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LBA8

IMvigor011: A phase III trial of circulating tumour (ct)DNA-guided adjuvant atezolizumab vs placebo in muscle-invasive bladder cancer

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Background

Serial monitoring of ctDNA-based molecular residual disease after radical cystectomy in patients (pts) with high-risk muscle-invasive bladder cancer shows promise in differentiating pts who need adjuvant therapy from those who can safely avoid treatment. We report the primary analysis of the global, randomised, double-blind, phase 3 IMvigor011 trial (NCT04660344) studying ctDNA-guided atezolizumab (atezo) vs placebo in this setting.

Methods

Pts with muscle-invasive bladder cancer and no radiographic evidence of disease enrolled in surveillance within 6–24 weeks of cystectomy and underwent serial ctDNA monitoring for up to 1 year after surgery. Eligible pts who tested ctDNA+ were randomised 2:1 to atezo 1680 mg or placebo every 4 weeks for 12 cycles or up to 1 year. The primary endpoint was investigator-assessed disease-free survival (DFS). Overall survival (OS) was a secondary endpoint with alpha control. Pts who persistently tested ctDNA– received no treatment.

Results

Overall, 761 pts were enrolled in surveillance. 250 eligible pts who tested ctDNA+ were randomised (atezo, n=167; placebo, n=83). At a median follow-up of 16.1 months, pts in the atezo arm had statistically significant improvements in DFS (HR, 0.64; 95% CI: 0.47, 0.87; *P*=0.0047) and OS (HR, 0.59; 95% CI: 0.39, 0.90; *P*=0.0131) vs pts in the placebo arm (Table). 28.5% of pts who received atezo (n=165) vs 21.7% who received placebo (n=83) had Grade 3/4 adverse events (treatment-related, 7.3% vs 3.6%); 3.0% vs 2.4% had fatal adverse events (treatment-related, 1.8% vs 0%). In 357 pts who persistently tested ctDNA–, the DFS rate was 95.4% at the end of the 1-year monitoring period and 88.4% at 2 years.Table: LBA8

Randomised ctDNA+

	Atezo (n=167)	Placebo (n=83)
DFS[a]		
Events, n	112	66
Median (95% CI), months	9.9 (7.2, 12.7)	4.8 (4.1, 8.3)
Stratified HR (95% CI)[b]	0.64 (0.47, 0.87); *P*=0.0047	
12-month rate, %	44.7	29.6
OS[c]		
Events, n	60	36
Median (95% CI), months	32.8 (27.7, NE)	21.1 (14.7, NE)

	Atezo (n=167)	Placebo (n=83)
Stratified HR (95% CI)[b]	0.59 (0.39, 0.90); *P*=0.0131	
12-month rate, %	85.1	70.0

[a]Per investigator. [b]Stratification factors: nodal status, tumour stage, programmed death-ligand 1 status and time from radical cystectomy to first ctDNA+ sample. [c]Prespecified interim analysis. CI, confidence interval; HR, hazard ratio; NE, not evaluable.

Conclusions

ctDNA-guided adjuvant atezo showed statistically significant and clinically meaningful DFS and OS improvements vs placebo. The atezo safety profile was tolerable, with no new findings. Pts who persistently tested ctDNA– had low risk of recurrence.

Clinical trial identification

NCT04660344.

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Legal entity responsible for the study

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Disclosure

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