Abstract Submission

16. Myeloproliferative neoplasms - Clinical

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COMPARISON OF LONG-TERM EFFICACY AND SAFETY OF ROPEGINTERFERON ALFA-2B VS. HU IN POLYCYTHEMIA VERA PATIENTS AGED BELOW OR ABOVE 60 YEARS: TWO-YEAR ANALYSIS FROM THE PROUD/CONTINUATION PHASE III TRIALS

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Background: Ropeginterferon alfa-2b (Ropeg) is a novel mono-pegylated IFNα, allowing convenient self-administration every 2 to 4 weeks. It is currently being developed for treatment of MPNs in particular PV. Hydroxyurea (HU) is the only licensed first-line therapy in high-risk patients with PV of all ages. Off-label IFNα as first-line therapy is primarily used in patients of younger age, partly because of the misconception that the risk-benefit ratio is not so favorable in elderly patients.

Aims: To analyse the difference in efficacy and safety of Ropeg and HU in two age cohorts (<60 years and ≥60 years).

Methods: 254 PV patients (WHO2008 criteria) had been randomized to receive Ropeg or HU in the PROUD Study. After 12 months of treatment, 89.6% of Ropeg treated patients and 68.5% of HU treated patients continued treatment in the CONTINUATION Study. Efficacy assessment consisted of complete hematological response (CHR) rate according ELN criteria, and the rate of CHR including symptom improvement (disease-related signs including clinically significant splenomegaly and PV-related symptoms). Secondary endpoints included *JAK2*V617F allelic burden assessed as rate of molecular response (modified ELN criteria). Efficacy and safety analysis was done for patients <60 years (Ropeg: n=49; HU: n=39) and ≥60 years (Ropeg: n=46; HU: n=37).

Results: After 24 months of treatment, Ropeg induced higher CHR rates compared to HU, irrespective of age: 77.6% vs. 55.9% (<60 years); 63.0% vs. 42.4% (≥60 years). Higher response rates were also shown for Ropeg vs. HU for CHR including symptom improvement, similar for both age cohorts: 55.1% vs. 37.1% (<60 years); 43.5% vs. 36.1% (≥60 years). CHR rate maintenance (response maintained from first occurrence to 24 months assessment) was also higher for Ropeg and age-independent for both study treatments (Ropeg <60 years: 49.0%, ≥60 years: 37.0%; HU <60 years: 17.9%, ≥60 years: 18.9%). A similar observation for response maintenance was shown for CHR rate including symptom improvement (Ropeg <60 years: 32.7%, ≥60 years: 28.3%; HU <60 years: 15.4%, ≥60 years: 18.9%). After 24 months of treatment, partial molecular response rates were higher for Ropeg compared to HU, irrespective of age: 78.1% vs. 33.3% (<60 years) and 59.5% vs 25.0% (≥60 years). Regarding safety, Ropeg and HU treated patients showed comparable numbers of both, adverse events (89.8% vs. 92.3% <60 years, 93.5% vs. 91.9% ≥60 years) and serious adverse events (6.1% vs. 10.3% <60 years, 21.7% vs. 24.3% ≥60 years) irrespective of age. The number of adverse drug reactions (ADRs) was comparable below 60 years (77.6% vs. 74.4%) but interestingly in the cohort ≥60 years, a trend towards a lower number of ADRs was evident for Ropeg (63.0%) vs. HU (89.2%). No serious ADRs were reported for Ropeg, but there were 4 serious ADRs (*Acute Leukemia, Anemia, Leukopenia, Granulocytopenia*) reported for HU (all patients aged ≥60 years).

Summary/Conclusion: A high CHR, symptom improvement and molecular response (*JAK2*V617F) achieved by long-term treatment with Ropeg was shown, with an advantage over HU independent of age. The safety analysis in patients ≥60 years also

showed a positive trend regarding less ADRs and less serious ADRs for Ropeg vs. HU. These data indicate that Ropeg provides a valuable, efficacious and safe new treatment option for PV patients of all ages including elderly.

Keywords: None