FIGHT: A Phase 3 Randomized, Placebo Controlled Study Evaluating Bemarituzumab (FPA144) and mFOLFOX6 in Patients with Previously Untreated Advanced Gastric and Gastroesophageal Cancer

Poster: TPS4135

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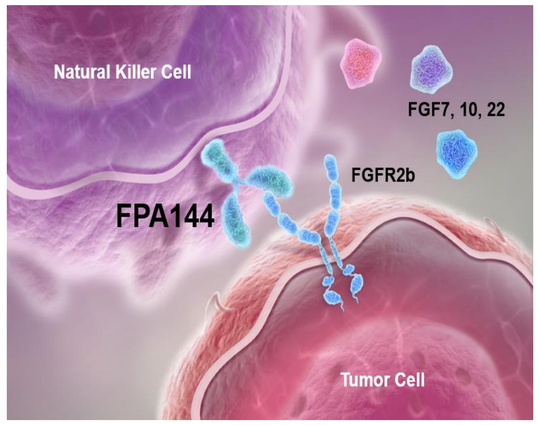
Gastric Cancer Background

- 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 prolong survival by 6 months compared to best 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 *FGFR2* amplification/overexpression is associated with a worse prognosis[1] and is present in approximately 10% of patients with GC/GEJ

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

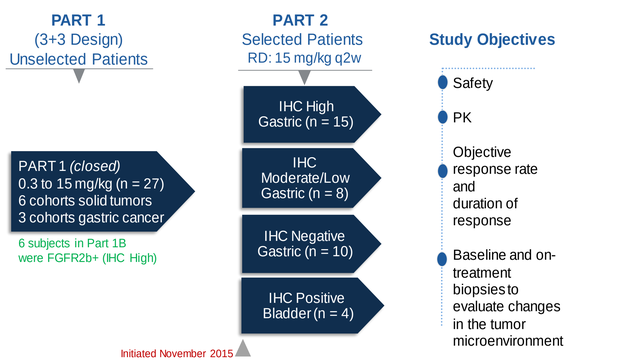
- FGFs can stimulate transformation and proliferation of tumor cells through signaling mediated by FGF receptors (FGFR 1-4)
- FGFR2 has 2 splice variants (b and c)
  - FGFR2b is expressed in tissues of epithelial origin
  - Alterations in FGF/FGFR2 pathway are associated with gastric, breast and other 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 the b isoform of FGFR2
- Bemarituzumab treatment is designed to deliver 2 distinct anti-tumor effects:
  1. Inhibits ligand binding to FGFR2b and blocks FGF7/10 receptor activation and downstream signaling (Gemo, 2014)
  2. Glycoengineered to enhance antibody-dependent cell-mediated cytotoxicity (ADCC)
- Isoform 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†



Initially patient selection required both tissue IHC and FISH amplification testing, but FISH was discontinued after demonstrating high correlation with IHC results (100%, n = 12).[2]

† Data as of 20 March 2017

Overall Safety Summary

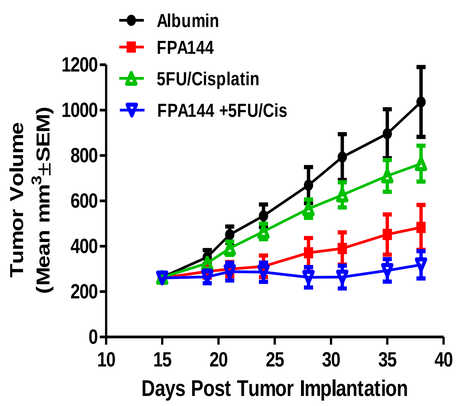
- No DLTs during dose escalation (MTD not reached)
- 58 AEs reported in 64 patients
- 30 patients (46.9%) experienced at least one Grade 3 event
  - 8 treatment-related events in 6 patients
- 16 SAEs reported, 4 treatment-related (across 3 patients):
  - Grade 2 ulcerative keratitis, Grade 3 hypersensitivity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

	All Part 1 and 2 Patients (Combined) N=64		
Preferred Term	**Grade 1/2 %**	**Grade 3 %**	**Total %**
Decreased Appetite	31.3	1.6	32.8
Fatigue	23.4	1.6	25.0
Nausea	20.4	3.1	23.4
Vomiting	18.6	1.6	20.3
Anemia	11.0	9.4	20.3
Dry Eye	15.6	0	15.6
Diarrhea	14.1	0	14.1
Hypoalbuminemia	11.0	1.6	12.5
Pyrexia	12.5	0	12.5
Decreased Weight	11.0	1.6	12.5
Constipation	9.4	1.6	10.9
Dehydration	10.9	0	10.9
Peripheral Edema	10.9	0	10.9
Increased AST	4.7	6.3	10.9

Strategic Decision to Pursue Front-line Bemarituzumab + Chemotherapy Combination Trial Based on Compelling Rationale

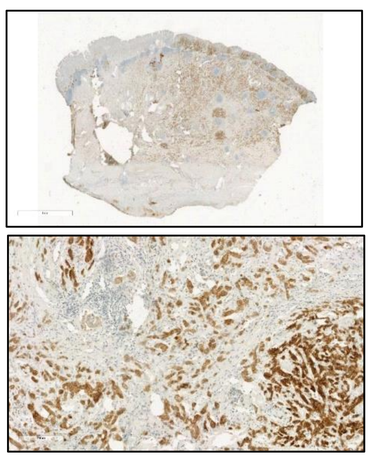
Preclinical data show additive efficacy of bemarituzumab + chemo

OCUM-2 gastric cancer xenograft model



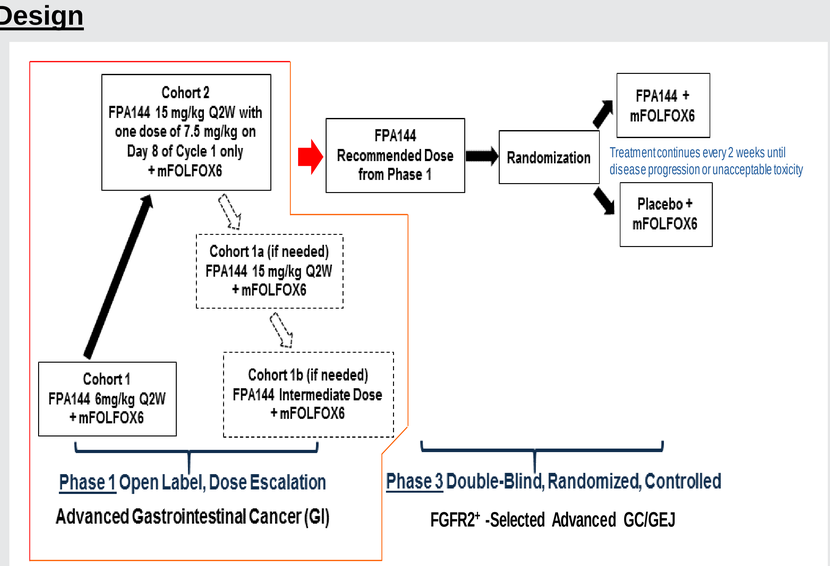
Mutational heterogeneity of GC/GEJ suggests that combining bemarituzumab + chemo will result in improved activity:

1. Acting on non-*FGFR2* amplified cells
2. Improving the activity of bemarituzumab in *FGFR2* amplified cells



FIGHT Trial: Study Design

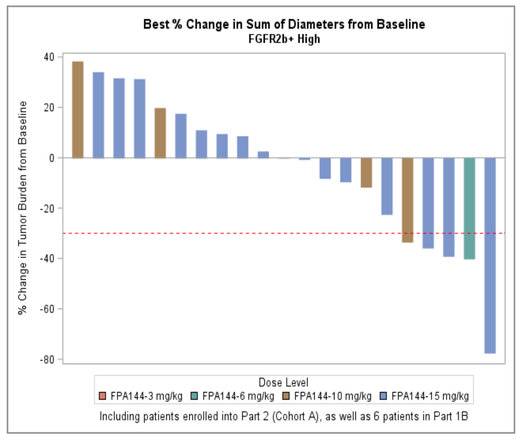
- Study has initiated with safety run-in including selection of dose with mFOLFOX6:
  - 6 mg/kg bemarituzumab every 2 weeks
  - 15 mg/kg bemarituzumab every 2 weeks with 1 dose of 7.5 mg/kg on Cycle 1, Day 8 only



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

Efficacy:

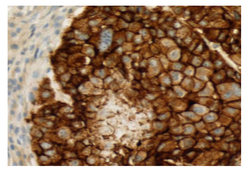
- In 21 treated patients with late-line GC/GEJ and strong IHC expression[3]:
  - ORR was 19.0% [95% CI (5.4%, 41.9%)] with 4 confirmed PRs
  - Disease control rate 55% (95% CI 38.5% - 70.7%)
  - Median duration of response 15.4 weeks (95% CI 9.1-19.1%)
- Overall safety:
  - Bemarituzumab is well tolerated
  - No DLT's and the MTD was not reached during dose escalation



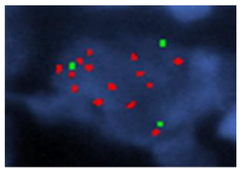
5 partial responses (4 confirmed. 1 unconfirmed) in 21 patients

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



3+ membrane staining in ≥10% of tumor with FPR2-D a proprietary anti-FGFR2b antibody



Positive - *FGFR2* probe correlates with FGFR2b overexpression

- ctDNA Analysis detects *FGFR2* gene amplification

Blood or plasma containing ctDNA

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 unresectable disease
  - 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

[1]Su, X. *FGFR2* amplification has prognostic significance in gastric cancer: results from a large international multicentre study. Br J Cancer 110:967, 2014
[2]Ahn S., et. al. FGFR2 in gastric cancer: protein overexpression predicts gene amplification and high H-index predicts poor survival. Mod Pathol 29:1095, 2016
[3]Catenacci D, Rha S, Bang YJ, et.al. Updated antitumor activity and safety of FPA144, an ADCC-enhanced, FGFR2b isoform-specific monoclonal antibody, in patients with FGFR2b+ gastric cancer. J Clin Oncol 35, 2017 (suppl; abstr 4067) 2017