

RATIONALE-315 (R315): Clinical Outcomes by Adjuvant (Adj) Treatment (Tx) Cycles in Perioperative (Periop) Tislelizumab (TIS) Plus Chemotherapy (CT) in Resectable NSCLC

Authors

Ernest Nadal,¹ Gustavo Schvartsman,² Dongsheng Yue,³ Jun Chen,⁴ Alona Zer,⁵ Julian Kretz,⁶ Kirsha Naicker,⁷ Na Zhao,⁸ Mesha Austin Taylor,⁹ Sun Min Lim,¹⁰ Peter Brossart,¹¹ Hua Zhong,¹² Qiang Pu,¹³ Changli Wang³

Affiliations

¹Catalan Institute of Oncology (ICO), IDIBELL, l'Hospitalet de Llobregat, Barcelona, Spain;

²Hospital Israelita Albert Einstein, São Paulo, Brazil; ³Tianjin Medical University Cancer Institute and Hospital, Tianjin, China; ⁴Tianjin Lung Cancer Institute, Tianjin Medical University General Hospital, Tianjin, China; ⁵Bruce and Ruth Rappaport Cancer Research Center, Rambam Medical Center, Haifa, Israel; ⁶BeOne Medicines, Ltd, Basel, Switzerland; ⁷BeOne Medicines, Ltd, London, UK; ⁸BeOne Medicines, Ltd, Shanghai, China; ⁹BeOne Medicines, Ltd, Cambridge, MA, USA; ¹⁰Yonsei University College of Medicine, Yonsei Cancer Center, Seoul, Republic of Korea; ¹¹Universitätsklinikum Bonn, Bonn, Germany; ¹²Shanghai Chest Hospital, Shanghai, China; ¹³West China Hospital, Sichuan University, Chengdu, China

Background

In R315 (NCT04379635), periop TIS + neoadjuvant (neoadj) CT significantly improved OS and event-free survival (EFS) vs placebo (PBO) + neoadj CT in patients (pts) with resectable NSCLC. More adj immunotherapy cycles after neoadj TIS + CT may improve outcomes in resectable NSCLC, yet the optimal number of cycles is undefined. We evaluated efficacy and safety of <8 vs 8 cycles of adj TIS vs adj PBO in R315.

Methods

Pts with untreated stage II-IIIa NSCLC were randomized (1:1) to neoadj TIS + CT or PBO + neoadj CT, then surgery and adj TIS or PBO. Pts with 1-8 cycles, ≈1 year, of adj tx were included. EFS was analyzed by completion of 8 vs <8 adj cycles. Landmark EFS analysis was performed at the end of adj tx to mitigate immortal time bias.

Results

As of 7 March 2025, 168 pts received adj TIS and 147 adj PBO. In pts with <8/8 cycles, respectively, 95.6/89.7% were male, 61.5/61.2% former smokers, 49.5/42.0% PD-L1 tumor proportion score <1%, 38.5/42.0% stage II, and 61.5/56.7% stage IIIA. Adj tx was not received in 9.7% TIS pts vs 11.5% PBO (4.4% vs 5.7% pt withdrawal; 3.1% vs 1.8% AE; 1.8% vs 3.1% physician decision; 0.4% vs 0.9% progressive disease [PD]). Adj tx was discontinued in 23.5% TIS pts vs 16.7% PBO (9.3% vs 14.1% PD; 6.6% vs 1.8% AE; 4.0% vs 0.9% pt withdrawal; 3.5% vs 0% physician decision).

Pts completing <8 vs 8 cycles of adj TIS had improved EFS vs PBO; pts completing 8 cycles had improved EFS vs <8, regardless of pCR status or disease stage (**table**). Grade ≥ 3 (11.3% and 6.1%) and serious (11.3% and 4.3%) tx-related AE (TRAE) incidence was higher for <8 vs 8 cycles, respectively, and generally low in both groups; TRAEs leading to tx discontinuation (17.0% and 0%) were more frequent with <8 cycles.

Conclusions

Periop TIS + CT was associated with improved EFS vs neoadj CT alone, with a manageable safety profile in R315. Outcomes appeared more favorable with a higher number of completed adj cycles; these exploratory findings should be validated prospectively.

	3-year EFS rate, % (95% CI)	
	<8 cycles n=91	8 cycles n=224
Adj TIS	n=53 36.3 (22.4-50.4)	n=115 86.0 (78.1-91.2)
Adj PBO	n=38 3.5 (0.3-15.2)	n=109 72.5 (62.9-80.1)
Landmark, adj TIS	n=37 40.3 (18.7-61.1)	n=109 81.1 (65.1-90.3)
Landmark, adj PBO	n=27 6.3 (0.4-24.3)	n=99 68.0 (53.9-78.7)
Landmark HR, adj TIS vs adj PBO	0.16 (0.07-0.34)	0.48 (0.25-0.92)
pCR, adj TIS	n=19 58.5 (31.6-77.9)	n=66 92.3 (82.5-96.7)
Non-PCR, adj TIS	n=34 22.3 (8.5-40.0)	n=49 77.4 (62.9-86.8)

Stage II, adj TIS	n=19 45.7 (19.1-69.0)	n=47 87.2 (73.7-94.0)
Stage IIIA, adj TIS	n=34 31.9 (16.6-48.3)	n=66 84.7 (73.4-91.5)
Median (range) follow-up was 41.5 (10.0-56.3) months. HR, hazard ratio; pCR, pathologic complete response.		