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Percutaneous Hepatic Perfusion (PHP) Vs. Best Alternative Care (BAC) for Patients (pts) With Melanoma Liver Metastases - Efficacy Update of the Phase 3 Trial (NCT00324727)

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Background: There is no standard of care for liver-dominant metastatic melanoma. Meta-analyses have reported median overall survival of 2–4 months. One-year survival is around 10%. PHP was designed to saturate the liver with high doses of chemotherapy, via a minimally invasive approach. We report updated efficacy results of the first-ever phase 3 multi-center randomized trial for pts with unresectable liver melanoma metastases, comparing PHP with melphalan to BAC.

Materials & Methods: Pts were prospectively randomized 1:1. On the PHP arm, melphalan (3mg/kg ideal body weight) was infused via the hepatic artery over 30 minutes. Hepatic venous return was captured from the intrahepatic IVC using a specially-designed double-balloon catheter, and directed through extra-corporeal filters to extract melphalan before return of filtered blood. The procedure was repeated every 4–8 weeks on recovery from hematological toxicity. The procedure was repeated every 4–8 weeks on recovery from hematological toxicity. The control arm was the investigators' pre-specified choice of therapy. The primary endpoint was hepatic progression-free survival (hPFS) using RECIST at pre-defined 6-week intervals on both study arms. Secondary endpoints included safety, ORR, PFS, OS. Cross-over to PHP on hepatic progression was permitted. All analyses were ITT. The NCI-led study with 9 additional US centers was sponsored by Delcath Systems, Inc., NY.

Results: From 2/2006 to 7/2009, 93 patients were randomized to PHP (n=44) or BAC (n=49). Mean age was 54.8yrs with no significant imbalances in baseline characteristics. AEs were primarily hematological (grade 3/4), as expected. As of 4/2011, investigator-assessed hPFS was significantly better in the PHP group, median 8.1 vs. 1.6 months, HR 0.34, p<0.0001, with a 6.5 month difference at the median. Overall PFS showed similar benefit (HR 0.41, p<0.0001, median 6.1 vs. 1.6 months). 1-year OS was 29% on PHP vs. 26% on BAC. OS was not significantly different (median PHP 11.4 vs. BAC 9.9 months, p=0.982) due to 51% crossover. Crossover pts had a median hPFS from crossover date of 9.2 months and overall PFS 6.5 months.

Conclusions: This first phase 3 study in pts with liver-dominant metastatic melanoma met its primary endpoint. hPFS, ORR and overall PFS were significantly improved with PHP vs. BAC. PHP with melphalan
should provide a new treatment option for unresectable metastatic melanoma in the liver.

- test: Melanoma
- test: Regional Therapy
- test: Liver

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