1386PD **IMpower150: Clinical safety, tolerability and immune-related adverse events in a phase III study of atezolizumab (atezo) + chemotherapy (chemo) ± bevacizumab (bev) vs chemo + bev in 1L nonsquamous NSCLC**

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Background: Atezo (anti–PD-L1) + bev + chemo prolonged PFS and OS vs bev + chemo in patients (pts) with 1L nonsquamous NSCLC in the randomized Phase III IMpower150 study. This combination was well tolerated and its safety profile was consistent with known safety risks. This study further evaluates safety, tolerability and immune-related AEs by treatment phase.

Table: 1386PD Immune-related AEs by treatment phase in arms B and C of IMpower150

Incidence, n (%)	Induction Phase[a]				Maintenance Phase[b]			
	Arm B: atezo + bev + CP (n = 393)		Arm C: bev + CP (n = 394)		Arm B: atezo + bev + CP (n = 312)		Arm C: bev + CP (n = 270)	
	All Grade	Grade 3-4	All Grade	Grade 3-4	All Grade	Grade 3-4	All Grade	Grade 3-4
AEs of special interest, including immune-related AEs[c]	131 (33.3)	30 (7.6)	85 (21.6)	12 (3.0)	116 (37.2)	20 (6.4)	35 (13.0)	1 (0.4)
Immune-related AEs[c] in ≥ 5 patients in any arm across treatment phases, n (%)								
Rash	81 (20.6)	9 (2.3)	46 (11.7)	2 (0.5)	48 (15.4)	0	9 (3.3)	0
Hepatitis Lab abnormalities	31 (7.9) 27 (6.9)	12 (3.1) 10 (2.5)	17 (4.3) 17 (4.3)	3 (0.8) 3 (0.8)	27 (8.7) 25 (8.0)	8 (2.6) 8 (2.6)	14 (5.2) 14 (5.2)	0 0
Hypothyroidism	17 (4.3)	1 (0.3)	10 (2.5)	0	41 (13.1)	0	8 (3.0)	0
Pneumonitis	6 (1.5)	3 (0.8)	4 (1.0)	1 (0.3)	6 (1.9)	2 (0.6)	1 (0.4)	1 (0.4)
Hyperthyroidism	8 (2.0)	1 (0.3)	2 (0.5)	0	9 (2.9)	0	3 (1.1)	0
Colitis	4 (1.0)	1 (0.3)	2 (0.5)	2 (0.5)	6 (1.9)	5 (1.6)	0	0

[a]Adverse events with an onset on or after the first study drug treatment and up to 1 day before the date of the first dose of the maintenance therapy.
[b]Adverse events with an onset on or after the first dose of the maintenance therapy and up to the data cutoff date. The denominator for the maintenance/follow up phase is adjusted to patients who received at least 1 dose of study treatment during the maintenance phase.
[c]Immune-related AEs were defined using MedDRA Preferred Terms that included both diagnosed immune conditions and signs/symptoms potentially representative of immune-related events, regardless of investigator-assessed causality.

Methods: Pts received atezo 1200 mg + bev 15 mg/kg + carboplatin (C) AUC 6 + paclitaxel (P) 200 mg/m^2 (Arm B) vs bev + CP (Arm C) IV q3w for 4 or 6 cycles per investigator decision, then maintenance atezo + bev or bev, respectively. AE incidence and severity in the induction and maintenance/follow-up phases were reported. Data cutoff: January 22, 2018.

Results: In the induction phase, 380/393 pts (97%) in Arm B and 389/394 pts (99%) in Arm C had an AE; 54% and 52% had Gr3-4, 4% and 3% had Gr5, and 29% and 27% had serious AEs, respectively. In the maintenance phase, 289/312 pts (93%) in Arm B and 219/270 pts (81%) in Arm C had an AE; 37% and 23% had Gr3-4, 3% had Gr5 in both arms, and 26% and 13% had serious AEs, respectively. 30% and 16% of pts received bev > 12 mo in Arms B and C. 36% of pts in Arm B received atezo > 12 mo. The incidence of AEs leading to all study treatment withdrawal in the induction phase was 6% and 5% in Arms B and C; chemo only withdrawal was 6% and 5% in Arms B and C. The incidence of AEs leading to bev withdrawal was 13% in both phases in Arm B and 11% and 9% in the induction and maintenance phases in Arm C; atezo withdrawal was 8% in Arm B in both phases. The incidence of immune-related AEs by treatment phase are shown in the table.

Conclusions: Atezo + bev + CP demonstrated a tolerable safety profile, with the majority of AEs occurring in the induction phase; most immune-related AEs observed were low grade. Incidence of AEs leading to treatment withdrawal were similar between arms, and withdrawal due to atezo or bev were similar across treatment phases.

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