

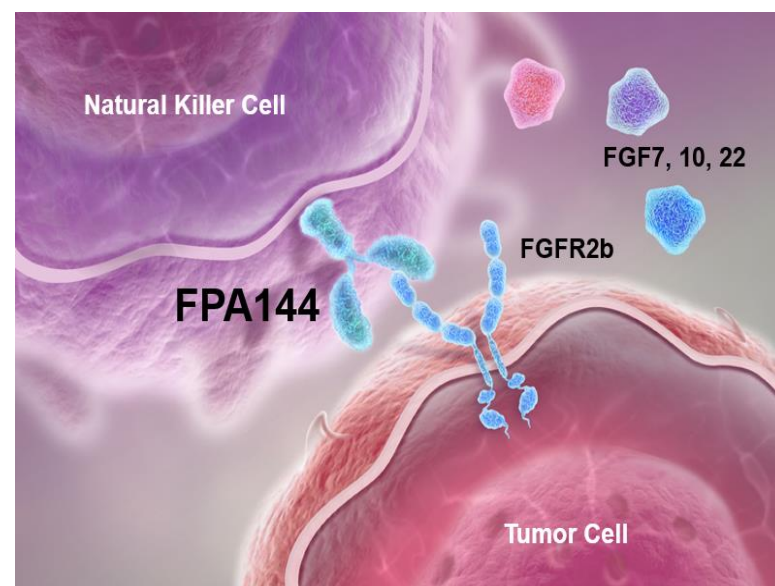
Updated Antitumor Activity and Safety of FPA144, an ADCC-enhanced, FGFR2b Isoform-specific Monoclonal Antibody, in Patients with FGFR2b+ Gastric Cancer

#59

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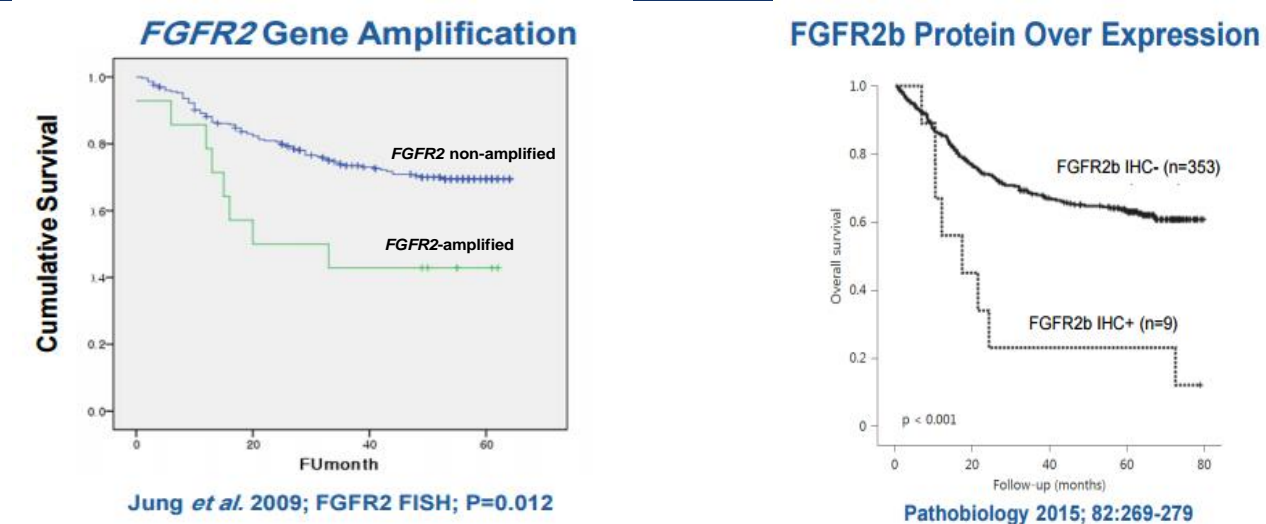
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Background on FPA144



- 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:
 - FPA144 inhibits ligand binding to FGFR2b and blocks receptor activation and downstream signaling (Gemo, 2014)
 - 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

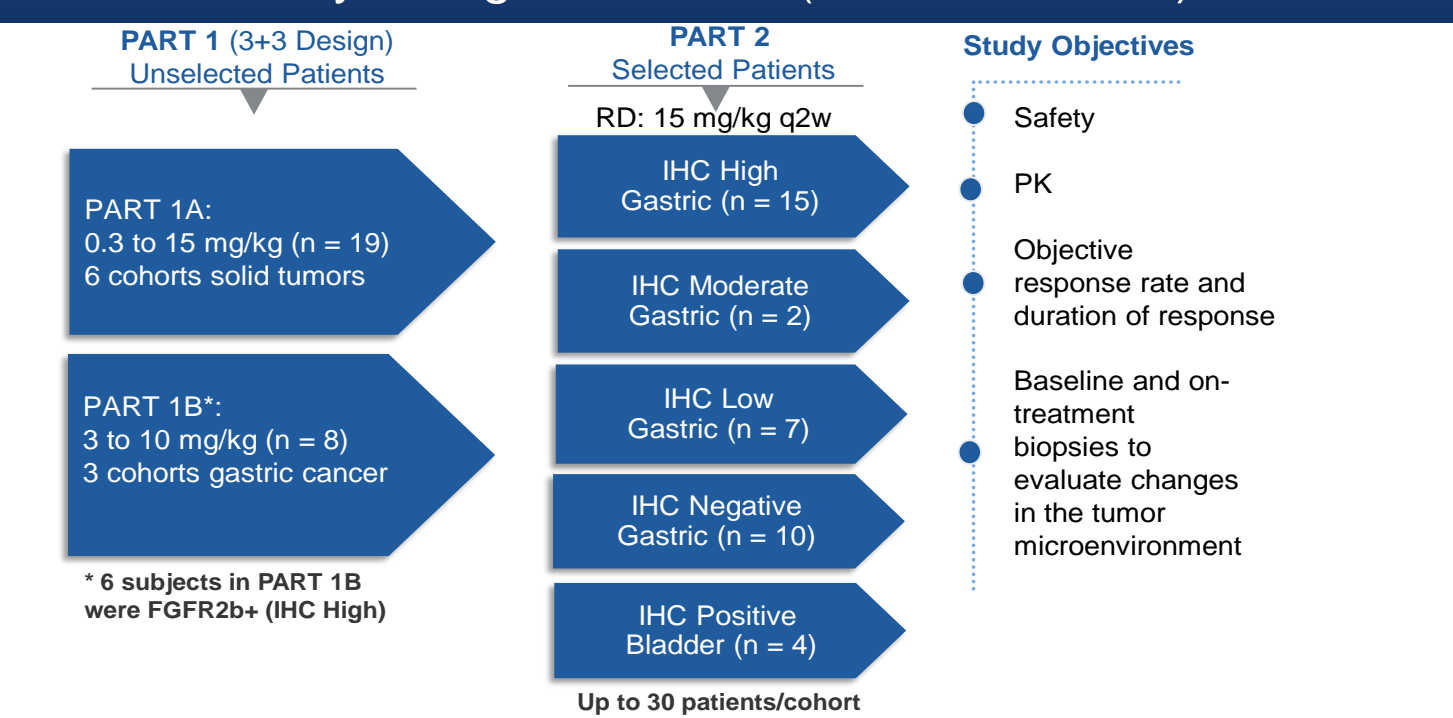
FGFR2b Overexpression and *FGFR2* Gene Amplification are Associated With Poor Prognosis



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

- Fluorescent *in situ* hybridization (FISH) analysis of *FGFR2* gene amplification in tumor tissue
- Immunohistochemistry (IHC) analysis of FGFR2b protein overexpression in tumor tissue
- 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

Patient Baseline Characteristics	All Patients N = 64	All Gastric Cancer* N = 41	IHC High Gastric Cancer N = 21	IHC Negative* 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)

* 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).
 † 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%)

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

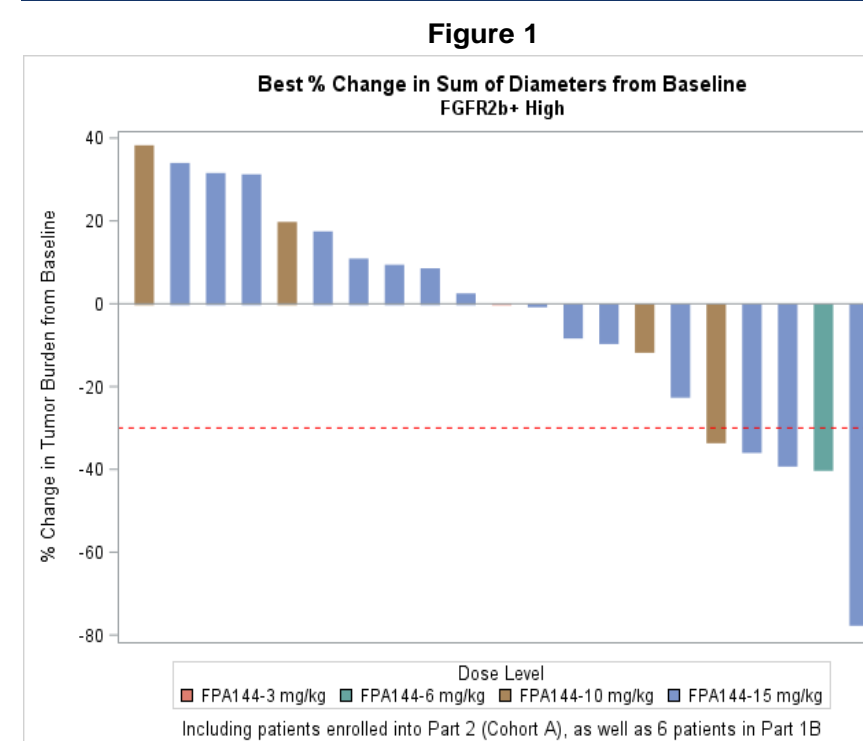
Ocular Toxicity

- 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

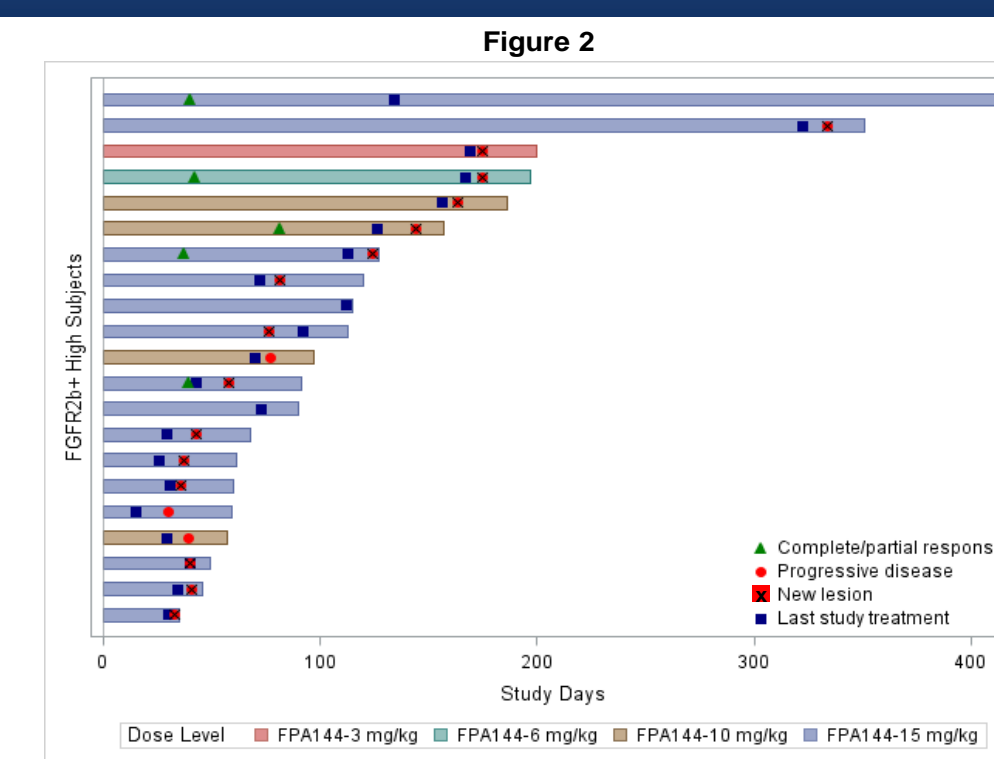
Ocular-related AE	Study Day Onset of Event	Dose	Action	Outcome
Grade 2 Ulcerative Keratitis	Day 100	15 mg/kg	Moxifloxacin administration and FPA144 interruption for 1 dose	Resolution of event. Patient continued treatment with no further ocular complaints.
Grade 2 Limbic Stem Cell Deficiency	Day 448	10 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



- 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

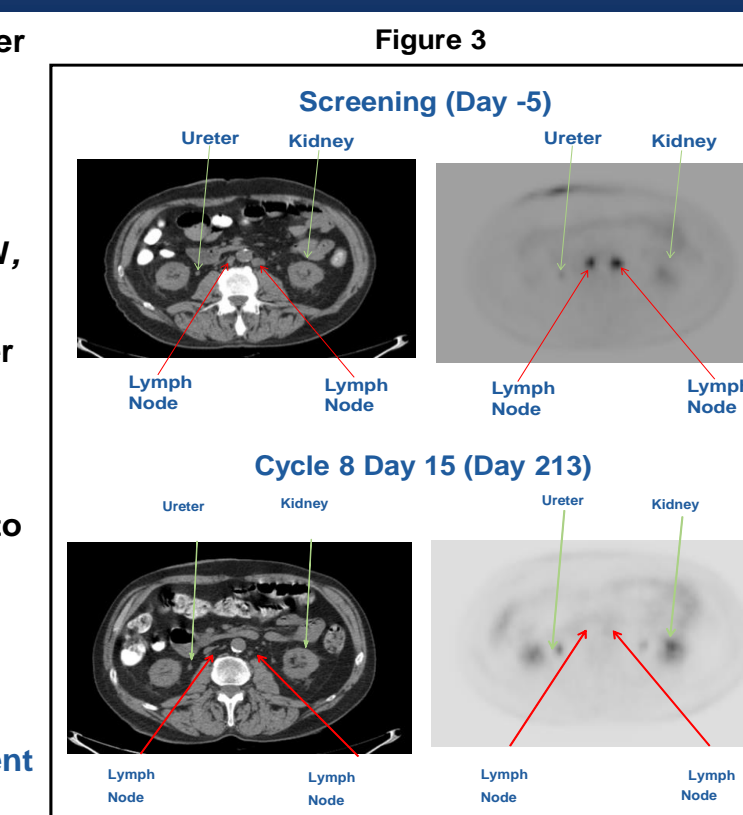
Duration of Treatment in FGFR2b+ (IHC High) Gastric Cancer Patients



- 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



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

References

Deng N, Goh L, Wang H, Das K, Tao J, Tan I, et al. A comprehensive survey of genomic alterations in gastric cancer reveals systematic patterns of molecular exclusivity and co-occurrence among distinct therapeutic targets. *Gut*. 2012; 61:673-84

Gemo A, Deshpande A, Palencia S, Bellocin D, Brennan TJ, Patil NS, et al. FPA144: A therapeutic antibody for treating patients with gastric cancers bearing *FGFR2* gene amplification. *Proc AACR*. 2014; 54:46

Han N, Kim MA, Lee HS, Kim WH. Evaluation of fibroblast growth factor receptor 2 expression, heterogeneity, and clinical significance in gastric cancer. *2015*; 82(6): 269-79

Hattori Y, Odagiri H, Nakatani H, Miyagawa K, Naito K, Sakamoto H et al. K-sam, an amplified gene in stomach cancer, is a member of the heparin-binding growth factor receptor genes. *PNAS*. 1990; 87(15): 5983-87

Hattori Y, Itoh H, Uchino S, Hosokawa K, Ochiai A, Ino Y et al. Immunohistochemical detection of K-sam protein in stomach cancer. *Clin Cancer Res*. 1996; 2:1373-81

Turner N, Grose R. Fibroblast growth factor signaling: from development to cancer. *Nat Rev Cancer*. 2010; 10:116-29

Fan EW, Li CC, Wu WJ, Huang CN, Li WM, Ke HL, Yeh HC, Wu TF, Liang PI, Ma LJ, Li CF. FGF7 Over Expression is an Independent Prognosticator in Patients with Urothelial Carcinoma of the Upper Urinary Tract and Bladder. *J Urol*. 2015 Jul;194(1):223-9.

Ahn S, Lee J, Hong M, Kim ST, Park SH, Choi MG, Lee JH, Sohn TS, Bae JM, Kim S, Jung SH, Kang WK, Kim KM. FGFR2 in gastric cancer: protein overexpression predicts gene amplification and high H-index predicts poor survival. *Mod Pathol*. 2016 Sep;29(9):1095-103.

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