

GAINER-AI: PREDICTING ACUTE RIMEGEPANT RESPONSE IN MIGRAINE USING MACHINE LEARNING IN A MULTICENTER REAL-WORLD COHORT

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Background. Rimegepant is the first calcitonin gene-related peptide (CGRP) receptor antagonist approved for both acute and preventive migraine treatment. Despite demonstrated efficacy in randomized trials and real-world studies, predictors of individual response remain poorly understood. Machine learning (ML) approaches may facilitate personalized treatment selection by identifying clinical features associated with treatment outcomes.

Objectives. To develop and evaluate an ML-based model to predict pain freedom 2 hours after acute rimegepant treatment and to create a web-based prediction tool using routinely available clinical variables.

Methods. We conducted a post hoc analysis of the prospective, multicenter, real-world GAINER study. Adults with episodic or chronic migraine treated up to four migraine attacks with rimegepant 75 mg orally disintegrating tablets. The primary outcome was pain freedom at 2 hours after treatment during the first treated attack. Multiple ML algorithms were evaluated, and a Random Forest model was selected based on performance. Data were randomly split into training (80%) and test (20%) sets. Feature selection was performed using sequential forward selection. Model explainability was assessed through SHapley Additive exPlanations (SHAP) analysis.

Results. A total of 191 participants (80.1% female; mean age 44.8 years) treated 377 migraine attacks. Overall, 44.6% of attacks achieved pain freedom at 2 hours, with higher response rates in episodic than chronic migraine (50.5% vs. 28.4%, p=0.001). The final Random Forest model retained 11 predictors and achieved a weighted F1-score of 0.671 in the independent test set. Monthly headache days (MHD) emerged as the most influential predictor, followed by concomitant anti-CGRP monoclonal antibody treatment, age, age at migraine onset, medication overuse headache, and monthly acute medication use. Higher MHD and older age were associated with lower probabilities of pain freedom. Based on the final model, a freely accessible web-based prediction tool was developed.

Conclusions. This study represents the first application of ML methods to predict response to any acute migraine treatment. Using readily available clinical variables, the GAINER-AI model demonstrated moderate predictive performance and enabled the development of a user-friendly web application. Although external validation is required, these findings support the potential of ML-based tools to advance personalized acute migraine management.

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