Sorafenib Improves Survival in Hepatocellular Carcinoma: Results of a Phase 3 Randomized, Placebo-Controlled Trial

The Sorafenib HCC Assessment Randomized Protocol (SHARP) trial demonstrated that treatment with sorafenib prolonged overall survival by 44% and prolonged time to progression by 73% for patients with advanced hepatocellular carcinoma (HCC).

Josep M. Llovet, MD

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"Sorafenib is the first systemic therapy to prolong survival in HCC patients after 30 years of research and more than 100 randomized controlled trials," said Josep M. Llovet, MD, Mount Sinai School of Medicine, who presented the findings of the study.

Dr. Llovet noted that patients with advanced stage HCC represent 40% of all patients with HCC in the United States and Europe and approximately 70% of all patients with HCC worldwide. "There are no first-line treatment options approved by FDA or European regulatory agencies for these patients," he said. Sorafenib is an antiangiogenic inhibitor and is the only approved inhibitor of Raf kinase. Raf kinase is overexpressed and activated in HCC.

The trial included 602 patients who were ineligible for local-regional therapy. The patients had not received previous systemic treatment, and had a good performance status and good liver function. Approximately 20% of the patients had undergone surgical resection and approximately 40% had received local-regional treatment. The patients were randomly assigned to treatment with sorafenib, 400 mg twice daily (n=299) or placebo (n=303).

Dr. Llovet said that the study was stopped earlier than planned when an interim analysis indicated a clear advantage in overall survival for the patients treated with sorafenib. The median overall survival and time to radiographic evidence of disease progression were significantly longer for the sorafenib group. The progression-free rate at four months was 62% for the sorafenib group and 42% for the placebo group. This difference was not significant.

According to RECIST criteria, the best response for most patients was stable disease (71% with sorafenib and 67% with placebo). There were no complete responses in either group. The rate of partial response was 2.3% for the sorafenib group and 0.7% for the placebo group.

The rate of toxicity was comparable in the two treatment groups. The most common grade 3 or 4 toxicities in the sorafenib group were diarrhea and hand-foot skin reactions.

In discussing the study, Philip J. Johnson, MD, University of Birmingham, United Kingdom, said that the cost of sorafenib will limit its use in many parts of the world. Prevention of hepatitis B virus transmission is still the most effective and cost-efficient way to reduce mortality related to HCC, he concluded.

Highlights from the
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