Safety and Feasibility of Percutaneous Hepatic Perfusion with Melphalan in Patients with Liver-Dominant Metastatic Breast Cancer

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Cornelia Lieselotte Angelika Dewald[1], Cagatay Arslan[2], Gurkan Guner[2], Frank Wacker[1], Thomas Wirth[1], Jasna Bruce[3], Gregory Wilson[4]

[1]Institute for Diagnostic and Interventional Radiology, Hannover Medical School, MHH, Hannover, Germany; [2]Izmir University of Economics, Medical Point Hospital, Izmir, Turkey; [3]Delcath Systems, Inc., Queensbury, NY, USA ; [4]The Christie NHS Foundation Trust, Manchester, United Kingdom

Background

Liver-dominant metastatic breast cancer (mBC) represents a clinical challenge, as hepatic progression frequently drives morbidity and limits effectiveness of systemic therapy. Percutaneous hepatic perfusion (PHP) enables whole-liver delivery of high-dose melphalan (M-PHP) with extracorporeal hemofiltration to reduce systemic exposure (**Fig. 1**). Data on M-PHP in mBC remain limited.

Materials and Methods

Patients with mBC were retrospectively identified based on treatment with M-PHP (CHEMOSAT®). Demographics and treatment characteristics were collected. Feasibility was assessed by successful delivery and completion of M-PHP cycles. Safety outcomes included peri-procedural complications, transfusion requirements, and adverse events (AEs). Tumor response was assessed by RECIST v1.1.

Results

Fifteen patients underwent PHP at 3 European centers between Sep 2015 and May 2024 (median age 51 years at first M-PHP) after a median of 4 prior systemic therapy lines (range, 1-6) (**Table 1**). Median follow-up (FU) was 55.6 months (95% CI, 53.7-NR). Patients received a median of 1 M-PHP cycle (range 1–7), typically followed by ICU admission of 1-2 days; 67% received blood transfusions, predominantly packed red blood cells (**Table 2**). Intra/periprocedural AEs occurred in 9 patients (60%), primarily peri-procedural hematologic or hemodynamic events, while Grade 3-4 post-procedure AEs occurred in 12 patients (80%) (**Fig. 2**) and included bone marrow suppression with neutropenic-related infection requiring supportive care. AEs typically occurred early (median onset 1 day) with median resolution in 7 days. Two patients had prolonged anemia that resolved with transfusions. Changes in liver function parameters are depicted in **Fig. 3**. Among evaluable patients, hepatic PR was observed in 60% (**Table 2**). At last FU, 33% (5/15) of patients were alive; median OS from first M-PHP was 6.0 months (95% CI, 2.9-NR; range, 0.1-76.5) (**Fig. 4**).

Fig. 1. *Schematic representation of the PHP procedure with melphalan.*

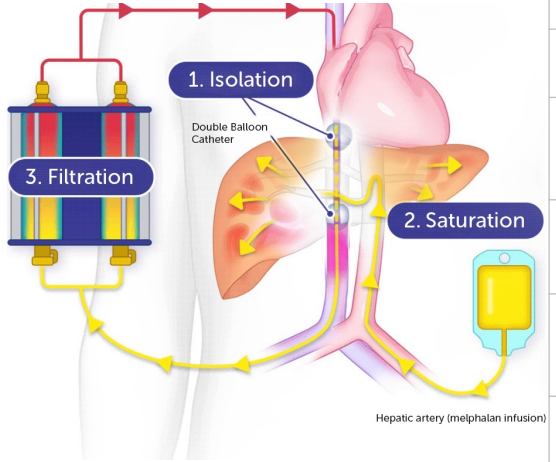


Fig. 2. *Maximum AE grade post-PHP (no AEs reported for one patient with best response of PR).*

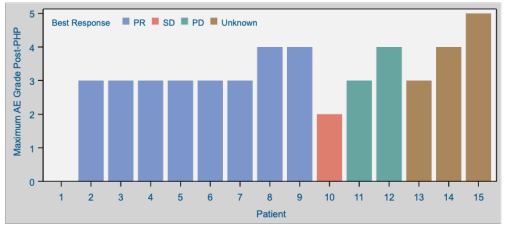


Fig. 3. *Individual patient-level changes in liver function parameters* following M-PHP cycle 1.

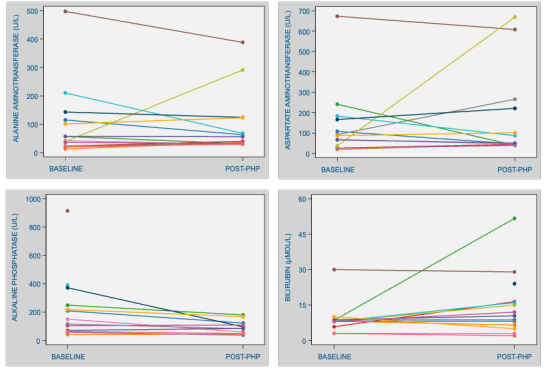


Table 1. *Baseline patient and disease characteristics (N=15).*

Histology	Invasive ductal carcinoma	11 (73.3%)
	Other	4 (26.7%)
Disease focality	Unifocal	11 (73.3%)
	Multifocal	4 (26.7%)
Primary tumor laterality	Left	5 (33.3%)
	Right	9 (60.0%)
	Bilateral	1 (6.7%)
Receptor status (missing 3 patients)	ER/PR+ (5 of which were HER2+)	10 (66.7%)
	Triple negative BC	2 (13.3%)
Tumor grade (missing 7 patients)	G1	1 (6.7%)
	G2	2 (13.3%)
	G3	5 (33.3)
pT stage at diagnosis (missing 5 patients)	pT1	2 (13.3%)
	pT2	5 (33.3%)
	pT3	3 (20.0%)
Outcome of primary breast cancer treatment (missing 1 patient)	Progression	9 (60.0%)
	Partial response	2 (13.3%)
	Complete regression	3 (20.0%)
Synchronous distant metastasis (any location)	Yes	3 (20.0%)
	No	12 (80.0%)
Time to distant metastasis (months)	Median (IQR)	19 (12-156)
Number of prior systemic therapy lines	Median (range)	4 (1–6)
Metastatic surgery prior to PHP	Yes	4 (26.7%)
	No	11 (73.3%)
Systemic therapy for metastatic disease (missing 1 patient)	Yes	13 (86.7%)
	No	1 (6.7%)

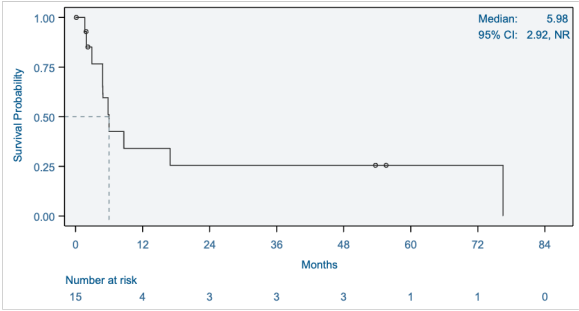
Conclusions

M-PHP was feasible and well tolerated in this limited cohort of heavily pre-treated patients with liver-dominant mBC. The safety profile is consistent with prior experiences in hepatic-dominant malignancies. M-PHP is currently evaluated in a randomized phase 2 trial (PHP-MBC-202; NCT06875128).

Table 2. *PHP treatments and safety outcomes.*

Age at first PHP cycle, years	Mean ± SD	51.7 ± 10.1
	Median (range)	51 (36-67)
Number of PHP cycles	Median (range)	1 (1-7)
ECOG performance status	0	6 (40.0%)
	1	9 (60.0%)
Blood transfusions required	Yes	10 (66.7%)
	No	5 (33.3%)
Intra-/periprocedural AEs (missing 1 patient)	Yes	9 (60.0%)
	No	5 (33.3%)
Maximum intra-/periprocedural complication grade	Median (range)	3 (3-4)
Maximum AE grade	Median (range)	3 (2-5)
AE onset, days from PHP	Median (IQR)	1 (0-7)
AE resolution, days	Median (IQR)	7 (1-73)
Best overall response (missing 3 patients)	CR	0
	PR	9 (60.0%)
	SD	1 (6.7%)
	PD	2 (13.3%)
Vital status at last follow-up	Alive	5 (33.3%)
	Dead	10 (66.7%)

Fig. 4. *Kaplan-Meier Plot of Overall Survival.*



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Declaration of interest C.L.A.D. reports honoraria from Delcath Systems. G.W. reports honoraria, consultancy, and shareholding in Delcath Systems. C.A. reports consultancy and honoraria from Delcath Systems. J.B. is an employee of Delcath Systems, Inc. All other authors declare no competing interests.