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FIRST REAL-WORLD CASE REPORT OF DANICOPAN AS AN ADD-ON THERAPY IN A PATIENT WITH PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA IN SWITZERLAND

Category: Hemostasis, transfusion medicine, vascular, laboratory medicine, benign hematology

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BACKGROUND

- In Switzerland, ravulizumab is currently first-line treatment for patients with haemolytic paroxysmal nocturnal haemoglobinuria (PNH).[1,2]
- Ravulizumab provides immediate, complete and sustained inhibition of terminal complete component 5 (**Figure 1**), resulting in control of intravascular haemolysis, reduced thrombosis and organ damage, and improved survival and quality of life for patients with PNH.[3,4]
- Approximately 10–20% of patients receiving the C5 inhibitors eculizumab or ravulizumab experience clinically significant extravascular haemolysis (csEVH; haemoglobin [Hb] level < 9.5 g/dL and absolute reticulocyte count [ARC] ≥ 120×10^9/L, as defined in clinical studies).[5,6]
- Danicopan is an oral factor D inhibitor that has demonstrated benefit as an add-on therapy (dual inhibition) to eculizumab and ravulizumab in patients with PNH and csEVH, leading to significant improvements in Hb level, ARC and fatigue, and a reduced need for transfusions.[6]
- Long-term clinical data (median treatment duration 427.5 days) have demonstrated that this treatment effect is maintained over 48 weeks.[7]
  - Intravascular breakthrough haemolysis with a lactate dehydrogenase (LDH) level > 2 × upper limit of normal (ULN) was observed in 1/84 patients only.
- However, real-world evidence in this rare disease population is lacking.[8]

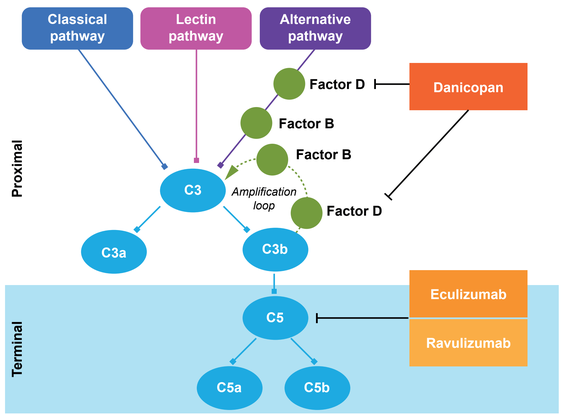

Figure 1. Overview of the complement cascade[9]

Danicopan inhibits complement factor D resulting in reduced deposition of C3 on erythrocytes and prevention of C3-mediated extravascular haemolysis (EVH). The terminal C5 inhibitors, ravulizumab and eculizumab, inhibit cleavage of C5 into C5b and C5a, preventing formation of the membrane attack complex and resultant intravascular haemolysis (IVH). Dual inhibition of the complement system by danicopan and eculizumab/ravulizumab prevents symptoms associated with clinically significant EVH and IVH.
C, complement component.

OBJECTIVE

- To present the first real-world case report of a patient with PNH in Switzerland who received danicopan in addition to ravulizumab.

METHODS

- This case report uses available clinical data from a patient with PNH in Switzerland collected between 2012 and 2024.

RESULTS

- A 34-year-old female presenting with fatigue and abdominal pain was diagnosed with PNH in the USA in 2007 (baseline laboratory data unavailable; **Figure 2**).
- In 2012, the patient relocated to Switzerland (Hb level 87 g/L, ARC 128 × 10^9/L, neutrophils 4 × 10^9/L, platelets 308 × 10^9/L; LDH 1200 U/L).
- Treatment with eculizumab (900 mg every 2 weeks) was initiated, resulting in control of symptoms related to intravascular haemolysis.
  - However, the patient remained anaemic and continued to experience fatigue (Hb level 80–90 g/L; LDH level normal).
- In 2020, the patient switched to ravulizumab for convenience (3300 mg every 8 weeks).
  - After this switch, symptoms related to intravascular haemolysis remained under control, but symptomatic anaemia was still present.

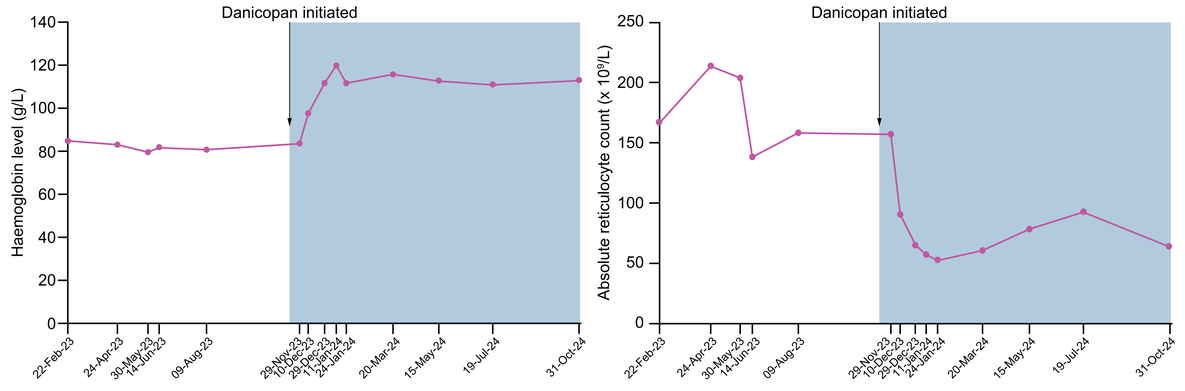

Figure 3. Haemoglobin level and absolute reticulocyte count over time

- In November 2023, owing to the symptomatic anaemia due to csEVH (Hb level 83 g/L), the patient began danicopan add-on therapy (150 mg three times daily).
- After 3.5 months of danicopan, Hb and ARC were almost normalized (115 g/L and 60 × 10^9/L, respectively; **Figure 3**).
  - The patient experienced improved quality of life with absence of anaemia-related fatigue.
- After 6 and 11 months of danicopan add-on therapy, effects on Hb level, ARC and fatigue were maintained (Hb level 112 g/L and 112 g/L, ARC 78 × 10^9/L and 63 × 10^9/L, respectively; **Figure 3**).
- No adverse events associated with danicopan were reported and the patient is continuing treatment.

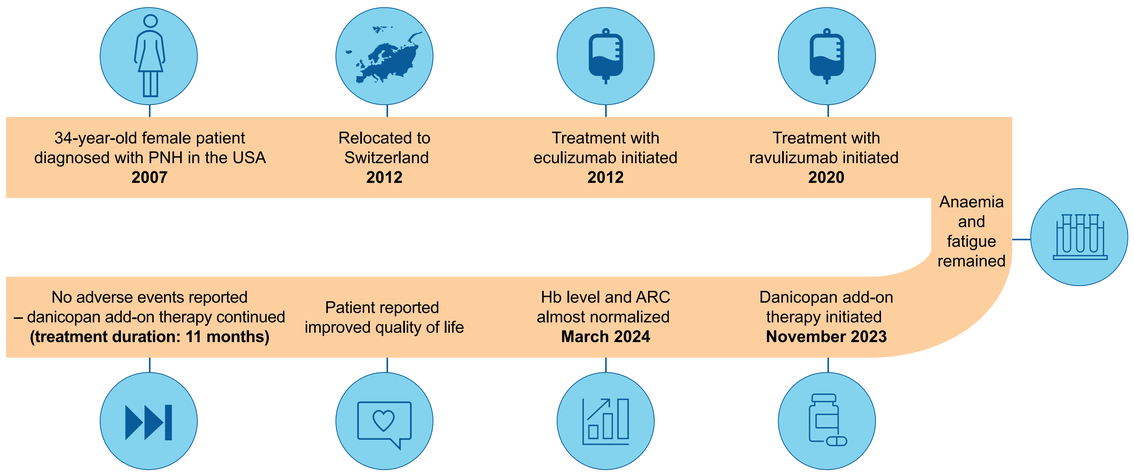

Figure 2. The patient journey

ARC, absolute reticulocyte count; Hb, haemoglobin; PNH, paroxysmal nocturnal haemoglobinuria.

CONCLUSIONS

- This is the first report of a patient treated with danicopan add-on therapy in real-world clinical practice in Switzerland.
- Danicopan add-on to ravulizumab improved symptoms associated with csEVH and quality of life, with no adverse events reported while maintaining control over intravascular haemolysis.
- This case will inform clinical practice in Switzerland and provide support for danicopan use in patients with csEVH.
  - Although long-term response has been demonstrated in clinical trials, real-world long-term response remains to be determined.

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AUTHOR DISCLOSURES

GG has participated in an advisory board for Alexion, AstraZeneca Rare Disease.

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