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Perioperative durvalumab with or without tremelimumab plus neoadjuvant enfortumab vedotin in muscle-invasive bladder cancer: Results from the phase 3 VOLGA trial

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Background

The standard of care continues to evolve for patients (pts) with muscle-invasive bladder cancer (MIBC). We evaluated if neoadjuvant durvalumab (D) ± tremelimumab (T) plus enfortumab vedotin (EV) followed by radical cystectomy (RC) and adjuvant D±T would be an effective option.

Methods

VOLGA (NCT04960709), a phase 3, randomised, open-label trial, enrolled pts with MIBC (cT2-T4aNO/1M0 or cT1N1M0) ineligible for or who refused treatment (tx) with cisplatin and were planned for RC. Pts were randomised 1:1:1 to D+EV, D+T+EV, or control. D+EV and D+T+EV arms: perioperative D±T (neoadjuvant: 3 cycles of D, 2 cycles of T; adjuvant: 9 cycles of D, 1 cycle of T) and 3 cycles of neoadjuvant EV; RC was completed after neoadjuvant tx. Control arm: RC and observation or locally approved adjuvant tx. Dual primary endpoints were event-free survival (EFS): D+EV vs control and D+T+EV vs control. Overall survival (OS) was the key secondary endpoint. Safety was also assessed. Here we present results from a pre-planned interim analysis (data cutoff: 02 Mar 2026).

Results

Overall, 233, 233, and 229 pts were randomised to the D+EV, D+T+EV, and control arms, respectively. RC was completed in 85% (D+EV), 79% (D+T+EV), and 78% (control) of pts; and 55% (D+EV) and 42% (D+T+EV) completed adjuvant tx. Median EFS follow-up was 22.9 mo. D+EV showed significant improvements in EFS (HR 0.51 [95% CI, 0.38–0.67], P<0.0001; 24-mo rate 64% vs 45%) and OS (HR 0.58 [95% CI, 0.40–0.83], P=0.0027; 24-mo rate 78% vs 69%) vs control. D+T+EV also showed a significant improvement in EFS vs control (HR 0.61 [95% CI, 0.47–0.80], P=0.0004; 24-mo rate 60% vs 45%) but did not meet significance for OS; follow-up is ongoing. Pathological complete response per local review was observed in 45% (95% CI, 38.6–51.7) of pts in the D+EV arm and 10% (95% CI, 6.1–14.2) in the control arm. In the D+EV and D+T+EV arms, max. Grade 3/4 tx-related adverse events occurred in 30% and 42% of pts, respectively. ctDNA results will also be presented.

Conclusions

Dual primary endpoints of EFS were met. Perioperative D plus 3 cycles of neoadjuvant EV also demonstrated a significant improvement in OS vs control. Safety profiles were consistent with those of the individual agents.

Clinical trial identification

NCT04960709; EudraCT 2023-507342-84-00.

Editorial acknowledgement

Sarah Hibbert, PhD, and Georgiana Manica, PhD, (both of Parexel International) provided medical writing and editorial assistance, funded by AstraZeneca.

Legal entity responsible for the study

AstraZeneca.

Funding

AstraZeneca.

Disclosure

T.B. Powles: Financial Interests, Personal, Advisory Board: AstraZeneca, Bristol Myers-Squibb, Exelixis, Incyte, Ipsen, Merck, Novartis, Pfizer, Seattle Genetics, Merck Serono, Astellas, Johnson & Johnson, Eisai, Roche, MSD; Financial Interests, Personal, Other, Travel/Accommodation/Expenses: Roche, Pfizer, MSD, AstraZeneca, Ipsen; Financial Interests, Personal, Other, Sponsorship for Uromigos Podcast: Mashup Ltd; Financial Interests, Institutional, Other, honoraria: Gilead; Financial Interests, Institutional, Research Grant: AstraZeneca, Roche, Bristol Myers-Squibb, Exelixis, Ipsen, Merck, MSD, Seattle Genetics, Novartis, Pfizer, Merck Serono, Astellas, Johnson & Johnson, Eisai; Financial Interests, Institutional, Other, Honoraria: Gilead. E. 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