



Prospective Studies – in mUM

1. Zager J. S., Orloff M. M., Ferrucci P. F., et al. (final results to be published soon)
 FOCUS phase 3 trial results: Percutaneous hepatic perfusion (PHP) with melphalan for patients with ocular melanoma liver metastases (PHP-OCM-301/301A). JCO, Volume 40, Number 16_suppl; doi.org/10.1200/JCO.2022.40.16_suppl.9510.

In this analysis of data from the FOCUS trial, PHP demonstrates superior ORR, DOR, DCR, PFS, and OS in comparison with BAC in the treatment of hepatic metastases from ocular melanoma.

2. Meijer T. S., Burgmans M. C., de Leede E. M., et al.
 Percutaneous Hepatic Perfusion with Melphalan in Patients with Unresectable Ocular Melanoma Metastases Confined to the Liver: A Prospective Phase II Study. Ann Surg Oncol (2021) 28:1130–1141; doi.org/10.1245/s10434-020-08741-x.

Although this prospective study was not designed for direct comparison, the results indicate that M-PHP using the GEN 2 filter is more effective in treating liver metastases from ocular melanoma than systemic therapies.

3. Meijer T. S., Burgmans M. C., Fiocco M., et al.
 Safety of Percutaneous Hepatic Perfusion with Melphalan in Patients with Unresectable Liver Metastases from Ocular Melanoma Using the Delcath Systems' Second-Generation Hemofiltration System: A Prospective Non-randomized Phase II Trial. Cardiovasc Intervent Radiol (2019) 42:841–852; doi.org/10.1007/s00270-019-02177-x

The purpose of this study was to investigate the safety and toxicity of percutaneous hepatic perfusion with melphalan (M-PHP) with the Delcath Systems' second generation (GEN 2) filter and compare the outcomes with historical data from studies using the first-generation filter.

4. Tong T. M. L., Burgmans M. C., Speetjens F. M., et al.
 Combining Melphalan Percutaneous Hepatic Perfusion with Ipilimumab Plus Nivolumab in Advanced Uveal Melanoma: First Safety and Efficacy Data from the Phase Ib Part of the Chopin Trial. Cardiovasc Intervent Radiol; doi.org/10.1007/s00270-022-03338-1.

Primary objective of this study was to define a safe treatment dose of ipilimumab (IPI) and nivolumab (NIVO) when applied in combination with percutaneous hepatic perfusion with melphalan (M-PHP) in metastatic uveal melanoma (mUM) patients. Secondary objective was response rate, PFS and OS.

Quality of Life Data – in mUM

5. Vigneswarana G., Malalasekera W., Smith V., et al.
 Quality of life after melphalan percutaneous hepatic perfusion for patients with metastatic Uveal Melanoma. Melanoma Res; DOI: 10.1097/CMR.0000000000000947.

QoL following M-PHP decreases immediately after therapy and is not significantly different from baseline by the day of discharge but by day 28 there is improved emotional well-being. This study could help to optimize the time between treatment cycles when combined with toxicity data and blood count recovery.

Retrospective Studies – comparative in mUM

6. Kolb M., Forschner A., Artzner C., et al.
 Selective Internal Radiotherapy (SIRT) and Chemosaturation Percutaneous Hepatic Perfusion (CS-PHP) for Metastasized Uveal Melanoma: A Retrospective Comparative Study. Cancers 2023, 15(20), 4942; doi.org/10.3390/cancers15204942.

This study demonstrates a possible small benefit of CS-PHP treatment over SIRT treatment in patients with liver-dominant metastasized uveal melanoma, especially concerning overall survival.

Retrospective Studies – safety and efficacy (in mUM)

7. Artzner C., Mossakowski O., Hefferman G., et al.
 Chemosaturation with percutaneous hepatic perfusion of melphalan for liver dominant metastatic uveal melanoma: a single center experience. Cancer Imaging (2019) 19:31; doi.org/10.1186/s40644-019-0218-4.

The aim of this study was to investigate the outcome and safety data of chemosaturation with percutaneous hepatic perfusion (CS-PHP) of melphalan in patients with liver-dominant metastatic uveal melanoma.

8. Brüning R., Tiede M., Schneider M., et al.
 Unresectable Hepatic Metastasis of Uveal Melanoma: Hepatic Chemosaturation with High-Dose Melphalan—Long-Term Overall Survival Negatively Correlates with Tumor Burden. Radiology Research and Practice, Volume 2020, Article ID 5672048, 7 pages; doi.org/10.1155/2020/5672048.

The purpose of this study was to enable better stratification of patient selection for chemosaturation in the future. It showed that PHP-M for nonresectable liver metastasis of uveal melanoma provides a safe and locally efficient liver directed procedure that offers patients a chance for long-term survival especially for patients with a low hepatic tumor burden.



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Retrospective Studies – safety and efficacy (in mUM) *continued*

- 9.** Dewald C. L. A., Warnke M., Brüning R., et al.
 Percutaneous Hepatic Perfusion (PHP) with Melphalan in Liver-Dominant Metastatic Uveal Melanoma: The German Experience. *Cancers* 2022, 14(1), 118; doi.org/10.3390/cancers14010118.
 The aim of this two-center retrospective study was to examine the safety, response, and survival after PHP. This study demonstrated that PHP is an efficacious, minimally invasive treatment modality, which offers local tumor control in appropriately selected UM patients with primarily liver-based disease.
- 10.** Modi S., Gibson T., Vigneswaran G., et al.
 Chemosaturation with percutaneous hepatic perfusion of melphalan for metastatic uveal melanoma. *Melanoma Research* 32(2):p 103-111, April 2022; DOI: 10.1097/CMR.0000000000000806.
 The aim of this retrospective cohort study was to evaluate the safety and efficacy of this intervention in the largest number of mUM patients treated in a single centre with M-PHP to date worldwide.
- 11.** Dewald C. L. A., Becker L. S., Maschke S. K., et al.
 Percutaneous isolated hepatic perfusion (chemosaturation) with melphalan following right hemihepatectomy in patients with cholangiocarcinoma and metastatic uveal melanoma: peri and post-interventional adverse events and therapy response compared to a matched group without prior liver surgery. *Clinical & Experimental Metastasis* (2020) 37:683–692; doi.org/10.1007/s10585-020-10057-9.
 In conclusion, the severity of adverse events following chemosaturation percutaneous hepatic perfusion in patients after right hemihepatectomy was comparable to a matched group without prior liver surgery. Therefore, CS-PHP with melphalan might be safely performed in patients following hemihepatectomy.

Retrospective Studies – mUM and other indication

- 12.** Vogel A., Ochsenreither S., Zager J. S., et al.
 Chemosaturation for primary and secondary liver malignancies: A comprehensive update of current evidence. *Cancer Treatment Reviews*; doi.org/10.1016/j.ctrv.2022.102501.
 Within the last decade, “isolated hepatic perfusion” (IHP) has evolved from an open surgical approach to a minimally invasive procedure, now termed “chemosaturation” (CS) with “percutaneous hepatic perfusion (PHP)”. The most conclusive data on CS-PHP is currently available for patients with hepatic metastases from uveal melanoma (UM). In this review we provide an overview on the technique, available clinical data, including safety and efficacy, and potential indications for CS-PHP.
- 13.** Veelken R., Maiwald B., Strocka S., et al.
 Repeated percutaneous hepatic perfusion with melphalan can maintain long-term response in patients with liver cancers. *Cardiovasc Intervent Radiol* (2022) 45:218–222; doi.org/10.1007/s00270-021-02983-2.
 The findings of this analysis are encouraging to study the repetitive long-term use of CS-PHP treatment as a novel therapeutic approach for hepatic OM metastasis. Also patients with primary liver tumors like iCCA and HCC might benefit from this treatment.
- 14.** Schönfeld L., Hinrichs J. B., Marquardt S., et al.
 Chemosaturation with percutaneous hepatic perfusion is effective in patients with ocular melanoma and cholangiocarcinoma. *Journal of Cancer Research and Clinical Oncology* (2020) 146:3003–3012; doi.org/10.1007/s00432-020-03289-5.
 The purpose of this study was to analyse the safety and efficacy of CS-PHP after 141 treatments in patients with primary and secondary hepatic tumors as last-line treatment at Hannover Medical School, Germany.
- 15.** Marquardt S., Kirstein M. M., Brüning R., et al.
 Percutaneous hepatic perfusion (chemosaturation) with melphalan in patients with intrahepatic cholangiocarcinoma: European multicentre study on safety, short-term effects and survival. *European Radiology*; doi.org/10.1007/s00330-018-5729-z.
 Cholangiocarcinoma is the second most common primary liver tumour with a poor overall prognosis. Percutaneous hepatic perfusion (PHP) is a directed therapy for primary and secondary liver malignancies, and its efficacy and safety have been shown in different entities. The purpose of this study was to prove the safety and efficacy of PHP in patients with unresectable intrahepatic cholangiocarcinoma (iCCA).

