Abstract: P1042

Title: A PHASE 2 STUDY OF PEMIGATINIB (FIGHT-203; INCB054828) IN PATIENTS WITH MYELOID/LYMPHOID NEOPLASMS WITH FIBROBLAST GROWTH FACTOR RECEPTOR 1 GENE REARRANGEMENT

Abstract Type: Poster Presentation

Topic: Myeloproliferative neoplasms - Clinical

Background:

Myeloid/lymphoid neoplasms with fibroblast growth factor receptor 1 (*FGFR1)* gene rearrangement (MLN*FGFR1*) are rare, aggressive hematologic malignancies caused by chromosome band 8p11 reciprocal translocations that result in *FGFR1* fusion genes and constitutive FGFR1 activation. Pemigatinib is a selective oral FGFR1-3 inhibitor approved for adult refractory/relapsed MLN*FGFR1*. Previous data from FIGHT-203 (Verstovsek et al. *Blood*. 2022;140(suppl 1):3980) demonstrated durable clinical and cytogenetic responses to pemigatinib in patients (pts) with MLN*FGFR1* (NCT03011372).

Aims:

To present updated data from FIGHT-203

Methods:

Eligible pts had MLN*FGFR1* and were not candidates for, or had relapsed after, allogeneic HCT (alloHCT) or other therapy. Pts received oral pemigatinib 13.5 mg once daily (intermittent dose [ID; 2 weeks on/1 week off] or continuous dose [CD]). The primary endpoint was complete response (CR) rate. Secondary endpoints included complete cytogenetic response (CCyR) rate, duration of CR (DOCR), and safety. Responses were investigator assessed locally and adjudicated by a central review committee (CRC) per CRC-defined criteria. CyR were quantified from decreased 8p11 translocated metaphases by cytogenetics (≥20 metaphases) or break-apart (BA) FISH. In exploratory analyses, changes from baseline in *FGFR1* fusion transcript copies were quantified by droplet digital PCR (ddPCR) using RNA from serial whole blood samples.

Results:

As of July 17, 2023, 47 pts were enrolled; 41 had received ≥1 prior therapy and 3 had received prior alloHCT. 45 pts had documented *FGFR1* rearrangement at screening and were analyzed for efficacy. Disease presentation characteristics are shown in **Table 1**. Median follow-up was 47.4 (range, 13.7-74.7) months. Treatment was ongoing in 15 pts (33.3%) and 13 pts (28.9%) had discontinued to bridge to alloHCT, enabled by improved clinical status and responses achieved after pemigatinib, among whom 12 had confirmed alloHCT receipt. Per CRC, CR rates were 71.1% (chronic phase [CP], 95.8%; blast phase [BP], 44.4%); CCyR rates were 71.1% (CP, 87.5%; BP, 44.4%) (**Table 1**). Among pts with ≥1 and without prior treatment, CR rates were 70.0% and 80.0%, respectively. Median time to CR was 1.5 (1.3-9.7) months. Median DOCR was not reached (NR; range, 27.9-NR) months; 85.8% of pts were estimated to have maintained a response at 24 months. *FGFR1* fusion transcript copy numbers in whole blood decreased during treatment in 30/33 pts (90.9%), rebounded following dose interruption (>5 weeks), and decreased upon rechallenge (**Figure 1A**). These dynamic changes were consistent with changes in the bone marrow by BA FISH (Pearson coefficient = 0.80), including improved responses in pts who transitioned from ID to CD (**Figure 1B**). Of the 47 pts evaluated for safety, most common treatment-emergent adverse events (TEAEs) were hyperphosphatemia (76.6%), diarrhea (61.7%), and alopecia (57.4%); most common grade ≥3 TEAEs were stomatitis (19.1%) and anemia (14.9%); 5 (10.6%), 30 (63.8%), and 28 pts (59.6%), respectively, discontinued, interrupted, or reduced dose owing to TEAEs.

Summary/Conclusion:

Pemigatinib is the first treatment to show deep and durable responses in pts with MLN*FGFR1*. High CR and

CCyR rates were achieved regardless of disease presentation or number of prior therapies; toxicities were manageable with dose modification and consistent with the known safety profile of pemigatinib. Pemigatinib may provide a long-term treatment option for pts with MLN*FGFR1* ineligible for alloHCT, or may facilitate eligible pts to bridge to alloHCT.

Keywords: Myeloid malignancies, Lymphoid malignancy, FGF