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7MO Oritinib (SH-1028) a third-generation EGFR tyrosine kinase inhibitor in locally advanced or metastatic NSCLC patients with positive EGFR T790M: Results of a single-arm phase II trial

C. Zhou¹, A. Xiong¹, J. Zhao², W. Li³, M. Bi³, J. Chen⁴, K. Li⁴, L. Miao⁵, Y. Mao⁶, D. Wang⁷, C. Liu⁸, A. Zeng⁹, R. Li¹⁰, Y. Pan¹¹, Y. Hu¹², X. Zhang¹³, H. Niu¹⁴, Y. Du¹⁵, Y. Sun¹⁶, Z. Liu¹⁷

¹Shanghai Pulmonary Hospital, Shanghai, China; ²Xuzhou Central Hospital, Xuzhou, China; ³The First Affiliated Hospital of Bengbu Medical College, Bengbu, China; ⁴Hunan Cancer Hospital, Changsha, China; ⁵Nanjing Drum Tower Hospital, Nanjing, China; ⁶The First Affiliated Hospital of Henan University of Science and Technology, Luoyang, China; ⁷Chongqing University Cancer Hospital, Chongqing, China; ⁸Center Hospital Affiliated to Xinjiang Medical University, Wulumuqi, China; ⁹Guangxi Medical University Affiliated Tumor Hospital, Nanning, China; ¹⁰Baoding NO.2 Central Hospital, Baoding, China; ¹¹The First Affiliated Hospital of University of Sciences and Technology of China, Hefei, China; ¹²Hubei Cancer Hospital, Wuhan, China; ¹³Nantong Tumor Hospital, Nantong, China; ¹⁴The First Affiliated Hospital of Xixiang Medical College, Xixiang, China; ¹⁵The First Affiliated Hospital of Anhui Medical University, Hefei, China; ¹⁶Jinan Central Hospital Affiliated to Shandong University, Jinan, China; ¹⁷Jiangxi Cancer Hospital, Nanchang, China

Background: Oritinib (SH-1028) is a third-generation EGFR-TKI selectively targeting both sensitive EGFR and EGFR T790M mutations. Herein, we report the efficacy and safety of oritinib in EGFR T790M-positive advanced NSCLC patients from the phase II study (NCT03823807).

Methods: Eligible patients were locally advanced or metastatic NSCLC patients aged ≥ 18 years, with centrally confirmed EGFR T790M mutation. Patients with asymptomatic, stable CNS metastases were eligible into the study. Oritinib 200 mg was given orally once daily until disease progression or unacceptable toxicity. Primary efficacy endpoint was objective response rate (ORR). Secondary efficacy endpoints included disease control rate (DCR), progression-free survival (PFS), duration of response (DOR) and overall survival (OS).

Results: Between December 2019 and March 2021, 228 patients were enrolled and 227 patients received at least one dose of oritinib. The median age of 227 patients was 62 years old, 57.3% of patients were female and 24.7% received systemic chemotherapies. At data cutoff (September 17, 2021), 137 of 227 patients achieved confirmed partial responses with ORR of 60.4% (95% CI: 42.4%, 68.8%) by IRaC. The DCR was 92.5% (88.3%, 95.6%), the mPFS was 12.6 months (95% CI: 9.7, 15.3), the mDOR was 12.5 months (95% CI: 11.2, NA) and the mOS was immature. The most common ($\geq 10\%$) treatment-emergent adverse events (TEAEs) included diarrhea (45.4%), increased blood creatine phosphokinase (26.0%), anaemia (20.3%), decreased white blood cell count (15.4%), decreased appetite (15.0%), increased blood creatine phosphokinase isoenzyme (13.2%), nausea (13.2%), vomiting (13.2%), increased serum creatine (12.8%), upper respiratory tract infection (12.3%), increased aspartate aminotransferase (11.9%), cough (11.9%), decreased platelet count (11.0%), constipation (10.6%). Grade ≥ 3 TEAEs included increased blood creatine phosphokinase (4.0%), hypertension (3.1%), death (2.6%), diarrhea (2.2%). No interstitial lung disease were reported.

Conclusions: Oritinib demonstrated potential clinical benefit and tolerable in advanced NSCLC patients with EGFR T790M mutation.

Clinical trial identification: NCT03823807; January 30, 2019.

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8MO The efficacy and safety of TQ-B3101 monotherapy in the first-line treatment in patients with ROS1-positive non-small cell lung cancer

S. Lu¹, H. Pan², L. Wu³, Y. Yao⁴, J. He⁵, Y. Wang⁶, X. Wang⁷, X. Wang⁸, X. Cai⁹, Y. Yu¹⁰, Z. Ma¹¹, X. Min¹², Z. Yang¹³, L. Cao¹⁴, H. Yang¹⁵, Y. Shu¹⁶, W. Zhuang¹⁷, S. Cang¹⁸, J. Fang¹⁹, K. Li²⁰

¹Medical Oncology Department, Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; ²Sir Run Run Shaw Hospital, Zhejiang University, Zhejiang, China; ³Hunan Provincial Tumor Hospital, Changsha, China; ⁴The First Affiliated Hospital of Xi'an Jiaotong University, Xian, China; ⁵The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; ⁶Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China; ⁷Qilu Hospital of Shandong University, Jinan, China; ⁸The First Affiliated Hospital/School of Clinical Medicine of Guangdong Pharmaceutical University, Guangzhou, China; ⁹Sun Yat-sen University Cancer Center, Guangzhou, China; ¹⁰Harbin Medical University Cancer Hospital, Harbin, China; ¹¹Henan Tumor Hospital, Zhengzhou, China; ¹²Anhui Chest Hospital, Hefei, China; ¹³Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; ¹⁴The First Affiliated Hospital of the University of Science and Technology of China, Hefei, China; ¹⁵Xiangya Hospital Central South University, Changsha, China; ¹⁶Department of Oncology, Jiangsu Province People's Hospital, Nanjing, China; ¹⁷Fujian Cancer Hospital and Fujian Medical University Cancer Hospital, Fuzhou, China; ¹⁸Henan Provincial People's Hospital, Zhengzhou, China; ¹⁹Peking University Cancer Hospital, Beijing, China; ²⁰Tianjin Medical University Cancer Institute and Hospital, Tianjin, China

Background: TQ-B3101 is a novel small molecule receptor tyrosine kinase inhibitor, which targets to ALK, ROS1 and MET. Preclinical studies showed that it had a good tumor inhibition activity and duration. This study aims to evaluate the efficacy and safety of TQ-B3101 monotherapy in the first-line treatment in patients with ROS1-positive non-small cell lung cancer (NSCLC).

Methods: This is a multicenter, single arm phase II trial (NCT03972189). ROS1 positive locally advanced or metastatic NSCLC patients with ROS1-TKI treatment naïve were enrolled. TQ-B3101 was orally administered at dose of 300 mg BID in a 28-day cycle, until disease progression or intolerable toxicity. The primary endpoint was independent review committee (IRC) assessed objective response rate (ORR). The secondary endpoints included IRC assessed disease control rate (DCR), duration of response (DoR), progression-free survival (PFS), overall survival (OS), intracranial ORR/DoR, intracranial time to progress and safety.

Results: As of October 15, 2021, 111 patients had received TQ-B3101 therapy (median age 52 yrs, 61.3% female, 71.2% ECOG PS 1, 92.8% stage IV, 29.7% with brain metastasis), with a median follow up of 12.1 months. 1 patient achieved complete response and 86 patients achieved partial response with ORR assessed by IRC of 78.4% (95% CI, 69.6%-85.6%) and DCR of 87.4% (95% CI, 79.7% - 92.9%). The median PFS assessed by IRC was 15.6 months (95% CI, 10.2 - 27.0) and median DoR was 20.3 (95% CI, 11.0 - 26.1). Median OS has not been reached and the 12- and 24-month OS rate were 98.1% and 88.1% respectively. Treatment related adverse events (TRAEs) occurred in 99.1% of patients (≥ 3 TRAEs occurred in 45.1%). Treatment-related SAEs occurred in 3.6% of patients, and only 2 (1.8%) patients had treatment discontinuation due to TRAEs. Most common TRAEs were AST increased (73.9%), ALT increased (72.1%), emesis (63.1%), neutrophils count decrease (56.8%), leukocyte count decrease (52.3%), sinus bradycardia (52.3%), and diarrhea (43.2%).

Conclusions: For the first-line treatment of ROS1-positive locally advanced or metastatic NSCLC patients, TQ-B3101 showed the promising efficacy with a manageable safety profile, offering a new first-line therapeutic strategy.

Clinical trial identification: NCT03972189.

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