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A Phase 2 Study of Pemigatinib (FIGHT-203; INCB054828) in Patients with Myeloid/Lymphoid Neoplasms (MLNs) with *Fibroblast Growth Factor Receptor 1 (FGFR1)* Rearrangement (MLN^{FGFR1})

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Speaker's Disclosures

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- **Research Funding:** Incyte, Novartis, Kartos, Blueprint Medicines, Deciphera, Cogent Biosciences, Abbvie, Celgene, BMS, Protagonist Therapeutics
- **Advisory Boards/Consulting/Honoraria:** Incyte, Novartis, Kartos, Blueprint Medicines, Deciphera, Cogent Biosciences, Abbvie, Protagonist Therapeutics, PharmaEssentia



MLNs With Fusion Tyrosine Kinase Genes

Rare hematologic malignancy with a WHO major category “MLN with eosinophilia and rearrangements of *PDGFRA*, *PDGFRB*, *FGFR1*, or with *PCM1-JAK2*”¹⁻³

- *PDGFRA*, *PDGFRB*, *FGFR1* rearrangements — activation of receptor tyrosine kinases
- *PCM1-JAK2* (provisional entity) — activation of *JAK2*, a non-receptor tyrosine kinase^{1,2}
- *FLT3* and *ABL1* rearrangements are reported but not yet added to the WHO classification¹
- Eosinophilia is characteristic but not universally present^{1,2}

MLN^{FGFR1}

- Patients may present with BM involvement only, extramedullary disease (EMD) only, or BM plus EMD¹⁻³
 - **BM involvement**
 - **Chronic phase (CP):** myeloid disease: most commonly MPN; MDS/MPN or MDS are also observed
 - **Blast phase (BP):** AML, T- or B-cell lymphoblastic lymphoma/leukemia, or mixed phenotype acute leukemia (MPAL)
 - **EMD involvement = BP disease:** AML, T- or B-cell lymphoblastic lymphoma/leukemia, or MPAL

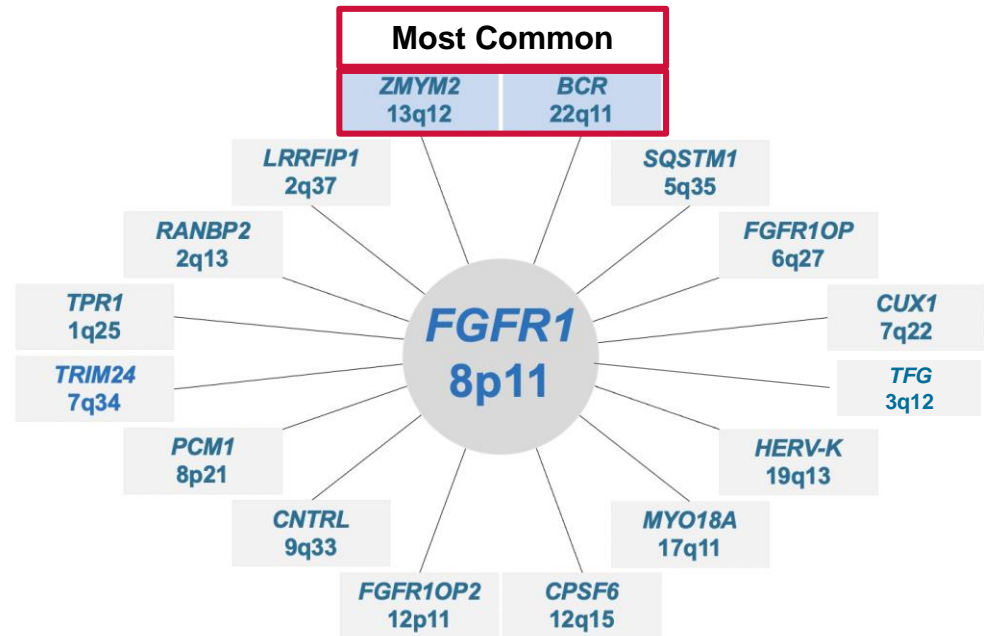
ABL1, ABL proto-oncogene 1, non-receptor tyrosine kinase; AML, acute myeloid leukemia; BM, bone marrow; FGFR1, fibroblast growth factor receptor 1; FLT3, fms related receptor tyrosine kinase 3; JAK2, Janus kinase 2; MDS, myelodysplastic syndrome; MLN, myeloid/lymphoid neoplasm; PCM1, pericentriolar material 1; PDGFRA, platelet derived growth factor receptor alpha; PDGFRB, platelet derived growth factor receptor beta; MPN, myeloproliferative neoplasm; WHO, World Health Organization.

1. Macdonald D, et al. *Leukemia*. 1995;9:1628–30. 2. Reiter A and Gotlib J. *Blood*. 2017;129:704–14. 3. Arber DA, et al. *Blood*. 2016;127:2391–405.

MLN^{FGFR1} Cytogenetics / Molecular Genetics

- Patients will have t(8;13)(p11;q12), t(8;22)(p11;q11), or another translocation involving chromosome band 8p11 that results in constitutive activation of *FGFR1*
 - Translocations are usually identified with conventional cytogenetic analysis and can be confirmed with break-apart FISH

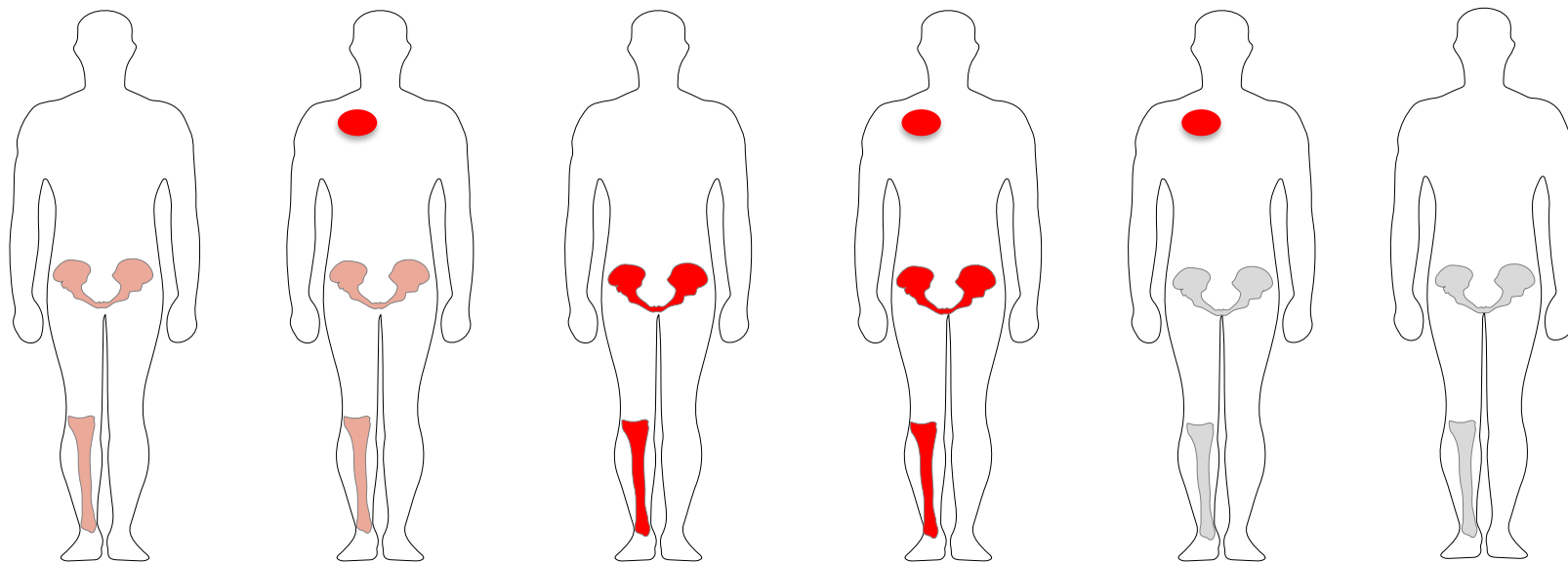
**16 currently known
fusion partners
of *FGFR1***



AML, acute myeloid leukemia; BM, bone marrow; BP, blast phase; CP, chronic phase; EMD, extramedullary disease; FGFR1, fibroblast growth factor receptor 1; FISH, fluorescence in-situ hybridization; MDS, myelodysplastic syndrome; MLN, myeloid/lymphoid neoplasm; MPAL, mixed phenotype acute leukemia; MPN, myeloproliferative neoplasm.

1. Jackson CC, et al. *Hum Pathol.* 2010;41:461–76.

MLN^{FGFR1}: Categories of Presentation



BM/PB: **Chronic Phase**
No EMD

BM/PB: **Chronic Phase**
with **EMD**

BM/PB: **Blast Phase**
No EMD

BM/PB: **Blast Phase**
with **EMD**

EMD Only

Treated, no morphologic
or radiologic evidence
of disease;
+ Cytogenetic/FISH, or
molecular evidence of
FGFR1 rearrangement

BM, bone marrow; EMD, extramedullary disease; FGFR, fibroblast-growth factor receptor; FISH, fluorescence in-situ hybridization; MLN, myeloid/lymphoid neoplasm; PB, peripheral blood.

Information derived from speaker's clinical experience.

Clinical Course of MLN^{FGFR1}

● Chronic phase

- The cumulative incidence of transformation to blast phase at 12 months has been reported to be almost 50%
- Median overall survival from diagnosis reported as low as 9 months in patients not receiving allogeneic HSCT before transformation
- Long-term remission has been reported in patients transplanted before transformation

● Blast phase

- 1-year overall survival from the development of blast phase was 30%
- Achievement of CR with induction therapy has been associated with superior survival
 - Long-term remissions reported in patients undergoing allogeneic HSCT

Current Treatment and Unmet Medical Need

- No established standard therapy^{1,2}
- NCCN Guidelines include recommendations for the diagnosis, staging, and treatment of any of the MLN-Eo associated with a TK fusion gene included in the 2017 WHO classification, as well as MLN-Eo with a *FLT3* or *ABL1* rearrangement³
- Current treatments for MLN^{FGFR1} often lead to partial or short-lived complete responses, however, complete cytogenetic responses are rare¹⁻⁴
 - **CP disease**
 - Hydroxyurea and multi-kinase inhibitors with anti-FGFR1 activity, including ponatinib and midostaurin
 - **BP disease**
 - Lineage-specific induction chemotherapy +/- TKI

NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY

Myeloid/Lymphoid Neoplasms with Eosinophilia and TK Fusion Genes, Version 3.2021

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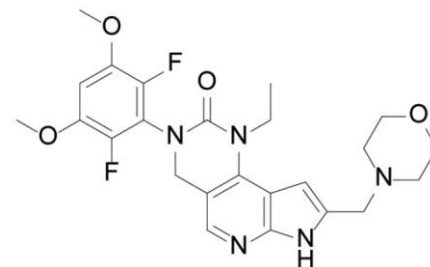
BP, blast phase; CP, chronic phase; Eo, eosinophilia; FGFR1, fibroblast growth factor receptor 1; MLN-Eo, Myeloid-lymphoid neoplasm with eosinophilia; TK, tyrosine kinase; TKI, TK inhibitor.

1. Jackson CC, et al. *Hum Pathol.* 2010;41:461–76. 2. Reiter A and Gotlib J. *Blood.* 2017;129:704–14. 3. Gerds A, et al. *J Natl Compr Canc Netw.* 2020;18:1248–269. 4. Kriel S, et al. *Blood.* 2015;126:2812.

Pemigatinib and FIGHT-203

- Pemigatinib (INCB054828) is a selective and potent inhibitor of FGFR1–3 approved in the US, EU, Japan, and Canada for the treatment of adults with previously treated, unresectable, locally advanced, or metastatic cholangiocarcinoma with an *FGFR2* fusion or other rearrangements¹⁻⁴
- This is an analysis of data from the ongoing FIGHT-203 study of pemigatinib in adults with MLN^{FGFR1} (NCT03011372)

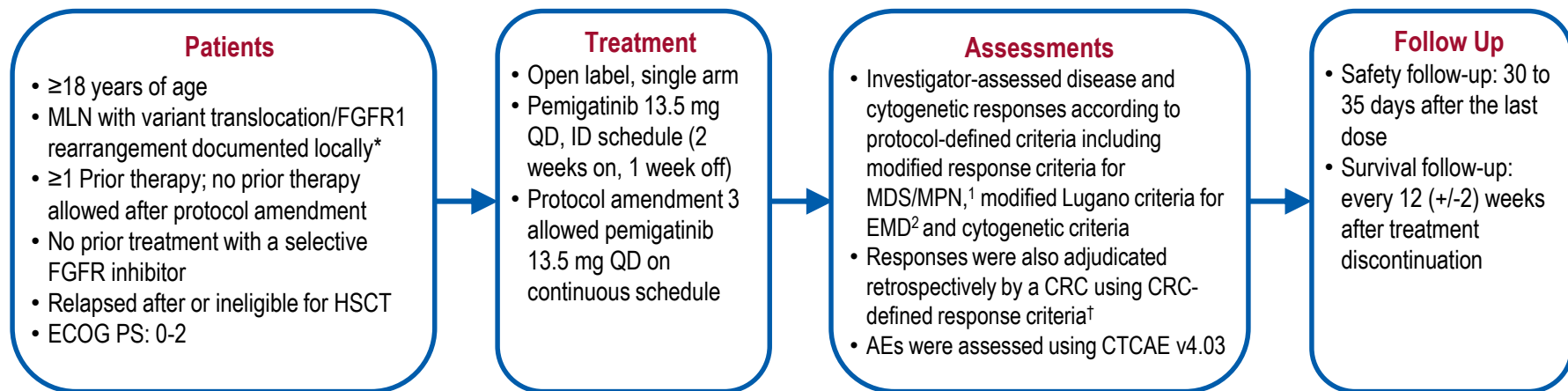
3-(2,6-difluoro-3,5-dimethoxyphenyl)-1-ethyl-8-(morpholin-4-ylmethyl)-1,3,4,7-tetrahydro-2H-pyrrolo[3',2':5,6]pyrido[4,3-d]pyrimidin-2-one



FGFR1, fibroblast growth factor receptor 1; MLN^{FGFR1}, Myeloid/Lymphoid Neoplasms (MLNs) with FGFR1 Rearrangement.

1. PEMAZYRE[®] (pemigatinib) tablets [prescribing information]. Wilmington, DE: Incyte Corporation; February 2021. 2. Pemazyre[®] (pemigatinib) overview. European Medicines Agency; 2021. 3. Incyte announces approval of Pemazyre[®] (pemigatinib) in Japan for the treatment of patients with unresectable biliary tract cancer (BTC) with a fibroblast growth factor receptor 2 (FGFR2) fusion gene, worsening after cancer chemotherapy [press release]. Wilmington, DE: Incyte Corporation; March 23, 2021. 4. <https://www.biospace.com/article/releases/incyte-announces-health-canada-conditional-approval-of-pemazyre-and-174-pemigatinib-as-first-targeted-treatment-for-adults-with-previously-treated-unresectable-locally-advanced-or-metastatic-cholangiocarcinoma/>

Study Design and Endpoints



- **Primary endpoint is CR rate**
- **Secondary endpoints include ORR (CR + PR), CCyR or partial CyR (PCyR), and Safety**

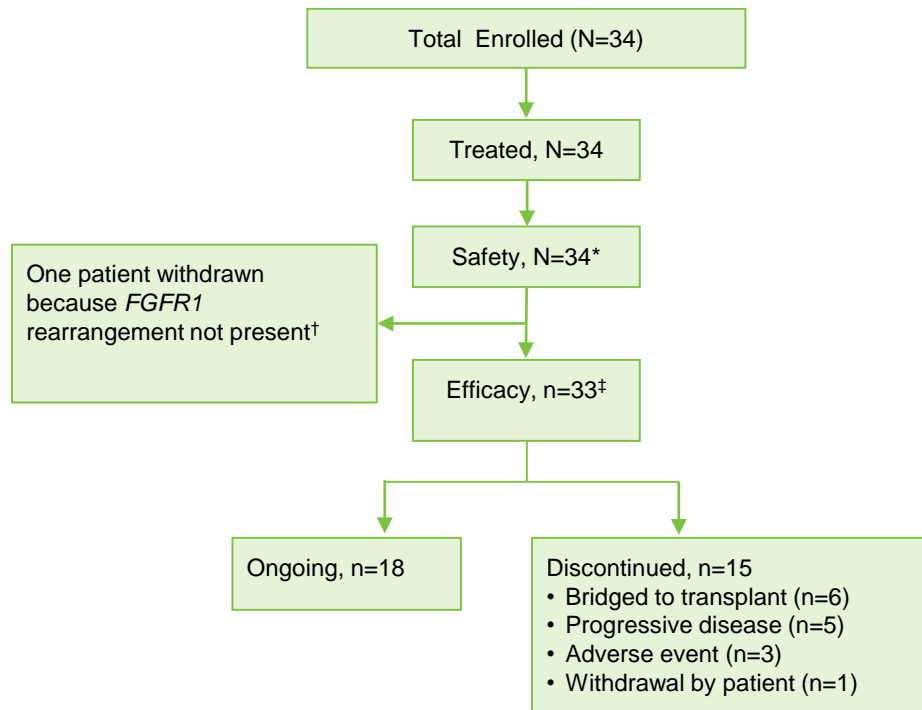
*Based on standard cytogenetic evaluation performed locally. [†]CRC-defined response criteria were based on local lab and radiologic results and central histopathology review; both local and central cytogenetic results were used by CRC with central results given priority.

AE, adverse event; CCyR, complete cytogenetic response; CD, continuous dose; CR, complete response; CRC, Central Review Committee; CTCAE, Common Terminology Criteria for Adverse Events; ECOG PS, Eastern Cooperative Oncology Group Performance Status; EMD, extramedullary sites; FGFR1, fibroblast growth factor 1; HSCT, hematopoietic stem cell transplant; ID, intermittent dose; MDS/MPN, myelodysplastic/myeloproliferative neoplasms; MLN, myeloid/lymphoid neoplasm; ORR, overall response rate; PCyR, partial cytogenetic response; PR, partial response; QD, daily.

1. Savona MR, et al. *Blood*. 2015;125:1857–865. 2. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059–068.

Patient Disposition and Exposure

Patient Disposition



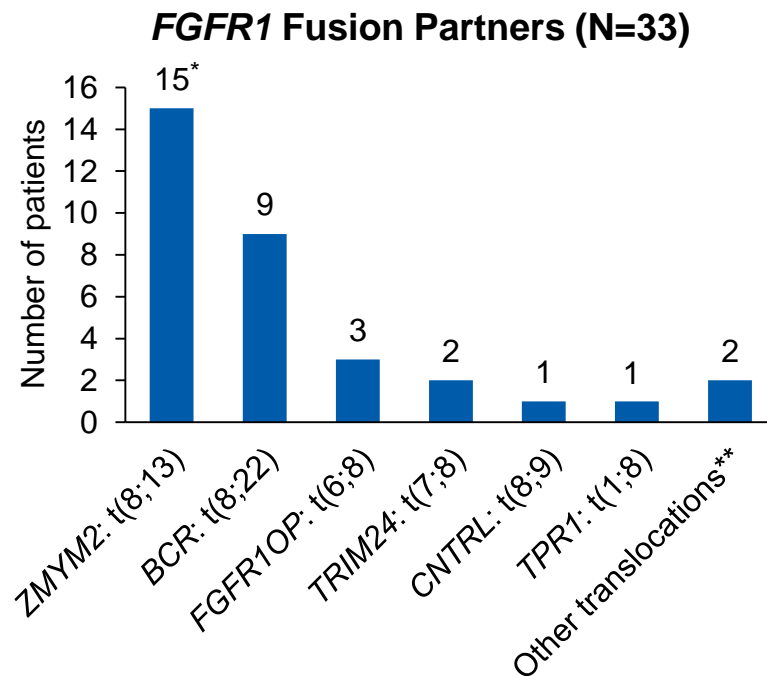
Pemigatinib exposure

Exposure, median (range)	Patients (N=34)
Daily dose (mg/day)	9.5 (4.0-14.7)
Number of treatment cycles completed	10.0 (2.0-65.0)
Duration of treatment, weeks	29.3 (4.3-192.4)

Data cut-off: 31 December 2020. *Safety population included all enrolled patients who received at least one dose of pemigatinib; †Physician decision; ‡ Efficacy evaluable population included all enrolled patients with an *FGFR1* rearrangement who received at least 1 dose of pemigatinib; 1 pt did not have *FGFR1* rearrangement and was excluded from efficacy analysis.

Baseline Characteristics (1 of 2)

Characteristic	Overall (N=33)
Age, median, years (range)	64.0 (36-78)
Female, n (%)	20 (61)
No. of patients with prior therapy for MLN ^{FGFR1} , n (%)	28 (85%)
No. of prior therapies, average (range)	1.6 (0-6)
Prior HSCT, n (%)	3 (9)
Peripheral blood eosinophilia (>0.5 × 10 ⁹ /L) at baseline (per CRC), n (%)	7 (21)



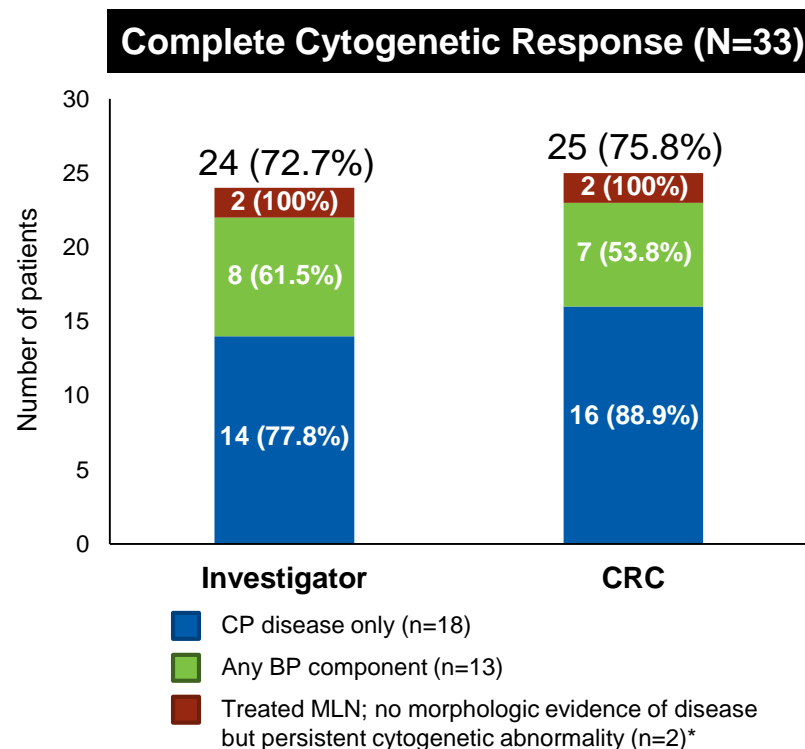
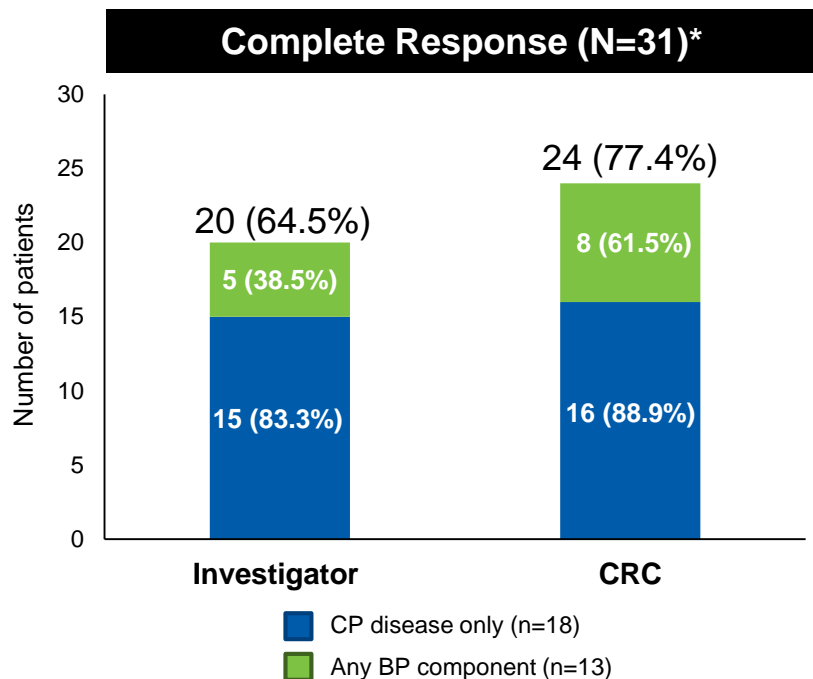
*One patient had 2 rearrangements on translational testing—a *TPR1* identified on cytogenetic testing and a *ZMYM2* rearrangement that was not identified on cytogenetics testing. **Other translocations were: t(5;8), t(8;10). *BCR*, breakpoint cluster region protein; CRC, Central Review Committee; *CNTRL*, Centriolin; *FGFR*, fibroblast growth factor receptor; *FGFR1OP*, Fibroblast Growth Factor Receptor 1 Oncogene Partner; HSCT, hematopoietic stem cell transplant; MLN, myeloproliferative neoplasm; t, translocation; *TPR1*, Tetratricopeptide repeat protein 1; *TRIM24*, Tripartite Motif Containing 24; *ZMYM2*, Zinc Finger MYM-Type Containing 2.

Baseline Characteristics (2 of 2)

Disease presentation, n (%)	Overall (N=33)
BM involvement by lineage (per CRC)	
No morphological evidence of disease	7 (21)
Myeloid neoplasm	23 (70)
CP (MPN, n=16; MDS/MPN, n=4)	20
BP (AML, n=3)	3
Lymphoid neoplasm	2 (6)
BP (B-ALL, n=2)	2
Mixed-phenotype neoplasm	1 (3)
BP (MPAL, n=1)	1
Presentation category (BM and/or EMD involvement; per CRC)	
CP only (no EMD)	18 (55)
BP disease (EMD represents a BP component)	13 (39)
CP with EMD	2 (6)
BP without EMD	5 (15)
BP with EMD	1 (3)
EMD only	5 (15)
Treated MLN without morphologic evidence of BM or EMD involvement (persistent 8p11 translocation and/or <i>FGFR</i> rearrangement)	2 (6)

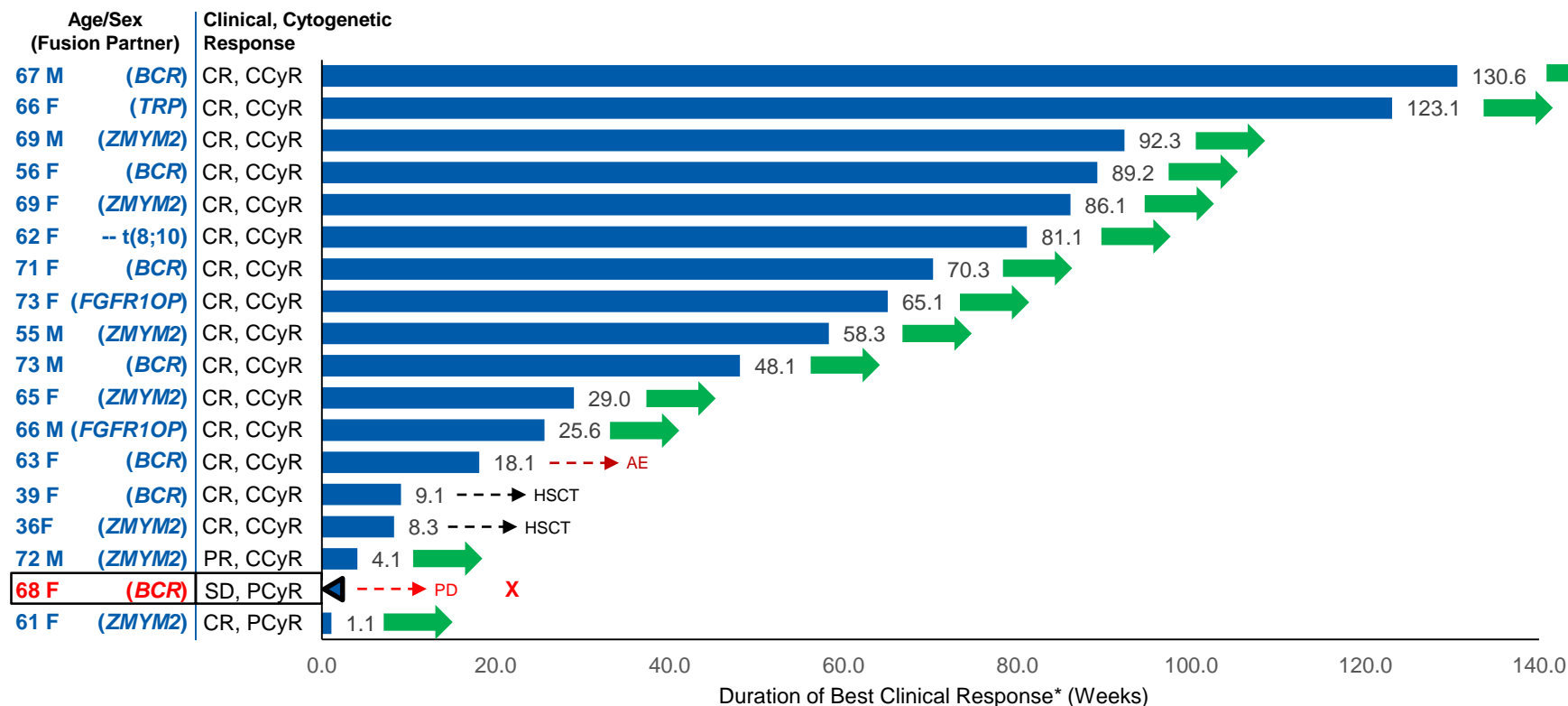
AML, acute myeloid leukemia; B-ALL, B-cell acute lymphoblastic leukemia; BM, bone marrow; BP, blast phase; CP, chronic phase; CRC, Central Review Committee; EMD, extramedullary disease; FGFR, fibroblast growth factor receptor; MDS, myelodysplastic syndrome; MLN, myeloid/lymphoid neoplasm; MPAL, mixed phenotype acute leukemia; MPN, myeloproliferative neoplasm.

Response Rates



Note: Central FISH was given priority over local cytogenetic results during CRC adjudications. *In the 2 patients with "treated MLN with no morphologic evidence of disease but persistent cytogenetic abnormality" clinical responses were not adjudicated but cytogenetic response were adjudicated. BP, blast phase; CCyR, cytogenetic response; CP, chronic phase; CRC, Central Review Committee; FISH, fluorescence in-situ hybridization; MLN, myeloid/lymphoid neoplasm.

Chronic Phase Disease Only (n=18): Best Clinical and Cytogenetic Responses per CRC

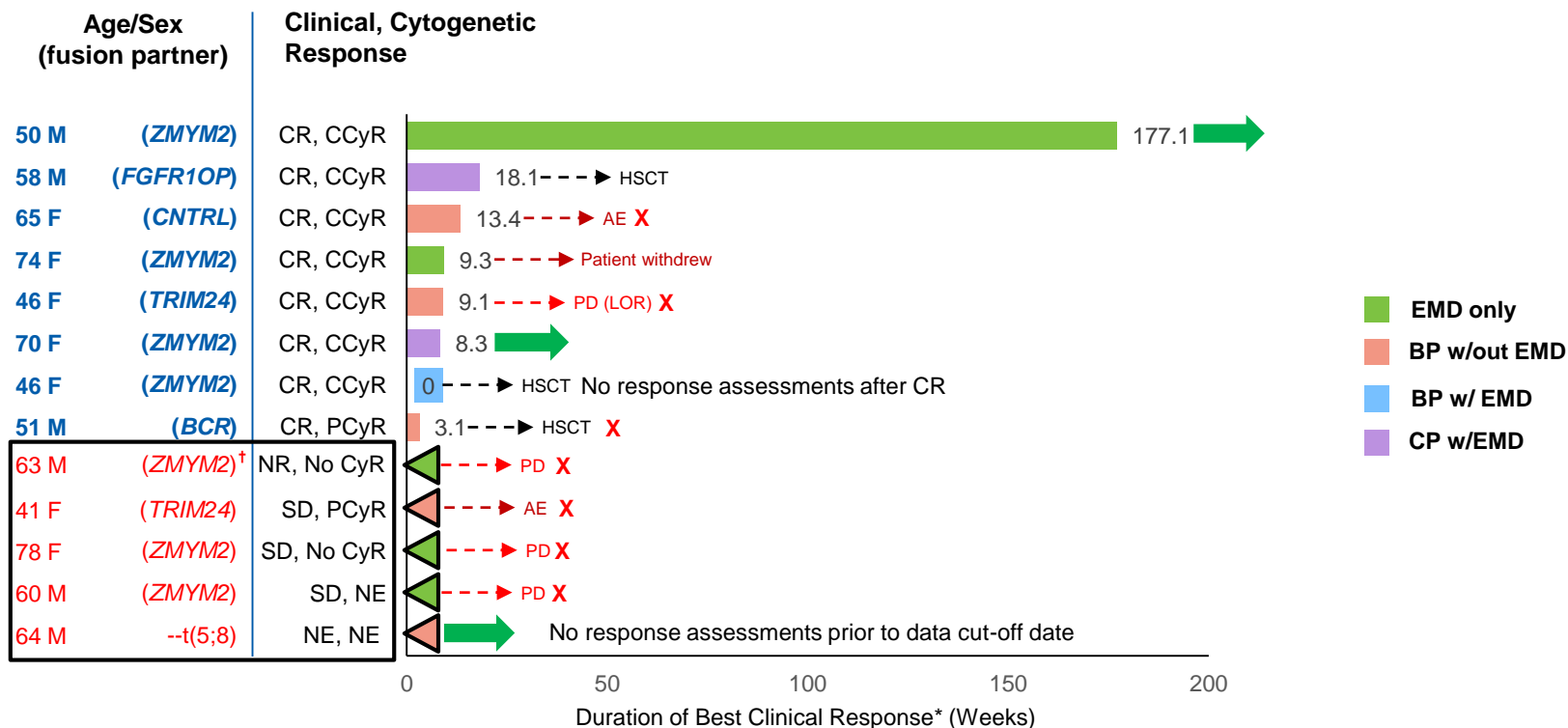


*Swimmer lane representative of duration of clinical response only.

X denotes death; green arrow shows patients still receiving treatment at the time of data cut-off; Black-outlined triangle shows non-responder.

AE, adverse event; CCyR, complete cytogenetic response; CR, complete response; CRC, Central Review Committee; HSCT, hematopoietic stem cell transplant; NE, not evaluable; PR, partial response; SD, stable disease.

Blast Phase (n=13): Best Clinical and Cytogenetic Responses per CRC



*Swimmer lane is representative of clinical response only.

X denotes death; [†]Patient had no response prior to PD; **green arrow** shows patients still receiving treatment at the time of data cut-off; **Black-outlined triangles** show non-responders.

AE, adverse event; BP, blast phase; CCyR, complete cytogenetic response; CP, chronic phase; CR, complete response; EMD, extramedullary disease; HSCT, hematopoietic stem cell transplant; LOR, loss of response; NE, not evaluable; PD, progressive disease; SD, stable disease.

Dose Modifications

Dose Modifications Due to Any TEAE

Dose modifications	Patients (N=34)*
Interruption	22 (65%)
Reduction	20 (59%)
Discontinuation	4 (12%)

- The TEAEs (in one patient each) that led to treatment discontinuation were:
 - Cardiac failure
 - Multiple organ dysfunction
 - Blood alkaline phosphatase increased
 - Calciphylaxis
- 9 deaths were reported in the study and none was considered related to pemigatinib**
 - Disease progression (n=7)
 - Progressive kidney failure and fungal pneumonia (n=1)
 - Unknown (n=1)

*Safety population included all enrolled patients who received at least one dose of pemigatinib; **Including one patient without *FGFR1* rearrangement who was withdrawn from the study and subsequently died. TEAE, treatment-emergent adverse event.

Treatment-Emergent Adverse Events

TEAE, n (%)	Patients (N=34)*	
	All Grades	Grade ≥3
Any TEAE	34 (100)	29 (85)
Hematologic (any frequency)		
Anemia	12 (35)	6 (18)
Thrombocytopenia	4 (12)	3 (9)
Neutropenia	1 (3)	0
Non-hematologic (occurring in ≥20% of all patients)		
Hyperphosphatemia	23 (68)	1 (3)
Alopecia	20 (59)	0
Diarrhea	17 (50)	1 (3)
Stomatitis	15 (44)	4 (12)
Constipation	11 (32)	1 (3)
Dry mouth	11 (32)	0
Blood alkaline phosphatase increased	10 (29)	1 (3)
Dry eye	10 (29)	0

TEAE, n (%)	Patients (N=34)*	
	All Grades	Grade ≥3
Non-hematologic (continued)		
Epistaxis	10 (29)	0
Pain in extremity	9 (27)	4 (12)
Asthenia	8 (24)	1 (3)
Decreased appetite	8 (24)	2 (6)
Dyspepsia	8 (24)	0
Rash	8 (24)	1 (3)
Abdominal pain	7 (21)	1 (3)
Back pain	7 (21)	2 (6)
Dizziness	7 (21)	0
Dry skin	7 (21)	0
Fatigue	7 (21)	2 (6)
Nausea	7 (21)	0
Edema peripheral	7 (21)	0
Vision blurred	7 (21)	1 (3)

*Safety population included all enrolled patients who received at least one dose of pemigatinib. TEAE, treatment-emergent adverse event.

Conclusions

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- Pemigatinib is the first therapy to demonstrate durable and high rates of CR and CCyR in patients with MLN^{FGFR1}, most of whom had progressed on prior therapies including intensive chemotherapy or HSCT.
- Kaplan-Meier median durations of CR and OR (CR+PR) have not been reached in the full efficacy population.
- Clinical and cytogenetic responses in patients with blast phase disease were less frequent and less durable than in the patients with chronic phase disease. However, 23% of the patients with blast phase disease were bridged to HSCT.
- The safety profile was consistent with FGFR inhibition with no unexpected toxicities.
- These results suggest that pemigatinib may offer a long-term treatment option for patients with MLN^{FGFR1} ineligible for HSCT or may facilitate bridging to HSCT in eligible patients.

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