Time to response (TTR) and depth of response (DpR) in non-squamous non-small cell lung cancer (nsq-NSCLC) patients (pts) treated with tislelizumab (TIS) plus chemotherapy (chemo) as first line therapy: an exploratory analysis of RATIONALE 304

Shun Lu[1], Xinmin Yu[2], Yanping Hu[3], Zhiyong Ma[4], Xingya Li[5], Weidong Li[6], Yunpeng Liu[7], Dong Wang[8], Xiuwen Wang[9], Zhehai Wang[10], Jingxun Wu[11], Diansheng Zhong[12], Gaofeng Li[13], Wanyu He[14], Yuanyuan Bao[15], Yuan Yuan[15], Jinghui Fan[14], Fangfang Bu[14]

[1]Shanghai Chest Hospital, Shanghai Jiao Tong University, Shanghai, China; [2]Zhejiang Cancer Hospital, Hangzhou, China;[3]Hubei Cancer Hospital, Wuhan, China; [4]Henan Cancer Hospital, Zhengzhou University, Zhengzhou, China; [5]The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [6]Cancer Center of Guangzhou Medical University, Guangzhou, China; [7]The First Hospital of China Medical University, Shenyang, China; [8]Daping Hospital, Third Military Medical University, Chongqing, China; [9]Qilu Hospital of Shandong University, Jinan, China; [10]Shandong Cancer Hospital, Jinan, China; [11]The First Affiliated Hospital of Xiamen University, Xiamen, China; [12]Tianjin Medical University General Hospital, Tianjin, China; [13]Yunnan Cancer Hospital, Kunming, China; [14]BeiGene (Beijing) Co., Ltd., Beijing, China; [15]BeiGene (Shanghai) Co., Ltd., Shanghai, China

Background: Primary results from Phase 3 RATIONALE 304 study (NCT03663205) showed efficacy and manageable safety/tolerability for TIS, an anti-PD-1 monoclonal antibody, plus chemo, as 1L treatment for locally advanced or metastatic nsq-NSCLC [1]. This exploratory analysis aims to characterize the profile of TTR and DpR in responders treated with TIS plus chemo from RATIONALE 304.

Methods: Eligible pts with histologically confirmed stage IIIB or IV nsq-NSCLC were randomized 2:1 to receive TIS plus platinum and pemetrexed for 4–6 cycles followed by maintenance TIS plus pemetrexed, or platinum and pemetrexed for 4–6 cycles followed by maintenance pemetrexed. Tumor assessments were scheduled every 6 weeks for the first 6 months, then every 9 weeks through the remaining 6 months of year 1 and every 12 weeks thereafter. TTR, DpR and safety were assessed in responders (pts who achieved complete or partial response per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1) per Independent Review Committee (IRC). TTR was defined as the time from randomization to the first occurrence of a CR or PR per RECIST v1.1. DpR was defined as the percentage of maximal tumor reduction from the baseline of target lesion sum of diameters.

Results: As of 23 January 2020, 128 pts (57.4% in ITT population) treated with TIS plus chemo achieved response (CR, 7 pts; PR, 121 pts) per IRC with a median TTR of 7.9 weeks (range: 5.1 - 33.3) and a median duration of response of 8.5 months (95% CI: 6.80 - 10.58). Initial detection of response (CR or PR) was achieved in 50.8% (n=65) of the 128 responders at the first post-

baseline tumor assessment (week 6), 31.3 % (n=40) at the second tumor assessment (week 12), 9.4% (n=12) at the third assessment (week 18), 4.7% (n=6) at the fourth assessment (week 24), and 3.9% (n=5) at the fifth assessment (week 33). DpR with tumor shrinkage of ≥ 70% to ≤ 100%, ≥ 50 to < 70%, and ≥ 30 to< 50% was observed in 26.6% (n=34), 28.1% (n=36) and 45.3% (n=58) of responders, respectively; and the median PFS (95% CI) was not reached (NR; 11.76, NR), 11.5 months (7.72, NR), and 9.0 months (7.66, 9.86), respectively. The profile of TTR and DpR of responders treated with chemo alone is summarized in the Table. The safety profile of responders treated with TIS plus chemo was generally consistent with that of the overall safety population. Grade ≥3 TEAE occurred in 68.0% of responders (67.6% in the overall safety population); immune-mediated adverse events occurred in 27.3% of the responders (25.7% in the overall safety population).

Conclusion: 82% of responders with nsq-NSCLC treated with TIS plus chemo achieve response within the first two tumor assessments (12 weeks), while still 18% of responders achieve response at later assessments (18-33 weeks). Responders treated with TIS plus chemo with deeper tumor response have a trend of longer PFS.

Table. TTR and DpR in nsq-NSCLC pts treated with TIS plus chemo and chemo alone.

	TIS plus chemo		**Chemo**	
	Responders (n=128)	**ITT (n=223)**	**Responders (n=41)**	**ITT (n=111)**
Pts who achieved response at each assessment, n (%)				
First tumor assessment (week 6)	65 (50.8)	65 (29.1)	18 (43.9) [a]	18 (16.2) [a]
Second tumor assessment (week 12)	40 (31.3) [b]	40 (17.9) [b]	15 (36.6) [c]	15 (13.5) [c]
Third tumor assessment (week 18)	12 (9.4)	12 (5.4)	3 (7.3)	3 (2.7)
Fourth tumor assessment (week 24)	6 (4.7)	6 (2.7)	5 (12.2)	5 (4.5)
Fifth tumor assessment (week 33)	5 (3.9)	5 (2.2)	0 (0.0)	0 (0.0)
DpR, n (%)				
≥ 30% to < 50%	58 (45.3)	58 (26.0)	20 (48.8)	20 (18.0)
≥ 50% to < 70%	36 (28.1)	36 (16.1)	17 (41.5)	17 (15.3)
≥ 70% to≤ 100%	34 (26.6)	34 (15.2)	4 (9.8)	4 (3.6)

[a] One patient only had one tumor assessment which was unscheduled with TTR of 63 days (week 9).

[b] One patient had the first tumor assessment (week 6) as non-response, and the first response was per unscheduled tumor assessment afterwards with TTR of 56 days (week 8).

[c] One patient had the first tumor response (week 6) as non-response, and the first response was per end of treatment tumor assessment afterwards with TTR of 80 days (week 11.4).

Reference:

[1]. Lu, S., et al., J Thorac Oncol, 2021. 16(9): p. 1512-1522.