

532P KEYNOTE-189 study of pembrolizumab (pembro) plus pemetrexed (pem) and platinum vs placebo plus pem and platinum for untreated, metastatic, nonsquamous NSCLC: Does choice of platinum affect outcomes?

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Background: In KEYNOTE-189 (NCT02578680), pembro plus pem and platinum provided superior OS (HR 0.49, $P < 0.00001$) and PFS (HR 0.52, $P < 0.00001$) and had manageable safety vs placebo plus pem and platinum as first-line therapy for metastatic nonsquamous NSCLC. In an exploratory analysis, we assessed outcomes by investigator's choice of carboplatin (carbo) or cisplatin (cis).

Methods: 616 patients (pts) with untreated metastatic nonsquamous NSCLC regardless of PD-L1 TPS without sensitizing EGFR or ALK alteration were randomized 2:1 to 4 Q3W cycles of pembro 200 mg or placebo + pem 500 mg/m² + carbo AUC 5 or cis 75 mg/m² followed by maintenance pembro or placebo + pem. Randomization was stratified by TPS ($<1\%$ vs $\geq 1\%$), platinum (carbo vs cis), and smoking status (current/former vs never). Primary end points were OS and PFS; ORR and safety were secondary.

Results: Carbo was chosen for 72% of pts in both arms. OS, PFS, and ORR were improved in the pembro plus pem and platinum arm in both carbo and cis recipients (Table). In the pembro vs placebo arm, 83% vs 72% received 4 carbo doses and 81% vs 79% received 4 cis doses. 76% vs 65% and 78% vs 72%, respectively, received ≥ 5 pem doses. Grade 3-5 AE rates for pembro vs placebo were 70% vs 66% with carbo and 59% vs 65% with cis. Rates of the most common any-grade AEs were generally similar for carbo and cis: nausea 54% with pembro vs 48% with placebo for carbo and 60% vs 63% for cis, anemia 45% vs 48% and 50% vs 44%, and fatigue 44% vs 43% and 33% vs 26%. Rates of acute kidney injury in the pembro arm were 5.1% with carbo and 5.4% with cis.

Table: 532P

	Carbo		Cis	
	Pembro + Chemo N = 297	Placebo + Chemo N = 148	Pembro + Chemo N = 113	Placebo + Chemo N = 58
OS, median (95% CI), mo	NR (NR-NR)	11.3 (8.0-NR)	NR (NR-NR)	10.8 (8.1-NR)
HR (95% CI)	0.52 (0.39-0.71)		0.41 (0.24-0.69)	
PFS, median (95% CI), mo	8.6 (7.1-9.2)	4.9 (4.6-5.6)	9.2 (6.9-11.1)	4.8 (4.7-6.0)
HR (95% CI)	0.55 (0.44-0.70)		0.44 (0.30-0.65)	
ORR, % (95% CI)	47 (41-53)	18 (12-25)	49 (39-58)	21 (11-33)

Conclusions: Pembro plus pem and platinum improved efficacy and was generally tolerable compared with placebo plus pem and platinum regardless of the chosen platinum. These data support the use of both carbo and cis in combination with pembro and pem as first-line therapy for metastatic nonsquamous NSCLC.

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