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LBA59

Combined percutaneous hepatic perfusion with ipilimumab plus nivolumab in metastatic uveal melanoma (CHOPIN): A single-center, open-label, randomized, phase II study

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Background

Metastatic uveal melanoma is a rare cancer with poor prognosis, with a reported median overall survival of around 11 months. Percutaneous hepatic perfusion has shown response rates of 27.3 to 72% in patients with liver-dominant or liver-only metastatic uveal melanoma, but remains ineffective against extrahepatic disease. Immune checkpoint inhibitors ipilimumab and nivolumab demonstrate limited efficacy in uveal melanoma, though retrospective studies suggest improved outcomes when combined with liver-directed therapies.

Methods

In this prospective, investigator-initiated, phase 2 trial, 76 patients with liver-only or liver-dominant metastatic uveal melanoma were randomized 1:1 to receive percutaneous hepatic perfusion alone (perfusion group) or combined with ipilimumab and nivolumab (combination group). The primary endpoint was one-year progression-free survival; secondary endpoints included overall survival, best overall response rate, and safety.

Results

The median follow-up was 24.9 months. The primary endpoint was met, with a one-year progression-free survival of 54.7% (95% CI, 36.8 to 69.5) in the combination group versus 15.8% (95% CI, 5.8 to 30.1) in the perfusion group (P<0.001). The combination also significantly improved overall survival (23.1 vs. 19.6 months, P=0.006), and best overall response rate (76.3% vs. 39.5%, P<0.001). Grade 3 or higher treatment-related adverse events were more frequent in the combination group (81.6% vs. 40.5%, P<0.001), but most were manageable with standard care or self-limiting.Table: LBA59

	Combination group (n = 38)	Perfusion group (n = 38)	P-value
Progression-free survival			
One-year: % (95% CI)	54.7 (36.8 - 69.5)	15.8 (5.8 - 30.1)	
Median: months (95% CI)	12.8 (9.2 - 15.4)	8.3 (6.0 - 9.6)	
Hazard ratio (95% CI)	0.34 (0.19 - 0.60)		<0.001
Overall survival			
One-year: % (95% CI)	82.8 (65.6 - 91.9)	82.2 (64.5 - 91.6)	
Two-year: % (95% CI)	49.6 (29.3 - 67.0)	22.1 (7.9 - 40.6)	
Median: months (95% CI)	23.1 (20.2 - 38.5)	19.6 (15.2 - 21.8)	
Hazard ratio (95% CI)	0.39 (0.20 - 0.77)		0.006
Best overall response rate			
number of patients	29	15	
% (95% CI)	76.3 (59.4 - 88.0)	39.5 (24.5 - 56.5)	<0.001
Safety			
Grade ≥ 3 adverse events: n (%)	31 (81.6)	15 (40.5)	<0.001

Conclusions

The addition of ipilimumab and nivolumab to percutaneous hepatic perfusion significantly improves progression-free survival, overall

survival and best overall response rate, but with manageable toxicity, offering a promising new treatment paradigm for patients with metastatic uveal melanoma.

Clinical trial identification

NCT04283890; EudraCT: 2018-004248-49.

Legal entity responsible for the study

LUMC, Leiden, the Netherlands.

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Disclosure

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