Abstract: 670P

Preliminary Efficacy and Safety of Tinengotinib (TT-00420) Monotherapy in Chinese Patients (pts) with Advanced Solid Tumors: Results from a Phase Ib/II Study

Panpan Zhang[1], MD; Jifang Gong[1], MD; Hongqian Guo[2], MD; Weiqing Han[3], MD; Zuoxing Niu[4], MD; Baoshan Cao[5], MD; Jian Zhang[6], MD; Ying Cheng[7], MD; Chaohong He[8], MD; Jean Fan[9], MD; Peng Peng[10], PhD; Caixia Sun[10], MD, PhD; Hui Wang[10], MS; Yingying Yu[10], MS; Yujia Zhu[10], MS; Yingtong Wu[10]; Qing Li[10]; Peng Huang[10]; Frank Wu[10], PhD; Lin Shen[1], MD, PhD
Beijing Cancer Hospital[1], Beijing, China; Nanjing Drum Tower hospital[2], Nanjing, China; Hunan Cancer Hospital[3], Changsha, China; Shandong Cancer Hospital[4], Jinan, China; Peking University Third Hospital[5], Beijing, China; Fudan University Shanghai Cancer Center[6], Shanghai, China; Jilin Cancer Hospital[7], Changchun, China; Henan Cancer Hospital[8], Zhengzhou, China; TransThera Sciences (US), Inc.[9], MD, USA; TransThera Sciences (Nanjing), Inc.[10] Nanjing, China.

INTRODUCTION

- Tinengotinib is a spectrum-selective multi-kinase inhibitor that targets cell proliferation, angiogenesis, and immune-oncology pathways by inhibiting Aurora kinases A/B, Janus kinases (JAK), and receptor tyrosine kinases (FGFRs, VEGFRs).
- Tinengotinib has shown promising efficacy in prostate cancer (PC), hormone receptor positive (HR+) human epidermal growth factor receptor 2 negative (HER2-) breast cancer (BC), triple-negative BC (TNBC) and cholangiocarcinoma (CCA) from several studies globally.
- NCT05253053 is a Phase Ib/II study assessing tinengotinib monotherapy or in combination with PD-L1/chemotherapy in patients with advanced/metastatic solid tumors. Here we present the interim data from monotherapy arm.

METHODS

Patients

- ≥18 years of age,
- advanced/metastatic solid tumors who have no available standard therapeutic treatment options,
- At least one measurable lesion as defined by RECIST V1.1 criteria,
- ECOG of 0~2,
- Adequate organ function

Arm A	Arm B		Arm C	
Tinengotinib Monotherapy	Tinengotinib + Atezolizumab Combination Therapy		Tinengotinib + Nab-paclitaxel Combination Therapy	
Phase Ib 8/10/12 mg, all-comer	**Phase II** 10 mg, specific tumor types	**Phase Ib** 8/10/12 mg, Biliary Tract Carcinoma	**Phase II** RP2D, Biliary Tract Carcinoma	**Phase Ib** 8/10/12 mg, HER2-BC	**Phase II** RP2D, HER2-BC

Tinengotinib tablet orally administered continuously in 21-day cycles

Objectives

- Safety and tolerability per CTCAE V5.0
- Preliminary efficacy per RECIST V1.1 (Arm A and Arm C), imRECIST (Arm B), PCWG3 (only for PC in Arm A)
- Clinical PK analyses
- Biomarker(s)

The interim data from monotherapy arm（Arm A）will be presented in the poster.

RESULTS

- As of September 8, 2023, 50 patients with solid tumors were enrolled and treated in monotherapy (Arm A). Based on the preliminary efficacy observed in the subjects with FGFR-altered CCA, metastatic castration-resistant prostate cancer (mCRPC), Pan-FGFR-altered advanced solid tumors (ASTs) in Arm A Ph Ib and several studies globally, the Ph II cohorts for FGFR-altered CCA, mCRPC, Pan-FGFR-altered ASTs have been opened for enrollment in Arm A.

Table 1. Baseline subject demographics and clinical characteristics

Characteristic Statistic	Phase I 8 mg AST (n = 3)	Phase I 10 mg AST (n = 3)	Phase I 12 mg AST (n = 3)	Phase II 10 mg CCA (n = 12)	Phase II 10 mg mCRPC (n = 19)	Phase II 10 mg Pan-FGFR (n = 10)	Total (N = 50)
Age (years)							
n	3	3	3	12	19	10	50
Mean (SD)	57.7 (8.51)	54.7 (13.20)	60.0 (14.73)	53.3 (15.16)	65.7 (8.20)	56.5 (13.73)	59.8 (12.47)
Median	58.0	52.0	68.0	54.0	67.5	58.0	64.0
Min, Max	49, 66	43, 69	43, 69	29, 76	52, 81	29, 71	29, 81
Sex, n (%)							
Male	2 (66.7)	2 (66.7)	2 (66.7)	4 (33.3)	19 (100)	3 (30.0)	32 (64.0)
Female	1 (33.3)	1 (33.3)	1 (33.3)	8 (66.7)	0	7 (70.0)	18 (36.0)
ECOG, n(%)							
0	0	0	1 (33.3)	5 (41.7)	1 (5.3)	2 (20.0)	9 (18.0)
1	3 (100)	3 (100)	2 (66.7)	7 (58.3)	18 (94.7)	8 (80.0)	41 (82.0)
Tumor Type, n(%)							
Bile ducts	2 (66.7)	0	0	12 (100)	0	0	14 (28.0)
Prostate	0	0	0	0	19 (100)	0	19 (38.0)
Lung	0	0	0	0	0	3 (30.0)	3 (6.0)
Colorectum	1 (33.3)	3 (100)	1 (33.3)	0	0	2 (20.0)	7 (14.0)
Stomach	0	0	0	0	0	3 (30.0)	3 (6.0)
Other	0	0	2 (66.7)	0	0	2 (20.0)	4 (8.0)
Prior Lines Antineoplastic Medication Therapy, n(%)							
1	1 (33.3)	1 (33.3)	0	6 (50.0)	0	2 (20.0)	10 (20.0)
2	1 (33.3)	1 (33.3)	0	2 (16.7)	3 (15.8)	2 (20.0)	9 (18.0)
≥3	1 (33.3)	1 (33.3)	3 (100)	4 (33.3)	16 (84.2)	6 (60.0)	31 (62.0)

Efficacy

- Among 39 efficacy-evaluable pts treated with tinengotinib monotherapy, the median follow up was 8.20 months (range 1.1-15.8). The median Progression-free survival (PFS) have reached 5.65 (95% CI, 4.17-8.54) months.
- For 31 efficacy-evaluable pts with measurable target lesions,
  - the objective response rate (ORR) and the disease control rate (DCR) were 19.4% (6/31) and 83.9% (26/31), respectively. Partial responses were observed in 6 pts with CCA, PC and urothelial carcinoma.
  - among all CCA pts (8 pts with FGFR alteration, 4 pts with FGFR wild type), ORR was 33.3% (4/12), DCR was 83.3% (10/12).
  - for 4 CCA pts who harbored FGFR2 fusion, ORR was 75%, DCR was 100%. Two responders with prior FGFR inhibitor treatments achieved tumor reduction of 44% and 32%. Another responder with no prior FGFR inhibitor treatment achieved 81% reduction.

Figure 1. Waterfall plot for the best percentage change of target lesion per RECIST v1.1 (N=31)

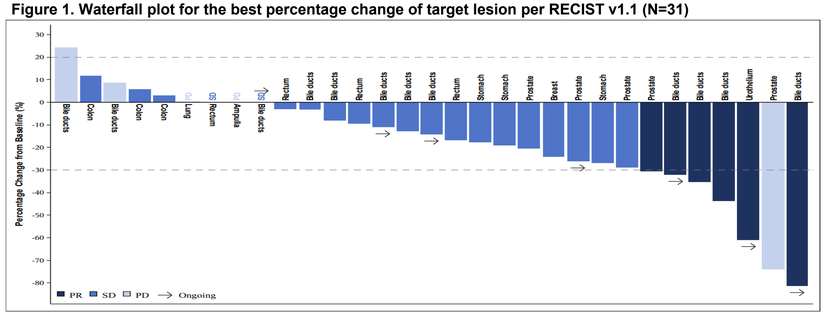


Figure 2. Waterfall plot for the best percentage change of target lesion per RECIST v1.1 for CCA (N=12)

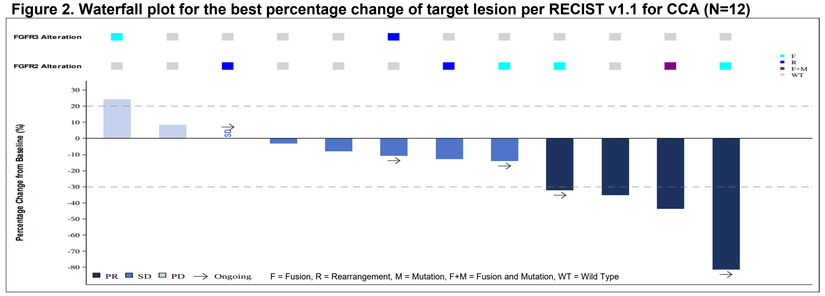
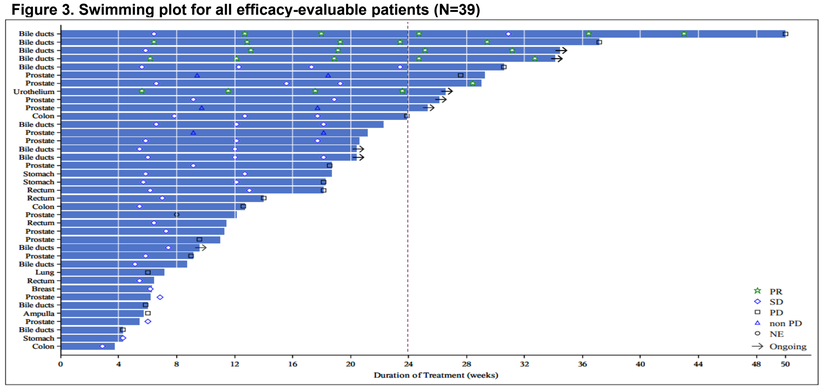


Figure 3. Swimming plot for all efficacy-evaluable patients (N=39)



Safety

- Tinengotinib treatment-related AEs (TRAEs) in monotherapy arms were reported in 49/50 (98.0%) pts. 20/50 (40.0%) were Grade (G) 1-2, 28/50 (56.0%) were G3, 1/50 (2.0%) were G4 (renal failure), no G5 TRAE reported; the most common ≥G3 TRAEs (≥5%) were hypertension, white blood cell count decreased, anaemia, neutrophil count decreased, platelet count decreased, proteinuria and palmar-plantar erythrodysesthesia syndrome.

Table 2. Tinengotinib Treatment related adverse events

	Total (N = 50)
Number of Subjects with at least one TRAE	49 (98.0%)
CTCAE Grade 1	4 (8.0%)
CTCAE Grade 2	16 (32.0%)
CTCAE Grade 3	28 (56.0%)
CTCAE Grade 4	1 (2.0%)
CTCAE Grade 5	0
Most Common ≥CTCAE Grade 3 TRAEs (≥5%)	
Hypertension	9 (18.0%)
White blood cell count decreased	5 (10.0%)
Anaemia	5 (10.0%)
Neutrophil count decreased	4 (8.0%)
Platelet count decreased	3 (6.0%)
Proteinuria	3 (6.0%)
Palmar-plantar erythrodysaesthesia syndrome	3 (6.0%)

CONCLUSION

- Tinengotinib monotherapy was well-tolerated and safety-manageable in Chinese pts and 10 mg QD was selected as RP2D.
- Encouraging efficacy of tinengotinib monotherapy was observed in pts with heavily pre-treated solid tumors, especially in CCA pts harboring FGFR2 alteration with prior treatment of FGFR targeted therapy.
- Breakthrough Therapy designation was granted for tinengotinib in CCA indication in China.
- A phase II and a phase III pivotal study are initiated to further evaluate the efficacy and safety of tinengotinib in patients with FGFR2-altered refractory/relapsed CCA in China (CTR20232860) and globally (NCT05948475).

Presenting Author: Jean Fan, MD

- Employment: TransThera Sciences (US), Inc. TransThera Sciences (Nanjing), Inc.
- Leadership: TransThera Sciences (US), Inc. TransThera Sciences (Nanjing), Inc.
- Stock and Other Ownership Interests: AstraZeneca
- Email: fan_jean@transtherabio.com

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