ELSEVIER

Blood 142 (2023) 4566–4568

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Retrospective Analysis of the Relationship between Transfusion Independence and Bone Marrow Fibrosis Reduction in Patients with Myelofibrosis Treated with Pacritinib Versus Ruxolitinib

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Background Pacritinib is a JAK1-sparing JAK2/IRAK1/ACVR1 inhibitor for treatment of myelofibrosis (MF). In addition to improving spleen volume and symptoms, pacritinib is associated with anemia benefit in MF patients. Recent *in vivo* studies have shown that dual JAK2/IRAK1 inhibition is associated with improvement in both cytopenias and bone marrow reticulin fibrosis (BMF) in an inflammation-driven murine MF model (*Cuenca Zamora E, et al. EHA 2023; P987 and P990*). Here, we retrospectively analyzed the relationship between achieving transfusion independence and reduction in BMF in MF patients treated with pacritinib 200 mg twice daily (BID) vs ruxolitinib (RUX) on the phase 3 PERSIST-2 study.
Methods: PERSIST-2 enrolled patients with platelet counts ≤100 x 10^9/L. This analysis focused on pacritinib 200 mg BID and on patients who received RUX as best available therapy (BAT) who enrolled ≥12 weeks prior to study termination and who required red blood cell (RBC) transfusions at baseline. The proportion of patients who achieved transfusion independence response (TI-R, any 12-week interval with no RBC transfusions) was ascertained for pacritinib vs RUX. The proportion of patients with BMF reduction (≥1 grade decrease in reticulin fibrosis from baseline at week 24) was reported among patients on pacritinib achieving TI-R vs. non-response (NR).
Results: The analysis included 41 patients on pacritinib (median dose intensity 100% through week 24) and 18 on RUX (median daily dose 10mg at week 24). Baseline characteristics were similar between the groups, including median platelet count (41 vs 38 x 10^9/L) and median hemoglobin (8.7 vs 8.6 g/dL). All patients required RBC transfusion at baseline.
A significantly greater proportion of patients treated with pacritinib vs RUX achieved TI through week 24: 37% (n=15/41) vs 6% (n=1/18), *P*=0.023. Nominally, this trend held for those with baseline platelets <50 x 10^9/L: 28% vs 8%, *P*=0.222. In addition, a greater percentage achieved a 50% reduction in RBC transfusions over any 12 weeks (49% vs 6%, *P*=0.001).
Paired bone marrow assessments at baseline and week 24 were available for 18/41 of patients on pacritinib, of whom 44% (8/18) achieved TI-R on study. The proportion of patients who experienced BMF reduction (>=1 grade at any point) was significantly greater among TI-R (62.5%, n=5/8) compared to TI-NR (10%, n=1/10) on pacritinib (*P*=0.043). Of the 5 patients who achieved TI-R and BMF reduction, all had grade 2-3 fibrosis at baseline, and 2 experienced a reduction from grade 3 to grade 1 (**Figure 1**). By contrast, paired bone marrow biopsies were available for 5 patients on RUX, and there was no association between fibrosis reduction in TI-R (0%, n=0/1) and TI-NR (25%, n=1/4).

Conclusions: In cytopenic MF patients from PERSIST-2, TI-R on pacritinib was associated with BMF improvement. Though these results are based on a small sample size, they contrast with recent data suggesting no correlation between BMF reduction and TI-R on the JAK1/2 inhibitors momelotinib and ruxolitinib (*Oh ST, et al. Blood 2022;140 (Supp 1):821-23*). While differences in study design could have impacted these results, these findings suggest that distinct inhibitory profiles may further distinguish the clinical impact of these treatments. Further studies are warranted to confirm the relationship between BMF reduction and anemia benefit in patients treated with pacritinib.
Study funded by CTI BioPharma Corp., a Sobi company

Disclosures Oh: *CTI BioPharma, Bristol Myers Squibb, Disc Medicine, Blueprint Medicines, PharmaEssentia, Constellation/MorphoSys, Geron, AbbVie, Sierra Oncology/GSK, Cogent, Incyte, Morphic, Protagonist:* Consultancy. **Shammo:** *Astra Zeneca:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *BMS:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *CTI BioPharma Corp., a Sobi company:* Consultancy, Honoraria, Research Funding; *Incyte:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Novartis:* Consultancy, Honoraria, Research Funding; *sanofi Aventis:* Consultancy, Honoraria, Speakers Bureau; *MJH:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Apellis:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *NS bio:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *GSK:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Protagonist:* Research Funding; *AbbVie:* Current equity holder in publicly-traded company, Research Funding; *Alexion:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *Blueprint:* Honoraria, Speakers Bureau; *otsuka:* Research Funding. **Gupta:** *Novartis, BMS Celgene, GSK:* Honoraria; *GSK:* Other: Travel to EHA 2023 for invited talk at GSK sponsored MPN education session ; *BMS, Celgene, Roche, Abb Vie, Pfizer, Sierra Oncology, CTI Biopharma:* Membership on an entity's Board of Directors or advisory committees; *Novartis, BMS Celgene, SMP Oncology, AbbVie, Constellation Biopharma, Pfizer, GSK Pharma, CTI Biopharma:* Consultancy; *BMS Celgene, Roche, AbbVie, Pfizer, Sierra Oncology, CTI Biopharma, GSK:* Other: Participation on a Data Safety Monitoring Board or Advisory Board; *Novartis, BMS Celgene, Sierra Oncology, AbbVie, Constellation Biopharma, Pfizer, GSK Pharma, CTI Biopharma:* Consultancy. **McMullin:** *Novartis:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *BMS:* Membership on an entity's Board of Directors or advisory committees, Other: Clinical trial support; *AbbVie:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *AOP:* Other: Clinical trial support, Speakers Bureau; *Incyte:* Membership on an entity's Board of Directors or advisory committees, Speakers Bureau; *CTI BioPharma Corp., a Sobi company:* Membership on an entity's Board of Directors or advisory committees; *GSK:* Membership on an entity's Board of Directors or advisory committees. **Bose:** *Incyte, BMS, CTI, Morphosys, Blueprint, Cogent, Sumitomo:* Honoraria, Research Funding; *GSK, Novartis, Karyopharm, AbbVie, Pharma Essentia, Jubilant, Morphic:* Honoraria; *Kartos, Telios, Ionis, Disc, Janssen, Geron:* Research Funding. **Mesa:** *Promedior:* Research Funding; *Samus:* Research Funding; *Abbvie:* Research Funding; *Constellation:* Consultancy, Research Funding; *LaJolla Pharma:* Consultancy; *Genetech:* Research Funding; *Celgene:* Research Funding; *Incyte:* Research Funding; *Sierra Onc:* Consultancy; *Novartis:* Consultancy; *Mays Cancer Center:* Research Funding; *CTI BioPharma., a Sobi Company:* Research Funding; *NCI:* Research Funding. **Lucchesi:** *Morphosys:* Consultancy; *Amgen:* Consultancy, Speakers Bureau; *Novartis:* Consultancy, Speakers Bureau; *Grifols:* Consultancy, Speakers Bureau; *Sanofi:* Consultancy, Speakers Bureau; *Protagonist:* Consultancy; *SOBI:* Speakers Bureau; *Pfizer:* Speakers Bureau; *Incyte:* Speakers Bureau; *BMS:* Speakers Bureau. **Buckley:** *CTI BioPharma Corp., a Sobi company:* Current Employment, Other: Company provided vested and unvested equity awards to author as a company employee as part of overall compensation package, and all such equity grants were subject to accelerated vesting and pay out following Company's sale to new ownership. **Suthar:** *CTI BioPharma Corp., a Sobi company:* Current Employment, Other: Company provided vested and unvested equity awards to author as a company employee as part of overall compensation package, and all such equity grants were subject to accelerated vesting and pay out following Company's sale to new ownership. **Roman-Torres:** *CTI BioPharma Corp., a Sobi company:* Consultancy, Other: Company provided vested and unvested equity awards to author as a company employee as part of overall compensation package, and all such equity grants were subject to accelerated vesting and pay out following Company's sale to new ownership. **Mascarenhas:** *Bristol Myers Squibb, Celgene, CTI BioPharma, Geron, Incyte Corporation, Janssen, Kartos Therapeutics, Merck, Novartis, PharmaEssentia, Roche; Participated in consulting or advisory committees - AbbVie, Bristol Myers Squibb, Celgene, Constellation Pharmac:* Research Funding; *Incyte, Novartis, Roche, Geron, GSK, Celgene/BMS, Kartos, AbbVie, Karyopharm, PharmaEssentia, Galecto, Imago, Sierra Oncology, Pfizer, MorphoSys, CTI Bio:* Consultancy; *Bristol Myers Squibb, Celgene, Constellation Pharmaceuticals/MorphoSys, CTI BioPharma, Galecto, Geron, GSK, Incyte Corporation, Karyopharm Therapeutics, Novartis, PharmaEssentia, Prelude Therapeutics, Pfizer, Merck, Roche, AbbVie, Kartos:* Consultancy, Membership on an entity's Board of Directors or advisory committees; *AbbVie, Bristol Myers Squibb, Celgene, CTI BioPharma, Geron, Incyte Corporation, Novartis, Janssen, Kartos Therapeutics, Merck, PharmaEssentia, Roche:* Research Funding; *AbbVie, CTI BioPharma Corp, a Sobi company, Geron, GlaxoSmithKline, Imago, Incyte, Kartos, Kayropharm, MorphoSys, Novartis, Pfizer, PharmaEssentia, Sierra:* Consultancy; *GSK:* Honoraria. **Ferrer Marin:** *Novartis Farmaceutica SA:* Honoraria; *Celgene S.L.U:* Consultancy; *INCYTE BIOSCIENCES INTERNATIONAL SARL:* Honoraria, Research Funding; *CTI BioPharma Corp., a Sobi company:* Research Funding.

OffLabel Disclosure: Pacritinib is a kinase inhibitor indicated for the treatment of adults with intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50x10

^{9}/L. This indication is approved under accelerated approval based on spleen volume reduction. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Figure 1. Bone Marrow Fibrosis in TI Responders vs Non-Responders
PERSIST-2, PAC 200 mg BID

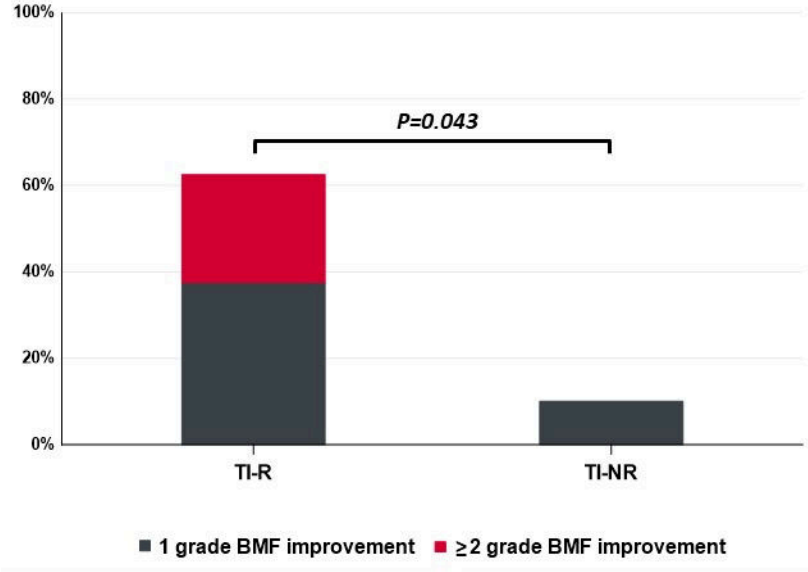

Figure 1

https://doi.org/10.1182/blood-2023-178753