MANIFEST-2, a Global, Phase 3, Randomized, Double-Blind, Active-Control Study of CPI-0610 and Ruxolitinib vs Placebo and Ruxolitinib in JAK Inhibitor-Naïve Myelofibrosis Patients

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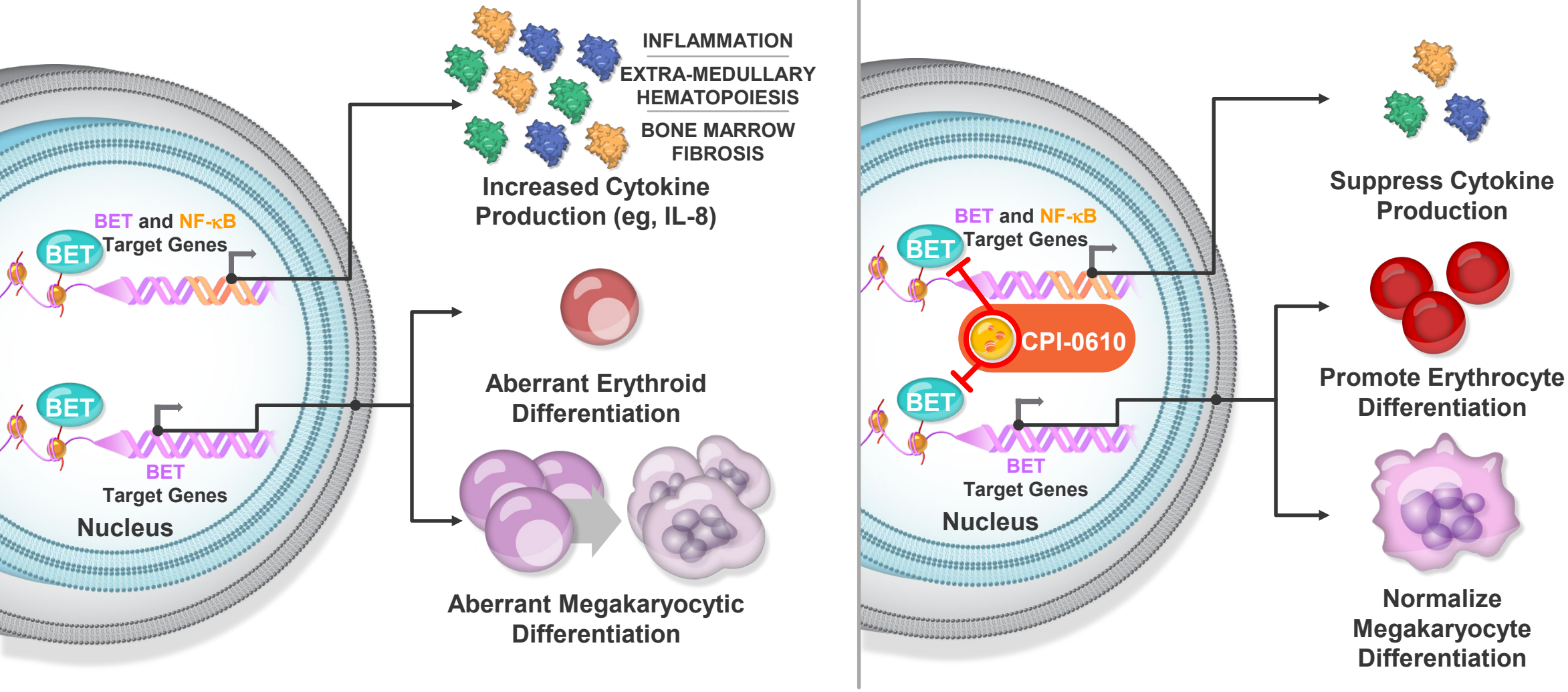
Abstract # 3085

NCT04603495

Disclosures

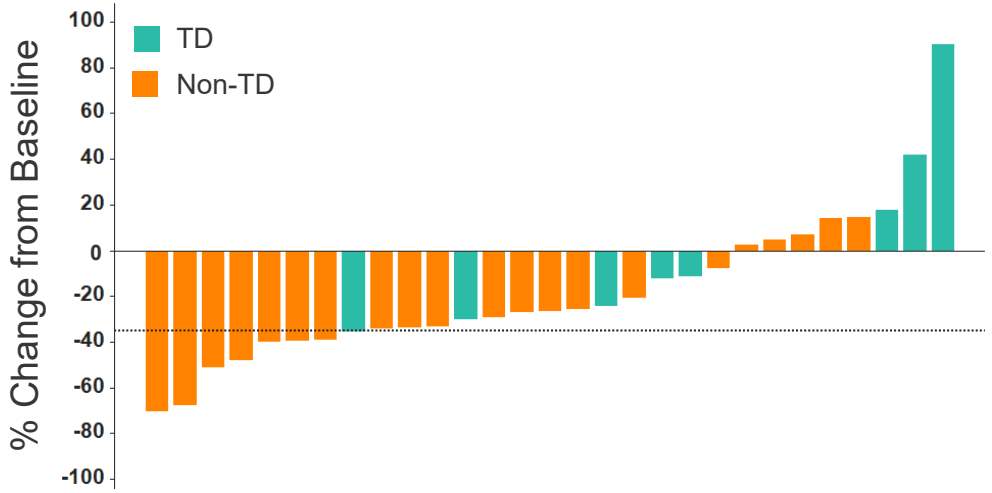
- Consultancy: Celgene, Prelude, Galecto, Promedior, Geron, Constellation, and Incyte
- Research funding: Incyte, Kartos, Roche, Promedior, Merck, Merus, Arog, CTI, Biopharma, Janssen, and PharmaEssentia

BET Inhibitor CPI-0610 in Myelofibrosis

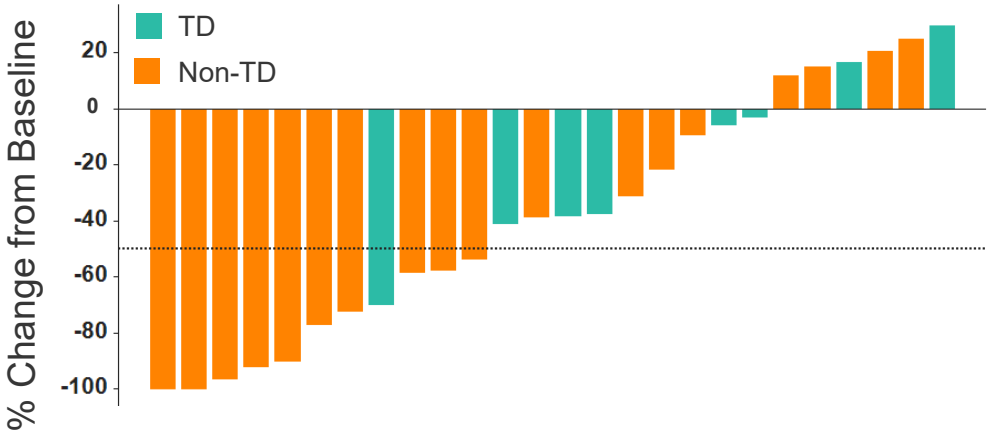


BETi CPI-0610 showed monotherapy activity in MF patients who are resistant/refractory, intolerant to ruxolitinib or ineligible for JAKi as evidenced by splenic response, symptoms improvement and hemoglobin improvement (Abstract # 2163)

Spleen Volume % Change at week 24



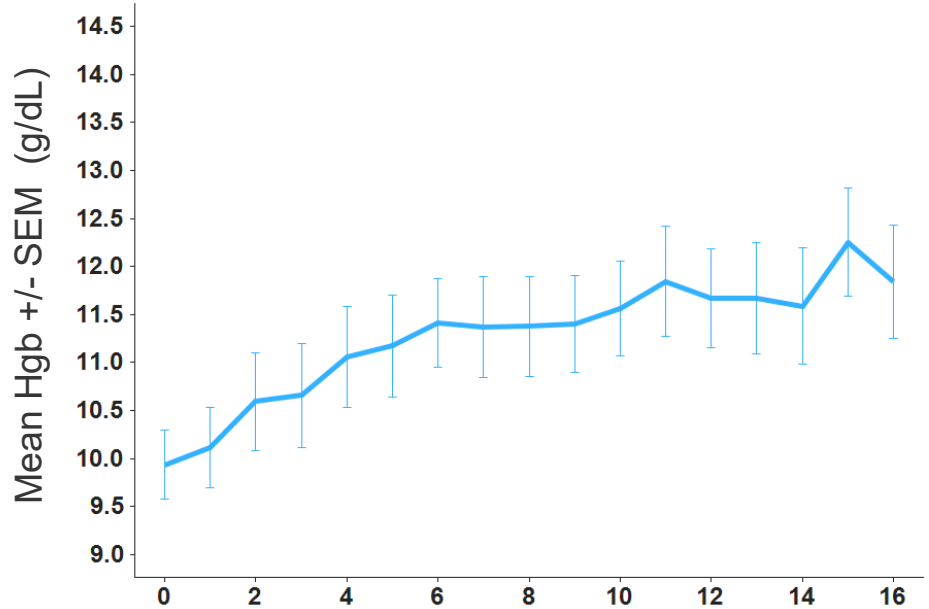
Total Symptom Score % Change at week 24



Transfusion Dependence and Hemoglobin Improvement

- In transfusion dependent cohort: 21% of patients converted to transfusion independence
- In non-transfusion dependent cohort: 10/20 (50%) patients had 1.5 g/dL Hgb increase without transfusion

Mean Hemoglobin Over Time- All patients[1]

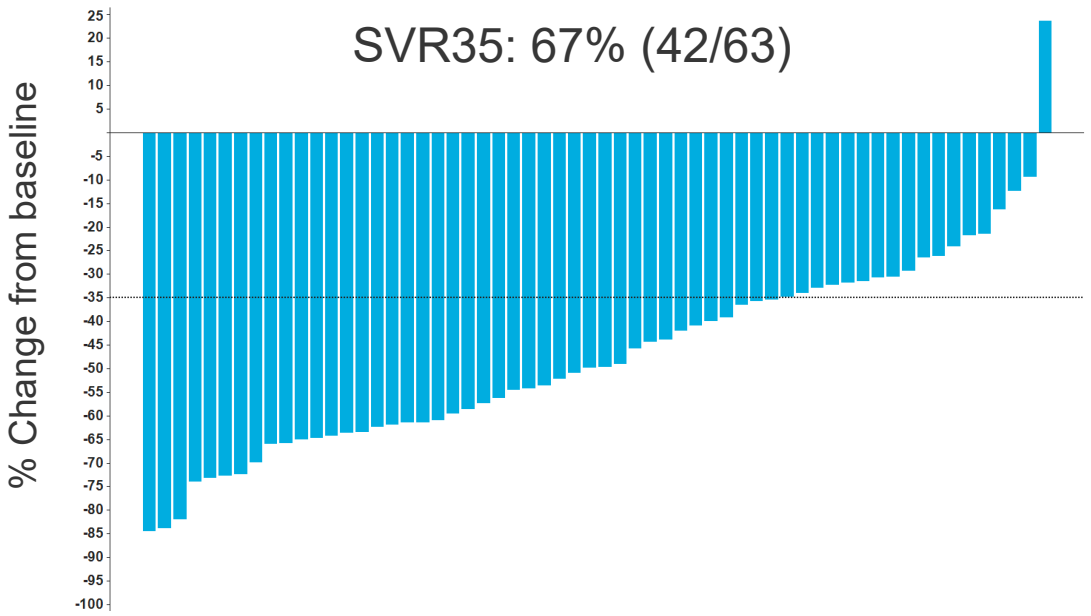


N	22	22	22	22	21	21	21	20	20	20	19	18	19	18	17	16	15

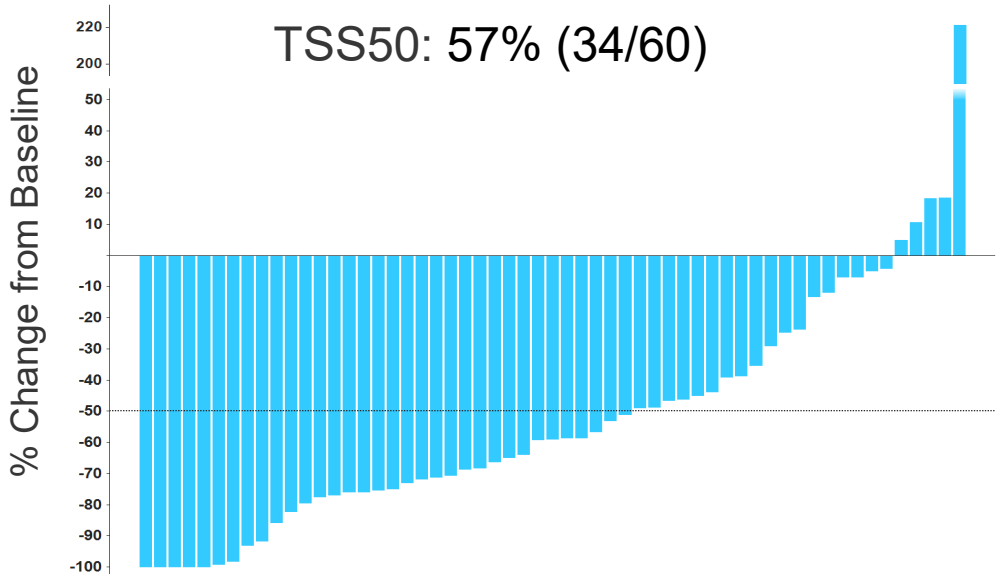
[1] Patients on treatment ≥ 12 wks

Combination of CPI-0610 + ruxolitinib leads to 67% SVR35 at week 24 in JAKi naïve pts (Abstract #55)

Spleen Volume % Change at week 24



Total Symptom Score % Change at week 24



- Encouraging response rates were observed in spleen volume reduction (SVR35 response) and symptom improvement (TSS50 response) at week 24 with the combination of CPI-0610 and ruxolitinib in JAKi naïve MF patients
  - 67% SVR35 (primary endpoint) and 57% TSS50 responses at week 24
- Based on these encouraging data from phase 2 trial, the phase 3, global, randomized, double-blind MANIFEST-2 trial of CPI-0610 + ruxolitinib vs placebo + ruxolitinib in a JAKi naïve MF patient population has been initiated and is open for enrollment

MANIFEST-2 Phase 3 study

Study Population

JAK-inhibitor-naïve primary MF or post-ET/PV MF patients with:

- Advanced MF requiring therapy
- Splenomegaly by CT/MRI
- Symptomatic
- DIPSS int-1 or higher

Design/Size

Double-Blind Randomization n: ~310

Treatment Arm/Cohort

CPI-0610 PO QD D1-14 + Ruxolitinib BID D1-21

Placebo PO QD D1-14 + Ruxolitinib BID D1-21

Patient randomization (1:1) will be stratified by:

- DIPSS risk category: Int-1 vs Int-2 vs High
- Platelet count: > 200 × 10^9/L vs 100–200 × 10^9/L
- Spleen volume: ≥ 1800 cm^3 vs < 1800 cm^3

Endpoints

Primary:

- **SVR35 at 24 weeks**

Key Secondary*:

- **TSS50 by MFSAF v4.0 at 24 weeks**

* Other secondary endpoints include safety; PK, PD; bone marrow morphology/fibrosis; duration of SVR35 and TSS50 responses; PFS, OS; conversion to transfusion independence; rate of RBC transfusion for first 24 wk; hemoglobin response; peripheral proinflammatory cytokines

Key eligibility criteria

Inclusion

- Age ≥ 18 years old
- Confirmed diagnosis of myelofibrosis (primary, post-polycythemia vera, or post essential thrombocythemia)
- Adequate hematologic, renal, & hepatic function
- Have at least 2 symptoms with an average score ≥ 3 or an average total score of ≥ 10 over the 7-day period prior to randomization using the MFSAF v4.0
- Prognostic risk-factor score of Intermediate-1 or higher per DIPSS scoring system
- Spleen volume of ≥ 450 cm^3
- ECOG performance status ≤ 2

Exclusion

- Splenectomy or splenic irradiation in the previous 6 months
- Chronic or active conditions and/or concomitant medication use that would prohibit treatment
- Had prior treatment with any JAKi or BET inhibitor for treatment of a myeloproliferative neoplasm

MANIFEST-2: NCT04603495

MANIFEST study ASH 2020 Abstracts

Abstract #: 55, Oral presentation, Saturday, 5 December, 8:30 am

CPI-0610, a Bromodomain and Extraterminal Domain Protein (BET) Inhibitor, in Combination with Ruxolitinib, in JAK-Inhibitor-Naïve Myelofibrosis Patients: Update of MANIFEST Phase 2 Study

Abstract #: 56, Oral presentation, Saturday, 5 December, 8:45 am

CPI-0610, Bromodomain and Extraterminal Domain Protein (BET) Inhibitor, As “Add-on” to Ruxolitinib, in Advanced Myelofibrosis Patients with Suboptimal Response: Update of MANIFEST Phase 2 Study

Abstract #: 2163, Poster presentation, Sunday, 6 December

CPI-0610, a Bromodomain and Extraterminal Domain Protein (BET) Inhibitor, As Monotherapy in Advanced Myelofibrosis Patients Refractory/Intolerant to JAK Inhibitor: Update from Phase 2 MANIFEST Study

Abstract #: 3079, Poster presentation, Monday, 7 December

The BET Inhibitor, CPI-0610, Promotes Myeloid Differentiation in Myelofibrosis Patient Bone Marrow and Peripheral CD34+ Hematopoietic Stem Cells

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