointestinal stromal tumor; PK: pharmacokinetics; QD: once daily; RP2D: recommended phase 2 dose

[1] Progression after treatment with imatinib and at least one kind of the other tyrosine kinase inhibitors (TKI), or intolerance of standard treatment, lack of standard treatment, or presence of a D842V mutation in the PDGFRA gene

Data cut-off date: 31 July 2020

Baseline Characteristics

- As of 31 Jul 2020, a total of 60 patients were treated, 6 received avapritinib 200 mg QD, 54 received avapritinib 300 mg QD
- 40 patients were still on treatment, 10 patients discontinued the treatment due to death, 9 due to disease progression and 1 due to adverse event

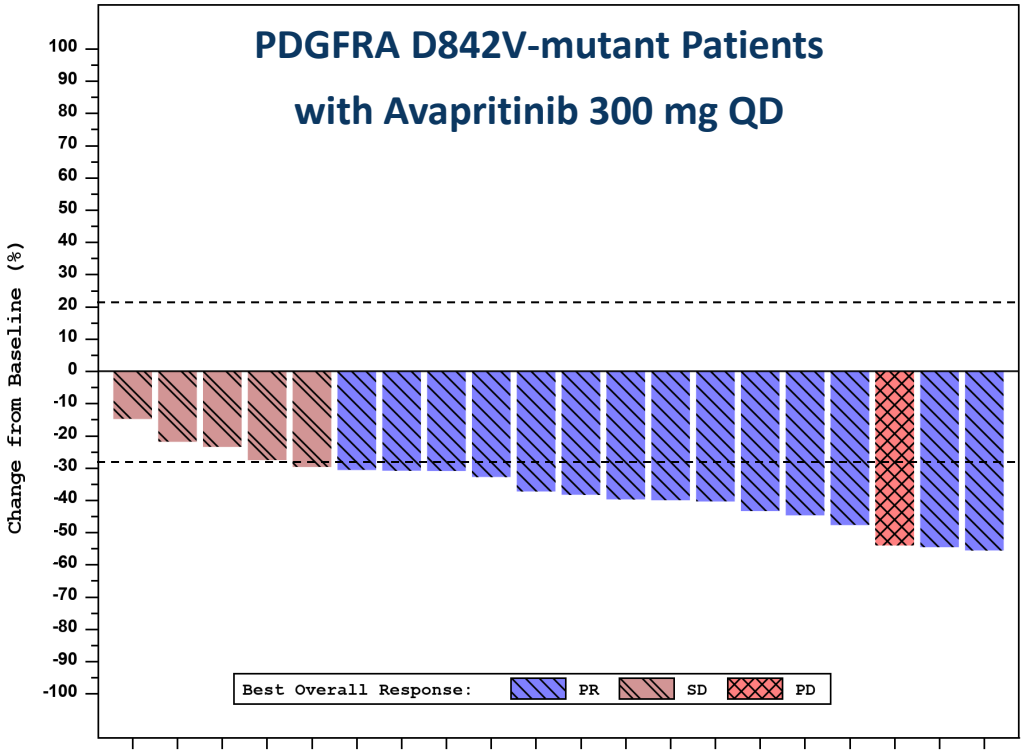
	Avapritinib Starting Dose		
	200 mg	300 mg	Total
	N=6	N=54	N=60
Median age (range), years	60 (45-68)	63 (43-70)	63 (43-70)
Male, n (%)	6 (100)	35 (65)	41 (68)
ECOG PS 1	5 (83)	40 (74)	45 (75)
Cancer stage at screening (TNM), Stage IV, n (%)	6 (100)	52 (96)	58 (97)
Metastases diagnosed, Y, n (%)	6 (100)	53 (98)	59 (98)
Time since initial diagnosis (years), Mean (min, max)	6 (2, 10)	6 (0, 16)	6 (0, 16)
Number of previous TKIs, n (%)			
0	0	7 (13)	7 (12)
1	0	10 (19)	10 (17)
2	1 (17)	14 (26)	15 (25)
3	4 (67)	18 (33)	22 (37)
4+	1 (17)	5 (9)	6 (10)
Prior cancer-related Surgery/Procedure, n (%)	6 (100)	53 (98)	59 (98)

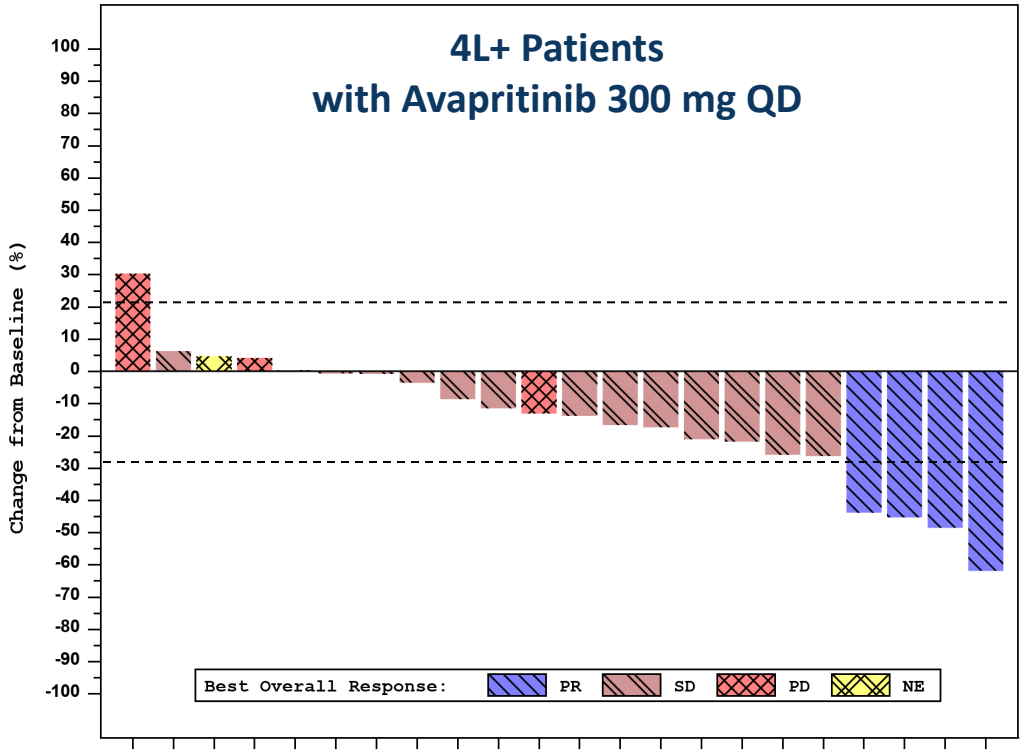
ECOG: Eastern Cooperative Oncology Group; PS: performance status; QD: once daily; TKI: tyrosine kinase inhibitor; TNM: tumor, node, metastasis
Data cut-off date: 31 July 2020

Efficacy Results

IRRC assessed Best Overall Response[1]

- A total of 20 patients in the PDGFRA D842V group and 23 patients in the 4L+ group were evaluable
- 14 patients achieved PR (ORR 70%; 95% CI 46%–88%) in PDGFRA D842V group, median PFS were not reached
- 4 patients achieved PR (ORR 17%; 95 CI 5%-39%) in 4L+ group, median PFS for 4L+ patients were 5.6 months
- The clinical benefit rate (CBR[2]) was 16 (80%) in PDGFRA D842V group, and 12 (52%) in 4L+ group





CI: confidence incidence; CR: complete response; IRRC: independent radiology review committee; ORR: objective response rate; PFS: progression free survival; PR: partial response; QD: once daily; SD: stable disease
One 4L+ GIST patient was classified as not applicable due to no post-baseline response assessment, thus was not shown in the waterfall plot

[1] assessed according to mRECIST v1.1

[2] CBR is defined as the proportion of patients with CR/PR or SD lasting ≥ 4 cycles from the start of treatment

Data cut-off date: 31 July 2020

Safety Results

Most Common TEAEs and AEs of Special Interest

Most common AEs (any cause and grade) in ≥ 20% of patients, n (%)	Avapritinib Starting Dose		
	200 mg N=6	300 mg N=54	200/300 mg N=60
Number of patients with at least one event	**6 (100)**	**54 (100)**	**60 (100)**
Anaemia	5 (83)	47 (87)	52 (87)
Blood bilirubin increased	5 (83)	43 (80)	48 (80)
White blood cell count decreased	5 (83)	29 (54)	34 (57)
Blood creatine phosphokinase increased	6 (100)	23 (43)	29 (48)
Aspartate aminotransferase increased	4 (67)	23 (43)	27 (45)
Face oedema	1 (17)	25 (46)	26 (43)
Eyelid oedema	6 (100)	19 (35)	25 (42)
Neutrophil count decreased	2 (33)	19 (35)	21 (35)
Hair colour changes	1 (17)	18 (33)	19 (32)
Hypokalaemia	2 (33)	15 (28)	17 (28)
Oedema peripheral	5 (83)	12 (22)	17 (28)
Periorbital oedema	0	16 (30)	16 (27)
Hypocalcaemia	3 (50)	12 (22)	15 (25)
Nausea	0	13 (24)	13 (22)
Alanine aminotransferase increased	2 (33)	10 (19)	12 (20)
Hypophosphataemia	1 (17)	11 (20)	12 (20)

AESI (any cause and grade), n (%)	Avapritinib Starting Dose		
	200 mg N=6	300 mg N=54	200/300 mg N=60
Number of patients with at least one event	**0**	**6 (11)**	**6 (10)**
Cognitive effects	0	6 (11)	6 (10)
Memory impairment	0	4 (7)	4 (7)
Cognitive disorder	0	2 (4)	2 (3)
Confusional state	0	0	0
Encephalopathy	0	0	0
Intracranial bleeding	0	0	0

- The median treatment duration was 25 (range: 2-49) weeks for the total safety population
- 59 (98%) patient reported treatment-related AEs, with the most common reported being anaemia (45, 75%)
- 41 (68%) patients had Grade ≥3 treatment-related AEs
- 41 (68%) patients reported AEs leading to drug interruption
- 11 (18%) patient reported AEs leading to death (mostly were disease progression, 7, 12%)
- A total of 6 (10%) patients experienced AESI, they all reported cognitive effects

AE: adverse event; AESI: adverse event of special interest; TEAE: treatment emergent adverse event
Data cut-off date: 31 July 2020

Conclusions

- Avapritinib as a precise target therapy provided promising clinical benefit in Chinese patients with PDGFRA D842V-mutant GIST, a GIST subtype that has a low response rate and poor clinical outcome when treated with other available kinase inhibitors
    - The IRRC-assessed ORR was 70%, CBR was 80%, median PFS was not reached
    - A substantial proportion of patients experienced significant tumor shrinkage
- Avapritinib has moderate clinical activity in fourth- and later-line (4L+) treatment of Chinese patients with GIST, making it a potential new treatment option for these population
    - The IRRC-assessed ORR was 17%; CBR was 52%; median PFS was 5.6 months
- Avapritinib demonstrated a tolerable safety profile in Chinese patients with GIST, consistent with the results seen in the global study

GIST: gastrointestinal stromal tumor; IRRC: independent radiology review committee; ORR: objective response rate; CBR: clinical benefit rate; PFS: progression free survival

Acknowledgement

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