Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

OPEN ACCESS ORIGINAL REPORTS March 20, 2023

Liver Metastases: A Multicenter, Randomized, Open-Label, Phase III Trial (the SCANDIUM Trial)

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Publication: Journal of Clinical Oncology Volume 41, Number 16
https://doi-org.ezproxy.ub.gu.se/10.1200/JCO.22.01705

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Isolated Hepatic Perfusion With Melphalan for Patients With Isolated Uveal Melanoma Liver Metastases: A Multicenter, Randomized, Open-Label, Phase III Trial (the SCANDIUM Trial)

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PURPOSE About half of patients with metastatic uveal melanoma present with isolated liver metastasis, in whom the median survival is 6-12 months. The few systemic treatment options available only moderately prolong survival. Isolated hepatic perfusion (IHP) with melphalan is a regional treatment option, but prospective efficacy and safety data are lacking.

METHODS In this multicenter, randomized, open-label, phase III trial, patients with previously untreated isolated liver metastases from uveal melanoma were randomly assigned to receive a one-time treatment with IHP with melphalan or best alternative care (control group). The primary end point was overall survival at 24 months. Here, we report the secondary outcomes of response according to RECIST 1.1 criteria, progression-free survival (PFS), hepatic PFS (hPFS), and safety.

RESULTS Ninety-three patients were randomly assigned, and 87 patients were assigned to either IHP (n = 43) or a control group receiving the investigator's choice of treatment (n = 44). In the control group, 49% received chemotherapy, 39% immune checkpoint inhibitors, and 9% locoregional treatment other than IHP. In an intention-to-treat analysis, the overall response rates (ORRs) were 40% versus 4.5% in the IHP and control groups, respectively ($P < .0001$). The median PFS was 7.4 months versus 3.3 months ($P < .0001$), with a hazard ratio of 0.21 (95% CI, 0.12 to 0.36), and the median hPFS was 9.1 months versus 3.3 months ($P < .0001$), both favoring the IHP arm. There were 11 treatment-related serious adverse events in the IHP group compared with seven in the control group. There was one treatment-related death in the IHP group.

CONCLUSION IHP treatment resulted in superior ORR, hPFS, and PFS compared with best alternative care in previously untreated patients with isolated liver metastases from primary uveal melanoma.

J Clin Oncol 41:3042-3050. © 2023 by American Society of Clinical Oncology

ASSOCIATED CONTENT
Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on February 9, 2023 and published at ascopubs.org/journal/jco on March 20, 2023: DOI https://doi.org/10.1200/JCO.22.

INTRODUCTION

Uveal melanoma is a rare disease accounting for approximately 3% of all melanomas. Even when the primary tumor is successfully eradicated from the eye with surgery or radiotherapy, approximately 50% of patients will develop metastases.[1] Metastases are strongly hepatotropic, with isolated liver metastases seen in over half of patients with metastatic disease. Among these patients, the median survival is approximately 10-12 months and only a few patients outcomes reflect generally poor responses to systemic chemotherapy, which shows minimal efficacy and delivers no detectable survival benefit.

In contrast to cutaneous melanoma, immune checkpoint inhibition (ICI) has been of only limited benefit in patients with uveal melanoma, with the combination of ipilimumab and nivolumab showing an overall response rate (ORR) of 10%-18% and an uncertain impact on survival.[3-5] The combination of pembrolizumab and epigenetic therapy with a

Prior Presentation

Presented at the 2022 ASCO annual meeting, Chicago, IL, June 3-7, 2022.

Support

Supported by grants from the Signe and Olof Wallenius Foundation, The Assar Gabrielsson Foundation, Gothenburg Society of Medicine, Wilhelm and Martina Lundgrens Foundation, The Erling-Persson Foundation, Knut and Alice Wallenberg Foundation, The Swedish Cancer Society, and The Swedish Research Council.

Clinical Trial Information

NCT01785316 (EudraCT number: 2013-000564-29)

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