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Durvalumab + BCG therapy in BCG-naïve, high-risk NMIBC: efficacy and safety analyses from POTOMAC

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Background: Durvalumab (D) plus BCG induction (I) + maintenance (M) vs BCG (I+M) demonstrated statistically significant, clinically meaningful improvement in disease-free survival (DFS) in patients with BCG-naïve, high-risk non-muscle-invasive bladder cancer (NMIBC; POTOMAC, NCT03528694). We report in-depth efficacy and safety analyses for D+BCG (I+M) vs BCG (I+M).

Methods: Patients were randomized 1:1:1 D+BCG (I+M), D+BCG (I), or BCG (I+M). For D+BCG (I+M) vs BCG (I+M), we report time to cystectomy (TTC; secondary endpoint), post-hoc exploratory analyses of time to high-risk event, BCG-unresponsive disease, median TTC, cystectomy-free survival (CFS; time from randomization to cystectomy/death); and outcomes in patients with papillary tumours.

Results: Fewer high-risk disease events with D+BCG (I+M) (53/339) vs BCG (I+M) (69/340). Median time to high-risk event was 14.1 vs 8.3mo; 45% (24/53) vs 61% (42/69) patients had early high-risk events (≤1 year from randomization). At recurrence, 65% (24/37) vs 81% (44/54) met BCG-unresponsive criteria, respectively. TTC had HR 0.63 (95% CI 0.31–1.24) with D+BCG (I+M) vs BCG (I+M), medians not reached in either arm (ITT population); among patients who underwent cystectomy, median TTC was 19.0 vs 14.1mo. CFS favoured D+BCG (I+M) (HR 0.69; 95% CI 0.48–0.99). Efficacy in papillary subgroups is summarised (Table), and safety was consistent with the overall population.

Conclusions: Fewer early high-risk events occurred with D+BCG (I+M) vs BCG (I+M), with delayed time to high-risk events, and fewer BCG-unresponsive recurrences. TTC and CFS favoured D+BCG (I+M) vs BCG (I+M). DFS benefit observed across papillary subgroups with D+BCG (I+M). Funding: AstraZeneca.

D+BCG (I+M) vs BCG (I+M)	DFS		Overall survival	
	HR (95% CI)	Reduction in risk of disease recurrence, progression or death	HR (95% CI)	Reduction in risk of death
Any papillary tumors (91% of ITT)	0.61 (0.43–0.85)	39%	0.76 (0.49–1.16)	24%
Papillary only (64−65% of ITT)	0.56 (0.37–0.84)	44%	0.68 (0.42–1.09)	32%
Any T1 (58−62% of ITT)	0.55 (0.36–0.83)	45%	0.67 (0.39–1.14)	33%
T1 only (40−43% of ITT)	0.48 (0.28–0.79)	52%	0.52 (0.27–0.93)	48%

T1 high grade/grade 3 only (30−34% of ITT)	0.55 (0.31–0.94)	45%	0.58 (0.29–1.12)	42%

HR <1 favours D+BCG (I+M) vs BCG (I+M).