SUPPLEMENTARY MATERIAL

FIGHT-102: A phase 1 study of pemigatinib in Japanese patients with advanced malignancies

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Supplementary Tables

Supplementary Table 1. *FGF/FGFR* status at baseline

Centrally confirmed *FGF/FGFR* alterations at baseline[a,b], n (%)	**Pemigatinib intermittent dosing**				**Pemigatinib continuous dosing**	
	9 mg (n = 3)	**13.5 mg (n = 23)**	**18 mg (n = 5)**	**Subtotal (n = 31)**	**13.5 mg (n = 13)**	**Total (n = 44)**
FGFR1 amplification	0	8 (34.8)	0	8 (25.8)	3 (23.1)	11 (25.0)
FGFR 2 amplification	0	2 (8.7)	0	2 (6.5)	1 (7.7)	3 (6.8)
FGFR2 translocation	0	1 (4.3)	0	1 (3.2)	0	1 (2.3)
FGFR3 alteration	0	0	0	0	1 (7.7)	1 (2.3)
FGFR3 mutation	0	2 (8.7)	0	2 (6.5)	0	2 (4.5)
FGFR3 translocation	0	0	0	0	1 (7.7)	1 (2.3)
FGF1 amplification	0	1 (4.3)	0	1 (3.2)	0	1 (2.3)
FGF3 amplification	0	6 (26.1)	0	6 (19.4)	3 (23.1)	9 (20.5)
FGF4 amplification	0	5 (21.7)	0	5 (16.1)	3 (23.1)	8 (18.2)
FGF6 mutation	0	1 (4.3)	0	1 (3.2)	0	1 (2.3)
FGF12 amplification	0	2 (8.7)	0	2 (6.5)	0	2 (4.5)
FGF19 amplification	0	5 (21.7)	0	5 (16.1)	3 (23.1)	8 (18.2)

FGF, fibroblast growth factor; FGFR, fibroblast growth factor receptor. [a]Locally identified *FGF/FGFR* alterations are not presented in the table.
[b]Some patients had more than 1 relevant alteration.

Supplementary Table 2. Treatment-related adverse events[a]

Number of events (%)	Pemigatinib intermittent dosing								Pemigatinib continuous dosing		Total (N = 44)	
	9 mg (n = 3)		13.5 mg (n = 23)		18 mg (n = 5)		Subtotal (n = 31)		13.5 mg (n = 13)			
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Hyperphosphatemia	2 (66.7)	0	18 (78.3)	0	5 (100.0)	0	25 (80.6)	0	11 (84.6)	0	36 (81.8)	0
Dysgeusia	1 (33.3)	0	7 (30.4)	0	2 (40.0)	0	10 (32.3)	0	8 (61.5)	0	18 (40.9)	0
Stomatitis	1 (33.3)	0	3 (13.0)	0	4 (80.0)	0	8 (25.8)	0	10 (76.9)	1 (7.7)	18 (40.9)	1 (2.3)
Alopecia	1 (33.3)	0	7 (30.4)	0	2 (40.0)	0	10 (32.3)	0	7 (53.8)	0	17 (38.6)	0
Nausea	0	0	7 (30.4)	0	3 (60.0)	0	10 (32.3)	0	4 (30.8)	0	14 (31.8)	0
Diarrhea	1 (33.3)	0	4 (17.4)	0	1 (20.0)	0	6 (19.4)	0	7 (53.8)	1 (7.7)	13 (29.5)	1 (2.3)
Decreased appetite	0	0	4 (17.4)	0	3 (60.0)	2 (40.0)	7 (22.6)	0	4 (30.8)	1 (7.7)	11 (25.0)	1 (2.3)
Blood creatinine increased	0	0	4 (17.4)	0	1 (20.0)	0	5 (16.1)	0	1 (7.7)	0	6 (13.6)	0
Fatigue	0	0	2 (8.7)	0	1 (20.0)	0	3 (9.7)	0	3 (23.1)	0	6 (13.6)	0
Paronychia	0	0	2 (8.7)	0	0	0	2 (6.5)	0	4 (30.8)	0	6 (13.6)	0
Alanine aminotransferase increased	1 (33.3)	0	2 (8.7)	0	0	0	3 (9.7)	0	2 (15.4)	1 (7.7)	5 (11.4)	1 (2.3)
Arthralgia	0	0	2 (8.7)	0	0	0	2 (6.5)	0	3 (23.1)	0	5 (11.4)	0

Aspartate aminotransferase increased	0	0	3 (13.0)	0	0	0	3 (9.7)	0	2 (15.4)	1 (7.7)	5 (11.4)	1 (2.3)
Dry mouth	0	0	1 (4.3)	0	0	0	1 (3.2)	0	4 (30.8)	0	5 (11.4)	0
Keratitis	1 (33.3)	0	2 (8.7)	0	0	0	3 (9.7)	0	2 (15.4)	0	5 (11.4)	0
Malaise	0	0	2 (8.7)	0	0	0	2 (6.5)	0	3 (23.1)	0	5 (11.4)	0
Onchyomadesis	0	0	2 (8.7)	0	0	0	2 (6.5)	0	3 (23.1)	0	5 (11.4)	0
Palmar-plantar erythrodysesthesia syndrome	0	0	2 (8.7)	0	0	0	2 (6.5)	0	3 (23.1)	0	5 (11.4)	0
Serous retinal detachment	1 (33.3)	0	3 (13.0)	0	0	0	4 (12.9)	0	1 (7.7)	0	5 (11.4)	0

[a]Reported in ≥10% of patients.

Supplementary Table 3. Pharmacokinetic parameters on Cycle 1 Day 1

Dose	Patients (n)	C_{max} (nM)	t_{max} (h)	AUC_{last} (h*nM)	AUC_{0-24h} (h*nM)
9 mg ID	3	114 ± 35.3 110 (32.1)	1.90 (0.783–3.95)	1120 ± 125 1120 (11.6)	1130 ± 133 1120 (12.2)
13.5 mg ID orCD	36	260 ± 136 216 (77.0)	1.43 (0.500–6.00)	1990 ± 748 1850 (41.2)	2020 ± 762 1880 (41.2)
18 mg ID	5	431 ± 272 344 (96.7)	1.02 (0.467–6.02)	3380 ± 1010 3240 (34.3)	3450 ± 1020 3310 (33.7)

Note: Values are presented as mean ± SD and geometric mean (CV%), except $t_{max,}$ which is reported as median (range).
AUC_{0-24h}, area under the plasma concentration-time curve from hours 0 to 24; AUC_{last}, area under the plasma concentration-time curve from time 0 to the last measurable concentration; CD, continuous dosing; C_{max}, maximum plasma drug concentration; ID, intermittent dosing; t_{max}, time to maximum plasma drug concentration.

Supplementary Table 4. Pharmacokinetic parameters at steady state (Cycle 1 Day 14)

Dose	Patients (n)	$C_{max, ss}$ (nM)	t_{max} (h)	$t_{½}$ (h)	$C_{min, ss}$ (nM)	$AUC_{ss,0-24h}$ (h*nM)	$CL_{ss/F}$ (L/h)	V_z/F (L)	Accumulation ratio
9 mg ID	3	155 ± 117 127 (89.9)	0.967 (0.917–1.00)	17.1 ± 7.44 16.1 (43.6)	74.7 ± 60.0 60.4 (92.9)	2540 ± 2100 2050 (91.0)	10.6 ± 6.31 8.99 (91.0)	224 ± 104 209 (48.1)	2.43 ± 2.29 1.83 (111)
13.5 mg ID or CD	33	238 ± 139 195 (77.8)	1.02 (0.750–24.0)	15.4 ± 9.03 13.6 (49.2)	66.2 ± 45.2 56.0 (61.0)	3090 ± 1680 2720 (55.5)	11.6 ± 6.52 10.2 (55.5)	258 ± 216 201 (76.9)	1.59 ± 0.767 1.43 (52.3)
18 mg ID	3	450 ± 285 385 (81.1)	0.833 (0.000–1.00)	20.7 ± 11.2 18.9 (54.3)	203 ± 52.1 199 (24.7)	6950 ± 2780 6560 (43.8)	5.96 ± 2.50 5.63 (43.8)	205 ± 188 154 (116)	1.86 ± 0.456 1.83 (23.5)

Note: Values are presented as mean ± SD and geometric mean (CV%), except t_{max} which is reported as median (range).

$AUC_{SS,0-24}$, area under the plasma concentration-time curve from hours 0 to 24 during steady state; CD, continuous dosing; CL_{ss}/F, apparent oral dose clearance at steady state; $C_{max,ss}$, maximum plasma drug concentration at steady state; $C_{min,ss}$, minimum plasma drug concentration at steady state; CV, coefficient of variation; ID, intermittent dosing; QD, once daily; SD, standard deviation; t_{max}, time to maximum plasma drug concentration; $t_{½}$, half-life; V_z/F, apparent oral volume of distribution.

Supplementary Table 5. Efficacy results by genomic alteration

Dose regimen	Solid tumor type	Genomic alteration		Best change in sum of target lesion diameters (%)	Best overall response
		Central laboratory	Local laboratory		
Part 1					
9 mg ID	Gastric cancer	Not tested	Not tested	–13.3	SD
9 mg ID	Other (medulloblastoma)	Not tested	No alteration detected	–[a]	PD
9 mg ID	Other (epithelioid hemangioendothelioma)	Not tested	Not tested	–12.6	SD
13.5 mg ID	Other (intrahepatic cholangiocarcinoma)	No alteration detected	Not tested	4.4	SD
13.5 mg ID	Cholangiocarcinoma	*FGF1* amp, *FGFR2* amp	Not tested	–8.5	SD
13.5 mg ID	Other (lower bile duct cancer)	*FGF6* mutation (p.S143N)	Not tested	–5.1	SD
13.5 mg ID	Colorectal cancer	*FGFR1* amp	*FGFR1* amp	–21.1	PD
13.5 mg ID	Lung cancer (NSCLC)	Not tested	Not tested	–29.0	SD
13.5 mg ID	Breast cancer	Not tested	No alteration detected	28.1	PD
18 mg ID	Other (intrahepatic cholangiocarcinoma)	No alteration detected	*FGFR2* fusion	0	SD
18 mg ID	Other (intrahepatic cholangiocarcinoma)	Not tested	Not tested	16.7	PD
18 mg ID	Other (Pancreatic head cancer)	Not tested	No alteration detected	1.0	PD
18 mg ID	Other (oropharyngeal cancer)	No alteration detected	Not tested	–[a]	–[a]

18 mg ID	Neuroendocrine cancer	Not tested	*FGF6/23* amp	37.5	PD
Part 2					
13.5 mg ID	Cholangiocarcinoma	*FGFR3* mutation	Not tested	30.9	PD
13.5 mg ID	Gallbladder cancer	No alteration detected	*FGFR3* mutation	25.0	PD
13.5 mg ID	Cholangiocarcinoma	*FGFR2* alteration	*FGFR2* translocation	–13.8	SD
13.5 mg ID	Other (intrahepatic cholangiocarcinoma)	*FGFR3* fusion	Not tested	65.2	PD
13.5 mg ID	Colorectal cancer	*FGFR1* amp	Not tested	44.7	PD
13.5 mg ID	Esophageal cancer	*FGFR1* amp	Not tested	6.5	SD
13.5 mg ID	Esophageal cancer	*FGF3/4/12/19* amp	Not tested	34.9	PD
13.5 mg ID	Esophageal cancer	*FGFR1* amp, *FGF3/4/19* amp	Not tested	37.8	PD
13.5 mg ID	Esophageal cancer	*FGFR1* amp, *FGF3/4/19* amp	Not tested	3.0	PD
13.5 mg ID	Esophageal cancer	*FGF3/4/19* amp	*FGF19* amp	–[a]	PD
13.5 mg ID	Breast cancer	*FGFR1* amp	Not tested	18.1	PD
13.5 mg ID	Urothelial tract/ bladder cancer (renal pelvis cancer)	*FGF3/4/19* amp	Not tested	24.2	PD
13.5 mg ID	Other (urachal cancer)	*FGF3* amp	Not tested	44.8	PD
13.5 mg ID	Pancreatic cancer (neuroendocrine)	*FGFR1* amp	*FGFR1* mutation (p.N577K)	40.8	PD
13.5 mg ID	Lung cancer (NSCLC)	*FGFR1* amp, *FGF12* amp	Not tested	22.2	PD

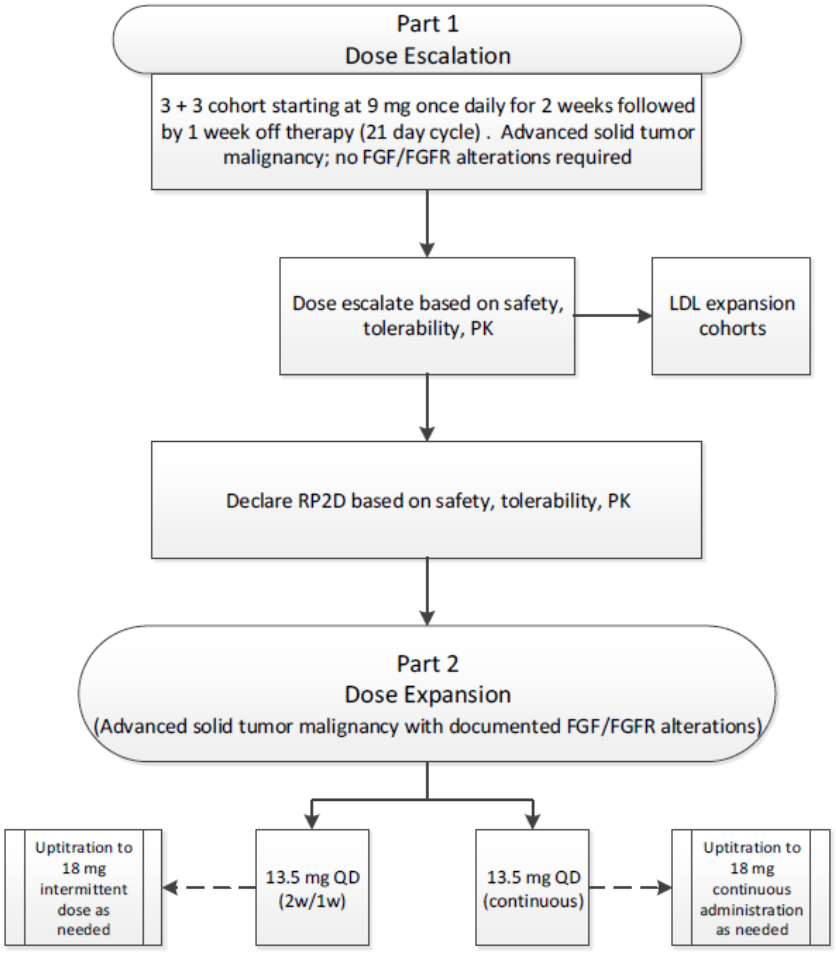
13.5 mg ID	Other (apocrine sweat gland carcinoma)	*FGFR2* amp	Not tested	–42.1	PR
13.5 mg ID	Urothelial tract/ bladder cancer (bladder cancer)	*FGFR3* mutation (p.Y373C)	Not tested	–19.6	SD
13.5 mg CD	Cholangiocarcinoma	No alteration detected	*FGFR2* translocation	–30.6	PR
13.5 mg CD	Gallbladder cancer	*FGF3/4/19* amp	Not tested	–43.8	PR
13.5 mg CD	Colorectal cancer	No alteration detected	*FGF19* amp	41.0	PD
13.5 mg CD	Colorectal cancer	*FGFR1* amp	Not tested	26.5	PD
13.5 mg CD	Breast cancer	Not tested	*FGFR2* amp	–26.2	SD
13.5 mg CD	Breast cancer	Not tested	*FGFR1* amp, *FGFR3* mutation	6.4	NE
13.5 mg CD	Breast cancer	Not tested	*FGFR2* amp	–44.4	PR
13.5 mg CD	Urothelial tract/ bladder cancer (bladder cancer)	*FGF3/4/19* amp, *FGFR3 alteration*	Not tested	–37.2	PR
13.5 mg CD	Other (rectal cancer)	*FGFR1* amp	Not tested	0.0	SD
13.5 mg CD	Other (uterine cervix carcinoma)	*FGFR2* amp	Not tested	22.7	PD
13.5 mg CD	Other (prostate cancer)	*FGFR1* amp	Not tested	15.2	PD
13.5 mg CD	Urothelial tract/ bladder cancer (renal pelvis cancer)	*FGF3/4/19* amp	Not tested	12.1	PD
13.5 mg CD	Esophageal cancer	*FGFR3* translocation: fusion	*FGFR3* translocation: fusion	–4.3	SD

[a] Missing baseline and/or postbaseline disease assessment.

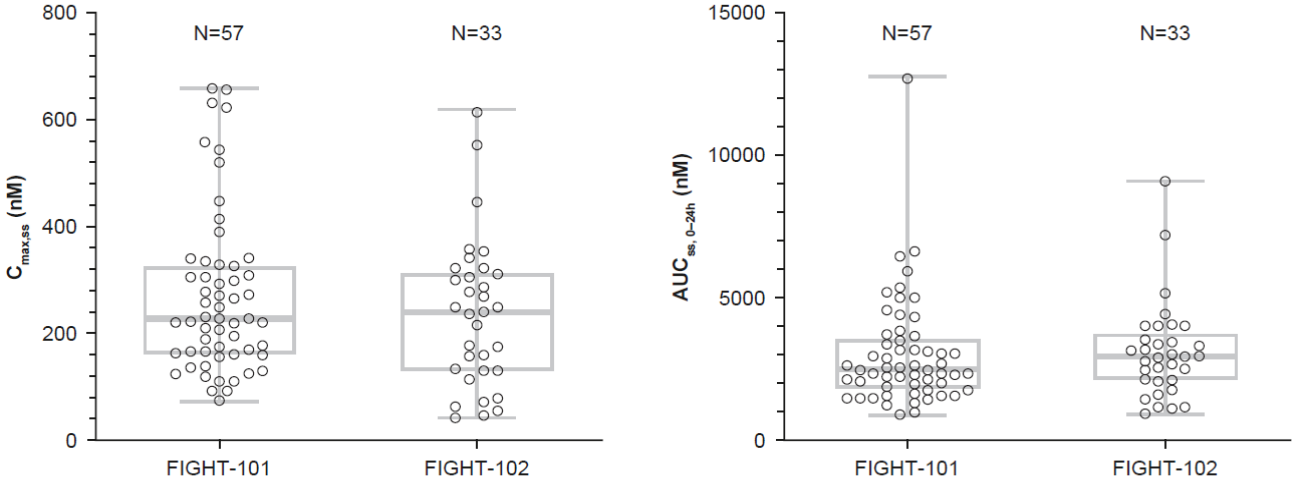
amp, amplification; CD, continuous dosing; FGFR, fibroblast growth factor receptor; ID, intermittent dosing; NE, not evaluable; NSCLC, non-small cell lung cancer; PD, progressive disease; PR, partial response; SD, stable disease.

Supplementary Figures

Supplementary Figure 1. FIGHT-102 study design. FGF, fibroblast growth factor; FGFR, fibroblast growth factor receptor; LDL, lower dose level; PK, pharmacokinetics; QD, once daily; RP2D, recommended phase 2 dose.

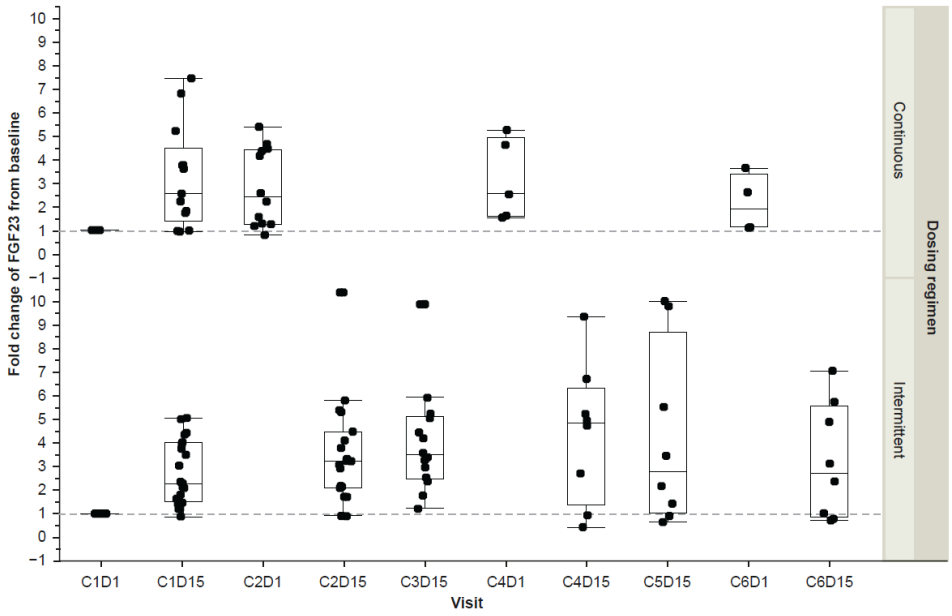


Supplementary Figure 2. Comparison of pemigatinib exposures at 13.5 mg once daily in FIGHT-101 and FIGHT-102. Data are presented as mean ± SD and geometric mean (CV%). [a]In FIGHT-101, 50 and 29 patients received 13.5 mg QD in the ID and CD regimens, respectively. [b]In FIGHT-102, 23 and 13 patients received 13.5 mg QD in the ID and CD regimens, respectively. AUC_{ss},0–24, area under the plasma concentration-time curve from hour 0 to 24 at steady state; CD, continuous dosing; $C_{max, ss}$, maximum plasma drug concentration at steady state; CV, coefficient of variation; h, hour; ID, intermittent dosing; nM, nanomolar; SD, standard deviation.



Population	Patients (n)	$C_{max,ss}$ (nM)	$AUC_{ss, 0–24h}$ (h*nM)
FIGHT-101	57	271 ± 151 236 (56.4)	3010 ± 1890 2620 (54.1)
FIGHT-102	33	238 ± 139 195 (77.8)	3090 ± 1680 2720 (55.5)

Supplementary Figure 3. Induction of plasma *FGF23* after treatment with pemigatinib 13.5 mg. Fold changes from baseline in *FGF23* expression were plotted for individual patients receiving pemigatinib 13.5-mg on ID or CD schedules. Boxes denote the first and third quartiles, lines represent the median, and the whiskers show the limits of 1.5 × IQR. Dashed grey line denotes no fold change from baseline. C, cycle; CD, continuous dosing; D, day; *FGF23*, fibroblast growth factor 23; ID, intermittent dosing; IQR, interquartile range.



Supplementary Figure 4. Inhibition of FGFR2α phosphorylation at trough pemigatinib concentration (Cycle 1 Day 15, 0 hours) in the KATO III *ex vivo* assay. Data are presented as mean ± SD. Dashed line shows 80% inhibition of FGFR2α phosphorylation. FGFR2α, fibroblast growth factor receptor 2-alpha; SD, standard deviation.