Leukemia insights

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Making Cancer History®

New Trials for Myelofibrosis, Advanced Systemic Mastocytosis, Chronic Neutrophilic Leukemia/Atypical Chronic Myeloid Leukemia, and Hypereosinophilic Syndrome/Chronic Eosinophilic Leukemia

In This Issue

INTRODUCTION

Management of myelofibrosis (MF) centers around amelioration of anemia, splenomegaly and constitutional symptoms, with the end goals of prolonging survival and curing the disease, which is currently achievable only with allogeneic stem cell transplantation. Anemia is typically treated with erythropoiesis-stimulating agents, corticosteroids, danazol and immunomodulatory drugs. Ruxolitinib, the only drug approved by the FDA for MF, significantly reduces splenomegaly, improves constitutional symptoms, and can prolong survival in many patients with symptomatic MF, regardless of JAK2 mutation status. A variety of ruxolitinib-based combination approaches are being explored, both with conventional agents and novel, mechanism-based medications. Newer JAK inhibitors, some with the potential for less myelosuppression, or even improvement of anemia, are in clinical trials for patients with MF. In addition, novel agents with different modes of action are being studied as well, both for MF and for advanced systemic mastocytosis, chronic neutrophilic leukemia/atypical chronic myeloid leukemia, and hypereosinophilic syndrome/chronic eosinophilic leukemia. Below, we discuss clinical trials currently recruiting these patients at the MD Anderson Cancer Center.

COMBINATION THERAPIES WITH RUXOLITINIB

Despite significant improvements in the clinical manifestations of MF elicited by ruxolitinib, significant reductions in bone marrow fibrosis or JAK2^{V617F} allele burden have remained elusive. Combining ruxolitinib with novel therapies that have distinct mechanisms of action is a promising strategy to improve outcomes and potentially reverse the disease process.

Phase II trial of ruxolitinib and oral pracinostat in subjects with MF

In addition to activating the signal transducer and activator of transcription (STAT) pathway, JAK2 can also act as a histone-modifying enzyme, which has downstream effects on other genes involved in hematopoiesis. Pracinostat is a histone deacetylase (HDAC) inhibitor that has shown modest activity in patients with MF.[1] Furthermore, HDAC inhibitors enhance the cytotoxic effects of JAK inhibitors in human MPN cells *in vitro*, providing a rationale for combining the two. A phase II trial of ruxolitinib and pracinostat in subjects with MF is currently enrolling patients at our center. Patients will receive ruxolitinib orally as a single agent for the first 3 months, at which point oral

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pracinostat will be added. Patients with MF not previously treated with a JAK inhibitor or who are currently on ruxolitinib for < 3 months are eligible.

Phase II study of ruxolitinib and azacytidine in patients with MF

Ruxolitinib, a JAK 1/2 inhibitor and azacytidine, a pyrimidine nucleoside analog with hypomethylating activity, are effective and tolerable treatments for patients with MF and myelodysplastic syndromes (MDS), respectively. Combination of these agents, which have different targets, may improve the overall clinical response without causing excessive toxicity. Patients with symptomatic MF or MDS/MPN overlap syndromes requiring therapy are eligible. Patients will receive oral ruxolitinib alone twice daily for the first 3 months, and then low-dose azacytidine will be added and given intravenously daily for the first 4 days of each 28-day cycle.

NOVEL JAK INHIBITORS

Phase III randomized trial of oral pacritinib vs. best available therapy in thrombocytopenic subjects with MF (PERSIST-2)

Two JAK inhibitors with kinase selectivity different from ruxolitinib have also shown promise in MF and are in advanced stages of clinical development. Pacritinib (SB1518), an oral JAK2 inhibitor that also targets FLT3, has been shown to be non-myelosuppressive.[2] In the phase III PERSIST-1 trial, which compared pacritinib with best available therapy (BAT), 19.1% of patients in the pacritinib arm experienced ≥ 35% reduction in spleen volume, compared with 4.7% of those receiving BAT.[3] In the subgroup of patients ineligible for ruxolitinib due to severe thrombocytopenia, 33% in the pacritinib arm had a ≥35% reduction in spleen volume vs. 0% in the control arm; these patients also experienced a 35% increase (average) in platelet counts. We are enrolling patients on the phase 3 PERSIST-2 trial comparing pacritinib vs. BAT in patients with MF and thrombocytopenia, including those previously treated with a JAK2 inhibitor. Crossover from the BAT arm to pacritinib is allowed and patients with MF and platelet counts ≤ 100 x 10^9/L are eligible.

Phase III randomized trial of momelotinib vs. best available therapy in anemic or thrombocytopenic subjects previously treated with ruxolitinib

Momelotinib (CYT387) is another novel, oral JAK1/2 inhibitor that produces not only spleen and symptom responses, but also anemia responses in patients with MF.[4] A phase 3 trial of momelotinib vs. BAT in anemic or thrombocytopenic subjects previously treated with ruxolitinib is currently enrolling patients. Patients will be randomized 2:1 to receive either momelotinib orally once daily or best available therapy for at least 24 weeks. Crossover from the BAT arm to momelotinib is allowed. Patients with anemia or thrombocytopenia who have received ruxolitinib for at least 28 days are eligible.

Phase II, open-label study of NS-018 in patients with MF previously treated with a JAK2 inhibitor

A third JAK2 inhibitor that has shown activity in a mouse model of MF is also in clinical development.[5] We are enrolling patients to a phase 2 open-label study of the oral inhibitor NS-018, which is selective for JAK2. Patients will receive 300 mg NS-018 orally twice daily. Only patients previously treated with a JAK2 inhibitor are eligible to enroll. Patients must be 18 or older, have reasonable kidney and liver function, and have a platelet count greater than 25 x 10^9/L.

IMMUNOTHERAPY

Phase II study of nivolumab in patients with MF

Immune checkpoint inhibitors such as ipilimumab and nivolumab have shown unprecedented efficacy in several types of cancer, including metastatic melanoma, non-small cell lung cancer (NSCLC) and metastatic renal cell carcinoma. Nivolumab is a fully human, IgG4 (kappa) monoclonal antibody against PD-1
that is FDA-approved for use in patients with previously treated metastatic melanoma[6] and NSCLC.[7] In addition, results have been highly promising in patients with relapsed or refractory Hodgkin's lymphoma, where overexpression of the PD-1 receptor ligands PD-L1/2 is mediated by the JAK-STAT pathway.[8] Although PD-L1/2 expression in MF has not yet been tested, the non-canonical effects of nuclear JAK2 lead to increased PD-L1/2 expression in hematologic malignancies. Patients with relapsed/refractory MF previously treated with ruxolitinib or those who are newly diagnosed but not a good candidate for ruxolitinib are eligible. Patients with autoimmune diseases are excluded and prior therapy with immune checkpoint inhibitors is not allowed. Nivolumab will be given intravenously at the standard dose of 3 mg/kg every 2 weeks for 8 doses, then every 3 months.

OTHER TARGETED AGENTS

Phase II, open-label study of sotatercept (ACE-011) in subjects with MF and significant anemia

Other novel agents with targets outside the JAK-STAT pathway are also being tested in MF. Anemia is a common

symptom of MF and is often exacerbated by treatment with ruxolitinib. We are testing the novel agent sotatercept (ACE-011) in a phase 2 study to determine its efficacy in patients with MF and significant anemia. Sotatercept is a human fusion protein consisting of the extracellular domain of activin receptor IIA linked to the human IgG1 Fc domain. It acts as an activin receptor IIA ligand trap, improving ineffective erythropoiesis and resulting in increased terminal erythroid differentiation, thus correcting anemia. This trial enrolls patients with MF who are anemic or RBC-transfusion-dependent. Sotatercept is administered by subcutaneous injection every 3 weeks for at least 6 months.

Phase II, open-label study of LCL-161 in patients with MF

LCL-161 is an oral, small-molecule antagonist of inhibitor of apoptosis (IAP) proteins, which promote cellular survival by antagonizing the activity of caspases.[9] In preclinical studies, IAP antagonists synergize with tumor necrosis factor alpha (TNFα) and TNF-related apoptosis inducing ligand (TRAIL) to induce apoptosis. In MPN cells, $JAK2^{V617F}$ upregulates TNFα, which plays a critical role in their clonal expansion. This phase 2 open-label trial enrolls patients with MF who are not candidates for, are intolerant of or have failed therapy with ruxolitinib.

Phase I/II trial of SL-401 in patients with advanced, high risk MPNs, including MF, CMML, advanced systemic mastocytosis and HES/CEL

Another potential target in MF is the interleukin-3(IL-3) receptor, which is overexpressed on leukemia stem cells and MPN cells.[10] A phase 1/2 trial is testing SL-401, a novel fusion protein consisting of human interleukin-3 conjugated to a truncated form of diphtheria toxin, in patients with advanced, high-risk MPNs, including MF, chronic myelomonocytic leukemia, and hypereosinophilic syndrome/chronic eosinophilic leukemia. Patients with symptomatic MF who are not candidates for, are intolerant of or have failed therapy with ruxolitinib are eligible. Patients with chronic myelomonocytic leukemia (CMML) or primary eosinophilic disorders who are not candidates for therapy with imatinib are also eligible, as are patients with advanced systemic mastocytosis (SM) who have failed at least 1 prior therapy.

Phase II, double-blind, placebo-controlled study of PF-04449913 in patients with MF previously treated with ≥1 JAK inhibitors.

PF-04449913 is an oral sonic hedgehog pathway (smoothened) inhibitor. Signaling through the hedgehog pathway, a key regulator of cell growth and differentiation during embryonic development, is critical for survival and self-renewal of cancer stem cells. Patients with relapsed/refractory MF who have been previously treated with a JAK inhibitor are eligible. Crossover is permitted for patients randomized to placebo upon disease progression or after completing 24 weeks on study.

Phase I, open-label study of AG-881 in patients with advanced hematologic malignancies with IDH1/2 mutations.

AG-881 is a novel, oral inhibitor of the Krebs' cycle enzymes isocitrate dehydrogenase 1 and/or 2 (IDH1/2). Activating mutations in IDH1/2 have been reported to be associated with shorter leukemia–free survival in Ph- MPNs. Patients with relapsed or refractory Ph- MPNs with IDH1/2 mutations are eligible for this first-in-human, phase I, dose-escalation study.

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CLL Treatment Priorities

1. Untreated

- Fludarabine + Cytoxan + Rituximab (FCR) (2008-0431)
- Ofatumumab (2011-0520)
- TRU-016 + Rituximab (2012-0626)
- Nivolumab + Ibrutinib (2014-0931)
- Lirilumab + Rituximab (2014-0933)

2. Prior Therapy

- Sapacitabine + Cytoxan + Rituximab (2010-0516)
- CD19 CAR (2011-1169)
- ROR1R CAR-T (2012-0932)
- GDC-0199 + Obinutuzumab (2013-0486)
- Ublituximab + TGR-1202 (2013-0566)
- Ibrutinib +/- Rituximab (2013-0703)
- PRT062070 (2013-0880)
- ACP-196 (2013-0907)
- ABT-199 (2014-0405)
- ACP-196 + ACP-319 (2014-0419)
- IPI-145 + Obinutuzumab (2014-0794)
- Urelumab + Rituximab (2014-0932)

3. Other Studies

- Ruxolitinib for CLL Fatigue (2013-0044)
- Lenalidomide (2013-0371)
- Richter's: Selinexor (2014-0601)

4. Hairy Cell

- 2CDA + Rituximab (2004-0223)
- PCI-32765 (2013-0299)

AML/MDS Treatment Priorities

1. Newly Diagnosed

A. Acute Promyelocytic Leukemia: cytogenetic feature: t(15;17):

- ATRA + Arsenic +/– Gemtuzumab (2010-0981)

B. Cytogenetic feature: Inv16 or t(8:21): Fludarabine + Ara-C + Idarubicin (2007-0147)

C. Younger Patients:

- CIA vs FAI (2010-0788)
- 3 + 7 vs IA+Vorinostat (S1203)
- PF-04449913 with 3 + 7 (2012-0062)
- Cladribine + IA + Sorafenib (2012-0648)
- Nivolumab + IA (2014-0907)

D. Older Patients:

- Omacetaxine + Decitabine (2013-0812)
- SGI-110 (2013-0843)
- Cladribine + LD Ara-C/DAC (2011-0987)
- PF-04449913 with LD Ara-C or DAC (2012-0062)
- DAC 5 vs. 10day (2012-1017)
- Vosaroxin + DAC (2013-0099)
- Sorafenib + Aza (2014-0076)
- Ruxolitinib + Decitabine (2014-0344)
- CPX-351 (2014-0548)
- Ibrutinib +/- Ara-C (2014-0950)
- SGI-110 vs. Treatment Choice (2014-1051)

E. Mixed Phenotype:

- Clofarabine + Idarubicin + Ara-C + Vincristine (2013-0073)

2. Salvage Programs

- Aza + Tosedostat (2011-0188)
- Clofarabine + LD Ara-C (2011-0660)
- Crenolanib (2012-0569)
- BL-8040 (2012-1097)
- AC220 + Aza or Ara-C (2012-1047)
- DAC + CIA (2012-1064)
- Trametinib + GSK2141795 (2013-0001)
- Rigosertib + Aza (2013-0030)
- Eltrombopag (2013-0225)
- ASP2215 (2013-0672)
- MEK162 + BYL719 (2013-0813)
- Omacetaxine (2013-0870)
- SGI-110 (2013-0901)
- SL-401 (2013-0979/2014-0860)
- AC220 vs Salvage Therapy (2014-0058)
- KPT-330 (2014-0187)
- Ruxolitinib + Dac (2014-0344)
- BVD-523 (2014-0391)
- AG-221 (2014-0408)
- ABT-199 + Aza or Dac (2014-0490)
- SGN-CD33A + DAC or Aza (2014-0615)
- SGN-CD33A (2014-0744)
- BGB324 (2014-0756)
- E6201 (2014-0777)
- Nivolumab + Aza (2014-0861)
- Lirilumab + Aza (2014-0862)
- ADI-PEG (2014-0865)
- AG-120 (2014-0800)
- Lorvotuzumab (2014-0926)
- FLX925 (2014-1000)
- IDH305 (2014-1006)
- CC-486 (2015-0056)

3. Low Risk MDS and CMML with <10% Blasts

- DAC vs. Aza (2012-0507/2014-0112)
- Horse ATG (2012-0334)
- Sotatercept (2012-0428)
- Bortezomib (2012-0562)

- Oral Aza vs. Best Supportive Care (2012-0733)
- Ruxolitinib (2013-0012)
- Eltrombopag + DAC (2013-0590)
- MEDI 4736 (2013-1041)
- FF-10501-01 (2014-0014)
- ASTX 727 (2014-0089)
- AZA +/– Birinapant (2014-0399)
- OPN-305 (2014-0432)

4. MDS/MPN

- Ruxolitinib + Aza (2012-0737)
- Ruxolitinib (2014-0764)

5. Maintenance/MRD

- Lenalidomide (2014-0116)
- Ixazomib (2014-0379)
- SGN-CD33A (2014-0744)
- SL-401 (2014-0860)

Phase I/II Agents for Hematologic Malignancies

- L-Grb2 Antisense (2003-0578)
- Nelarabine (2009-0717)
- KB004 (2010-0509)
- CWP232291 (2011-0253)
- PRI-724 (2011-0527)
- DFP-10917 (2012-0262)
- KPT-330 (2012-0372)
- EPZ-5676 (2012-0374)
- MEK 162 (2013-0116)
- GSK525762 (2013-0527)
- CB-839 (2014-0152)
- Bosutinib + Inotuzumab (2014-0435)
- APTO-253 (2014-0528)
- DS-3032B (2014-0565)
- ABL001 (2014-1019)
- AG-881 (2015-0343)

CML Treatment Priorities

1. CML Chronic Phase

- Bosutinib vs Imatinib (2014-0437)

2. TKI Failures, T315I Mutations or Advanced Phases

- Dasatinib + DAC (2011-0333)
- Ponatinib (2015-0212)
- Omacetaxine (2014-0229)
- Nilotinib + MEK-162 (2014-0128)
- Dasatinib + Nivolumab (2015-0068)

3. Minimal Residual Disease

- Ruxolitinib (2012-0697)

Myeloproliferative Disorders

1. Myelofibrosis

- NS-018 (2011-0090)
- Sotatercept (2012-0534)
- Ruxolitinib + Aza (2012-0737)
- PRM-151 (2013-0051)
- LCL-161 (2013-0612)
- Momelotinib vs. Ruxolitinib (2013-0741)
- Oral Pacritinib vs Best Available Therapy (2013-1001)
- Momelotinib (2014-0145)
- Momelotinib vs. Best Available Therapy (2014-0258)
- PF-04449913 vs. Placebo (2014-0415)
- Ruxolitinib + Pracinostat (2014-0445)
- Lorvotuzumab (2014-0926)
- Nivolumab (2014-0962)
- SL-401 (2014-0976)

2. Systemic Mastocytosis

- Brentuximab (2012-0734)

ALL Treatment Priorities

1. Newly Diagnosed or Primary Refractory

(one non-hyper-CVAD induction)

- Age >60: Low dose Hyper CVD + CMC-544 (2010-0991)
- Hyper CVAD + Ofatumumab (2010-0708)
- Hyper CVAD + Liposomal Vincristine (2008-0598)
- T cell: Hyper CVAD + Nelarabine (2006-0328)
- Ph+: Hyper CVAD + Ponatinib (2011-0030)
- Burkitts: EPOCH + Ofatumumab (2014-0123)

2. Salvage Programs

- Low Dose Hyper CVAD + CMC-544 (2010-0991)
- Rituximab (2011-0844)
- BMS-906024 (2011-0382)
- DAC + CIA (2012-1064)
- Moxetumomab (2012-1143)
- Ibrutinib (2013-0459)
- EPOCH + Ofatumumab (2014-0123)
- Ruxolitinib or Dasatinib + Hyper CVAD (2014-0521)

3. CNS Disease

- Intrathecal Rituximab (2011-0844)

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STUDIES IN ADVANCED SYSTEMIC MASTOCYTOSIS, ATYPICAL CHRONIC MYELOID LEUKEMIA (ACML)/ CHRONIC NEUTROPHILIC LEUKEMIA (CNL), AND HYPEREOSINOPHILIC SYNDROME (HES)/CHRONIC EOSINOPHILIC LEUKEMIA (CEL)

Phase II study of brentuximab vedotin in CD30+ systemic mastocytosis

Brentuximab vedotin is a novel, CD30-targeted antibody-drug conjugate approved for the treatment of relapsed Hodgkin lymphoma and anaplastic large cell lymphoma.[11] CD30 is preferentially expressed on neoplastic mast cells in aggressive SM (ASM) and mast cell leukemia (MCL).[12] Patients with CD30-positive disease and evidence of organ damage with or without an associated hematologic non-mast cell-lineage disease are eligible for a phase 2 trial of this agent. Brentuximab vedotin will be administered intravenously every 3 weeks for 8 cycles. As noted above, patients with ASM or MCL who have failed ≥ 1 prior therapy are also eligible to participate in the phase 1/2 trial of SL-401.

Prospective evaluation of ruxolitinib for patients with chronic neutrophilic leukemia (CNL) or atypical chronic myeloid leukemia (aCML) and mutated CSF3R

Activating mutations in the colony stimulating factor 3 receptor *(CSF3R)* gene occur in 59% of cases of CNL or atypical CML.[13] Different types of CSF3R mutations activate distinct downstream pathways, including JAK-STAT, and responsiveness to ruxolitinib has been shown both *in vitro* and clinically. To test this, we are conducting a prospective clinical study of ruxolitinib in patients with CNL or aCML. Patients with CNL or aCML and mutated CSF3R with baseline platelets > 25 x 10^9/L are eligible. Subjects already taking ruxolitinib are also eligible.

Phase I/II trial of SL-401 in patients with advanced, high risk MPNs, including MF, CMML, advanced systemic mastocytosis and HES/CEL

As noted above, patients with advanced systemic mastocytosis and HES/CEL who have failed ≥ 1 prior therapy are eligible for this study.

REFERENCES

1. Quintas-Cardama A, Kantarjian H, Estrov Z, Borthakur G, Cortes J, Verstovsek S. Therapy with the histone deacetylase inhibitor pracinostat for patients with myelofibrosis. Leukemia research 2012;36:1124-7.
2. Komrokji RS, Seymour JF, Roberts AW, et al. Results of a phase 2 study of pacritinib (SB1518), a JAK2/JAK2(V617F) inhibitor, in patients with myelofibrosis. Blood 2015;125:2649-55.

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3. Mesa RA, Egyed M, Szoke A, et al. Results of the PERSIST-1 phase III study of pacritinib (PAC) versus best available therapy (BAT) in primary myelofibrosis (PMF), post-polycythemia vera myelofibrosis (PPV-MF), or post-essential thrombocythemia-myelofibrosis (PET-MF). ASCO Meeting Abstracts 2015;33:LBA7006.

4. Pardanani A, Laborde RR, Lasho TL, et al. Safety and efficacy of CYT387, a JAK1 and JAK2 inhibitor, in myelofibrosis. Leukemia 2013;27:1322-7.

5. Verstovsek S, Talpaz M, Ritchie EK, et al. A Phase 1/2, Open-Label, Dose-Escalation, Multi-Center Study to Assess the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of Orally Administered NS-018 in Patients with Primary Myelofibrosis (PMF), Post-Polycythemia Vera Myelofibrosis (ASH Annual meeting abstracts) 2014;124:1839.

6. Weber JS, D'Angelo SP, Minor D, et al. Nivolumab versus chemotherapy in patients with advanced melanoma who progressed after anti-CTLA-4 treatment (CheckMate 037): a randomised, controlled, open-label, phase 3 trial. The Lancet Oncology 2015;16:375-84.

7. Brahmer J, Reckamp KL, Baas P, et al. Nivolumab versus Docetaxel in Advanced Squamous-Cell Non-Small-Cell Lung Cancer. N Engl J Med 2015;373:123-35.

8. Ansell SM, Lesokhin AM, Borrello I, et al. PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. N Engl J Med 2015;372:311-9.

9. Gyrd-Hansen M, Meier P. IAPs: from caspase inhibitors to modulators of NF-kappa B, inflammation and cancer (vol 10, pg 561, 2010). Nature Reviews Cancer 2010;10:561-74.

10. Frolova O, Benito J, Brooks C, et al. SL-401 and SL-501, targeted therapeutics directed at the interleukin-3 receptor, inhibit the growth of leukaemic cells and stem cells in advanced phase chronic myeloid leukaemia. Br J Haematol 2014;166:862-74.

11. Pro B, Perini GF. Brentuximab vedotin in Hodgkin's lymphoma. Expert opinion on biological therapy 2012;12:1415-21.

12. Valent P, Arock M, Akin C, et al. The classification of systemic mastocytosis should include mast cell leukemia (MCL) and systemic mastocytosis with a clonal hematologic non-mast cell lineage disease (SM-AHNMD). Blood 2010;116:850-1.

13. Maxson JE, Gotlib J, Pollyea DA, et al. Oncogenic CSF3R mutations in chronic neutrophilic leukemia and atypical CML. N Engl J Med 2013;368:1781-90.

CONCLUSION

In the last few years treatment of myelofibrosis and the other myeloproliferative neoplasms has expanded considerably past the relief of the signs and symptoms of these diseases. Ruxolitinib-based combinations, newer JAK inhibitors, and novel agents are now being tested in clinical trials.

For information about these studies, the Myeloproliferative Neoplasms program, or the Leukemia program in general, contact Prithviraj Bose, Srdan Verstovsek, or any Leukemia physician.

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