original reports

Phase I Escalation and Expansion Study of Bemarituzumab (FPA144) in Patients With Advanced Solid Tumors and FGFR2b-Selected Gastroesophageal Adenocarcinoma

Daniel V.T. Catenacci, MD, PhD[1]; Drew Rasco, MD[2]; Jeeyun Lee, MD[3]; Sun Young Rha, MD, PhD[4]; Keun-Wook Lee, MD, PhD[4]; Yung Jue Bang, MD, PhD[5]; Johanna Bendell, MD[6]; Peter Enzinger, MD[7]; Neyssa Marina, MD[8]; Hong Xiang, PhD[8]; Wei Deng, PhD[8]; Janine Powers, PhD[8]; and Zev A. Wainberg, MD[9]

abstract

PURPOSE To evaluate the safety, pharmacokinetics, and preliminary activity of bemarituzumab in patients with FGFR2b-overexpressing gastric and gastroesophageal junction adenocarcinoma (GEA).

PATIENTS AND METHODS FPA144-001 was a phase I, open-label, multicenter trial consisting of the following 3 parts: part 1a involved dose escalation in patients with recurrent solid tumors at doses ranging from 0.3 to 15 mg/kg; part 1b involved dose escalation in patients with advanced-stage GEA; and part 2 involved dose expansion in patients with advanced-stage GEA that overexpressed FGFR2b at various levels (4 cohorts; high, medium, low, and no FGFR2b overexpression) and 1 cohort of patients with FGFR2b-overexpressing advanced-stage bladder cancer.

RESULTS Seventy-nine patients were enrolled; 19 were enrolled in part 1a, 8 in part 1b, and 52 in part 2. No dose-limiting toxicities were reported, and the recommended dose was identified as 15 mg/kg every 2 weeks based on safety, tolerability, pharmacokinetic parameters, and clinical activity. The most frequent treatment-related adverse events (TRAEs) were fatigue (17.7%), nausea (11.4%), and dry eye (10.1%). Grade 3 TRAEs included nausea (2 patients) and anemia, neutropenia, increased AST, increased alkaline phosphatase, vomiting, and an infusion reaction (1 patient each). Three (10.7%) of 28 patients assigned to a cohort receiving a dose of $\geq$ 10 mg/kg every 2 weeks for $\geq$ 70 days reported reversible grade 2 corneal TRAEs. No TRAEs of grade $\geq$ 4 were reported. Five (17.9%; 95% CI, 6.1% to 36.9%) of 28 patients with high FGFR2b-overexpressing GEA had a confirmed partial response.

CONCLUSION Overall, bemarituzumab seems to be well tolerated and demonstrated single-agent activity as late-line therapy in patients with advanced-stage GEA. Bemarituzumab is currently being evaluated in combination with chemotherapy in a phase III trial as front-line therapy for patients with high FGFR2b-overexpressing advanced-stage GEA.

J Clin Oncol 38:2418-2426. © 2020 by American Society of Clinical Oncology

ASSOCIATED CONTENT

Protocol

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on February 3, 2020 and published at ascopubs.org/journal/jco on March 13, 2020: DOI https://doi.org/10.1200/JCO.19.01834

INTRODUCTION

Gastroesophageal adenocarcinoma (GEA) represents the third most common cause of cancer death worldwide.[1] The majority of patients globally present with advanced-stage disease, in whom the median overall survival is approximately 11 months with combination chemotherapy.[2] Later lines of systemic therapy such as ramucirumab,[3,4] immunotherapy,[5,6] and trifluridine/tipiracil[7] improve survival by only 1 to 2 months compared with placebo. New effective therapeutics are needed.

Potential therapeutic targets include the fibroblast growth factor (FGF)/fibroblast growth factor receptor (FGFR) pathway, which stimulates angiogenesis, transformation, and proliferation of tumor cells.[8] This pathway is mediated by a family of transmembrane tyrosine kinase receptors encoded by 4 genes (*FGFR1-FGFR4*).[8] Oral tyrosine kinase inhibitors have demonstrated efficacy in bladder cancer and cholangiocarcinomas with genetic alternations, such as mutations or fusions of *FGFR1*, *FGFR2*, and *FGFR3* (although minimal activity with *FGFR* amplification), but toxicities such as hyperphosphatemia, stomatitis, and retinal toxicities have been reported in association with these agents.[9-11] The FGFR2 receptor has a splice variant, FGFR2b (also known as FGFR2IIIb, KGFR, or K-sam),[12] that is overexpressed in 2.5%-31.1% of GEAs depending on the antibody and assay used.[13-16] Overexpression of FGFR2b has been

demonstrated to be a result of either amplification or aberrant transcriptional upregulation of the *FGFR2* gene,[8,17-20] and in GEA, both FGFR2b overexpression and *FGFR2* gene amplification have been associated with a worse prognosis.[21-23] Amplification of the *FGFR2* gene is associated with both the chromosomal instability and genomically stable subgroups of The Cancer Genome Atlas.[15,17-20,24]

Bemarituzumab (FPA144) is a first-in-class humanized immunoglobulin G1 monoclonal antibody specific to the splice-variant FGFR2b that inhibits binding of the ligands FGF7, FGF10, and FGF22.[25] Specifically, bemarituzumab does not inhibit binding of FGF23, the ligand responsible for phosphate and vitamin D metabolism,[26] thereby potentially avoiding the risk of hyperphosphatemia associated with pan-FGFR tyrosine kinase inhibitors.[9-11] Bemarituzumab is also glycoengineered for increased affinity for the human Fc gamma RIIIA receptor expressed on natural killer cells, enabling enhanced antibody-dependent cell-mediated cytotoxicity.[25] Bemarituzumab has demonstrated inhibition of FGFR2b phosphorylation and cell proliferation in FGFR2b-overexpressing gastric cancer xenograft models.[25] Preclinical in vitro and in vivo studies identified that a bemarituzumab target trough serum concentration of $\geq$ 60 μg/mL achieves maximum efficacy (data on file; Five Prime Therapeutics, South San Francisco, CA).

In preclinical toxicity studies, bemarituzumab was tolerated in doses up to 100 mg/kg administered weekly for 13 weeks to cynomolgus monkeys. Dose-dependent microscopic corneal atrophy and mammary gland atrophy were observed in animals receiving treatment but not in the animals killed at the end of the 15-week recovery phase, suggesting the findings were reversible (data on file; Five Prime Therapeutics). This first-in-human, phase I, dose-escalation and expansion trial of bemarituzumab (FPA144-001 trial) was designed to evaluate the safety and recommended dose (RD) of bemarituzumab in patients with solid tumors and to evaluate the preliminary efficacy in patients with FGFR2b-overexpressing advanced-stage GEA or bladder cancer.

PATIENTS AND METHODS

Phase I Patient Population and Trial Design

FPA144-001 was an open-label, multicenter, nonrandomized trial (ClinicalTrials.gov identifier: NCT02318329).[27,28] Please see Protocol (online only). Informed consent was obtained for all patients, and the trial was conducted in compliance with local and national regulations and in accordance with the ethical principles based on the Declaration of Helsinki.

The trial was designed with 3 parts, 2 parallel dose escalations (parts 1a and 1b) and a part 2 expansion (Fig 1).

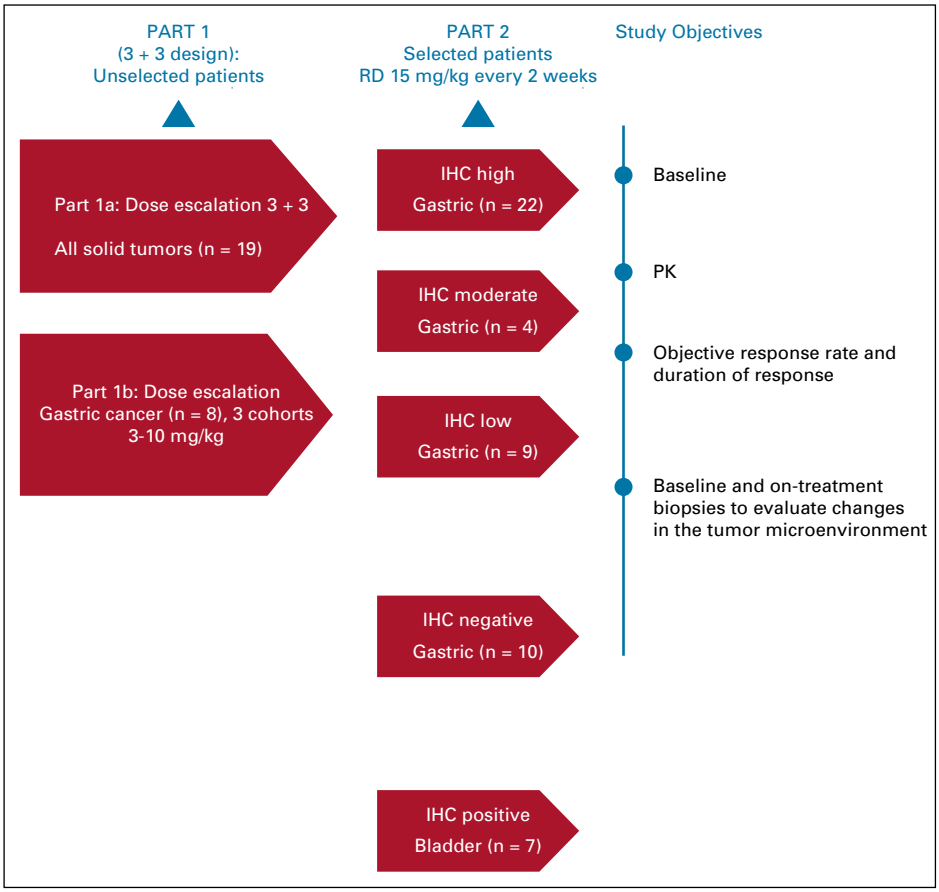

FIG 1. Study design. IHC, immunohistochemistry; PK, pharmacokinetics; RD, recommended dose.

Patients in part 1a were required to have any locally advanced or metastatic solid tumor that had progressed after standard treatment or that was not appropriate for standard treatment. For parts 1b and 2, patients were required to have histologically documented recurrent or metastatic GEA or bladder cancer (part 2 only), measurable disease by RECIST version 1.1, and available tumor tissue for retrospective or prospective evaluation of FGFR2b expression and *FGFR2* amplification.

Part 1a. The primary end point of part 1a was to determine the incidence of grade 3 or 4 adverse events (AEs) and clinical laboratory abnormalities defined as dose-limiting toxicities (DLTs). Part 1a followed a standard 3 + 3 dose-escalation design with 6 cohorts of patients receiving bemarituzumab at doses of 0.3, 1, 3, 6, 10, and 15 mg/kg administered intravenously every 2 weeks. Intrapatient dose escalation was not permitted. Dose-escalation decisions were agreed upon by the investigators and the study sponsor and based on an assessment of DLTs, AEs, and laboratory data during a 28-day DLT window.

Part 1b. The primary end point of part 1b was to evaluate safety and pharmacokinetics (PK) in patients with GEA based on literature suggesting therapeutic antibodies may achieve lower serum concentrations in patients with GEA compared with other solid tumors.[29]

Part 2. After identification of the RD from parts 1a and 1b, part 2 enrolled patients with GEA who were assigned to one of the following cohorts based on the level of FGFR2b expression in their tumor sample using a centrally performed validated laboratory-developed prototype immunohistochemistry (IHC) assay (LabCorp, Burlington, NC): cohort 1, high staining ($\geq$ 10% of tumor cells with 3+ membranous staining); cohort 2, moderate staining ($\geq$ 10% of tumor cells with 2+ staining and/or $<$ 10% of tumor cells with 3+ staining); cohort 3, low staining (1+ staining and/or $<$ 10% of tumor cells with 2+ staining); and cohort 4, negative staining. Initially, enrollment into the high FGFR2b group also required demonstration of *FGFR2* amplification (FGFR2-to-CEN10 ratio $\geq$ 2.0) by fluorescence in situ hybridization (FISH). After observing a 100% correlation in the first 12 patients between high overexpression by IHC and gene amplification by FISH, testing for amplification was conducted retrospectively. Cohort 5 enrolled patients with FGFR2b-overexpressing bladder cancer.

Treatment and Assessments

Patients were administered bemarituzumab as a 30-minute intravenous infusion at a dose based on body weight every 2 weeks until disease progression, unacceptable toxicity, patient or physician decision, or death. Safety was monitored throughout the study and for 28 days after the last dose of treatment by history, physical examination, ECG, blood laboratory testing, and ophthalmologic exams. AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (version 4.03). A DLT was defined as any of the following events occurring in the first 28 days: absolute neutrophil count (ANC) of $< 0.5 \times 10^9$/L for $>$ 5 days; febrile neutropenia (fever $>$ 38.3°C with ANC $< 1.0 \times 10^9$/L); platelets $< 25 \times 10^9$/L or $< 50 \times 10^9$/L with bleeding requiring medical intervention; grade 3 thrombocytopenia for $>$ 7 days; grade 4 anemia; any grade $\geq$ 2 ophthalmologic AE that did not resolve within 7 days; AST or ALT $> 3\times$ the upper limit of normal (ULN) and concurrent total bilirubin $> 2\times$ ULN; or any nonhematologic AE of grade $\geq$ 3 (except controlled nausea, vomiting, and diarrhea).

Comprehensive ophthalmologic assessments (fundoscopy, slit lamp, ocular coherence tomography, and visual acuity) were conducted during the trial at screening, after 2 doses, at the time of any ophthalmologic symptoms, and at end of treatment. Any adverse ophthalmologic events were deemed events of special interest and followed until resolution. Additional slit lamp evaluations of the cornea were conducted every 6 weeks for the first 6 months (later amended to be conducted throughout therapy regardless of duration). Interim safety reviews were conducted by an independent data safety monitoring board (DSMB) during part 2 of this study in accordance with the DSMB Charter.

Multiple serum PK samples were collected during the first dose, followed by collection before and at the end of infusions, at subsequent dosing cycles, and approximately 28 days after the last dose. Tumor assessments were performed according to RECIST version 1.1 during screening and every 6 weeks from the first dose of bemarituzumab until week 24 and then every 12 weeks until study treatment discontinuation or withdrawal of consent. A complete response (CR) or partial response (PR) required confirmation within 4 to 6 weeks.

Statistical Methods

Up to 30 patients were planned for each cohort in part 2. Safety and PK analyses were conducted in all patients who received $\geq$ 1 dose of bemarituzumab. Patients were evaluable for efficacy if they had measurable disease at study entry and at least 1 postbaseline disease assessment. Descriptive summary statistics were provided for patient characteristics, safety, and PK variables.

Objective response rate (ORR) was calculated as the proportion of patients with best overall response as CR or PR per RECIST version 1.1. Disease control rate (DCR) was calculated as the proportion of patients with a best overall response of CR, PR, or stable disease. Duration of response (DOR) was calculated as the number of days from the first documentation of response to the first documentation of progressive disease or death, whichever occurred earlier.

RESULTS

Baseline Patient Characteristics

From November 24, 2014, to February 16, 2018, 79 patients at 17 sites across the United States, South Korea, and Taiwan were enrolled onto the study. Nineteen patients with solid tumors were enrolled in part 1a (including 3 patients

with GEA, 6 with colorectal cancer, 2 with biliary cancer, and 1 each with neuroendocrine, submandibular, lung, peritoneal, esophageal, breast, bladder, and pancreatic cancer), 8 patients with GEA were enrolled in part 1b, and 52 patients with GEA (n = 45) or bladder cancer (n = 7) were enrolled in part 2 (Fig 1). Baseline characteristics are listed in Table 1. The median number of bemarituzumab infusions across all patients was 4 (range, 1-97 infusions), and for patients with GEA, the median number of infusions was 5 (range, 1-34 infusions). As of the data cutoff date of February 20, 2019, 1 patient with bladder cancer remained on treatment. The majority of patients (72.2%) discontinued the study as a result of radiographic disease progression.

Safety

No DLTs were observed during the part 1a and 1b dose escalations, and no maximum-tolerated dose was identified. Seventy-four (93.7%) of 79 patients reported treatment-emergent AEs (TEAEs). TEAEs reported in ≥ 10% of patients by study part are listed in Table 2. The most frequently reported TEAEs were generally consistent with an advanced cancer population and included decreased appetite (30.4%), abdominal pain (29.1%), and fatigue (26.6%).

Treatment-related AEs (TRAEs) were reported in 40 (50.6%) of 79 patients. Fatigue (17.7%), nausea (11.4%), and dry eye (10.1%) were the most common TRAEs. Three patients reported infusion reactions (grades 1-3, in 1 patient each). Grade 3 or 4 TEAEs occurred in 40 patients (50.6%), and 6 of those patients (7.6%) had grade 3 or 4 TEAEs that were considered by the investigator to be treatment related. Eight grade 3 AEs were reported in the 6 patients (nausea [2 patients] and anemia, neutropenia, increased AST, increased alkaline phosphatase, vomiting, and an infusion reaction [1 patient each]).

Serious AEs (SAEs) occurred in 23 patients (29.1%), with 6 events in 5 patients (6.3%) assessed as treatment related.

TABLE 1. Patient Characteristics

Characteristic	All Patients (N = 79)	Patients With GEA				
		All (n = 56)	FGFR2b High (n = 28)	FGFR2b Moderate (n = 4)	FGFR2b Low (n = 13)	FGFR2b Negative or Unknown (n = 11)
Median age, years (range)	59 (25-86)	56 (29-77)	54 (29-70)	60 (50-61)	63 (50-68)	57 (44-77)
Sex, No. (%)						
Male	46 (58.2)	31 (55.4)	11 (39.3)	3 (75)	11 (84.6)	6 (54.5)
Female	33 (41.8)	25 (44.6)	17 (60.7)	1 (25)	2 (15.4)	5 (45.5)
Race, No. (%)						
Asian	46 (58.2)	42 (75)	23 (82.1)	3 (75)	8 (61.5)	8 (72.7)
White	31 (39.2)	12 (21.4)	3 (10.7)	1 (25)	5 (38.5)	3 (27.3)
American Indian	1 (1.3)	1 (1.8)	1 (3.6)	0	0	0
African American	1 (1.3)	1 (1.8)	1 (3.6)	0	0	0
ECOG PS, No. (%)						
0	24 (30.4)	16 (28)	6 (21.4)	0	6 (42.2)	4 (36.4)
1	55 (69.6)	40 (71.4)	22 (78.6)	4 (100)	7 (53.8)	7 (63.6)
Median No. of prior therapies (range)	3 (1-8)	3 (1-6)	2.5 (1-6)	1.5 (1-4)	3 (2-5)	4 (2-5)
Prior treatment, No. (%)						
Platinum/pyrimidine		55 (98.2)	28 (100)	3 (75)	13 (100)	11 (100)
Taxanes		41 (73.2)	19 (67.9)	1 (25)	12 (92.3)	9 (81.8)
Irinotecan		26 (46.4)	9 (32.1)	2 (50)	9 (69.2)	6 (54.5)
Ramucirumab		12 (21.4)	6 (21.4)	0	5 (38.5)	1 (9.1)
FGFR2b overexpression, No. (%)						
Strong		28 (50)				
Moderate		4 (7.1)				
Low		13 (23.2)				
None		11 (19.6)				

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; GEA, gastroesophageal adenocarcinoma.

TABLE 2. Adverse Events Occurring > 10% of Patients in the Overall Patient Population

	No. of Patients (%)		
Preferred Term	**All Events (N = 79)**	**Grade 3 or 4 Events**	**Grade 5 Events**
Decreased appetite	24 (30.4)	1 (1.3)	0
Abdominal pain	23 (29.1)	5 (6.3)	0
Fatigue	21 (26.6)	1 (1.3)	0
Nausea	17 (21.5)	2 (2.5)	0
Anemia	16 (20.3)	7 (8.9)	0
Vomiting	15 (19.0)	1 (1.3)	0
Dry eye	14 (17.7)	0	0
Diarrhea	11 (13.9)	0	0
Edema, peripheral	11 (13.9)	1 (1.3)	0
Pyrexia	11 (13.9)	0	0
Constipation	9 (11.4)	1 (1.3)	0
Weight decreased	9 (11.4)	1 (1.3)	0
Dyspnea	8 (10.1)	1 (1.3)	0
Hypoalbuminemia	8 (10.1)	1 (1.3)	0
Pruritus	8 (10.1)	0	0

Nausea and vomiting were reported in 1 patient, and an infusion reaction was reported in 1 patient. Any ocular event that required intervention or drug discontinuation was deemed an event of special interest and categorized as an SAE. Three patients reported such ocular events (ulcerative keratitis, limbal stem-cell deficiency, and corneal dystrophy in 1 patient each). These 3 ocular events were all corneal and grade 2, were reported at doses ≥ 10 mg/kg, and were reported ≥ 70 days after the patient's first dose of bemarituzumab. The patient with ulcerative keratitis presented with ocular pain on study day 100 while receiving treatment at a dose of 15 mg/kg. Bemarituzumab was held for 1 dose, and the patient received a topical ophthalmologic antibiotic and then resumed bemarituzumab without recurrence of the AE. The patient with limbal stem-cell deficiency presented with decreased visual acuity on study day 448 while receiving treatment at a dose of 10 mg/kg. Ophthalmologic examination revealed conjunctivalization, bemarituzumab was permanently discontinued, the patient received an antibiotic ointment, and the AE resolved 60 days after the last dose of study drug. This AE was the only TRAE on the study resulting in treatment discontinuation. The patient with corneal dystrophy developed myopia on study day 104 (33 days after the sixth and final dose of bemarituzumab at 15 mg/kg), which resolved with corticosteroid eye drops. Of the 28 patients who received bemarituzumab at doses of ≥ 10 mg/kg for ≥ 70 days, ocular events of special interest were reported in 3 patients (10.7%). In addition, low-grade (grade 1 or 2) ocular TEAEs were reported in 23 (29.1%) of 79 patients, with the most common events being dry eye (17.7%) and increased lacrimation (6.3%). No retinal toxicity was reported.

Four patients died on study; 1 patient died as a result of septic shock, and 3 died as a result of progressive disease, with no deaths deemed by the investigator as related to bemarituzumab. No notable difference in the safety profile was identified based on tumor type (GEA *v* non-GEA) or level of FGFR2b expression.

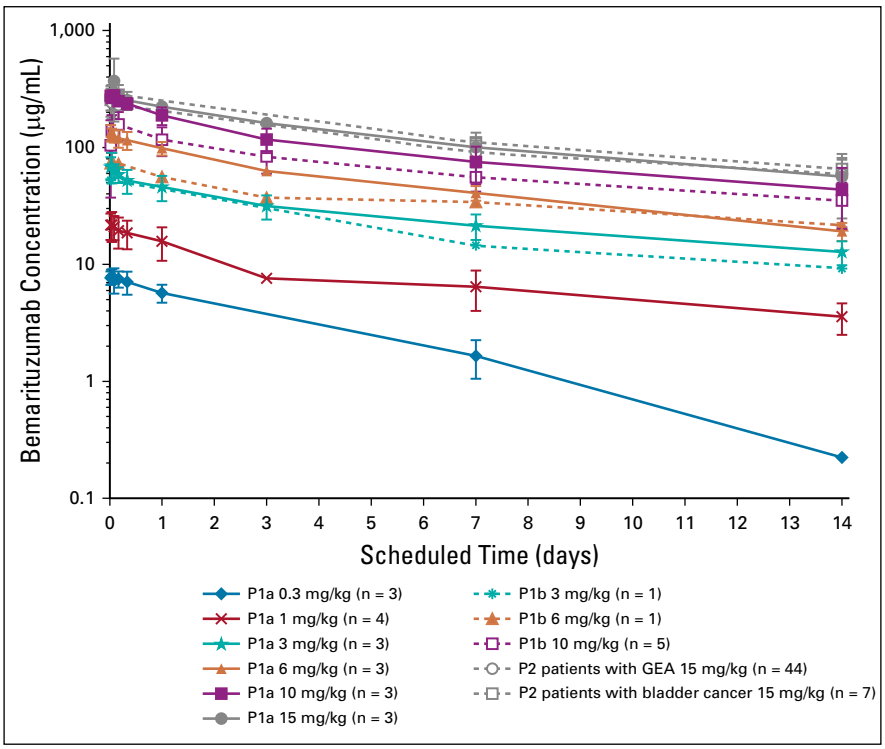

FIG 2. Mean (± standard deviation) bemarituzumab serum concentration versus time profiles after first dose (cycle 1, day 1). GEA, gastroesophageal adenocarcinoma; P1a, part 1a; P1b, part 1b; P2, part 2.

PK

Bemarituzumab serum concentration versus time profiles (group mean ± standard deviation) from cycle 1, dose 1 for 77 of 79 patients (excluding the 2 patients without full dose) are displayed in Figure 2. Group mean estimated PK parameters using noncompartmental analysis from 75 of 79 patients (excluding the 4 patients without enough data or without full dose) are listed in Table 3 by cohort. Bemarituzumab demonstrated nonlinear clearance from 0.3 mg/kg to 1 mg/kg and approximately linear clearance from 1 mg/kg to 15 mg/kg in patients, suggesting target-mediated clearance. Maximum concentration (C_{max}) increased the dose proportionally, whereas exposure (area under the curve [AUC]) did not increase dose proportionally in the nonlinear dose range (0.3-1 mg/kg). In the linear dose range (1-15 mg/kg), both C_{max} and AUC increased dose proportionally. A slight accumulation of C_{max} and trough concentration (C_{trough}) was observed with repeated every-2-week dosing.

A comparison of the PK parameters in the 3 patients with corneal toxicity versus those in the 25 patients who were dosed at ≥ 10 mg/kg for ≥ 70 days without corneal toxicity did not identify a clear association based on C_{max}, C_{trough}, or AUC; however, analyses are limited by the number of patients. The dose of 15 mg/kg every 2 weeks was identified as the RD, based on the observed clinical activity, the safety, and the ability of this dose to achieve the target trough of ≥ 60 μg/mL in most of the patient population. In patients with high FGFR2b-overexpressing GEA, responses were observed in the 1 patient dosed at 6 mg/kg, 1 of 4 patients dosed at 10 mg/kg, and 3 of 22 patients dosed at 15 mg/kg. All 5 patients with PRs achieved the predicted target C_{trough} at steady-state of ≥ 60 μg/mL.

Antitumor Activity

Fifty-two (92.9%) of 56 patients with GEA enrolled across the study (parts 1a and 1b combined) were efficacy evaluable per protocol, and all received a dose of at least 6 mg/kg every 2 weeks. Twenty-eight of these patients had tumors that had high FGFR2b overexpression (all *FGFR2* amplified by FISH), 4 patients had tumors with moderate expression, 12 patients had tumors with low expression, and 8 patients had tumors with no or unknown expression. All tumors with moderate, low, or no or unknown FGFR2b expression were nonamplified by FISH (Table 1). The ORR was 17.9% (95% CI, 6.1% to 36.9%) in patients with GEA with high FGFR2b overexpression, with a median DOR of 12.6 weeks (range, 9.1-19.1 weeks; Fig 3). Stable disease was the best observed response in 13 additional patients, leading to an overall DCR (PR plus stable disease) of 64.3% (95% CI, 44.1% to 81.4%) in the subgroup with high FGFR2b overexpression (Fig 4).

TABLE 3. Bemarituzumab Pharmacokinetic Parameter Estimates Using Noncompartmental Analysis for Patients Enrolled in FPA144-001 After First Dose

		Mean ± SD		
Study Part and Dose (mg/kg)	**No. of Patients Enrolled**	**Cmax (μg/mL)**	**Ctrough (μg/mL)**	**AUClast (d*μg/mL)**
Part 1a (all solid tumors including GEA)				
0.3	3	7.96 ± 1.14	0.224[a]	28.3 ± 9.50
1	4	22.2 ± 6.12	3.57 ± 1.07[b]	115 ± 36.2
3	3	71.5 ± 18.2	12.8 ± 2.98	355 ± 82.5
6	3	136 ± 17.5	19.2 ± 3.39	672 ± 83.5
10	3	288 ± 7.30	43.6 ± 23.4	1,320 ± 340
15	3	393 ± 185	56.4 ± 31.7	1,710 ± 310
Part 1b (GEA)				
3	1	52.5	9.22	288
6	1	77.0	21.6	529
10	6[c]	164 ± 43.8	35.3 ± 14.6	885 ± 191
Part 2				
15 (GEA)	45[d]	276 ± 59.3	59.5 ± 19.2	1,610 ± 329
15 (bladder)	7	297 ± 57.0	65.4 ± 16.0	1,840 ± 324

Abbreviations: AUC_{last}, area under the observed concentration-time curve from the time of dosing to the last quantifiable concentration after first dose; C_{max}, maximum observed serum concentration after first dose; C_{trough}, observed serum concentration at the end of the first dose interval; GEA, gastroesophageal adenocarcinoma; SD, standard deviation.

[a]Only 1 patient included as a result of 2 of 3 patients with C_{trough} below the lower limit of quantification.

[b]Only 3 patients included as a result of no data from cycle 1, day 15 for 1 patient as a result of early termination on study.

[c]Only 5 patients included as a result of 1 patient receiving a partial dose for first dose.

[d]Only 42 patients included as a result of missing data for 3 patients.

In the 12 patients with GEA with low FGFR2b overexpression, there was 1 confirmed response (ORR, 8.3%; 95% CI, 0.2% to 38.5%), with a DOR of 18.1 weeks. The blood from this patient with tumor response tested negative for *FGFR2* circulating tumor DNA amplification. There were no responses in the subgroups with moderate (n = 4) and no or unknown (n = 10) FGFR2b overexpression.

Six patients with bladder cancer selected for FGFR2b overexpression (high, n = 5; and low, n = 1) were evaluable for efficacy. No responses were observed. Four patients experienced a best response of stable disease for a median of 11.3 weeks (range, 10.1-17.6 weeks). Of note, 1 additional patient with FGFR2b-overexpressing bladder cancer was enrolled in part 1a at a dose of 3 mg/kg every 2 weeks. The patient had a history of surgically resected bladder cancer with recurrent disease that was diagnosed by positron emission tomography (PET) scan and, on study, experienced a complete metabolic response by PET scan, which was ongoing at the time of data cutoff (49 months).

DISCUSSION

This first-in-human study demonstrated that bemarituzumab, an afucosylated monoclonal antibody directed against FGFR2b, can be safely administered in patients with advanced cancer at doses up to 15 mg/kg every 2 weeks. Evidence of monotherapy activity was observed in heavily pretreated patients with high FGFR2b-overexpressing GEA. The RD was determined to be 15 mg/kg every 2 weeks based on safety and clinical responses observed at dose levels that achieved the target trough concentration of bemarituzumab. Consistent with selective targeting of FGFR2b by bemarituzumab, AEs associated with the pan-FGFR oral tyrosine kinase inhibitors, such as stomatitis and hyperphosphatemia, were not observed with bemarituzumab. However, reversible TRAEs of grade 2 symptomatic corneal events, which required intervention and in one case drug discontinuation, were reported in 3 (10.7%) of 28 patients who were treated with a dose of ≥ 10 mg/kg for ≥ 70 days. An analysis of PK parameters did not identify a clear association between C_{max}, C_{trough}, or AUC for corneal events; however, the small number of patients limits definitive conclusions.

The mechanism of the corneal toxicity is hypothesized to be a result of inhibition of FGF10, 1 of the 3 growth factors inhibited by bemarituzumab, and involved in the regulation of corneal epithelial wound healing.[30,31] No predisposing clinical factors were identified by medical history review or baseline ophthalmologic examinations in patients who developed corneal events compared with those who did not. In addition, no precursor findings were identified during the every-6-week ophthalmologic evaluations in the patients who developed corneal toxicity compared with those who did not. These analyses are limited because of the small number and poor prognosis of patients enrolled in a phase I trial, which lead to a low number of patients exposed to prolonged dosing (> 70 days) of bemarituzumab.

Monotherapy efficacy has been disappointing with noncytotoxic agents in GEA.[3,5,32-35] The ORR observed in this study in advanced-stage patients with high FGFR2b-overexpressing GEA was 17.9% (95% CI, 6.1% to 36.9%), and the DCR was 64.3% (95% CI, 44.1% to 81.4%). This ORR compares favorably with that of other noncytotoxic agents in GEA, such as ramucirumab (ORR, 3.2%)[3] and checkpoint inhibitors (ORR, 12%-16%)[5,6] in the late-line GEA setting, warranting further evaluation.

Because of the poor prognosis of GEA with first-line therapy, the majority of patients do not receive third-line and later therapies.[4,36-38] The monotherapy activity of bemarituzumab and its lack of significant overlapping toxicities

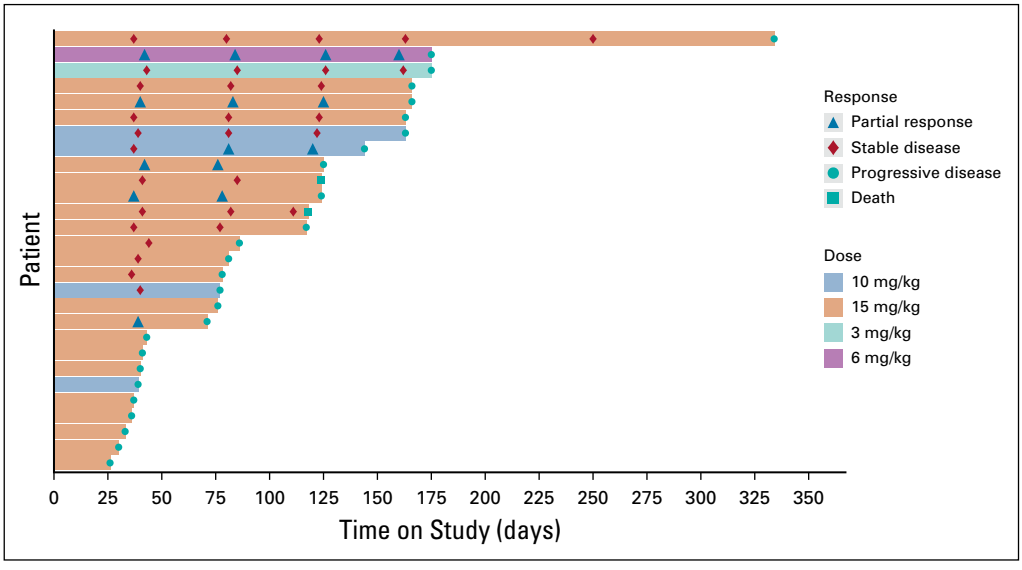

FIG 3. Objective response and duration of follow-up in FGFR2b-positive gastric cancer.

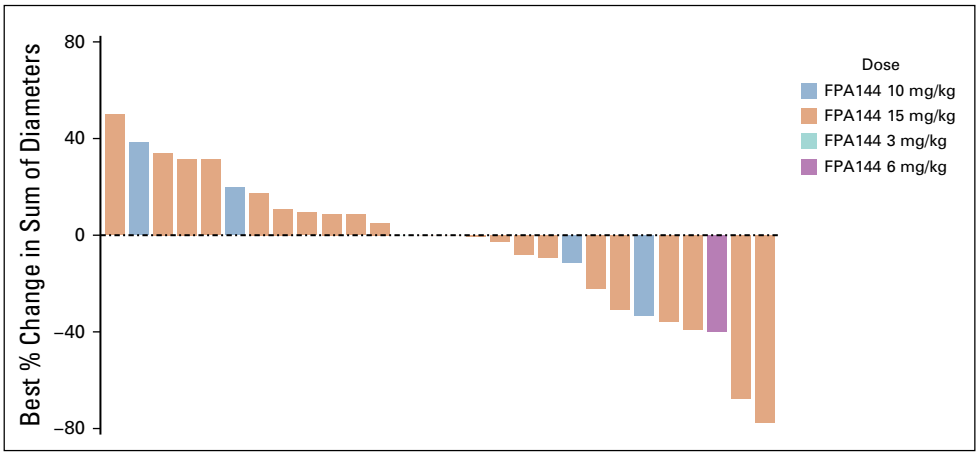

FIG 4. Waterfall plot of best percent change in sum of diameters from baseline in FGFR2b-positive gastric cancer. FPA144, bemarituzumab.

with standard platinum and fluoropyrimidine chemotherapeutic agents suggest that combining bemarituzumab with chemotherapy may potentially benefit more patients in the front-line setting of FGFR2b-overexpressing GEA. Early safety data suggest that bemarituzumab combined with oxaliplatin, fluorouracil, and leucovorin (mFOLFOX6) is olerable in patients with advanced-stage GI cancers,[39] and a randomized, placebo-controlled, phase III study of mFOLFOX6 with bemarituzumab in patients with newly diagnosed advanced-stage GEA, the FIGHT trial (ClinicalTrials.gov identifier: NCT03694522), initiated enrollment in September 2018.[40]

AFFILIATIONS

[1]University of Chicago, Chicago, IL
[2]The START Center for Cancer Care, San Antonio, TX
[3]Samsung Medical Center, Seoul, South Korea
[4]Seoul National University College of Medicine, Seoul National University Bundang Hospital, Seoul, South Korea
[5]Seoul National University College of Medicine, Seoul, South Korea
[6]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN
[7]Dana-Farber Cancer Institute, Boston, MA
[8]Five Prime Therapeutics, South San Francisco, CA
[9]University of California, Los Angeles, Los Angeles, CA

CORRESPONDING AUTHOR

Daniel V.T. Catenacci, MD, PhD, Associate Professor of Medicine, University of Chicago, 900 E 57th St, Ste 7120, Chicago, IL, 60637; Twitter: @DocCatenacci; e-mail: dcatenac@bsd.uchicago.edu.

PRIOR PRESENTATION

Presented in part at the 52nd Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, June 3-7, 2016, and in part at the 53rd Annual Meeting of the American Society of Clinical Oncology, Chicago, IL, June 2-6, 2017.

CLINICAL TRIAL INFORMATION

NCT02318329

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/JCO.19.01834.

AUTHOR CONTRIBUTIONS

Conception and design: Daniel V.T. Catenacci, Yung Jue Bang, Peter Enzinger, Hong Xiang, Zev A. Wainberg
Provision of study materials or patients: Daniel V.T. Catenacci, Drew Rasco, Yung Jue Bang, Johanna Bendell, Hong Xiang, Zev A. Wainberg
Collection and assembly of data: Daniel V.T. Catenacci, Drew Rasco, Jeeyun Lee, Sun Young Rha, Keun-Wook Lee, Yung Jue Bang, Johanna Bendell, Peter Enzinger, Neyssa Marina, Hong Xiang, Zev A. Wainberg
Data analysis and interpretation: Daniel V.T. Catenacci, Jeeyun Lee, Yung Jue Bang, Johanna Bendell, Peter Enzinger, Neyssa Marina, Hong Xiang, Wei Deng, Janine Powers, Zev A. Wainberg
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, et al: Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 68:394-424, 2018
2. Wagner AD, Syn NL, Moehler M, et al: Chemotherapy for advanced gastric cancer. Cochrane Database Syst Rev 8:CD004064, 2017
3. Fuchs CS, Tomasek J, Yong CJ, et al: Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): An international, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet 383:31-39, 2014
4. Wilke H, Muro K, Van Cutsem E, et al: Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): A double-blind, randomised phase 3 trial. Lancet Oncol 15:1224-1235, 2014
5. Kang YK, Boku N, Satoh T, et al: Nivolumab in patients with advanced gastric or gastro-oesophageal junction cancer refractory to, or intolerant of, at least two previous chemotherapy regimens (ONO-4538-12, ATTRACTION-2): A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 390:2461-2471, 2017

6. Fuchs CS, Doi T, Jang RW, et al: Safety and efficacy of pembrolizumab monotherapy in patients with previously treated advanced gastric and gastroesophageal junction cancer: Phase 2 clinical KEYNOTE-059 trial. JAMA Oncol 4:e180013, 2018
7. Shitara K, Doi T, Dvorkin M, et al: Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): A randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 19:1437-1448, 2018
8. Turner N, Grose R: Fibroblast growth factor signalling: From development to cancer. Nat Rev Cancer 10:116-129, 2010
9. Tabernero J, Bahleda R, Dienstmann R, et al: Phase I dose-escalation study of JNJ-42756493, an oral pan-fibroblast growth factor receptor inhibitor, in patients with advanced solid tumors. J Clin Oncol 33:3401-3408, 2015
10. Bahleda R, Italiano A, Hierro C, et al: Multicenter phase I study of erdafitinib (JNJ-42756493), oral pan-fibroblast growth factor receptor inhibitor, in patients with advanced or refractory solid tumors. Clin Cancer Res 25:4888-4897, 2019
11. Nogova L, Sequist LV, Perez Garcia JM, et al: Evaluation of BGJ398, a fibroblast growth factor receptor 1-3 kinase inhibitor, in patients with advanced solid tumors harboring genetic alterations in fibroblast growth factor receptors: Results of a global phase I, dose-escalation and dose-expansion study. J Clin Oncol 35:157-165, 2017
12. Miki T, Bottaro DP, Fleming TP, et al: Determination of ligand-binding specificity by alternative splicing: Two distinct growth factor receptors encoded by a single gene. Proc Natl Acad Sci USA 89:246-250, 1992
13. Angal S, King DJ, Bodmer MW, et al: A single amino acid substitution abolishes the heterogeneity of chimeric mouse/human (IgG4) antibody. Mol Immunol 30: 105-108, 1993
14. Han N, Kim MA, Lee HS, et al: Evaluation of fibroblast growth factor receptor 2 expression, heterogeneity and clinical significance in gastric cancer. Pathobiology 82:269-279, 2015
15. Ahn S, Lee J, Hong M, et al: FGFR2 in gastric cancer: Protein overexpression predicts gene amplification and high H-index predicts poor survival. Mod Pathol 29:1095-1103, 2016
16. Nagatsuma AK, Aizawa M, Kuwata T, et al: Expression profiles of HER2, EGFR, MET and FGFR2 in a large cohort of patients with gastric adenocarcinoma. Gastric Cancer 18:227-238, 2015
17. Cancer Genome Atlas Research Network: Comprehensive molecular characterization of gastric adenocarcinoma. Nature 513:202-209, 2014
18. Cancer Genome Atlas Research Network, Analysis Working Group, Asan University, et al: Integrated genomic characterization of oesophageal carcinoma. Nature 541:169-175, 2017
19. Klempner SJ, Madison R, Pujara V, et al: FGFR2-altered gastroesophageal adenocarcinomas are an uncommon clinicopathologic entity with a distinct genomic landscape. Oncologist 24:1462-1468, 2019
20. Ali SM, Sanford EM, Klempner SJ, et al: Prospective comprehensive genomic profiling of advanced gastric carcinoma cases reveals frequent clinically relevant genomic alterations and new routes for targeted therapies. Oncologist 20:499-507, 2015
21. Su X, Zhan P, Gavine PR, et al: FGFR2 amplification has prognostic significance in gastric cancer: Results from a large international multicentre study. Br J Cancer 110:967-975, 2014
22. Seo S, Park S, Ryu M, et al: Prognostic impact of fibroblast growth factor receptor 2 gene amplification in patients receiving fluoropyrimidine and platinum chemotherapy for metastatic and locally advanced unresectable gastric cancers. Oncotarget 8:33844-33854, 2017
23. Kim HS, Kim JH, Jang HJ, et al: Pathological and prognostic impacts of FGFR2 overexpression in gastric cancer: A meta-analysis. J Cancer 10:20-27, 2019
24. Matsumoto K, Arao T, Hamaguchi T, et al: FGFR2 gene amplification and clinicopathological features in gastric cancer. Br J Cancer 106:727-732, 2012
25. Gemo AT, Deshpande AM, Palencia S, et al: FPA144: A therapeutic antibody for treating patients with gastric cancers bearing FGFR2 gene amplification. Cancer Res 74, 2014 (abstr 5446)
26. Saito T, Fukumoto S: Fibroblast growth factor 23 (FGF23) and disorders of phosphate metabolism. Int J Pediatr Endocrinol 2009:496514, 2009
27. Bendell JC, Rogers S, Xiang H, et al: FPA144-001: A first in human study of FPA 144, an ADCC-enhanced, FGFR2b isoform-selective monoclonal antibody in patients with advanced solid tumors. J Clin Oncol 34, 2016 (suppl; abstr 140)
28. Catenacci DVT, Rha SY, 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 15; abstr 4067)
29. Cosson VF, Ng VW, Lehle M, et al: Population pharmacokinetics and exposure-response analyses of trastuzumab in patients with advanced gastric or gastroesophageal junction cancer. Cancer Chemother Pharmacol 73:737-747, 2014
30. Emoto H, Tagashira S, Mattei MG, et al: Structure and expression of human fibroblast growth factor-10. J Biol Chem 272:23191-23194, 1997
31. Itoh N: FGF10: A multifunctional mesenchymal-epithelial signaling growth factor in development, health, and disease. Cytokine Growth Factor Rev 28:63-69, 2016
32. Bang YJ, Kang YK, Kang WK, et al: Phase II study of sunitinib as second-line treatment for advanced gastric cancer. Invest New Drugs 29:1449-1458, 2011
33. Dragovich T, McCoy S, Fenoglio-Preiser CM, et al: Phase II trial of erlotinib in gastroesophageal junction and gastric adenocarcinomas: SWOG 0127. J Clin Oncol 24:4922-4927, 2006
34. Iqbal S, Goldman B, Fenoglio-Preiser CM, et al: Southwest Oncology Group study S0413: A phase II trial of lapatinib (GW572016) as first-line therapy in patients with advanced or metastatic gastric cancer. Ann Oncol 22:2610-2615, 2011
35. Ohtsu A, Ajani JA, Bai YX, et al: Everolimus for previously treated advanced gastric cancer: Results of the randomized, double-blind, phase III GRANITE-1 study. J Clin Oncol 31:3935-3943, 2013
36. Davidson M, Cafferkey C, Goode EF, et al: Survival in advanced esophagogastric adenocarcinoma improves with use of multiple lines of therapy: Results from an analysis of more than 500 patients. Clin Colorectal Cancer 17:223-230, 2018
37. Hess LM, Michael D, Mytelka DS, et al: Chemotherapy treatment patterns, costs, and outcomes of patients with gastric cancer in the United States: A retrospective analysis of electronic medical record (EMR) and administrative claims data. Gastric Cancer 19:607-615, 2016
38. Fanotto V, Uccello M, Pecora I, et al: Outcomes of advanced gastric cancer patients treated with at least three lines of systemic chemotherapy. Oncologist 23: 272, 2018
39. Tejani MA, Cheung E, Eisenberg PD, et al: Phase I results from the phase 1/3 FIGHT study evaluating bemarituzumab and mFOLFOX6 in advanced gastric/GEJ cancer (GC). J Clin Oncol 37, 2019 (suppl; abstr 91)
40. Catenacci DVT, Tesfaye A, Tejani M, et al: Bemarituzumab with modified FOLFOX6 for advanced FGFR2-positive gastroesophageal cancer: FIGHT Phase III study design. Future Oncol 15:2073-2082, 2019

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Phase I Escalation and Expansion Study of Bemarituzumab (FPA144) in Patients With Advanced Solid Tumors and FGFR2b-Selected Gastroesophageal Adenocarcinoma

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/authors/author-center.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

Daniel V.T. Catenacci
Honoraria: Genentech, Eli Lilly, Amgen, Foundation Medicine, Taiho Pharmaceutical, Guardant Health, Merck, Bristol-Myers Squibb, Gritstone Oncology, Five Prime Therapeutics, Astellas Pharma, Tempus, Seattle Genetics
Consulting or Advisory Role: Genentech, Amgen, Merck, Eli Lilly, Taiho Pharmaceutical, Bristol-Myers Squibb, Astellas Pharma, Seattle Genetics
Speakers' Bureau: Guardant Health, Foundation Medicine, Genentech, Eli Lilly, Merck

Drew Rasco
Consulting or Advisory Role: Boehringer Ingelheim, Eli Lilly
Research Funding: Celgene (Inst), Five Prime Therapeutics (Inst), Asana Biosciences (Inst), Eisai (Inst), Aeglea Biotherapeutics (Inst), Merck (Inst), Ascentage Pharma (Inst), Macrogenics (Inst), Apexian Pharmaceuticals (Inst), AbbVie (Inst), Constellation Pharmaceuticals (Inst), Syndax (Inst), Astex Pharmaceuticals (Inst), Compugen (Inst), Coordination Therapeutics (Inst), GlaxoSmithKline (Inst), Incyte (Inst), Gossamer Bio (Inst), Seven and Eight Biopharmaceuticals (Inst)
Travel, Accommodations, Expenses: Asana Biosciences

Sun Young Rha
Consulting or Advisory Role: MSD Oncology, Celltrion, Ipsen, Novartis, AbbVie, Bristol-Myers Squibb, Cellid, Daiichi Sankyo, Eisai
Speakers' Bureau: Eli Lilly, MSD Oncology, Ipsen
Research Funding: MSD Oncology, Bristol-Myers Squibb

Keun-Wook Lee
Honoraria: Bristol-Myers Squibb, Eli Lilly, Genexine
Research Funding: Macrogenics (Inst), MSD (Inst), Ono Pharmaceutical (Inst), Green Cross (Inst), ASLAN Pharmaceuticals (Inst), AstraZeneca/MedImmune (Inst), Five Prime Therapeutics (Inst), LSK BioPharma (Inst), Merck KGaA (Inst), Array BioPharma (Inst), Pharmacyclics (Inst), Pfizer (Inst), ALX Oncology (Inst), Zymeworks (Inst)

Yung Jue Bang
Consulting or Advisory Role: Samyang, BeiGene, Green Cross, Taiho Pharmaceutical, Merck Serono, AstraZeneca/MedImmune, Novartis, MSD Oncology, Bayer, Hanmi, Genentech, Eli Lilly, Daiichi Sankyo, Astellas Pharma, Bristol-Myers Squibb, Genexine, GlaxoSmithKline
Research Funding: AstraZeneca/MedImmune (Inst), Novartis (Inst), Genentech (Inst), MSD (Inst), Merck Serono (Inst), Bayer (Inst), GlaxoSmithKline (Inst), Bristol-Myers Squibb (Inst), Pfizer (Inst), Eli Lilly (Inst), Boehringer Ingelheim (Inst), Macrogenics (Inst), Boston Biomedical (Inst), Five Prime Therapeutics (Inst), CKD (Inst), Ono Pharmaceutical (Inst), Taiho Pharmaceutical (Inst), Takeda (Inst), BeiGene (Inst), Curis (Inst), Green Cross (Inst), Daiichi Sankyo (Inst), Astellas Pharma (Inst), Genexine (Inst)

Johanna Bendell
Consulting or Advisory Role: Gilead Sciences (Inst), Genentech (Inst), Bristol-Myers Squibb (Inst), Five Prime Therapeutics (Inst), Eli Lilly (Inst), Merck (Inst), MedImmune (Inst), Celgene (Inst), EMD Serono (Inst), Taiho Pharmaceutical (Inst), Macrogenics (Inst), GlaxoSmithKline (Inst), Novartis (Inst), OncoMed (Inst), Leap Therapeutics (Inst), TG Therapeutics (Inst), AstraZeneca (Inst), Boehringer Ingelheim (Inst), Daiichi Sankyo (Inst), Bayer (Inst), Incyte (Inst), Apexigen (Inst), Array BioPharma (Inst), Sanofi (Inst), ARMO BioSciences (Inst), Ipsen (Inst), Merrimack (Inst), Oncogenex (Inst), FORMA Therapeutics (Inst), Arch Oncology (Inst), Prelude Therapeutics (Inst), Phoenix Biotech (Inst), Cyteir (Inst), Molecular Partners (Inst), Innate Pharma (Inst), Torque (Inst), Tizona Therapeutics (Inst), Janssen (Inst), Tolero Pharmaceuticals (Inst), TD2 (Inst), Amgen (Inst), Seattle Genetics (Inst), Moderna Therapeutics (Inst), Tanabe Research (Inst), Beigene (Inst), Continuum Clinical (Inst), Cerulean Pharma (Inst), Kyn (Inst), Bicycle Therapeutics (Inst), Relay Therapeutics (Inst), Evelo Therapeutics (Inst)
Research Funding: Eli Lilly (Inst), Genentech (Inst), Incyte (Inst), Gilead Sciences (Inst), Bristol-Myers Squibb (Inst), Leap Therapeutics (Inst), AstraZeneca/MedImmune (Inst), Boston Biomedical (Inst), GlaxoSmithKline (Inst), Novartis (Inst), Array BioPharma (Inst), Taiho Pharmaceutical (Inst), Celgene (Inst), OncoMed (Inst), Daiichi Sankyo (Inst), Bayer (Inst), Apexigen (Inst), Kolltan Pharmaceuticals (Inst), SynDevRx (Inst), Merck (Inst), Macrogenics (Inst), Five Prime Therapeutics (Inst), EMD Serono (Inst), TG Therapeutics (Inst), Boehringer Ingelheim (Inst), Forty Seven (Inst), Stem CentRx (Inst), Onyx (Inst), Sanofi (Inst), Takeda (Inst), Abbott/AbbVie (Inst), Eisai (Inst), Celldex (Inst), Agios (Inst), ARMO BioSciences (Inst), CytomX Therapeutics (Inst), Nektar (Inst), Ipsen (Inst), Merrimack (Inst), Tarveda Therapeutics (Inst), Tyrogenex (Inst), Oncogenex (Inst), Marshall Edwards (Inst), Pieris Pharmaceuticals (Inst), Mersana (Inst), Calithera Biosciences (Inst), Blueprint Medicines (Inst), Gritstone Oncology (Inst), Evelo Therapeutics (Inst), FORMA Therapeutics (Inst), Forty Seven (Inst), EMD Serono (Inst), Merus (Inst), Jacobio (Inst), eFFECTOR Therapeutics (Inst), Novocure (Inst), Sorrento Therapeutics (Inst), Arrys (Inst), TRACON Pharma (Inst), Sierra Oncology (Inst), Innate Pharma (Inst), Prelude Therapeutics (Inst), Arch Oncology (Inst), Harpoon therapeutics (Inst), Phoenix Biotech (Inst), Unum Therapeutics (Inst), Vyriad (Inst), Harpoon Therapeutics (Inst), Cyteir (Inst), Molecular Partners (Inst), Innate Pharma (Inst), ADC Therapeutics (Inst), Torque (Inst), Tizona Therapeutics (Inst), Janssen (Inst), Amgen (Int), BeiGene (Inst), Pfizer (Inst), Millennium Pharmaceuticals (Inst), ImClone Systems (Inst), Acerta Pharma (Inst), Rgenix (Inst), Bellicum (Inst), Arcus Biosciences (Inst), Gossamer Biopharma (Inst), Seattle Genetics (Inst), TempestTx (Inst), Shattuck Labs (Inst), Synthorx (Inst), Revolution Medicines (Inst), Bicycle Therapeutics (Inst), Zymeworks (Inst), Relay Therapeutics (Inst), Evelo Therapeutics (Inst)
Travel, Accommodations, Expenses: Merck, Genentech, Celgene, Daiichi Sankyo, Gilead Sciences, Bristol-Myers Squibb, Eli Lilly, MedImmune, Taiho Pharmaceutical, Novartis, OncoMed, Boehringer Ingelheim, ARMO BioSciences, Ipsen, FORMA Therapeutics

Peter Enzinger
Consulting or Advisory Role: Merck, Astellas Pharma, Taiho Pharmaceutical, Loxo Oncology, Celgene, Zymeworks, Daiichi Sankyo

Neyssa Marina
Employment: Five Prime Therapeutics, Genentech (I), Synthorx
Stock and Other Ownership Interests: Five Prime Therapeutics, Genentech (I), Synthorx
Travel, Accommodations, Expenses: Five Prime Therapeutics, Synthorx

Hong Xiang
Employment: Five Prime Therapeutics, Genentech
Stock and Other Ownership Interests: Five Prime Therapeutics, Genentech, Amgen, Dynavax, Gilead Sciences, Immunogen, Johnson & Johnson

Wei Deng
Employment: Five Prime Therapeutics, Jazz Pharmaceuticals
Employment: Portola Pharmaceuticals (I), Santen (I)
Stock and Other Ownership Interests: Gilead

Janine Powers
Stock and Other Ownership Interests: Five Prime Therapeutics

Zev A. Wainberg
Consulting or Advisory Role: Array BioPharma, Five Prime Therapeutics, Novartis, Eli Lilly, Merck, Merck KGaA, Bristol-Myers Squibb, Genentech, Bayer, AstraZeneca/MedImmune
Research Funding: Novartis (Inst), Plexxikon (Inst), Pfizer (Inst), Merck (Inst), Five Prime Therapeutics (Inst)
Travel, Accommodations, Expenses: Genentech

No other potential conflicts of interest were reported.