

Percutaneous Hepatic Perfusion (CHEMOSAT® or CS-PHP) of Melphalan vs. Best Alternative Care (BAC) in Patients (pts) with Hepatic Metastases from Melanoma: Update of a Randomized Phase 3 Study

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Background: CS-PHP (Chemostat®; Delcath Systems Inc, New York, NY) is a regional therapy which isolates and perfuses the liver with high-dose chemotherapy. Unwanted systemic exposure is minimized by extracorporeal filtration of hepatic venous blood. **Methods:** A prospective randomized multicenter phase 3 study compared CS-PHP of melphalan with BAC in pts with proven unresectable hepatic metastases from ocular or cutaneous melanoma. A survival update was performed on 31 March 2011. CS-PHP melphalan 3.0 mg/kg ideal body weight was infused into the hepatic artery over 30 min with concurrent extracorporeal filtration for 60 min. Up to 6 treatments were given every 4–8 wks. In the BAC group, crossover to CS-PHP melphalan was permitted after hepatic disease progression. The primary endpoint was investigator-assessed hepatic progression-free survival (hPFS). An exploratory *post-hoc* analysis of pts who crossed from BAC to CS-PHP vs. BAC-only pts was also performed. **Results:** 93 pts were randomized to CS-PHP (n=44) or BAC (n=49). After hepatic disease progression, 28 pts crossed over to CS-PHP. Results are shown in the Table. The most common grade 3/4 toxicities in CS-PHP pts (n=40) were hematological peri-procedural thrombocytopenia (73%) and anemia (55%) and post-procedural (beyond day 4 post-treatment) neutropenia (93%) or thrombocytopenia (83%). The safety profile in crossover pts was similar to that in pts randomized to CS-PHP melphalan. **Conclusions:** CS-PHP melphalan significantly prolonged hPFS compared with BAC in pts with liver-dominant metastatic melanoma, thereby meeting the primary study objective. Efficacy was similar after hepatic disease progression in BAC-CS-PHP crossover pts as in those randomized initially to CS-PHP.

Treatment group	n	Median hPFS, mo	Hazard ratio (95% CI)	Median OS, mo	Hazard ratio (95% CI)
CS-PHP	44	8.0	0.35 (0.23-0.54)	9.8	1.08 (0.69-1.68)
BAC	49	1.6	P<0.0001	9.9	NS
BAC only	21	1.6	0.32	4.1	0.33
BAC→CS-PHP crossover	28	8.8		15.3	

Key words: melphalan; hepatic perfusion; melanoma; efficacy

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