Leukemia insights

MARCH 2022

MONTHLY EDITION

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

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In this month's Leukemia Insights newsletter, written by Prithviraj Bose, M.D., and Srdan Verstovsek, M.D., Ph.D., and sponsored in part by the Charif Souki Cancer Research Fund, we provide a summary of clinical trials for patients with polycythemia vera, essential thrombocythemia, systemic mastocytosis and myeloid/lymphoid neoplasms with eosinophilia. Learn more about our Leukemia program.

Clinical trials for patients with polycythemia vera (PV), essential thrombocythemia (ET), systemic mastocytosis (SM) and myeloid/lymphoid neoplasms with eosinophilia (MLNEo)

In parallel with the explosive growth of new drug development in myelofibrosis, several novel agents, some with unique mechanisms of action, have emerged to potentially expand our therapeutic arsenal for the more indolent classic myeloproliferative neoplasms (MPNs), PV and ET, as well as for rare neoplasms such as systemic mastocytosis and myeloid/lymphoid neoplasms with eosinophilia. Recent regulatory approvals include avapritinib for advanced SM and ropeginterferon alfa-2b for PV. Here, we discuss clinical trials for these conditions at MD Anderson.

1. Polycythemia vera

Rusfertide

Rusfertide (formerly PTG-300) is a hepcidin mimetic administered subcutaneously weekly. Mimicking the action of hepcidin in patients with PV leads to sequestration of iron in the reticuloendothelial system, rendering it unavailable for erythropoiesis. In a phase 2 trial in PV patients requiring ≥3 phlebotomies in the preceding 6 months, the addition of rusfertide to baseline therapy resulted in near elimination of phlebotomy requirement, corrected iron deficiency and improved symptoms (Hoffman…Verstovsek, ASH 2021). This drug now is being studied in a placebo-controlled, registrational phase 3 trial as an "add-on" therapy in phlebotomy-requiring patients with PV (NCT05210790). This will open to enrollment soon at MD Anderson.

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Sapablursen

Sapablursen (formerly ISIS 702843) is an anti-sense oligonucleotide directed against TMPRSS6, a negative regulator of hemojuvelin, which is a positive regulator of hepcidin production. Sapablursen thus increases endogenous hepcidin, invoking a similar mechanism of action to that of rusfertide in PV, but by a different strategy. Sapablursen is administered subcutaneously every 4 weeks. A phase 2 trial in phlebotomy-dependent patients with PV (NCT05143957) will open soon at MD Anderson.

2. Essential thrombocythemia

Ropeginterferon alfa-2b

Ropeginterferon alfa-2b (formerly P1101) is a mono-pegylated interferon alfa-2b that can be administered once every 2 weeks (and potentially less frequently over time). It recently was FDA-approved for patients with PV and is being compared to anagrelide in high-risk ET patients with resistance to or intolerance of hydroxyurea in the phase 3 SURPASS-ET trial. A white blood cell count of ≥10 x 10^9/L at screening is required. This trial is open at MD Anderson.

Pelabresib

The bromodomain and extra-terminal (BET) protein inhibitor pelabresib (formerly CPI-0610), best known for its promising results in patients with myelofibrosis in the MANIFEST trial, particularly in combination with ruxolitinib, is also being studied in patients with high-risk, hydroxyurea-resistant/intolerant ET in a separate arm of the same trial (NCT04603495). A minimum white blood cell count is not required. This trial is open at MD Anderson.

3. Systemic mastocytosis

Despite the success of avapritinib in advanced SM, some problems remain. The drug is associated with intracranial bleeding, particularly in patients with severe thrombocytopenia (platelets <50 x 10^9/L), in whom avapritinib is not indicated because it may impair platelet function. Cognitive impairment, although usually low grade, also can be an issue. For these reasons, a potent and selective inhibitor of mutant KIT that only minimally penetrates the blood-brain barrier could be a welcome addition. Such an agent, bezuclastinib (previously CGT9486), is being studied in the phase 2 APEX (NCT04996875) and SUMMIT (NCT05186753) trials in advanced and non-advanced (indolent and smoldering) SM, respectively. The APEX trial is open and the SUMMIT trial about to open at MD Anderson. A trial evaluating a similar agent, BLU-263 (NCT04910685, HARBOR), in patients with indolent SM will also open soon.

4. Myeloid/lymphoid neoplasms (MLN) with rearrangements of FGFR1 ("8p11 syndrome")

MLN with rearranged FGFR1, the gene encoding the type 1 fibroblast growth factor receptor located at chromosome 8p11, is a rare and aggressive neoplasm with no standard of care. Blast phase transformation is common, eosinophilia is often absent, and hematopoietic stem cell transplantation offers the only possibility of long-term remission. The most common fusion partners of FGFR1 are ZMYM2 (13q12) and BCR (22q11). Pemigatinib, an oral, small-molecule inhibitor of FGFR1/2/3, is FDA-approved for FGFR2-rearranged, locally advanced or metastatic cholangiocarcinoma. In the phase 2 FIGHT203 trial, pemigatinib led to high rates of complete and complete cytogenetic responses in 33 patients with FGFR1-rearranged MLN (Gotlib…Verstovsek, ASH 2021). This trial is open at MD Anderson.

Leukemia Faculty Contacts

Completing these studies in a timely manner will allow us to move quickly on positive leads. We appreciate referrals and will make every effort, once a patient is enrolled on a study, to continue as much of the care as possible through the referring oncologist. We also will keep you apprised of the patient's progress. View our faculty roster.

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