

Adverse Events Linked to Improved Outcomes for Hepatocellular Carcinoma

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CHICAGO—Patients may dread the side effects of cancer treatment, but the occurrence of certain adverse events during treatment of advanced hepatocellular carcinoma with cabozantinib predicted improved overall survival and progression-free survival in a retrospective review of data from the CELESTIAL trial.

The study results were presented on June 3 at the 2019 American Society of Clinical Oncology Annual Meeting in Chicago.¹

The Phase III CELESTIAL trial demonstrated that treatment with cabozantinib, an inhibitor of VEGFR, MET and AXL, improved both overall survival and progression-free survival in patients with advanced hepatocellular carcinoma (HCC) who had previously received sorafenib. The study involved 707 patients who were randomized 2:1 to receive cabozantinib or placebo. On the basis of these results, the U.S. Food and Drug Administration approved cabozantinib for advanced HCC in this setting.

Veterans face an elevated risk of HCC because of the historic high rate of hepatitis C infection and high rates of cirrhosis, the two most significant risk factors for the malignancy. Some risk remains even for veterans cured of hepatitis C, particularly if they were cured after age 65, have diabetes or had genotype 3 infection, according to research done by VA researchers.²

The study presented at ASCO analyzed outcomes for patients who developed any grade palmar-plantar erythrodysesthesia or hypertension of grade 3 or higher within the first eight weeks of the CELESTIAL study. During this period, 188 (40%) patients in the cabozantinib arm developed PPE compared to 11 (5%) in the placebo arm. Sixty-one patients (13%) who received cabozantinib experienced grade 3 or higher hypertension vs three in the placebo arm.

Patients in the cabozantinib arm who developed PPE of any grade had a median overall survival of 14.4 months compared to 8.4 months for those who did not experience this adverse event. Progression-free survival showed a similar benefit 6.5 months for those with PPE and 3.7 months for those without it.

Likewise, the median overall survival of patients treated with cabozantinib who developed grade 3 or higher hypertension was 16.1 months and the median progression free survival was 7.4 months, compared to 9.5 months and 4.4 months, respectively, for those who did not.

1. Abou-Alfa G, Meyer T, Cheng A-L, Cicin I, Bolondi L, et al. Association of adverse events with efficacy outcomes for cabozantinib in patients with advanced hepatocellular carcinoma in the phase III CELESTIAL trial. *J Clin Oncol* 37, 2019 (suppl; abstr 4088).
2. El-Serag HB, Kanwal F, Richardson P, Kramer J. Risk of hepatocellular carcinoma after sustained virological response in Veterans with hepatitis C virus infection. *Hepatology*. 2016 Jul;64(1):130-7. doi: 10.1002/hep.28535. Epub 2016 Apr 19. Erratum in: *Hepatology*. 2016 Sep;64(3):1010.