Updated Antitumor Activity and Safety of FPA144, an ADCC-enhanced, FGFR2b Isoform-specific Monoclonal Antibody, in Patients with FGFR2b+ Gastric Cancer

#59

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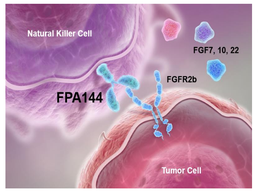
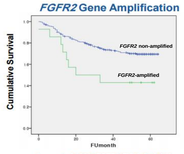
Background on FPA144



- **FPA144, an afucosylated humanized IgG1 monoclonal antibody, selectively binds the b isoform of FGFR2**
- **FPA144 therapy is designed to deliver 2 distinct anti-tumor effects:**
  1. **FPA144 inhibits ligand binding to FGFR2b and blocks receptor activation and downstream signaling (Gemo, 2014)**
  2. **FPA144 is glycoengineered for enhanced antibody-dependent cell-mediated cytotoxicity (ADCC)**
- **Isoform specificity of FPA144 may improve tolerability**
- **FPA144 is a potential therapy for patients whose gastric or bladder cancers overexpress FGFR2b or amplify the *FGFR2* gene**

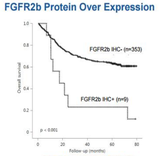
FGFR2b Overexpression and *FGFR2* Gene Amplification are Associated With Poor Prognosis

***FGFR2* Gene Amplification**



Jung *et al.* 2009; FGFR2 FISH; P=0.012

FGFR2b Protein Over Expression

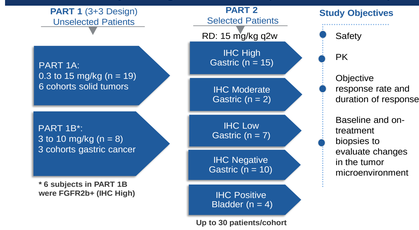


Pathobiology 2015; 82:269-279

Patients with gastric or gastroesophageal cancer (GE Cancer) for whom FPA144 is a potential therapy can be identified by 3 methods:

1. **Fluorescent *in situ* hybridization (FISH) analysis of *FGFR2* gene amplification in tumor tissue**
2. **Immunohistochemistry (IHC) analysis of FGFR2b protein overexpression in tumor tissue**
3. **Circulating DNA (ctDNA) analysis of *FGFR2* gene amplification in the peripheral blood**

Clinical Study Design Overview (NCT 02318329)



- **Initially patient selection for PART 2 required both tissue IHC and FISH amplification testing (n = 12), but FISH was discontinued after demonstrating high correlation with IHC results (100%, n = 12)**
- **High correlation between FGFR2b protein overexpression (IHC) and *FGFR2* gene amplification (FISH) was also supported by external data (Ahn S., *et. al.*, Mod Pathol. 2016)**

Study Population as of Data Cut-off March 20, 2017

Table 1

Patient Baseline Characteristics	All Patients N = 64	All Gastric Cancer[a] N = 41	IHC High Gastric Cancer N = 21	IHC Negative[b] Gastric Cancer N = 11
Median Age (yrs) (min, max)	58 (29, 86)	55 (29, 77)	**46 (29, 67)**	57 (44, 77)
Gender Male N (%)	36 (56.3%)	21 (51.2%)	**7 (33.3%)**	6 (54.5%)
Race N (%)				
White	27 (42.2%)	7 (17.1%)	**3 (14.3%)**	3 (27.3%)
Asian	35 (54.7%)	32 (78.0%)	**16 (76.2%)**	8 (72.7%)
ECOG N (%)				
0	20 (31.3%)	13 (31.7%)	**4 (19.0%)**	4 (36.4%)
1	44 (68.8%)	28 (68.3%)	**17 (81.0%)**	7 (63.6%)
Prior Therapies Median (N) (min, max)	3 (1, 8)	3 (1,6)	**3 (1, 6)**	4 (2,5)

[a] **Includes both FGFR2b+ and FGFR2b- gastric cancer patients (with 15 patients meeting the criteria of IHC High, 2 as IHC Moderate, 7 as IHC Low, and 11 as IHC Negative or with an unknown FGFR2b status).**
[b] **IHC Negative Gastric Cancer population includes patients with unknown FGFR2b status (n = 2) from Part 1A.**

Overall Safety Summary

- **No DLTs during dose escalation (MTD not reached)**
- **No grade 4 or higher treatment-related AEs**
- **16 reported SAEs, 5 treatment-related (across 4 patients):**
  - **Grade 2 ulcerative keratitis**
  - **Grade 3 hypersensitivity infusion reaction**
  - **Grade 3 nausea and vomiting in a single patient**
  - **Grade 2 ocular limbic stem cell deficiency* (drug discontinued)**
- **No hyperphosphatemia or retinal toxicity**

*Reported after the data cut-off date

Table 2: Most Common Treatment-Related Treatment-Emergent Adverse Events (Incidence ≥10%)

	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

Ocular Toxicity

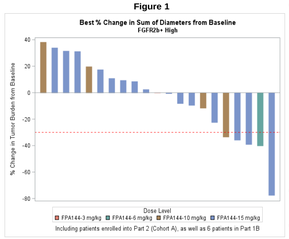
- **Toxicology studies have identified dose-dependent thinning of the corneal epithelium with FPA144**
- **Therefore, comprehensive ophthalmologic exams, including serial slit lamp examinations, were included in the FPA144-001 clinical trial to monitor for ocular toxicities**
- **23.4% (15/64) of patients reported ≥1 ocular toxicities (all grade 2 or less)**
  - **Most common (≥ 5%) ocular events were dry eye (10 patients, 15.6%) and increased lacrimation (4 patients, 6.3%)**
  - **2 symptomatic cases associated with corneal toxicity (Table 3)**

Table 3: Cases of Symptomatic Corneal Toxicity

Ocular-related AE	Study Day Onset of Event	Dose	Action	Outcome
Grade 2 Ulcerative Keratitis	Day 100	15 mg/kg	Moxifloxacin administration and FPA144 interruption for 1 dose	Resolution of event. Patient continued treatment with no further ocular complaints.
Grade 2 Limbic Stem Cell Deficiency	Day 448	10 mg/kg	FPA144 permanently discontinued	Within two months of last FPA144 administration, improvement of limbic stem cell deficiency and near complete symptomatic resolution.

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

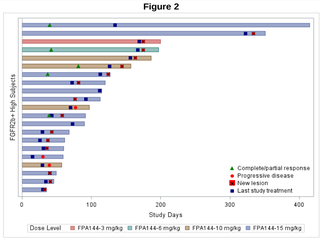
Figure 1



- **5 Partial Responses (4 confirmed, 1 unconfirmed) in 21 patients. Objective Response Rate: 19.0% (5.4%, 41.9%)**
  - **Median number of prior therapies = 3**
  - **Of the 4 confirmed Partial Responders, one received prior pembrolizumab therapy, another received ramucirumab, and a third received onartuzumab**
- **Disease Control Rate at 6 weeks: 57.1% (34.0%, 78.2%)**
- **No tumor responses observed in gastric cancer patients with Moderate or Low IHC status as of March 20, 2017**

Duration of Treatment in FGFR2b+ (IHC High) Gastric Cancer Patients

Figure 2

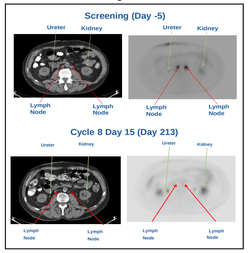


- **Median Duration of Response (weeks) = 15.4 (9.1, 19.1)**
- **Median PFS (weeks): 11.0 (5.7, 20.6)**

FGFR2b in Urothelial Bladder Cancer (UBC)

- **FGFR2b overexpression by IHC in bladder cancer is ~11% in primary tumors and ~14% in metastases**
- **FGF7 (a ligand that binds to FGFR2b) overexpression in bladder cancer correlates with reduced survival (Fan EW, *et. al.*, J Urol. 2015)**
- **In PART 1A, a patient with bladder cancer (IHC 2+) treated with 3mg/kg of FPA144 had a complete response which is on-going (706 days) (Figure 3)**
- **This observation provided the rationale to explore the use of FPA144 in bladder cancer**
- **FGFR2b-selected bladder cancer cohort in PART 2 is on-going:**
  - **4 patients enrolled to date (on treatment 0.1-10 weeks)**
  - **Too early to evaluate efficacy**

Figure 3



Conclusions

- **FPA144 was well tolerated in doses tested up to 15 mg/kg in patients with advanced solid tumors, including patients with gastric cancer**
  - **No hyperphosphatemia reported**
  - **Ocular adverse events were all ≤ Grade 2. No retinal toxicity reported.**
- **Confirmed radiographic responses of 19.0% (95% CI; 5.4%, 41.9%) with median duration of response of 15.4 weeks (9.1, 19.1)**
- **FPA144 efficacy data compare favorably with approved targeted agents in late-line gastric cancer which demonstrated low response rates as monotherapy and subsequently demonstrated greater benefit when combined with standard chemotherapy in earlier lines of therapy**
  - **Internal non-clinical data (not shown) demonstrates additive benefit of FPA144 to platinum and 5-FU chemotherapy**
- **Toxicities observed in this study (n = 64) suggest no overlapping toxicities with platinum and 5-FU chemotherapy**
- **Data supports further evaluation of the combination of FPA144 with chemotherapy or immunotherapy in FGFR2b-selected gastric and bladder cancer**

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