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FIGHT-202: A PHASE 2 STUDY OF PEMIGATINIB IN PATIENTS WITH PREVIOUSLY TREATED LOCALLY ADVANCED OR METASTATIC CHOLANGIOCARCINOMA

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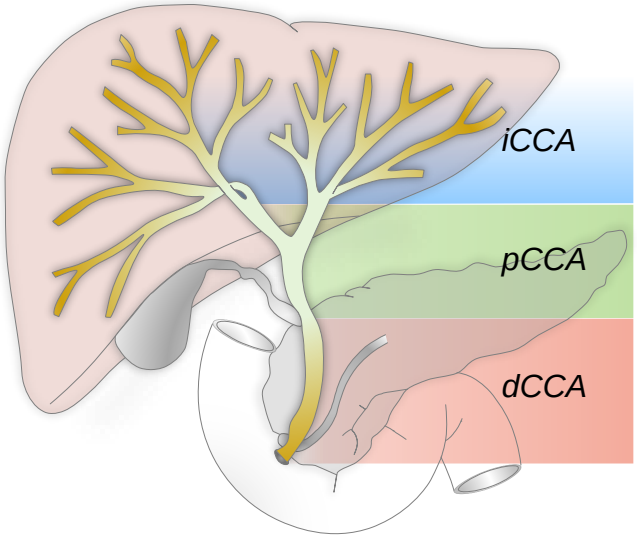
DISCLOSURE

Dr Vogel received honoraria from Incyte during the conduct of this study and has received honoraria from the following companies for services unrelated to this study: Amgen, AstraZeneca, Bayer, Beigene, BMS, Celgene, Delcath, Eisai, Hengrui, Incyte Corporation, Ipsen, Lilly, Medac, Merck, Pieris, QED, Roche, Sanofi, Servier, Shire.

This study was sponsored by Incyte Corporation.

BACKGROUND

Cholangiocarcinoma



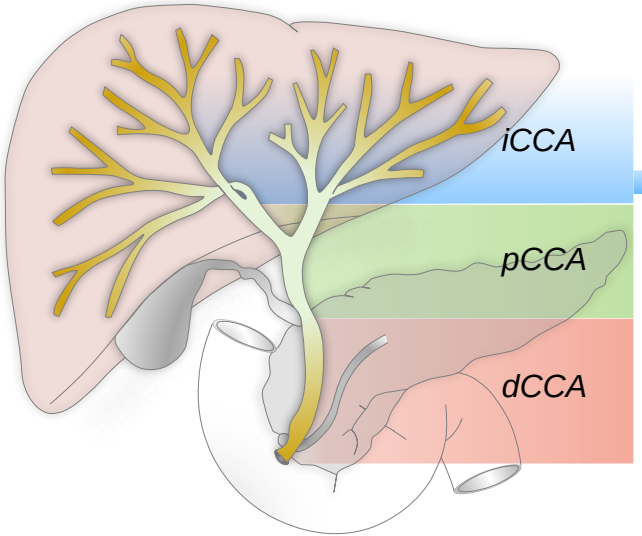
iCCA, pCCA, and dCCA correspond to intrahepatic, perihilar, and distal cholangiocarcinoma, respectively.

- Most common primary malignancy of the bile duct[1]
  - Worldwide incidence varies regionally (0.3–3.4 per 100,000 in North America and Europe)[2]
    - Substantially higher incidence in certain regions of Asia, particularly Thailand
- First-line treatment for locally advanced or metastatic cholangiocarcinoma (CCA) is gemcitabine/cisplatin[3]
- Second-line chemotherapies have shown limited efficacy[4–7]
  - Progression-free survival: median 2.6–3.2 months
  - Overall survival: median 6.2–7.2 months
  - Objective response rate: 7.7–9.5%

1. Saha SK, et al. *Oncologist.* 2016;21:594–9. **2.** Banales JM, et al. *Nat Rev Gastroenterol Hepatol.* 2016;13:261–80. **3.** Valle J, et al. *N Engl J Med.* 2010;362:1273–81. **4.** Goff LW, et al. *J Clin Oncol.* 2016;34:e15636. **5.** Lamarca A, et al. *J Clin Oncol.* 2019;37(15 Suppl):4003 [abstract]. **6.** Ying J, Chen J. *Crit Rev Oncol Hematol.* 2019;139:134–42. **7.** Lowery MA, et al. *Cancer.* 2019 Aug 27. doi: 10.1002/cncr.32463.

BACKGROUND

Cholangiocarcinoma



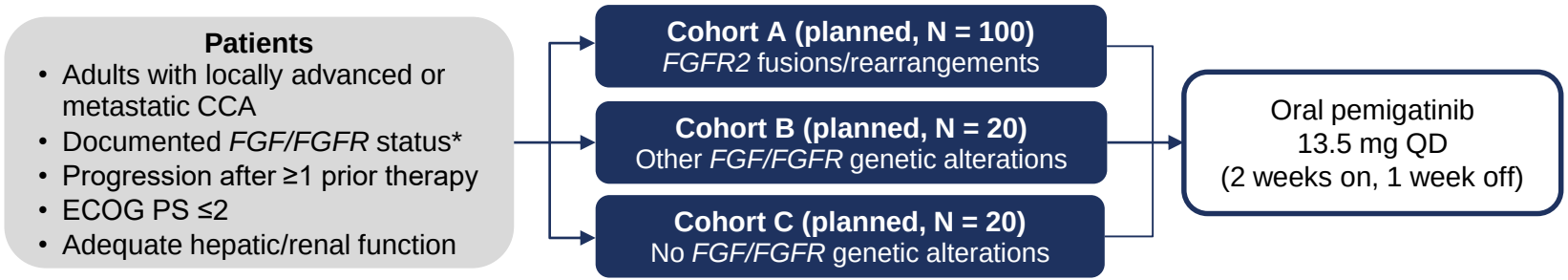
iCCA, pCCA, and dCCA correspond to intrahepatic, perihilar, and distal cholangiocarcinoma, respectively.

- Several actionable oncogenic alterations have been identified in CCA, including alterations involving FGFR2[1–3]
- *FGFR2* fusions or rearrangements are
  - Almost exclusively found in iCCA
  - Present in 10–16% of patients with iCCA in the United States and Europe[4–6]
- Pemigatinib is a selective, potent, oral inhibitor of FGFR1, 2, and 3[7]

1. Lowery MA, et al. *Clin Cancer Res.* 2018;24:4154–61. **2.** Nakamura H, et al. *Nat Genet.* 2015;47:1003–10. **3.** Pellino A, et al. *Transl Gastroenterol Hepatol.* 2018;3:40. **4.** Ross JS, et al. *Oncologist.* 2014;19:235–42. **5.** Farshidfar F, et al. *Cell Rep.* 2017;19:2878–80. **6.** Graham RP, et al. *Hum Pathol.* 2014;45:1630–8. **7.** Liu PCC, et al. *Cancer Res.* 2015;75(15 Suppl):771 [abstract].

FIGHT-202 STUDY DESIGN

- Phase 2 open-label, single-arm study evaluating the efficacy and safety of pemigatinib in patients with previously treated locally advanced or metastatic CCA (NCT02924376)
  - Sites opened in the United States, Europe, Middle East, and Asia



* Patients prescreened for *FGF/FGFR* status, documented either centrally (FoundationOne®, Foundation Medicine), based on local assessment, or an existing Foundation Medicine report. Retrospective central confirmation of locally documented *FGF/FGFR* status was required.

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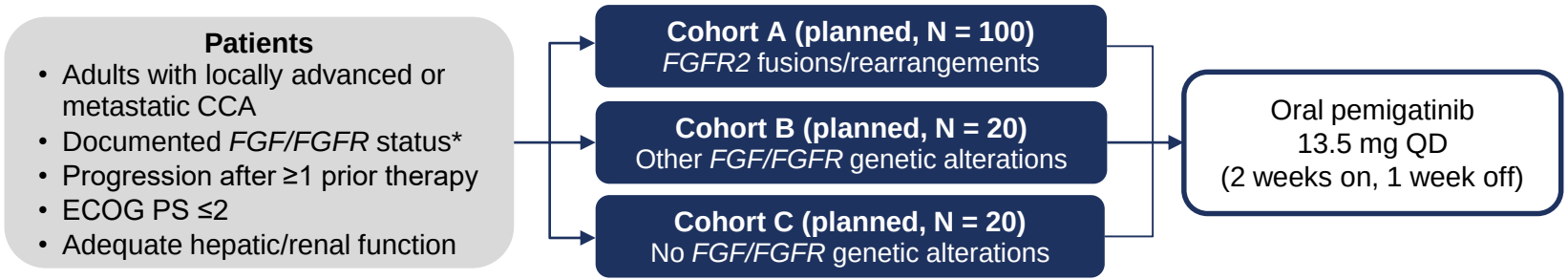

Primary endpoint: Confirmed ORR in cohort A by independent central review
Secondary endpoints: ORR in cohorts B, A + B, and C; duration of response, disease control rate, PFS, OS, and safety in all cohorts

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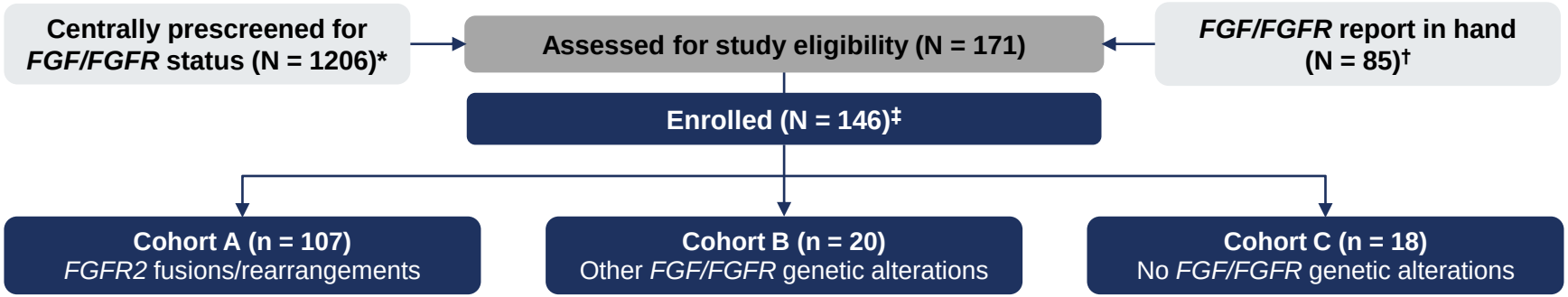
STATISTICAL ANALYSIS

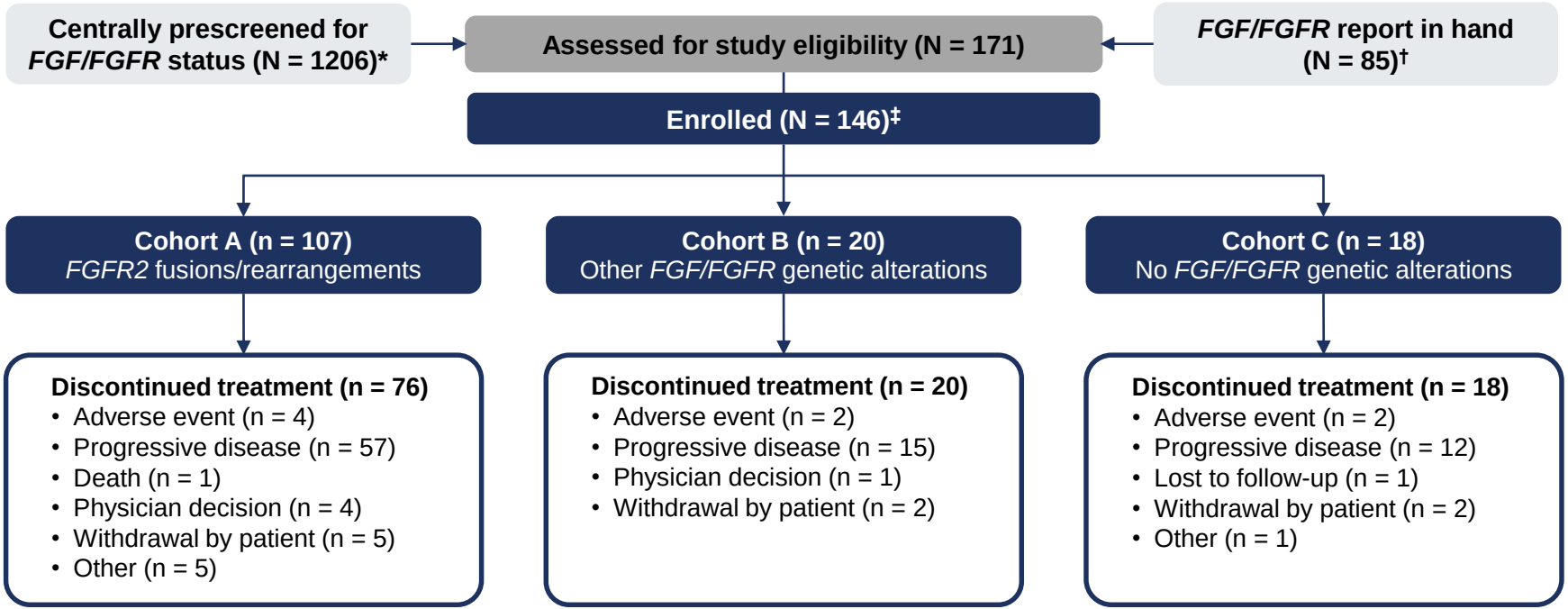
- Efficacy population: all patients with centrally confirmed *FGF/FGFR* status receiving ≥1 dose
- In a planned futility analysis, cohort A could be stopped if ≤2 patients achieved a response
- In cohorts B and C, up to 20 patients were planned for enrollment
- Survival analyses were conducted using Kaplan-Meier method; 95% CI for ORR was estimated using the Clopper-Pearson method
- For the primary endpoint, patients with insufficient baseline or on-study data for adequate assessment of response status were considered nonresponders
- *The study was not designed to make statistical comparisons between cohorts; no formal hypothesis testing or inferential analyses were conducted*

DISPOSITION



* FoundationOne®, Foundation Medicine.
† Most patients with report in hand had undergone FoundationOne® testing for *FGF/FGFR* status.
‡ One patient received pemigatinib but had undetermined *FGF/FGFR* status; analyzed for safety but not efficacy, and was not assigned to a cohort.

DISPOSITION



Data cutoff date: March 22, 2019

* FoundationOne®, Foundation Medicine.
† Most patients with report in hand had undergone FoundationOne® testing for *FGF/FGFR* status.
‡ One patient received pemigatinib but had undetermined *FGF/FGFR* status; analyzed for safety but not efficacy, and was not assigned to a cohort.

DEMOGRAPHICS

Characteristics	Cohort A (n = 107) *FGFR2* Fusions/ Rearrangements	Cohort B (n = 20) Other *FGF/FGFR* Genetic Alterations	Cohort C (n = 18) No *FGF/FGFR* Genetic Alterations	Total (N = 146)*
Age, median (range), years	56 (26–77)	63 (45–78)	65 (31–78)	59 (26–78)
<65, n (%)	**82 (77)**	**10 (50)**	**7 (39)**	**100 (68)**
65–<75, n (%)	20 (19)	7 (35)	8 (44)	35 (24)
≥75, n (%)	5 (5)	3 (15)	3 (17)	11 (8)
Sex, n (%)				
Men	42 (39)	9 (45)	10 (56)	62 (42)
Women	**65 (61)**	**11 (55)**	**8 (44)**	**84 (58)**
Region, n (%)				
North America	64 (60)	6 (30)	18 (100)	89 (61)
Western Europe	32 (30)	3 (15)	0	35 (24)
Rest of world†	11 (10)	11 (55)	0	22 (15)

* The total includes 1 patient who received pemigatinib but had undetermined *FGF/FGFR* status; analyzed for safety but not efficacy, and was not assigned to a cohort.

† Rest of world includes Israel, South Korea, Taiwan, Thailand, and Japan.

CLINICAL CHARACTERISTICS

Characteristics	Cohort A (n = 107) *FGFR2* Fusions/ Rearrangements	Cohort B (n = 20) Other *FGF/FGFR* Genetic Alterations	Cohort C (n = 18) No *FGF/FGFR* Genetic Alterations	Total (N = 146)*
ECOG PS, n (%)				
0	45 (42)	7 (35)	7 (39)	59 (40)
1	57 (53)	10 (50)	8 (44)	76 (52)
2	5 (5)	3 (15)	3 (17)	11 (8)
Number of prior regimens,† n (%)				
1	65 (61)	12 (60)	12 (67)	89 (61)
2	29 (27)	7 (35)	2 (11)	38 (26)
≥3	13 (12)	1 (5)	4 (22)	19 (13)
Prior cancer surgery, n (%)	38 (36)	6 (30)	4 (22)	48 (33)
Prior radiation, n (%)	28 (26)	3 (15)	5 (28)	36 (25)
CCA location, n (%)				
Intrahepatic	105 (98)	13 (65)	11 (61)	130 (89)
Extrahepatic	1 (1)	4 (20)	7 (39)	12 (8)
Other/Missing	1 (1)	3 (15)‡	0	4 (3)

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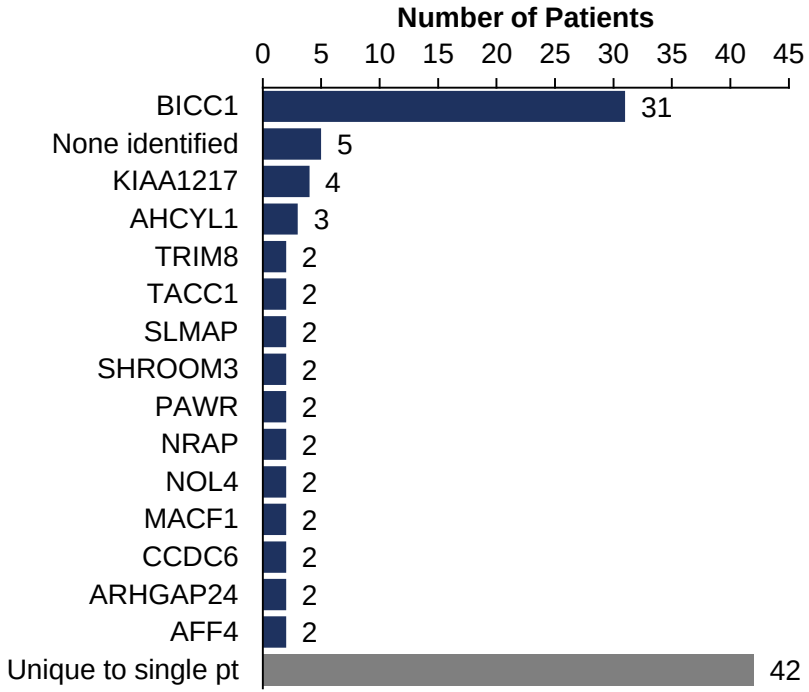
* The total includes 1 patient who received pemigatinib but had undetermined *FGF/FGFR* status; analyzed for safety but not efficacy, and was not assigned to a cohort.
† Maximum number of 5 therapies in cohort A and 3 in cohort B/C.
‡ Other includes gallbladder (n = 2) and ampulla of vater (n = 1) cancer.

FGFR2 FUSIONS/REARRANGEMENTS (COHORT A)



- Fusions are a product of chromosomal rearrangement
  - Consistent with Foundation Medicine terminology, rearrangements are classified as fusions if the partner gene is previously described or in-frame
- Among 107 patients in cohort A:
  - 92 fusions; 15 rearrangements
  - 56 different partner genes
  - 42 partners unique to single patients
  - Most common:
    - *BICC1* (29%)
    - No partner identified (5%)

For further information on genomic analyses in FIGHT-202, see ESMO Poster #720P presented Sunday, September 29, 2019.

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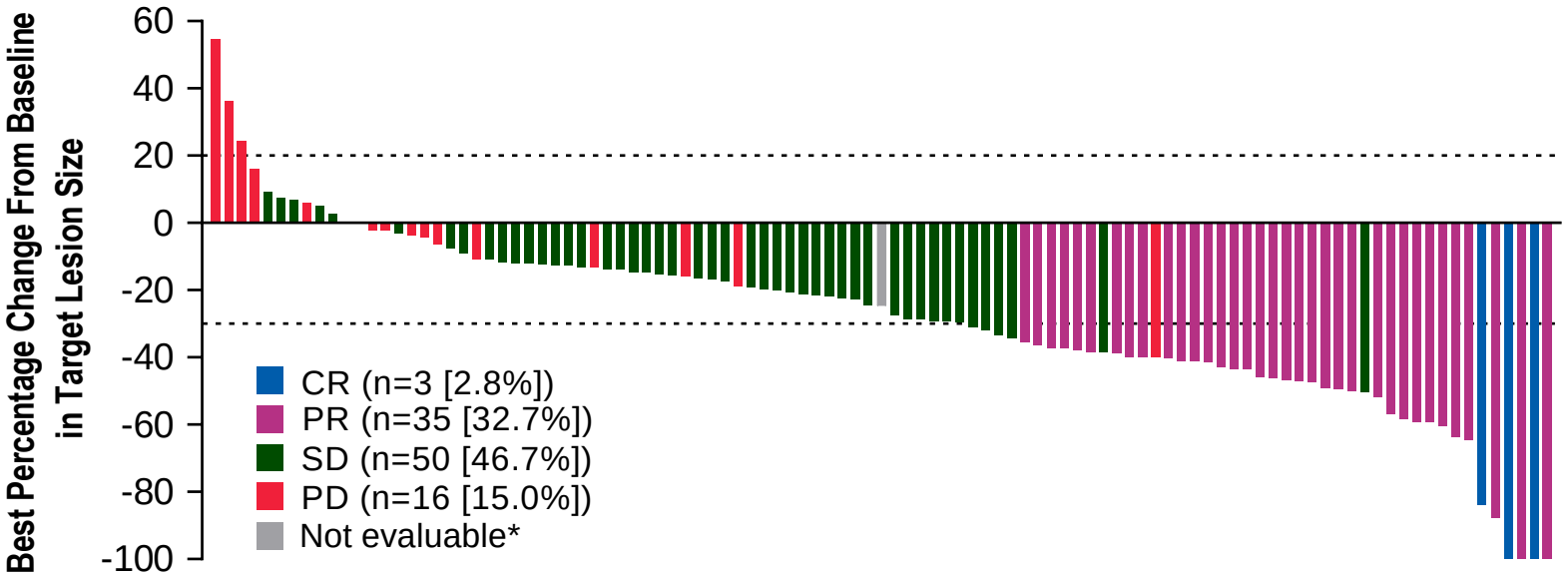
RESPONSE

Variable	Cohort A (n = 107) *FGFR2* Fusions/ Rearrangements	Cohort B (n = 20) Other *FGF/FGFR* Genetic Alterations	Cohort C (n = 18) No *FGF/FGFR* Genetic Alterations
ORR (95% CI), %	**35.5 (26.50–45.35)**	0	0
Best OR,* n (%)			
CR	3 (2.8)	0	0
PR	35 (32.7)	0	0
SD	50 (46.7)	8 (40.0)	4 (22.2)
PD	16 (15.0)	7 (35.0)	11 (61.1)
Not evaluable†	3 (2.8)	5 (25.0)	3 (16.7)
Median DOR (95% CI), mo	7.5 (5.7–14.5)	—	—
DCR (CR + PR + SD) (95% CI), %	82 (74–89)	40 (19–64)	22 (6–48)

* Assessed and confirmed by independent central review.
† Postbaseline tumor assessment was not performed owing to study discontinuation (2 participants in cohort A, 4 participants in cohort B, 3 participants in cohort C) or was performed prior to the minimum interval of 39 days for an assessment of SD (1 participant in cohort A, 1 participant in cohort B).

CHANGE FROM BASELINE IN TARGET LESION SIZE (COHORT A)



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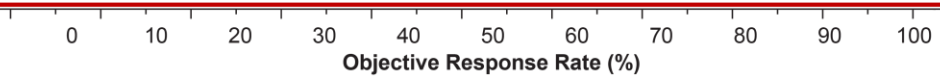
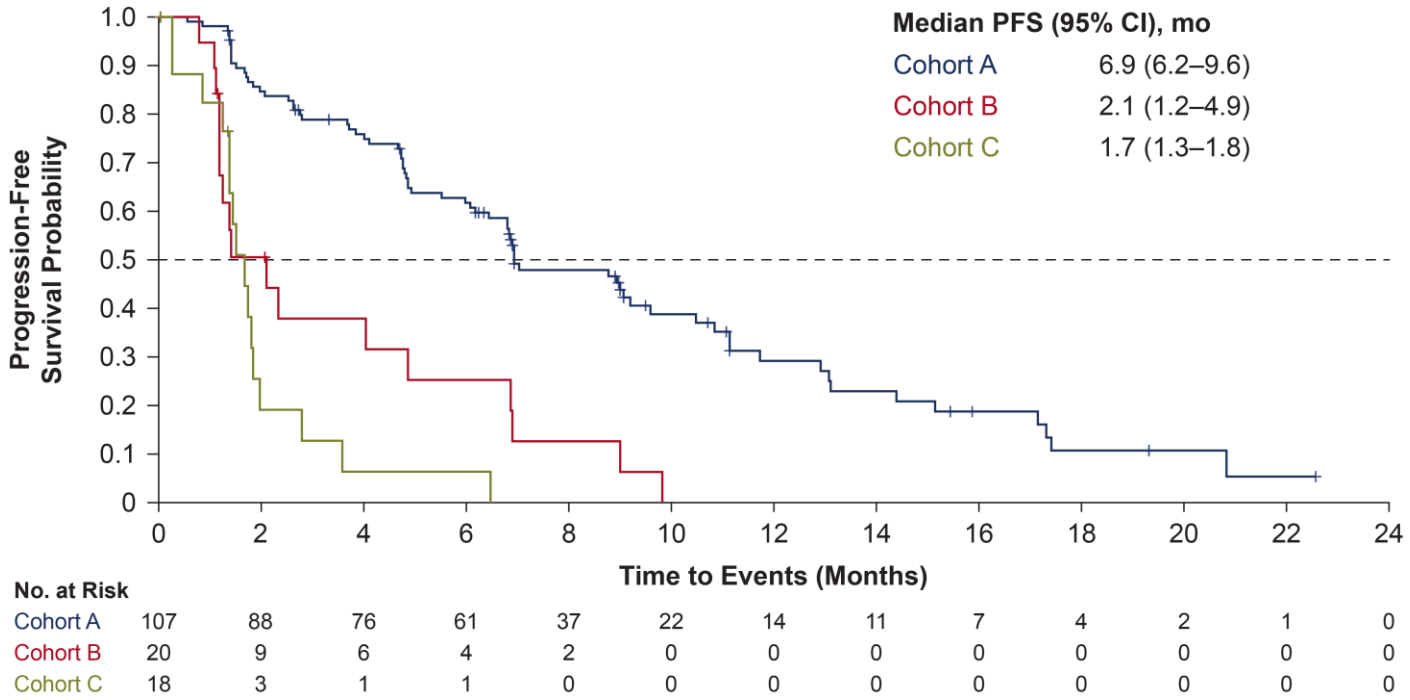
Colored bars: confirmed responses per RECIST.
* Patient had decrease in target lesion size but was not evaluable for response per RECIST.

ORR BY SUBGROUP (COHORT A)

Subgroup	No. of Patients	Objective Response Rate (95% CI)
All patients	107	35.5 (26.50–45.35)
Age group		
<65 years	82	34.1 (24.03–45.45)
65–<75 years	20	40.0 (19.12–63.95)
≥75 years	5	40.0 (5.27–85.34)
Sex		
Male	42	31.0 (17.62–47.09)
Female	65	38.5 (26.65–51.36)
Race		
White	79	34.2 (23.87–45.71)
Asian	11	36.4 (10.93–69.21)
Other	17	41.2 (18.44–67.08)
Region		
North America	64	35.9 (24.32–48.90)
Western Europe	32	40.6 (23.70–59.36)
Rest of world	11	18.2 (2.28–51.78)
ECOG status		
0	45	48.9 (33.70–64.23)
1 or 2	62	25.8 (15.53–38.50)
Metastatic disease present		
Yes	88	33.0 (23.30–43.79)
No	16	50.0 (24.65–75.35)
Lines of prior therapy		
1 line	65	36.9 (25.28–49.80)
2 lines	29	34.5 (17.94–54.33)
≥3 lines	13	30.8 (9.09–61.43)
FGFR2 rearrangement partner		
BICC1	31	32.3 (16.68–51.37)
Other	76	36.8 (26.06–48.69)

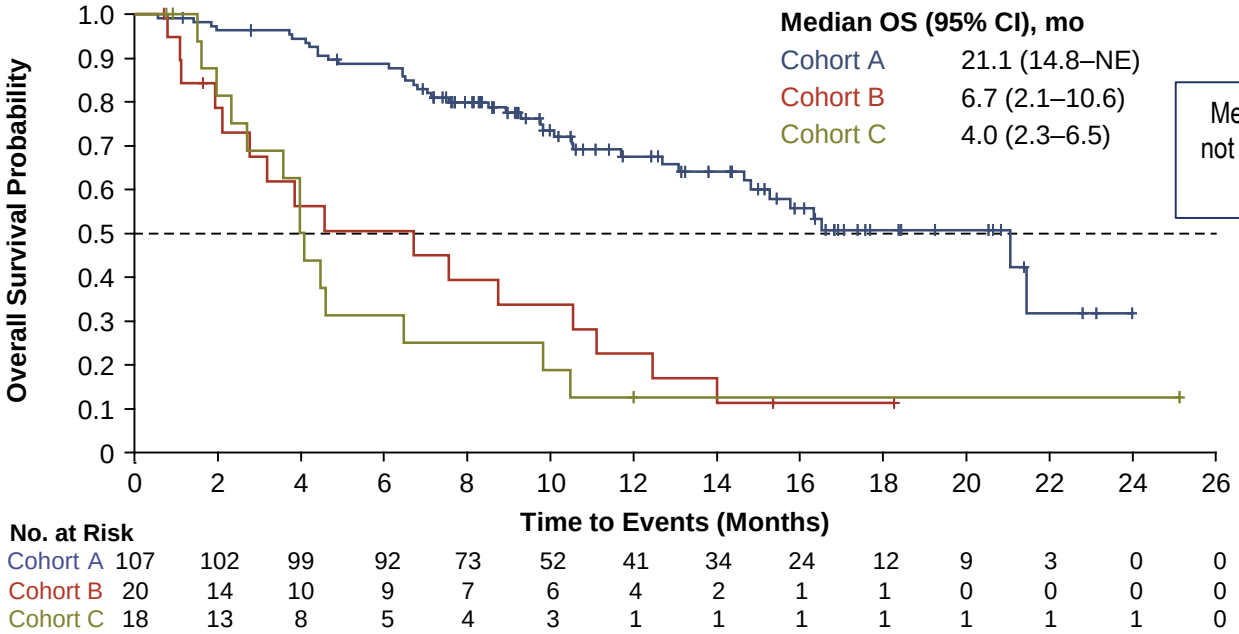


PROGRESSION-FREE SURVIVAL



The study was not designed to compare cohorts.

OVERALL SURVIVAL



	Cohort A	Cohort B	Cohort C
Median (range) duration of follow-up, mo	15.4 (7.0–24.7)	19.9 (16.2–23.5)	24.2 (22.0–26.1)
Median (range) duration of treatment, mo	7.2 (0.2–24.0)	1.4 (0.2–12.9)	1.3 (0.2–4.7)

The study was not designed to compare cohorts.

ADVERSE EVENTS OCCURRING IN ≥25% OF PATIENTS

Adverse Event, n (%)	Any AEs (N = 146)*	
	All Grades	Grade ≥3
Hyperphosphatemia†	**88 (60)**	**0**
Alopecia	72 (49)	0
Diarrhea	68 (47)	4 (3)
Fatigue	**62 (42)**	**7 (5)**
Nail toxicities†	62 (42)	3 (2)
Dysgeusia	59 (40)	0
Nausea	58 (40)	3 (2)
Constipation	51 (35)	1 (1)
Stomatitis	**51 (35)**	**8 (5)**
Dry mouth	49 (34)	0
Decreased appetite	48 (33)	2 (1)
Vomiting	40 (27)	2 (1)
Dry eye	37 (25)	1 (1)
Arthralgia	36 (25)	9 (6)

- **Hyperphosphatemia**† managed with a low phosphate diet, phosphate binders, and diuretics, or dose reduction/interruption
  - All grade 1 or 2
  - Few (n = 3) required dose reductions/interruptions
- **Hypophosphatemia**† occurred in 23% of patients
  - Most common grade ≥3 AE (12%)
  - None clinically significant/serious; none led to discontinuation/dose reduction
- **Serous retinal detachment**† occurred in 4% of patients
  - Mostly grade 1/2 (grade ≥3, 1%)
  - None resulted in clinical sequelae

* Safety analysis includes 1 patient who did not have confirmed *FGF/FGFR* status by central laboratory and was not assigned to any cohort.
† Combined MedDRA Preferred Terms.

DOSE MODIFICATIONS AND MANAGEMENT OF ADVERSE EVENTS

- **Discontinuations due to AEs: 9%**
  - Most frequent, intestinal obstruction and acute kidney injury (each, n = 2)
- **Dose reductions due to AEs: 14%**
  - Most frequent, stomatitis, palmar-plantar erythrodysesthesia syndrome, and arthralgia (each, n = 5), and asthenia and onychomadesis (each, n = 2)
- **Dose interruption due to AEs: 42%**
  - Most frequent, stomatitis (n = 11), palmar-plantar erythrodysesthesia syndrome (n = 8), arthralgia (n = 7), fatigue (n = 6), and abdominal pain (n = 4)
- **Median final pemigatinib dose: 13.5 mg** (range, 6.0–13.5 mg), received by 81% of patients

CONCLUSIONS

- 56 unique *FGFR2* fusion genes were observed in cohort A (*FGFR2* fusions or rearrangements), supporting the use of fusion partner–agnostic testing
- Adverse events were manageable and consistent with the mechanism of action of pemigatinib
- In cohort A, pemigatinib treatment resulted in
  - ORR of 35.5% with durable responses
  - Median PFS of 6.9 months
- These results demonstrate the potential therapeutic benefit of pemigatinib for patients with previously treated locally advanced or metastatic CCA and *FGFR2* fusions or rearrangements
- A phase 3 study is ongoing in the first-line setting to evaluate pemigatinib versus gemcitabine plus cisplatin in patients with CCA and *FGFR2* fusions or rearrangements (NCT03656536)

ACKNOWLEDGEMENTS

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