

Clinical burden of classical homocystinuria in the United States: a retrospective analysis of Optum Market Clarity

Mahim Jain¹, Lionel Pinto², Kamlesh M. Thakker³, Mehul Shah², Andrew Rava⁴, Colette Ndiba-Markey⁴, Diana T. Amari⁴

¹Kennedy Krieger Institute, Johns Hopkins Medicine, Baltimore, MD, USA, ²Travere Therapeutics, Inc, San Diego, CA, USA, ³Notting Hill Consulting LLC, Celebration, FL, USA, ⁴Genesis Research, Hoboken, NJ, USA

Background: Classical homocystinuria (HCU) is a rare genetic disorder characterized by elevated total homocysteine (tHcy) levels and a heterogeneous clinical presentation. This study aimed to describe clinical outcomes by tHcy levels in patients with HCU.

Case Study/Methods: This was a retrospective analysis using Optum's de-identified Market Clarity Data (2007-2021) and proprietary Natural Language Processed (NLP) Data. Expert clinical input was incorporated to develop a patient identification algorithm. Patients were included if they had ≥ 1 ICD-10 diagnosis code for HCU (E72.11) or HCU-related terms in the NLP dataset. In patients with tHcy < 50 μM , those with secondary causes of elevated tHcy were excluded unless they had other clinical presentations indicative of HCU. Major clinical events were defined as ≥ 1 condition-related emergency department or outpatient visit, or inpatient admission. tHcy levels were defined using the highest tHcy value at any time during the study period.

Results: 601 patients with HCU met the inclusion criteria. Mean age was 50 years, 46.1% female, and 79.0% White. Overall, the clinical burden of HCU was high (mean highest tHcy at any time: 68.4 μM) with $\sim 50\%$ experiencing at least one major clinical event and $\sim 14\%$ experiencing > 1 events over a median (Q1, Q3) follow-up of 29.2 (14.2, 45.5) months. Thrombotic/thromboembolic events (30.9%) were most common, followed by skeletal (16.6%) and ocular (10.5%). Clinical event rates were generally higher in patients with tHcy ≥ 50 μM vs. < 50 μM (thrombotic/thromboembolic 38.4% vs. 22.3% $p < 0.05$, skeletal 18.3% vs. 14.7% $p = 0.273$, ocular 11.1% vs. 9.7% $p = 0.596$, neurological 10.5% vs. 5.8% $p < 0.05$, mortality 8.4% vs. 2.5% $p < 0.05$).

Discussion/Conclusion: Clinical burden of HCU is substantial, particularly in those with total homocysteine levels above 50 μM . These data suggest that treatments focused on lowering homocysteine levels are needed to reduce significant clinical events for patients with HCU.

1,995/2000 characters including spaces