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634.MYELOPROLIFERATIVE SYNDROMES: CLINICAL AND EPIDEMIOLOGICAL

Real-World Experience of Ropeginterferon-Alfa Treatment of PV and ET - Two Centers Experience

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BACKGROUND AND AIM: Interferon alpha is an effective treatment for Polycythemia Vera (PV) and Essential Thrombocythemia (ET) and is the only treatment known to induce sustained molecular responses by decreasing JAK2 mutation allelic burden. Long-acting pegylated interferons are better tolerated. Ropeginterferon-alfa is a monopegylated interferon with a longer half-life and is the first interferon to be FDA-approved for the treatment of PV. It is not yet approved for ET, but clinical trials are ongoing. Given the similar disease biology between PV and ET and the efficacy of pegylated interferon-alfa in both PV and ET, this study aims to look at a real-world experience of treating PV and ET with ropeginterferon-alfa since its approval.
METHODS: We conducted a retrospective chart review of all our PV and ET patients treated with ropeginterferon-alfa at Huntsman Cancer Institute, University of Utah (SLC cohort), and at the University of North Carolina at Chapel Hill (UNC cohort), since the drug's approval for PV from November 2021 through June 2023. The complete hematologic response (CHR) was defined as the normalization of blood counts within the reference range of the local lab standards. Prior to ropeginterferon-alfa, the participants were managed with therapeutic phlebotomies, or cytoreduced with either hydroxyurea, pegylated interferon-alpha 2a (*Pegasys*), JAK2 inhibitors, or were newly diagnosed and previously untreated.
RESULTS: A total of 120 patients (76 in SLC cohort and 44 in UNC cohort) were included in this study. Of those, 75 (62.5%) were diagnosed with PV, 37 (31%) with ET, and 1 with congenital polycythemia due to germline *JAK2* mutation. Twenty-three (19%) patients had a prior history of thrombosis. *JAK2* mutation was present in 100 (83%) patients, while 9 (7.5%) were *CALR* mutated, 1 with *MPL* mutation, and 1 with triple-negative ET. Extended myeloid gene panel sequencing was available in 64 (53.3%) patients and 35 of them (54.6%) patients had additional somatic mutations. Most common somatic mutations include *TET2* (11 patients) and *DNMT3A* (8 patients) and *CBL* (3 patients), among others. Of the cohort, 15 (12%) patients discontinued ropeginterferon-alfa due to various adverse events, which included: fatigue, joint aches, skin rash, and increased anxiety and depression.
Of the 105 patients who are on ropeginterferon-alfa, 9 patients were previously untreated patients while 96 (91.4%) were pretreated with other therapies and switched to ropeginterferon-alfa. In many patients, the switch to ropeginterferon-alfa was done because of the increased frequency and aggressivity of squamous cell skin cancers while on hydroxyurea treatment. All of them started ropeginterferon-alfa at a dose of either 50 mcg or 100 mcg every two weeks and were increased at an increment of 50 mcg to achieve a goal of CHR. As most of the patients were switching from prior therapies, 51 (49%) were already in CHR at the time of initiating ropeginterferon-alfa. The median ropeginterferon-alfa dose to maintain CHR was 50mcg in the SLC cohort and 100mcg in the UNC cohort. (See table for more details).
We have 6 patients with *DNMT3A* mutation, 4 (66.6%) have achieved CHR at a median ropeginterferon-alfa dose of 100 mcg (range 50 mcg - 150 mcg), and 2 patients are undergoing dose titration. Of the 11 patients with *TET2* mutation, 7 (63.3%) achieved CHR at a median ropeginterferon-alfa dose of 150 mcg (range 50 mcg - 500 mcg). The analysis of *JAK2* V617F and *CALR* allelic burden, transcripts of inflammatory, prothrombotic, and hypoxia-regulated (HIFs) genes, and evaluation of females for reversal of clonal to polyclonal myelopoiesis is ongoing.
CONCLUSION: Ropeginterferon-alfa is effective in PV and ET, however, the dose that achieves CHR is highly individualized, necessitating an incremental titration approach. The patients already in CHR from prior therapy needed relatively lower doses of ropeginterferon-alfa to maintain CHR. Clinical trials are ongoing with an alternate accelerated dosing scheme and results are awaited.

Disclosures Tashi: *Cogent Biosciences:* Membership on an entity's Board of Directors or advisory committees; *Blueprint Medicine:* Membership on an entity's Board of Directors or advisory committees; *PharmaEssentia:* Membership on an entity's Board of Directors or advisory committees. **Reeves:** *PharmaEssentia, Incyte, BMS:* Honoraria.

OffLabel Disclosure: Ropeginterferon in ET

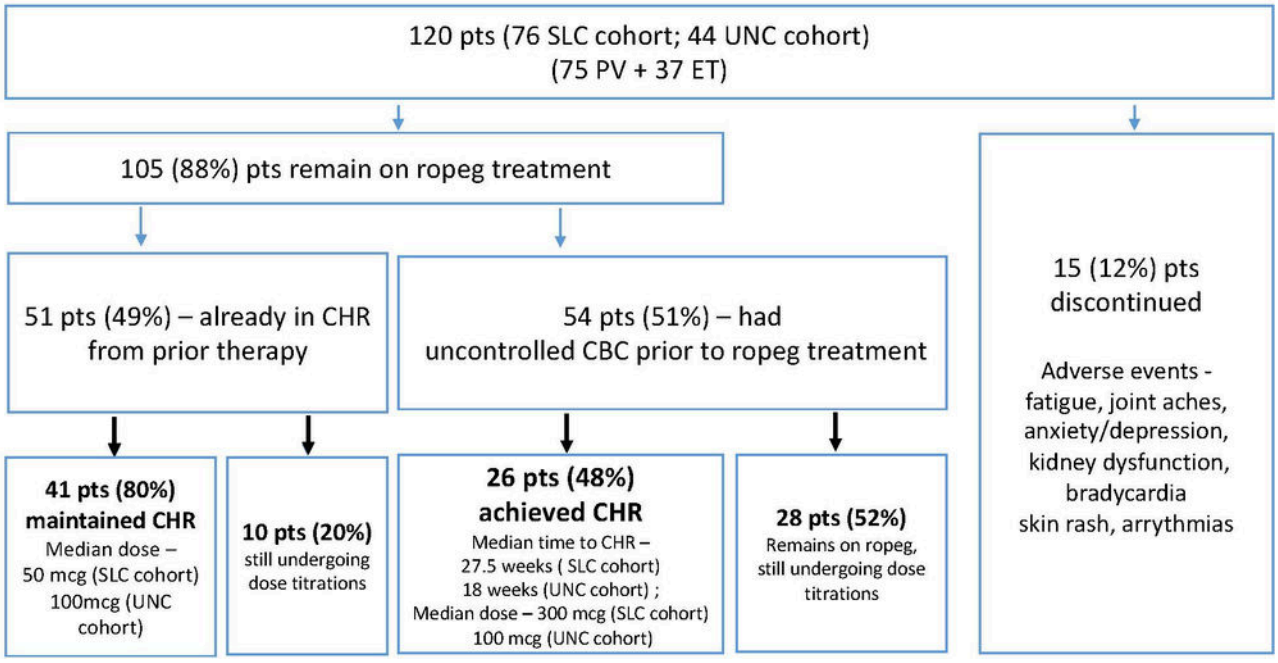

Figure 1

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