Phase 1 Results from the Phase 1/3 FIGHT Study Evaluating Bemarituzumab and mFOLFOX6 in Advanced Gastric/GEJ Cancer (GC)

#91

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Background

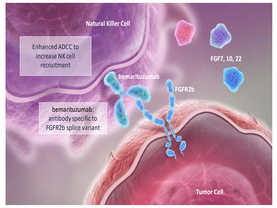
FGFR2b in Gastric Cancer

- Gastric cancer (GC)/gastroesophageal junction (GEJ) cancer is the 3rd most common cause of cancer death globally
  - Currently available treatments have limited benefit
- The presence of *FGFR2* amplification/ FGFR2b overexpression is associated with a worse prognosis[1-3] and is present in approximately 5-10% of patients with GC/GEJ
- FGFR2b expression is limited to a subset of tumors and epithelial tissue

Bemarituzumab (bema) is:

- an afucosylated, humanized IgG1 monoclonal antibody that selectively binds the b isoform of FGFR2
- an inhibitor of ligand binding to FGFR2b and blocks FGF7/10 receptor activation
- glycoengineered to enhance antibody-dependent cell-mediated cytotoxicity (ADCC)
- isoform-specific, potentially improving tolerability

Bemarituzumab



[1]Su, X. Br J Cancer 2014; [2]Jung, E. Hum Path 2011; [3]Ahn, S. Mod Path 2016

Methods

Phase 1 Primary Objective

Determine recommended dose of bema in combination with mFOLFOX6 to initiate Phase 3 FIGHT study

Dose and Schedule

Phase 1 Dose Levels

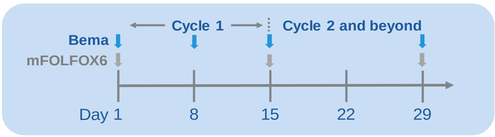
Dose Escalation	Cohort Design	Bema Dose/Schedule
Cohort 1	3+3	6 mg/kg Q2W
Cohort 2	Rolling 6	15 mg/kg Q2W + 7.5 mg/kg D8

Rationale for Dose Levels

- Bema 15mg/kg q2w was tolerable as monotherapy (Study FPA144-001)
- To achieve target trough concentration more rapidly, an additional dose of bema (7.5 mg/kg on D8) was added

Methods (continued)

Treatment Schedule



Phase 1 Endpoints

Primary Endpoint:
- Incidence of Dose-Limiting Toxicities (DLTs)

Secondary Endpoints:
- Incidence of treatment-emergent adverse events (AEs), lab abnormalities, corneal or retinal findings, ECG abnormalities
- PK parameters
- Incidence of treatment-emergent antibody response to bema

Exploratory Endpoints:
- Biomarker analysis of FGFR2 pathway in blood

Phase 1 Patient Population

Key Inclusion Criteria
- Adult with incurable GI cancer for whom mFOLFOX6 is appropriate
- ECOG 0-1
- Evaluable disease by RECIST v1.1

Key Exclusion Criteria
- Prior treatment with selective inhibitor of FGF-FGFR pathway
- Known HER2+
- Symptomatic CNS disease
- Treatment with radiotherapy or on other study within 28 days of enrollment

Distinct from the Phase 3 FIGHT Study Population; Phase 1 was:
- Not restricted to gastric/GEJ
- Not selected for FGFR2b status
- Not limited to patients without prior chemo for advanced/metastatic disease

Definition of Dose Limiting Toxicities

Attributed to bema within the first 28 days after starting treatment
- Any Grade 5 AE
- Grade 4 ophthalmologic AE or Grade 2-3 ophthalmologic AE that does not resolve in 7 days
- Non-hematologic adverse event Grade 3 or higher except nausea, vomiting and diarrhea
  - Grade 3 nausea, vomiting, or diarrhea that does not resolve with supportive care in 72 hours
  - Grade 4 nausea, vomiting, or diarrhea
- Febrile Neutropenia or ANC < 0.5 x 10^9/L greater than 5 days in duration
- Platelets < 25 x 10^9/L or < 50 x 10^9/L
  - for greater than 3 days duration
  - or with clinically significant bleeding
- Grade 4 anemia
- AST/ALT ≥ 3xULN with total bilirubin ≥ 2xULN not related to liver involvement of disease
- Grade 4 lab abnormality
- Incidental Grade 3 lab abnormalities that do not resolve in 72 hours

Results

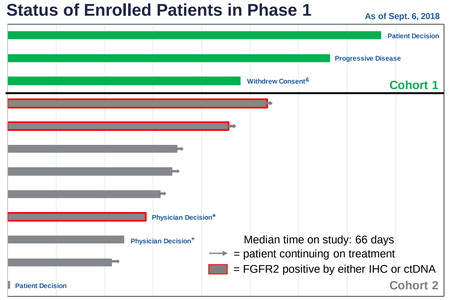
Phase 1 Patient Characteristics

	Cohort 1	Cohort 2	Total
Number of Patients	3	9	12
Number of Prior Treatments			
Mean	4	3.1	3.3
Median	4	2	2
Min	2	1	1
Max	6	8	8
Baseline ECOG status			
0	0	6 (67%)	6 (50%)
1	3 (100%)	3 (33%)	6 (50%)

Disease Type	Cohort 1	Cohort 2	Total
Gastric/Esophageal	0	3	3
Colorectal	3	5	8
Pancreatic	0	1	1

Cohort 1: 6 mg/kg Q2W + mFOLFOX6
Cohort 2:15 mg/kg Q2W + 7.5 mg/kg at D8 only + mFOLFOX6

Status of Enrolled Patients in Phase 1



[4]Weight loss and decline in clinical status
*Decision triggered by decline in clinical status
*Radiographic disease progression

Phase 1 Preliminary Efficacy Results

Pt #	GI Malignancy	Investigator-assessed BOR* as of Dec. 2018	FGFR2b+ (IHC)[a]	*FGFR2* amp by ctDNA[b]
02	Colorectal	SD	-	NA
03	Colorectal	SD	-	NA
06	Colorectal	SD	-	NA
08	Colorectal	NE^	NS	NA
12	Gastric/Esophageal	PR	NS	+
13	Gastric/Esophageal	SD	+	NA
14	Pancreatic	PD	+	NA
15	Colorectal	PR	-	NA
16	Colorectal	SD	NS	NA
17	Colorectal	SD	NS	NA
18	Colorectal	SD	-	NA
19	Gastric/Esophageal	SD	NS	NA

*Best overall response by RECISTv1.1: PD: progressive disease, SD: stable disease, PR: partial response, NE: Not evaluable
^Discontinuation of study due to port access issue on Day 1
[a]NS: not submitted (tissue for IHC was not required), negative: -, positive: +
[b]NA: Not yet available; positive: +

FGFR2+ Gastric/Esophageal Cancer Patients

- Patient 12: Study enrollment after progression on prior treatment with FOLFOX (1L) and FOLFIRI (2L). PR on CT, clinical response, ctDNA response at 4 months on study
- Patient 13: Study enrollment after relapse following resection and adjuvant FOLFIRINOX; subsequent treatment with Carboplatin/Paclitaxel. Complete metabolic response on PET (below) at 2 months with response in tumor markers, ctDNA prior to progression at 4 months

Treatment Emergent Adverse Events

(as of completion of DLT evaluation period: July 24, 2018)

At completion of DLT evaluation period for Phase 1:
- **No DLTs**
- No Grade ≥ 4 AEs, no deaths
- 1 Serious Adverse Event
  - Dyspnoea due to pulmonary involvement of GI malignancy (unrelated to bema)

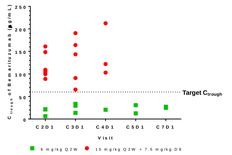
Treatment Emergent AEs in more than 1 Patient

	Cohort 1 N=3	Cohort 2 N=9	Total N=12
Any AE	3	8	11
Fatigue	1	5	6 (50%)
Vomiting	1	4	5 (42%)
Nausea	3	2	5
Diarrhea	2	3	5
Decreased appetite	2	2	4 (33%)
Stomatitis	2	2	4
Mucosal inflammation	1	2	3 (25%)
Constipation	1	2	3
Thrombocytopenia	1	2	2 (17%)
Abdominal Pain	1	1	2
Dysgeusia	0	2	2
Dyspnoea	0	2	2
Epistaxis	1	1	2
Neutropenia	0	2	2
Lymphocyte count decreased	0	2	2
Chills	0	2	2
Feeling Cold	0	2	2

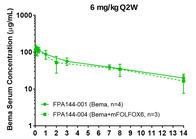
Treatment Emergent ≥Grade 3 AEs

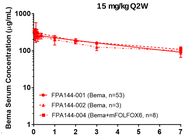
	Cohort 1 N=3	Cohort 2 N=9	Total N=12
Any Grade ≥ 3 AE	1	3	4 (33%)
Fatigue	0	2	2 (17%)
Neutropenia	0	2	2
Diarrhea	1	0	1 (8%)
Abdominal pain	1	0	1
Mucosal inflammation	0	1	1
Dyspnoea	0	1	1
Lymphocyte count decrease	0	1	1

Target Bema C_{trough} was Achieved by All Patients in Cohort 2



PK Profile of Bemarituzumab is Not Affected by Addition of mFOLFOX6



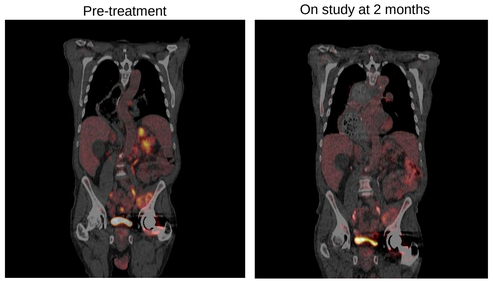


FPA144-001: Phase 1 FPA144 monotherapy; Bendell J., *et al*, ASCO Gastrointestinal Cancers Symposium, 2016

FPA144-002: Phase 1 FPA144 monotherapy (Japan); Data on file at Five Prime Therapeutics

FPA144-004: Phase 1 FPA144 + mFOLFOX6 (FIGHT study)

Patient 13: Complete Metabolic Response on PET



PET/CT Coronal Views demonstrate interval resolution of hypermetabolic activity in subpleural, retrocrural, and porta hepatis lymph nodes and distal pancreatic body and tail

Conclusions

- Bema in combination with mFOLFOX6 had acceptable toxicity in previously-treated patients with GI malignancies in Phase 1 safety run-in
  - Bema 15 mg/kg Q2W + 7.5 mg/kg D8 has been selected for combination with mFOLFOX6 in the global Phase 3 study
- PK results support 15 mg/kg Q2W + 7.5 mg/kg D8
  - Bema exposure was not affected by combination with mFOLFOX6
  - Additional D8 bema dose achieved target C_{trough} in all patients treated with bema 15mg/kg Q2W by D15
  - Bema continues to show activity in patients with heavily pre-treated GI malignancies
- FIGHT Phase 3, a randomized, double-blind, placebo-controlled study (NCT03694522) is currently enrolling worldwide
  - Patients with FGFR2b over-expressing or *FGFR2* gene-amplified gastric/GEJ cancer who have not received prior chemotherapy for advanced disease are eligible
  - For more information please visit : stomachcancertrial.com

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