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European Association of Urology

Words of Wisdom

Re: ctDNA-guided Adjuvant Atezolizumab in Muscle-invasive Bladder Cancer

Powles T, Kann AG, Castellano D, et al.

N Engl J Med 2025;393:2395–408

Experts' summary:
The phase 3 IMvigor011 trial evaluated a personalized adjuvant approach for muscle-invasive bladder cancer (MIBC) by selecting treatment on the basis of postoperative circulating tumor DNA (ctDNA) positivity [1]. Among patients who underwent radical cystectomy, only those who tested ctDNA-positive were randomized to receive adjuvant atezolizumab or placebo. The study demonstrated significant improvements in both disease-free survival and overall survival for patients treated with atezolizumab, and provides the first randomized evidence that molecular residual disease (MRD) can serve as a clinically actionable biomarker in urothelial cancer. Importantly, ctDNA positivity identified a population at substantial risk of relapse, which supports its role as a strong prognostic tool. The trial builds on findings from CheckMate 274 [2] and AMBASSADOR [3] but advances the field by moving beyond clinicopathologic selection towards a truly molecularly guided strategy.

Experts' comments:
IMvigor011 represents a decisive step towards precision oncology in urothelial cancer, and establishes ctDNA as a dynamic biomarker capable not only of risk stratification but also of guiding therapeutic intervention. The trial design ensured that only patients with evidence of residual disease received adjuvant immunotherapy, with potential to reduce overtreatment and limit unnecessary toxicity, which is an important advantage over universal adjuvant strategies.

However, the operational complexity of IMvigor011 should not be underestimated. The need for personalized ctDNA assays every 6 wk for a full year, centralized molecular testing, and rapid turnaround times all pose substantial challenges. Even in leading academic institutions, sustaining this infrastructure is difficult. Moreover, only one-third of the patients enrolled became ctDNA-positive and eligible for randomization, which highlights both the specificity and the inefficiency of this approach in its current form.

For Europe, the key question is feasibility. Implementation of ctDNA-guided adjuvant therapy will require harmonized molecular platforms, validated thresholds, streamlined workflows, and integration within national health systems. Broader adoption will depend on the development of cost-effective assays and standardized reporting pipelines.

IMvigor011 proves that molecular precision can refine adjuvant therapy in MIBC. The next challenge is to ensure that such innovation becomes accessible, scalable, and equitable to transform a complex concept into a real-world clinical tool.

Conflicts of interest: The authors have nothing to disclose.

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