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LBA50

IMbrave152/SKYSCRAPER-14: A phase III study of first-line tiragolumab (tira) + atezolizumab (atezo) + bevacizumab (bev) vs placebo (pbo) + atezo + bev for patients (pts) with untreated locally advanced or metastatic hepatocellular carcinoma (HCC)

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Background

Atezo + bev is a standard first-line therapy for advanced HCC; however, not all pts experience clinical benefit and novel treatment options are needed. IMbrave152/SKYSCRAPER-14 (NCT05904886) is a phase 3 study evaluating the addition of tira (an anti-TIGIT antibody) to atezo + bev in pts with advanced HCC.

Methods

Eligible pts with treatment-naïve, unresectable locally advanced or metastatic HCC were randomised 1:1 to receive tira 600 mg + atezo 1200 mg + bev 15 mg/kg or pbo + atezo 1200 mg + bev 15 mg/kg via intravenous infusion every 3 weeks until loss of clinical benefit or unacceptable toxicity. Dual primary endpoints were investigator-assessed progression-free survival (INV-PFS) and overall survival (OS). Secondary endpoints included objective response rate (ORR), duration of response (DOR), and safety.

Results

As of 08 May 2025 (median follow-up: 12.5 months) 669 pts were randomised to receive tira + atezo + bev (n=331) or pbo + atezo + bev (n=338). Baseline characteristics were similar between arms. Median INV-PFS was 8.3 months for tira + atezo + bev and 8.2 months for pbo + atezo + bev (HR 0.97 [95% CI 0.80–1.17]; Table); median OS data were immature (HR 0.94 [95% CI 0.72–1.22]). ORR was 29.9% for tira + atezo + bev and 26.0% for pbo + atezo + bev. Grade 3–5 treatment-related adverse events (TRAEs) were reported in 147 pts (44.3%) in the tira + atezo + bev arm and 122 pts (36.6%) in the pbo + atezo + bev arm. Overall, safety results were similar in both treatment arms and generally consistent with previous data from IMbrave150 (Table).Table: LBA50

	IMbrave152/SKYSCRAPER-14		IMbrave150[1]
Median follow-up, months	12.5*	8.9†	
Efficacy	Tira + atezo + bev (n=331)	Pbo + atezo + bev (n=338)	Atezo + bev (n=336)
Median INV-PFS,‡ months	8.3	8.2	7.1
Stratified HR (95% CI)	0.97 (0.80–1.17)	–	
ORR,‡ %	29.9	26.0	25.6
Median DOR,‡ months	15.0	13.2	13.1§
Safety¶	Tira + atezo + bev (n=332)	Pbo + atezo + bev (n=333)	Atezo + bev (n=329)

	IMbrave152/SKYSCRAPER-14		IMbrave150[1]
Grade 3–5 TRAEs, %	44.3	36.6	37.4[§]
AEs leading to treatment withdrawal, %	17.8	12.6	15.5

*PA CCOD: 08 May 2025. †PA CCOD: 29 Aug 2019. ‡Per RECIST v1.1. §Roche, data on file. ¶Includes all patients who received ≥1 dose of study drug. [1]Finn NEJM 2020. CCOD, clinical cut-off date; CI, confidence interval; HR, hazard ratio; PA, primary analysis.

Conclusions

The IMbrave152/SKYSCRAPER-14 study did not meet its primary endpoint of INV-PFS; combining tira with atezo + bev did not show an added benefit in pts with advanced HCC. OS data are not expected to reach statistical significance. The study has been unblinded and long-term survival follow-up is ongoing.

Clinical trial identification

NCT05904886.

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Legal entity responsible for the study

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Disclosure

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