Immune-related adverse events with PD-1 vs PD-L1 inhibitors: a meta-analysis of 8730 patients from clinical trials

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A trial-level meta-analysis investigating potential differences in immune-related adverse events reported in phase I-IV trials of anti–PD-1 (nivolumab and pembrolizumab) and anti–PD-L1 antibodies (atezolizumab, avelumab, durvalumab)

Data analyzed from 8730 patients treated with anti–PD-1/PD-L1 monotherapy

Meta-analysis explored 5 anti-PD-1 and PD-L1 antibodies that have been administered to the highest numbers of patients in clinical trials: atezolizumab, avelumab, durvalumab, nivolumab and pembrolizumab

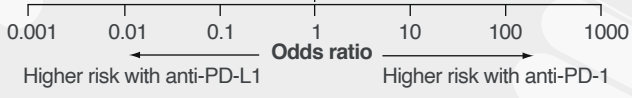
Anti-PD-1 antibodies: nivolumab and pembrolizumab

Anti-PD-L1 antibodies: atezolizumab, avelumab and durvalumab

For anti–PD-L1 vs anti–PD-1 antibodies, we identified trends for a lower risk of rash: any-grade and grade ≥3, colitis: any-grade and grade ≥3, elevated ALT: any-grade, hypothyroidism: grade ≥3.

Number of events/ total number of patients, n/N

		Anti-PD-L1	Anti-PD-1	Odds ratio (95% CI)
Rash	Any grade	141/4510	171/1797	4.34 (2.25–8.39)
	Grade ≥3	5/3174	12/1510	4.38 (1.62–11.82)
Pneumonitis	Any grade	110/4786	103/3497	1.74 (0.71–4.26)
	Grade ≥3	31/3450	25/2820	1.10 (0.49–2.46)
Hypothyroidism	Any grade	179/3270	280/3536	1.44 (0.86–2.41)
	Grade ≥3	5/2960	7/2776	2.85 (1.15–7.04)
Elevated AST	Any grade	54/3725	43/1351	2.63 (0.71–9.82)
	Grade ≥3	13/2699	18/1351	2.31 (0.52–10.26)
Elevated ALT	Any grade	9/1543	32/1116	4.64 (1.36–15.83)
	Grade ≥3	2/517	13/1116	2.31 (0.45–11.84)
Colitis	Any grade	31/3094	56/2933	2.53 (1.29–4.95)
	Grade ≥3	9/3094	31/2562	3.79 (1.92–7.51)
All irAEs	Any grade	618/4200	493/2307	1.44 (0.87–2.40)
	Grade ≥3	90/3174	106/1747	1.89 (1.05–3.41)



Incidence and odds ratios were calculated for irAEs overall, selected individual irAEs for individual agents, and pooled estimates for anti-PD-1 PD-L1 antibodies.

For individual agents, we found potential trends for a reduced risk of overall any-grade irAEs for atezolizumab vs pembrolizumab and grade ≥3 irAEs for avelumab vs pembrolizumab

Overall, these hypothesis-generating findings from this large meta-analysis suggest that safety profiles for irAEs may differ among individual anti–PD-1 and anti– PD-L1 antibodies

Glossary:

ALT: Alanine aminotransferase; irAE: Immune-related adverse event; PD-1: Programmed cell death 1 protein; PD-L1: Programmed cell death 1 ligand 1.