Chemosaturation Therapy with Percutaneous Hepatic Perfusions of Melphalan Versus Standard of Care in Patients with Hepatic Metastases from Melanoma: A Randomized Multicenter Phase 3 Study

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Purpose: Chemosaturation therapy with percutaneous hepatic perfusions (CS-PHP) isolates the liver from the systemic circulation using a system of catheters and filters (Delcath Systems Inc, New York, NY). The CS-PHP catheters are positioned using fluoroscopic and arteriographic techniques under general anesthesia. CS-PHP allows repeated delivery of chemotherapy to the liver, while limiting unwanted systemic exposure by extracorporeal filtration of hepatic venous blood.[1] A prospective randomized multicenter phase 3 study was conducted to compare CS-PHP delivery of melphalan with best alternative care (BAC) in patients (pts) with unresectable hepatic metastases from melanoma.

Materials and Methods: Pts with histologically/cytologically proven ocular or cutaneous melanoma with hepatic metastases were eligible. Pts with Childs B or C cirrhosis or portal hypertension were excluded. CS-PHP melphalan 3.0 mg/kg ideal body weight was delivered via the hepatic artery over 30 minutes followed by an additional 30 minutes of extracorporeal filtration. Up to 6 treatments were given every 4–8 weeks. BAC was active treatment or supportive care as selected by the investigator and patient. 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).

Results: A total of 93 pts were randomized to CS-PHP melphalan (n=44) or BAC (n=49); 28 (57%) BAC pts crossed over per protocol to CS-PHP melphalan after hepatic disease progression. Median hPFS was 8.0 months with CS-PHP melphalan versus 1.6 months with BAC (hazard ratio [HR] 0.35, 95% CI 0.23–0.54; p<0.0001). Overall PFS times were 6.7 and 1.6 months, respectively (HR=0.42, 95% CI 0.28-0.65; p<0.0001). Median overall survival was 9.8 months with CS-PHP melphalan and 9.9 months with BAC (HR=1.08, 95% CI 0.69-1.68; p=0.740). Hepatic response rate was statistically superior with CS-PHP melphalan versus BAC. The most common grade 3/4 adverse events associated with CS-PHP melphalan were hematological (anemia, thrombocytopenia, late-onset neutropenia).

Conclusion: CS-PHP melphalan prolongs hPFS compared with BAC in patients with hepatic metastases from ocular and cutaneous melanoma. The strong treatment effect

was replicated in the secondary efficacy outcomes of overall PFS and hepatic response rate.

References

1. Pingpank JF, et al: J Clin Oncol 2005;23:3465-74.

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