PRECISION:

A Canadian In-practice Needs Assessment in Management of PV in Canada*

Expert Consensus Recommendations

*This program was made possible through funding from Novartis Pharmaceuticals Canada.

BACKGROUND INFORMATION

PRECISION is a national program designed to assess management of PV in Canadian daily practice, in particular, the applicability of European LeukemiaNet (ELN) criteria for hydroxyurea (HU) resistance and intolerance. The objective is to identify potential gaps and unmet needs in the management of PV patients upon which a new and/or modified set of criteria and practical guidelines can be developed. Such guidelines could provide more value to clinicians involved in the management of PV patients on a daily bases than ELN guidelines which were developed primarily for use in clinical trials.

The program was led by the following Canadian experts:

NATIONAL LEAD

Shireen Sirhan, MD
Montreal, QC

REGIONAL CHAIRS

Pierre Laneuville, MD	**Jeannie Callum, MD**	**Charles Li, MD**
Montreal, QC	Toronto, ON	Vancouver, BC

A total of 20 hematologists participated and provided information on at least 3 of their PV patients (N=60 patients in total) meeting one of the following 4 descriptions (i.e., one patient per description):

1. Meets ELN criteria for HU resistance / intolerance
2. Borderline case (does not fully meet ELN criteria; may benefit from other therapy)
3. Optimally managed with HU
4. On cytoreductive treatment other than HU

Three small regional meetings held in Toronto, Vancouver and Montreal during the spring of 2016 provided participants an opportunity to discuss their specific cases and management of PV in their individual practices.

The regional chairs and the national lead discussed the outcomes of the regional meetings and formulated consensus recommendations for the use of HU in Canadian daily practices.

The following is the summary of their discussions, conclusions, and the consensus recommendations.

KEY CONCLUSIONS:

- The experts across the country unanimously agreed that the ELN criteria were developed for research purposes and as such are not fully applicable to daily clinical practice, especially since not all patients who can benefit from the switch from HU to other therapies are captured.
- Furthermore, the only recommendation that is supported by clinical trial evidence is for hematocrit (Hct) to be < 45%.

Below is the summary of consensus recommendations regarding the proposed criteria for HU resistance/intolerance for Canadian daily practice:

Hydroxyurea dose

- It was noted that in daily practice, resistance to HU is less common than intolerance, mainly because many patients develop toxicities (i.e., cytopenias) before reaching the recommended maximum dose of 2g/day.
    - It was agreed that since efficacy and tolerability of HU vary from patient to patient, it would be difficult to define the minimum recommended dose. To that end, clinicians should rely on regular blood tests to define the appropriate dose for a particular patient.

Recommendation 1	Selection of HU dose in daily practice should be selected based on and tailored to patient specific needs and tolerability profile.
Recommendation 2	When determining resistance to HU, maximum dose of HU of 2g/day, as recommended by the ELN criteria, is acceptable.
Recommendation 3	Intolerance to HU should be defined as presence of adverse events that affect patient quality of life at any dose.

Myeloproliferation

- Lack of background clinical data makes it difficult to assign specific values for white blood cells (WBC) and platelet counts, in particular in patients who are otherwise well controlled (without symptoms and/or toxicity-related problems).
- Thus, it was agreed that a progressive increase in blood counts is more relevant than isolated high but stable values.
    - It was acknowledged that there are some suggestions that high WBC counts might contribute to the risk of thrombosis
- Signs of progressive disease (i.e., progressive increase in blood counts, symptom burden, and spleen volume) at any dose of HU are indicators that the therapy should be modified.

Recommendation 4	Due to lack of clinical data, specific values cannot be assigned to WBC and platelet counts. Progressive increase in blood counts is a more relevant sign of treatment resistance than an isolated high but stable value in an otherwise well controlled patient. In any case, other potential underlying causes of high blood counts should be assessed.

Disease-related symptoms

Recommendation 5	Enlarging spleen and/or presence of inadequately controlled disease-related symptoms that have a significant impact on patients' quality of life are indicators of HU resistance.

Phlebotomy–related concerns

- The need for frequent phlebotomies (i.e., more frequently than every 3-4 months) despite HU is an indicator that treatment modification should be considered, especially in patients with phlebotomy-related issues.
    - However, the need and willingness to undergo frequent phlebotomy varies between patients. Some patients would rather undergo frequent phlebotomy and stay on low HU dose than change therapy.
    - Patients who cannot tolerate phlebotomies (i.e., those experiencing fatigue, restless leg syndrome, etc.) as well as those for whom frequent phlebotomies may be challenging (i.e., patients with poor vein access, frequent travellers, those who live far from clinics) are candidates for treatment modification.

Recommendation 6	Poorly tolerated phlebotomies (patients experiencing iron deficiency, fatigue, restless leg syndrome, etc.) as well as phlebotomies that may pose significant inconvenience for patents should be considered as indicators of the need for treatment modification.

Common HU-related adverse events

- Common adverse events associated with HU treatment such as but not limited to leg ulcers and other skin-related manifestations, gastrointestinal symptoms, pneumonitis, or fever should be included.

Recommendation 7	Any treatment-related adverse effect (including but not limited to leg ulcers and other mucocutaneous manifestations, gastrointestinal symptoms, and fatigue) that has an impact on patient quality of life should be considered as HU intolerance.

Specific situations

- The experts acknowledge that there is a lack of data regarding the treatment of a patient who experiences thromboembolic events despite normal blood counts and Hct. Such patients should be discussed and managed on a case-by-case basis.

Recommendation 8	Specific situations (i.e., patients with thromboembolic events) should be discussed amongst the experts and managed on a case-by-case basis. Thromboembolic complications in a patient with a hematocrit <45% on acetylsalicylic acid (ASA) warrant treatment modification.