

Comparative Efficacy of Cabozantinib and Regorafenib for Advanced Hepatocellular Carcinoma

Hello, I'm Professor Katie Kelley and I'm a Gastrointestinal Oncologist at the UCSF Helen Diller Family Comprehensive Cancer Center. I'm going to spend a few minutes considering the clinical implications of our recent matching-adjusted indirect comparison of cabozantinib versus regorafenib in patients with advanced hepatocellular carcinoma, or "HCC".

Cabozantinib and regorafenib are both tyrosine kinase inhibitors approved for the second-line treatment of advanced HCC in patients who have been previously treated with sorafenib.

Now, in the absence of head-to-head trials comparing cabozantinib with regorafenib, we conducted a matching-adjusted indirect comparison to compare the efficacy and safety of the two drugs for the second-line treatment of advanced HCC. w

We used data from the pivotal phase 3 trials for cabozantinib (also known as CELESTIAL) and regorafenib (or RESORCE). We aligned the individual patient data from CELESTIAL with the aggregate patient baseline characteristics from RESORCE and then we compared the outcomes for both treatments in the matched adjusted cohorts. Because CELESTIAL had include both second- and third-line patients, while RESORCE had included only second-line, only the second-line patients from CELESTIAL were included in this analysis.

This next graph shows a Kaplan Meier plot for overall survival for cabozantinib versus placebo and for regorafenib versus placebo in the matched populations. In this case, the median overall survival was numerically longer with cabozantinib than with regorafenib, but the difference was not statistically significant.

Here is a Kaplan Meier plot for progression-free survival, or "PFS", for cabozantinib versus placebo and for regorafenib versus placebo. Median PFS was 5.6 months for cabozantinib while median PFS was 3.1 months for regorafenib in this matched, adjusted population.

The odds of experiencing serious treatment-related adverse events were similar for the two therapies, with the exception of grade 3 or higher diarrhoea, which occurred in a higher proportion of patients in the matched, adjusted cabozantinib cohort for which the odds were significantly lower with regorafenib than with cabozantinib.

Although matching aims to remove bias and differences between comparator populations, differences still can persist because of unobserved factors that the matching cannot account and, therefore, a matched adjusted indirect comparison really can't replace a head-to-head randomized controlled trial.

Without any randomized trial data available to compare cabozantinib and regorafenib directly, however, this matched adjusted indirect comparison does offer clinicians additional data to help guide their decision making when choosing between second-line systemic treatment options for their patients with advanced HCC.

In summary, this indirect comparison found that progression free survival was longer with cabozantinib. Both drugs had similar safety profiles, though rates of diarrhoea may be higher with cabozantinib.

Despite possible residual differences between the comparator populations, these data may help guide decision making in the second-line treatment of patients with advanced HCC. Thank you for your attention.