ALK1 Pathway Background

- ALK1 is a receptor in tumor cell signaling that promotes tumor cell proliferation and survival.
- BMP9 is overexpressed in advanced HCC.
- Inhibition of ALK1 by Dalantercept is associated with decreased tumor angiogenesis.

Dalantercept Background

- Dalantercept inhibits the proliferation of vascular and reparative cells.
- It promotes vascular maturation.
- In preclinical models, treatment with dalantercept + sorafenib has shown significant additive antitumor activity.

BEL-7402 Xenograft Tumor Models

- The BEL-7402 cell line is derived from a primary human hepatocellular carcinoma (HCC) tumor with a known ALK1 mutation.
- Inhibition of ALK1 with dalantercept + sorafenib leads to decreased tumor growth.

DASH Study Rationale

- A randomized, open-label trial to evaluate the safety and tolerability of dalantercept + sorafenib in patients with advanced HCC.
- The primary endpoint is safety and tolerability of dalantercept plus sorafenib.
- The trial is open for enrollment.

Key Eligibility Criteria

- Histologically confirmed advanced HCC.
- Child-Pugh Class A liver disease.
- ECOG = 0.
- No prior systemic therapy in the advanced setting.

Summary

- Dalantercept inhibits vascular endothelial growth factor (VEGF) and disrupts tumor angiogenesis.
- The combination of dalantercept and sorafenib demonstrated additive antitumor activity.

References