Ramucirumab as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP) following first-line sorafenib: Pooled efficacy and safety across two global randomized Phase 3 studies (REACH-2 and REACH)

**BACKGROUND**

- Hepatocellular carcinoma (HCC) is the second most common cause of cancer-related mortality globally.
- Sorafenib (Nexavar®) and regorafenib (Stelara®) are the only globally approved drugs for treatment of HCC. ramucirumab (4L) is approved in US, Europe and Asia.
- There are no data on the efficacy and safety of ramucirumab as second-line therapy in patients with HCC.

**OBJECTIVES & METHODS**

- REACH-2 and REACH were both phase III, randomized, placebo-controlled phase 3 trials with similar study eligibility, protocol endpoints, and trial regimens, comparing ramucirumab to placebo in patients with advanced HCC, following prior sorafenib-based treatment, a posteriori analysis.
- Ramucirumab (4L) is a human IgG1 monoclonal antibody (mAb) that selectively targets vascular endothelial growth factor (VEGF) receptor 2 (VEGFR2) on endothelial cells.

**RESULTS**

- Efficacy analyses were prespecified prior to REACH-2 database lock.
- No heterogeneity in treatment effect observed across both studies.

**CONCLUSIONS**

- REACH-2 (N=929) confirmed the ramucirumab treatment benefit observed in the REACH subgroup of patients with AFP ≥400 ng/mL.
- The confidence and precision of efficacy and safety assessments were increased by performing pooled analyses of REACH-2 and REACH (AFP ≥400 ng/mL).

- Ramucirumab OS treatment benefit was consistent and robust across all subgroups. Sensitivity analyses, including random effects model, were consistent with the primary efficacy analysis.

**References**


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- All authors are for the investigation, methods and clinical trials and REACH trials.
- All authors have contributed to the writing of the manuscript.