Aim: We report interim data from a phase 1 study of nivolumab (N), a fully human IgG4 programmed death-1 (PD-1) immune checkpoint inhibitor antibody, combined with PT-DC or ERL in advanced chemotherapy-naive NSCLC patients (pts).

Methods: Pts (n = 56) were assigned by histology to receive N 10 mg/kg IV Q3W + concurrent IV gemcitabine 1250 mg/m² + cisplatin 75 mg/m² (squamous [sq]) or pemetrexed 500 mg/m² + cisplatin 75 mg/m² (non-sq), or N 5 or 10 mg/kg IV Q3W + IV paclitaxel 200 mg/m² + carboplatin AUC6 (sq + non-sq). N + PT-DC was given for 4 cycles, with continued N to progression/unacceptable toxicity. EGFR mutant (EGFR MT) NSCLC pts (n = 21) received N 3 mg/kg IV Q2W + ERL 150 mg PO daily until progression/unacceptable toxicity. Objective response rate (ORR) was assessed by RECIST 1.1.

Results: Across N + PT-DC arms (median follow-up [mF/U] 75 wks), grade 3–4 related AEs occurred in 45% of pts (25–73% across arms); 4 pts (7%) had grade 3–4 pneumonitis; 0–33% discontinued due to related AEs, any-grade pneumonitis (7%) most common. ORR with N + PT-DC was 33–47%; PD as best overall response (BOR) was infrequent (7%). Progression-free survival (PFS) rate at wk 24 was 38–71%; 1-yr OS rate was 50–87%. With N + ERL (mF/U 72 wks), grade 3–4 related AEs occurred in 5 pts; no pneumonitis was observed. Related AEs led to discontinuation in 4 pts (grade 3 AST 1, grade 3 diarrhea, grade 2 nephritis, grade 2 flushing). ORR was 19% (median duration of response [DOR] not reached; range 60.1, 72.3+ wks); 24-wk PFS rate was 51%. Three of 20 pts (15%) with acquired ERL resistance achieved PR (DOR 60.1, 64.6+, 70+ wks; 2 ongoing); 9/20 pts had BOR of SD, with 3/9 not progressed (time to progression/death 9.9+–53 wks); 1 pt had an ongoing unconventional response. One pt was EGFR TKI naïve and achieved PR (DOR 72.3+ wks; ongoing).

Conclusions: N + PT-DC demonstrated acceptable antitumor activity and safety reflecting additive nivolumab and PT-DC toxicities in pts with advanced NSCLC. N + ERL may provide durable clinical benefit and an acceptable safety profile in TKI-refractory, EGFR MT pts. These data support further evaluation of nivolumab combination regimens in pts with advanced NSCLC.

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