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MOIO: Interim analyses of a phase III randomized non inferiority trial assessing reduced frequency immune checkpoint inhibitors in responding patients with advanced/metastatic cancer

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Background

Immunotherapy (IO) has transformed metastatic cancer management, with durable responses and sustained target engagement beyond standard dosing intervals. MOIO assesses whether reduced IO dose-intensity preserves efficacy in responding advanced/metastatic patients (pts).

Methods

MOIO is an academic, multicentre, phase III non-inferiority trial conducted across 36 French centres. Pts with locally advanced/metastatic solid tumors in partial or complete response (CR) after 6 months of standard-dose IO were eligible (melanoma in CR excluded). Up to 646 pts were planned to be randomized to standard or reduced dose-intensity IO every 3 months (mo) at the same dose. The primary endpoint was PFS, with non-inferiority defined by a hazard ratio (HR) margin of 1.3. Two interim futility analyses were planned at 25% (125) and 50% (249) of 498 planned events, with stopping if the one-sided P-value for HR=1 was <0.0192. Secondary endpoints were overall survival (OS), response duration and safety.

Results

Between 03/2022 and 11/2025, 340 pts were randomized. At the data cut-off (median follow-up 18.6 mo), modified intent-to-treat analysis set (N=308) the median PFS was 25 mo (95% CI 19.4-NE) in standard vs 21.9 mo (95% CI 12.1-31.6) in reduced IO (HR 1.35 95% CI 0.9-2.0 p=0.0635) exceeding the prespecified futility boundary. Reduced IO was associated with a higher risk of death (HR 2.0 95%CI 1.1-3.9; p=0.0143). Treatment effect differed across stratification factors: tumour type and treatment line. The HR (95%CI) for PFS was 2.9 (1·3–6·7) in urothelial, 1.6 (0·8–3·1) in lung, 0.7 (0·3–1·5) in renal cell and 0.6 (0·1–2·4) in head and neck cancer. Beyond first line HR was 2.9 (0·9-4·9). Grade 3-4 immune related AE occurred in 10·5% versus 9·5% and SAE in 26·3% vs 25·0% in standard versus reduced IO, respectively.

Conclusions

Reduced IO dose intensity did not achieve PFS non-inferiority, showed no meaningful safety advantage, and was associated with a signal of inferior survival. Differential treatment effects according to tumour type and treatment line argue against a uniform de-escalation strategy. Biomarker-driven strategies warrant further study.

Clinical trial identification

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Legal entity responsible for the study

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Disclosure

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