

Nipocalimab for Warm Autoimmune Hemolytic Anemia: Updates From the Phase 2/3 Randomized Double-Blind ENERGY Study

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Background

- Warm autoimmune hemolytic anemia (wAIHA) is a life-threatening, relapsing-remitting, antibody-driven disease¹
- Immunoglobulin G (IgG) autoantibodies mediate premature destruction of red blood cells (RBCs), and most patients have severe anemia at onset^{1,2}
- wAIHA results in significant patient burden
 - Symptoms include debilitating fatigue⁴
 - Main complications include infections and thrombosis¹
 - Approximately 50% of patients require transfusions and hospital admission^{2,3}
 - 5-year mortality was ~30% in a Swedish database study²
- Management involves off-label broadly immunosuppressive regimens that are associated with relapse and adverse events
 - With corticosteroids, two-thirds of patients relapse or do not respond¹
 - With rituximab, ~50% of patients relapse and median time to response is 90 days after the first treatment course^{6,7}
- Nipocalimab is the first US Food and Drug Administration–approved treatment for wAIHA and is indicated for patients ≥12 years of age previously or currently treated with corticosteroids⁸
 - Nipocalimab is a fully human monoclonal antibody and binds the neonatal Fc receptor (FcRn) with high specificity and affinity to block the IgG-recycling pathway⁹

Objective

To evaluate the efficacy and safety of intravenous (IV) nipocalimab in wAIHA

Methods

- The phase 2/3, multicenter, randomized ENERGY trial (ClinicalTrials.gov identifier: NCT04119050) evaluated the efficacy and safety of IV nipocalimab for the treatment of wAIHA (Figure 1)
- Key eligibility criteria: adults (≥18 years of age) with primary or secondary wAIHA for ≥3 months (Hgb <10 g/dL, laboratory evidence of hemolysis, positive direct antiglobulin test) who received ≥1 prior therapy
- Participants were randomized 1:1:1 to nipocalimab 30 mg/kg IV every 4 weeks (q4w), 15 mg/kg IV every 2 weeks (q2w), or placebo during the 24-week double-blind period
- Stable doses of concomitant corticosteroids or immunosuppressants were allowed
 - Participants on corticosteroids who met the primary end point were required to taper corticosteroids by 10% q2w
- Primary end point: durable Hgb response (Hgb ≥10 g/dL and ≥2 g/dL increase from baseline at ≥3 consecutive visits [≥28 days] starting by Week 16, without rescue therapy or new/increased steroids/immunosuppressants)
- Key secondary end points
 - Mean change from baseline in Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-Fatigue) at Week 24
 - Percent reduction in corticosteroid dose at Week 24 (mandatory taper for Hgb responders only)
- Multiplicity was controlled via equal weight analysis for each dose arm, with a 1-sided $\alpha = 0.02499$

