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Hydroxyurea intolerance and resistance

Treating patients with **polycythaemia vera**

For UK healthcare professionals only.

This material has been developed and funded by Novartis.
Hydroxyurea is synonymous with/refers to Hydroxycarbamide throughout.

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Hydroxyurea treatment for PV

PV treatment is based on the risk profile of patients.
Those who are deemed high risk require a cytoreductive therapy such as HU, which is often the first-line recommendation[1]

High risk PV*[2]

- Aged ≥65 years
- And/or a history of thrombosis

HU intolerance and resistance

While the majority of PV patients gain adequate control with HU treatment with an acceptable tolerance, a significant minority develop resistance or intolerance (137 of 888 patients assessed)[3]

15–40%

of patients become intolerant or resistant to HU treatment, which could lead to increased mortality[3–5]

Risk factors[6]

Splenomegaly

Aged ≥60 years

Low baseline haemoglobin

* Based on The British Society of Haematology definition.[2]

Recognising the signs and symptoms of HU resistance and intolerance

A working group of the ELN agreed on the definition of HU intolerance and resistance which has since been modified for everyday clinical practice:[7,8]

HU intolerance

- **Haematologic toxicities**
  - Absolute neutrophil count <1.0 × 10^9/L
  - Platelet count <100 × 10^9/L
  - Haemoglobin <10 g/dL
- **Non-haematological toxicities**
  - Fever
  - Manifestations of the mucous membrane
  - Gastrointestinal symptoms
  - Pneumonitis
  - Leg ulcers

HU resistance

- Thrombosis or bleeding
- Unacceptable number of phlebotomies to keep HCT <45%†
- Persisting disease-related symptoms
- Platelet count >400 x 10^9/L and/or white blood cell count >10 x 10^9/L†
- No reduction of splenomegaly or a reduction <50%

Monitor patients closely as HU intolerance or resistance often requires a change of therapy or therapeutic strategy[8]

† To be assessed after 3 months of treatment of at least 2 g/day of HU, or the maximum tolerated dose.[8]

HU intolerance and resistance demands fast detection[3–5,7,8]

HU resistance impacts patients' prognoses and clinical strategy.[3–5,7,8]
A change in therapy is required if HU resistance or intolerance is detected.[5]

HU resistance: increased risk of negative outcomes[3,5,8]

- No control of already burdensome symptoms
- Transformation to myelofibrosis
- Transformation to acute myeloid leukaemia
- Death

HU intolerance: clinical relevance[5]

- Patients now eligible for second-line therapies

Maintaining a patient dialogue

Talking to patients can tease out underdiagnosed or underappreciated symptoms.[9] A close patient dialogue, in conjunction with routine clinical examinations, may help improve HU intolerance and resistance detection.

ELN, European LeukemiaNet; Hb, haemoglobin; HCT, haematocrit; HU, hydroxyurea; PV, polycythaemia vera.

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