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1262P Randomized, open-label phase III study of pembrolizumab (pembro) vs docetaxel (doce) in patients (pts) with previously treated NSCLC with PD-L1 tumour proportion score (TPS) ≥1%: KEYNOTE-033

C. Zhou[1], J. Feng[2], S. Ma[3], H. Chen[4], Z. Ma[5], C. Huang[6], L. Zhang[7], J. He[8], C. Wang[9], J. Zhou[10], P. Danchaivijtr[11], H-C. Huang[12], I.O. Vynnychenko[13], K. Wang[14], F. Orlandi[15], V. Sriuranpong[16], B. Li[17], J. Ge[18], T. Dang[19]

[1]Department of Medical Oncology, Shanghai Pulmonary Hospital, Shanghai, China; [2]Oncology, Jiangsu Cancer Hospital, Nanjing, China; [3]Oncology, Hangzhou First People's Hospital, Zhejiang, China; [4]Oncology, Guangdong Provincial People's Hospital, Guangdong, China; [5]Medical Oncology, Henan Cancer Hospital, Zhengzhou, China; [6]Oncology, Fujian Provincial Cancer Hospital, Fuzhou, China; [7]Oncology, Sun Yat-sen University, Guangzhou, China; [8]Thoracic surgery, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; [9]Medical Oncology, Tianjin Medical University Cancer Institute & Hospital, Tianjin, China; [10]Medical Oncology, The First Affiliated Hospital of Zhejiang University, Hangzhou, China; [11]Medical Oncology, Siriraj Piyamaharajkarun Hospital, Bangkok, Thailand; [12]Medical Oncology, Chang Gung Medical Foundation, Taoyuan, Taiwan; [13]Medical Oncology, Sumy State University, Sumy, Ukraine; [14]Medical Oncology, The Second Affiliated Hospital of Zhejiang University College of Medicine, Hangzhou, China; [15]Medical Oncology, Orlandi Oncologia, Region Metropolitana De Santiago, Chile; [16]Medical Oncology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand; [17]Oncology, MSD China, Beijing, China; [18]Oncology, MSD China, Shanghai, China; [19]Oncology, Merck & Co., Inc., Kenilworth, NJ, USA

Background: In KEYNOTE-010, pembro improved OS vs doce as 2L+ therapy for advanced NSCLC with PD-L1 TPS ≥1% and ≥50%. KEYNOTE-010 did not enroll any pts from mainland China, which has high NSCLC mortality. KEYNOTE-033 (NCT02864394) evaluates pembro vs doce in pts with previously treated advanced NSCLC with PD-L1 TPS ≥1%, with most pts enrolled in mainland China.

Methods: Eligible pts (≥18 y) were randomized to pembro 2 mg/kg Q3W (35 cycles) or doce 75 mg/m^2 Q3W (per local standard of care), stratified by TPS (≥50% vs 1–49%). Response was assessed Q9W per RECIST v1.1 by BICR. PD-L1 expression was assessed centrally (PD-L1 IHC 22C3 pharmDx assay). OS and PFS (primary objectives) were evaluated sequentially using stratified log-rank tests, first in pts with TPS ≥50% and then in pts with TPS ≥1% (1-sided α=0.025).

Results: 425 pts were enrolled. At data cutoff (Sep 9, 2019), median follow-up was 18.8 (range, 0.2-38.8) mo, and 291 (68%) pts had died. Pembro numerically improved OS in all groups analyzed, but did not achieve predefined statistical significance in pts with PD-L1 TPS ≥50% (Table); thus, sequential testing of OS and PFS ceased. HR for OS in TPS ≥1% pts from mainland China (n=311) was 0.68 (95% CI, 0.51–0.89). In all treated pts, incidence of treatment-related AEs was lower with pembro vs doce (any grade, 70% vs 88%; grade 3-5, 11% vs 47%).

Table: 1262P

		Pembro	Doce
PD-L1 TPS ≥50%		N=114	N=113
OS	Median (95% CI), mo HR (95% CI) *P*	12.3 (10.0-16.3) 0.83 (0.61-1.14) 0.1276	10.9 (8.3-13.1)
PFS	Median (95% CI), mo HR (95% CI)	4.0 (2.1-8.0) 0.76 (0.54-1.07)	2.5 (2.1-4.2)
ORR	% (95% CI)	28.1 (20.1-37.3)	7.1 (3.1-13.5)
PD-L1 TPS ≥1%		N=213	N=212
OS	Median (95% CI), mo HR (95% CI)	12.9 (10.3-16.5) 0.75 (0.60-0.95)	10.6 (8.7-12.5)
PFS	Median (95% CI), mo HR (95% CI)	3.3 (2.1-4.1) 0.84 (0.66-1.08)	3.0 (2.3-4.0)
ORR	% (95% CI)	20.7 (15.4-26.7)	5.7 (3.0-9.7)

Conclusions: While pembro did not meet statistical significance for OS in pts with PD-L1 TPS ≥50%, HRs for OS and PFS numerically favored pembro and ORR was higher with pembro in both the PD-L1 TPS ≥50% and ≥1% groups. Toxicity was consistent with the established pembro safety profile. These data support the value of pembro for previously treated advanced NSCLC in China.

Clinical trial identification: NCT02864394.

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1263P Tislelizumab + chemotherapy vs chemotherapy alone as first-line treatment for locally advanced/metastatic nonsquamous NSCLC

S. Lu[1], Y. Yu[2], X. Yu[3], Y. Hu[4], Z. Ma[5], X. Li[6], W. Zhuang[7], Y. Liu[8], W. Li[9], J. Cui[10], D. Wang[11], W. Liao[12], M. Wang[13], J. Zhou[14], Z. Wang[15], Y. Sun[16], J. Gao[17], Y. Bao[18], L. Liang[19], J. Wang[20]

[1]Medical Oncology, Shanghai Chest Hospital, Shanghai, China; [2]The 3rd Department of Thoracic Oncology, Affiliated Tumor Hospital of Harbin Medical University, Harbin, China; [3]Medical Oncology, Zhejiang Cancer Hospital, Hangzhou, China; [4]Oncology, Hubei Cancer Hospital, Wuhan, China; [5]The Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China; [6]Oncology, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China; [7]Medical Oncology, Fujian Cancer Hospital, Fuzhou, China; [8]Medical Oncology, The First Hospital of China Medical University, Shenyang, China; [9]Medical Oncology, Cancer Center of Guangzhou Medical University, Guangzhou, China; [10]Cancer Center, The First Hospital of Jilin University, Changchun, China; [11]Third Military Medical University, Daping Hospital, Chongqing, China; [12]Oncology, Nanfang Hospital of Southern Medical University, Guangzhou, China; [13]Medical Oncology, Peking Union Medical College Hospital, Beijing, China; [14]Medical Oncology, The First Affiliated Hospital of Zhejiang University, Hangzhou, China; [15]Department of Internal Medicine-Oncology, Shandong Cancer Hospital, Jinan, China; [16]Oncology, Jinan Central Hospital, Jinan, China; [17]Clinical Development, BeiGene (Beijing) Co., Ltd., Beijing, China; [18]Biostatistics, BeiGene (Beijing) Co., Ltd., Beijing, China; [19]Clinical Biomarker, BeiGene (Beijing) Co., Ltd., Beijing, China; [20]Department of Internal Medicine, Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China

Background: Tislelizumab + chemotherapy has shown antitumor activity with a favorable tolerability profile in patients (pts) with histologically confirmed nsq-NSCLC.

Methods: In this open-label phase 3 study (NCT03663205), Chinese pts were randomized 2:1 to receive tislelizumab 200 mg + platinum (carboplatin AUC 5 or cisplatin 75 mg/m^2) + pemetrexed 500 mg/m^2, followed by maintenance tislelizumab + pemetrexed (*Arm A*); pts in *Arm B* received platinum + pemetrexed and maintenance pemetrexed. Patients with known *EGFR* mutations or *ALK* rearrangement were ineligible. Patients were stratified by disease stage (IIIB vs IV) and tumor cell PD-L1 expression (<1% vs 1-49% vs ≥50%) assessed using the Ventana PD-L1 (SP263) Assay. Platinum was administered for 4-6 cycles at investigator's discretion; crossover to tislelizumab was allowed. Treatment beyond progression was allowed for tislelizumab. The primary endpoint, progression-free survival per RECIST v1.1, was assessed by Independent Review Committee (PFS_{IRC}); key secondary endpoints included overall survival (OS), objective response rate (ORR_{IRC}), duration of response (DoR_{IRC}), and safety/tolerability.

Results: As of 23 Jan 2020, 334 pts with nsq-NSCLC (*A*, n=223; *B*, n=111) were randomized; median study follow-up was 9.8 mo (95% CI: 9.23,10.38). PFS_{IRC} was significantly longer with tislelizumab combination therapy than chemotherapy alone (*P*=0.0044; HR=0.645 [95% CI: 0.462, 0.902]; median PFS_{IRC}, 9.7 mo vs 7.6 mo). ORR_{IRC} was 57% (95% CI: 50.6, 64.0) and 37% (95% CI: 28.0, 46.6) in *Arms A* and *B*, respectively. Median DoR in *Arm A* was 8.5 mo (95% CI: 6.80, 10.58) and 6.0 mo (95% CI: 4.99, NE) in *Arm B*. A total of 221 pts (99.5%) had a treatment-related AE (TRAE) in *Arm A*; 185 pts (83%) had AEs related to tislelizumab. Of 140 pts (63%) with grade ≥3 TRAEs, 69 (31%) were considered related to tislelizumab by the investigator. In *Arm B*, 107 pts (97%) experienced ≥1 TRAE, of which 50 (46%) were grade ≥3. Across the entire study, four pts (1%) had fatal pneumonitis; 3 of which were considered possibly related to tislelizumab.

Conclusions: Tislelizumab plus chemotherapy was generally well tolerated and demonstrated antitumor activity in pts with nsq-NSCLC.

Clinical trial identification: NCT03663205.

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