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16ESMO
36ESTRO
30

9304: Melanoma and Skin Cancer: Melanoma and Skin Cancer

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 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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