Gastric Cancer Background

- Gastric cancer (GC), including gastroesophageal junction (GEJ) cancer, is the 5th most common cancer worldwide and 3rd leading cause of cancer death
- More than 50% of gastric cancer cases occur in eastern Asia
- Current first-line chemotherapy treatments prolonging survival by 6 months compared to supportive care, but median OS remains poor with literature range of approximately 10 to 11 months and PFS from 5 to 5.6 months
- Few treatment options following progression are available after first-line chemotherapy
- An unmet medical need exists in the treatment for GC/GEJ
- The presence of FGFFR2 amplification/overexpression is associated with a worse prognosis and is present in approximately 10% of patients with GC/GEJ

Relevance of Fibroblast Growth Factor Receptor 2 (FGFR2) in Cancer

- FGFRs can stimulate transformation and proliferation of tumor cells through signaling mediated by FGF receptors (FGFR 1-4)
- FGFR2 has 2 splice variants (b and c)
- FGFR2 is expressed in tissues of epithelial origin
- Alterations in FGFR/FGFR2 pathway are associated with gastric, breast and other cancers
- Targeting this pathway may be important in GC/GEJ cancer treatment

Bemarituzumab (FPA144)

- Bemarituzumab is an afucosylated, humanized IgG1 monoclonal antibody that selectively binds to FGFR2b
- Bemarituzumab treatment is designed to deliver 2 distinct anti-tumor effects:
  1. Inhibits ligand binding to FGFR2b and blocks FGFR7/10 receptor activation and downstream signaling (Gamo, 2014)
  2. Glycoengineered to enhance antibody-dependent cell-mediated cytotoxicity (ADCC)
- Isometric specificity may improve tolerability

FPA144-001: A Phase 1 Dose-escalation and Expansion Study of Bemarituzumab in Patients with Solid Tumors With and Without FGFR2b+ Overexpression

Overall Safety Summary

- No DLTs during dose escalation (MTD not reached)
- 58 AEs reported in 64 patients
- 30 patients (46.9%) experienced at least one Grade 3 event
- 16 SAEs reported, 4 treatment-related (across 3 patients):
  - Grade 2 ulcerative keratitis, Grade 3 hypersensitivity infusional reaction and nausea and vomiting
  - Grade 6 surgery
- One grade 5 SAE not treatment related (septic shock)
- No treatment-related hyperprolactinemia or retinal toxicity

Best Response in FGFR2b+ (IHC High) Gastric Cancer Patients

Efficacy:

- In 21 treated patients with late-line GC/GEJ and strong IHC expression:
  - ORR was 19.0% (95% CI (4.5%, 41.9%)) with 4 confirmed PRs
  - Disease control rate 55% (95% CI 38.5% - 70.7%)
- Median duration of response 15.4 weeks (95% CI 9.1-19.1%)
- Overall Safety:
  - Bemarituzumab is well tolerated
  - No DLTs and the MTD was not reached during dose escalation

Companion Diagnostic (CDx) for FGFR2b in Gastric Cancer Patients

- FGFR2b overexpression/FGFR2 gene amplification identified using 2 CDx assays
- Both assays used to select patients for the FIGHT trial with FGFR2b positivity and/or FGFR2 gene amplification (~10% of GC and GEJ tumors)
- IHC uses a Five Prime proprietary antibody to specifically detect FGFR2b protein expression
- ctDNA Analysis detects FGFR2 gene amplification

FIGHT Trial: Key Eligibility Criteria

- Unresectable, locally advanced or metastatic GC/GEJ
- FGFR2b overexpression by immunohistochemistry (IHC) or FGFR2 gene amplification by circulating tumor DNA (ctDNA)
- Age ≥ 18 years; standard performance status and laboratory parameters
- Candidate for mFOLFOX6; no prior chemotherapy for metastatic or adjuvant/neoadjuvant
- May receive one cycle of mFOLFOX6 while waiting for IHC/ctDNA results
- More than 6 months between end of adjuvant treatment and confirmation of disease progression
- Eligible patients randomized 1:1 to bemarituzumab + mFOLFOX6 versus placebo + mFOLFOX6
- Study treatment continues every 2 weeks until radiographic/clinical progression or intolerable toxicity

FIGHT Trial: Endpoints

- Primary: Overall survival (OS) is event based
- Stratification factors:
  - Geographic region
  - Prior treatment (de novo vs. adjuvant/neoadjuvant)
  - One cycle of mFOLFOX6 (yes/no)
- Secondary:
  - Progression-free survival (PFS)
  - Objective response rate (ORR)
  - Safety profile
  - PK parameters

Summary

- Bemarituzumab is a first-in-class, FGFR2b antibody with monotherapy activity in late-line gastric/GEJ cancer patients
- Well-tolerated with no dose-limiting toxicities at all dose levels tested
- FIGHT study is evaluating bemarituzumab versus placebo in patients with newly diagnosed gastric cancer and FGFR2b overexpression/FGFR2 gene amplification
- Global trial involving over 250 institutions worldwide
- Eligible patients randomized to bemarituzumab + mFOLFOX6 or placebo + mFOLFOX6
- FIGHT Phase 1 study is currently enrolling

References

1Su X. FGFR2 amplification has prognostic significance in gastric cancer: results from a large international multicentre study. Br J Cancer 110:967, 2014