Evaluation of ischemic cardiovascular and cerebrovascular adverse events by 10-year cardiovascular risk score in patients with migraine treated with erenumab

David Kudrow[1*], Amaal Starling[2], Jessica Ailani[3], Rima Dafer[4], Feng Zhang[5], Fei Xue[5], Nishil Patel[5], Rob Nelson[5]

[1]California Medical Clinic for Headache, Santa Monica, CA, USA; [2]Mayo Clinic, Scottsdale, AZ,USA; [3]MedStar Georgetown University Hospital, Washington, DC, USA; [4]Rush University Medical Center, Chicago, IL, USA; [5]Amgen Inc, Thousand Oaks, CA, USA

One Sentence Summary: Ischemic cardiovascular and cerebrovascular adverse events were uncommon in DBTP data and the incidence rates in combined data of DBTP and extension phase were similar across CV risk categories.

Background: Anti-calcitonin gene-related peptide (CGRP) pathway monoclonal antibodies (mAb), including erenumab (erenumab-aooe in the US), have demonstrated efficacy as preventive treatments for episodic and chronic migraine. However, many health care providers are concerned about a lack of information to support anti-CGRP mAb selection for patients with cardiovascular and cerebrovascular medical history and/or comorbidities. Although, erenumab safety has been assessed in patients with coronary artery disease and with vascular risk factors, data from the pivotal trials limits the ability to characterize the risk to patients, particularly in patients at moderate to high 10-year cardiovascular (CV) risk, through a practical treatment timeframe. The objective of this analysis was to assess ischemic cardiovascular and cerebrovascular adverse events (ICCAE) of erenumab in clinical trial patients based on 10-year CV risk score.

Methods: Data were pooled from two Phase 2 (NCT02066415 [12-week double-blind treatment phase (DBTP)] and NCT01952574 [12-week DBTP]) and two Phase 3 (NCT02456740 [24-week DBTP] and NCT02483585 [12-week DBTP]) clinical trials that evaluated erenumab 70 mg and 140 mg versus placebo for migraine prevention and their extensions. Using a CV risk assessment algorithm incorporating the National Cholesterol Education Program, Adult Treatment Panel III, and Framingham Risk Score, patients were classified into no risk factors, low risk, moderate risk, and high risk categories at baseline. Narrow MedDRA terminology was used to identify ICCAEs.

Results: In an analysis of the first 12 weeks of the double-blind treatment phase (DBTP), patients in the erenumab group (70 mg/140 mg combined, total=1400) had the following 10-year CV risk at baseline: no risk factors (n=1020 [72.9%]), low risk (n=273 [19.5%]), moderate risk (n=67 [4.8%]), and high risk (n=40 [2.9%]). Comparatively, the placebo group (total=1043) had the following at baseline: no risk factors (n=747 [71.6%]), low risk (n=204 [19.6%]), moderate risk (n=50 [4.8%]), and high risk (n=42 [4.0%]). There was a

Single ICCAE, a cerebral venous thrombosis, observed in the low risk erenumab group. In the analysis of combined DBTP and extension phase data of up to 5 years in duration, patients ICCAEs were assessed across risk groups by exposure-adjusted incidence rates (EAIR) and were numerically similar (Table). Treatment discontinuation due to ICCAEs was low across all risk groups.

Conclusion: In the DBTP, there were no patients with moderate or high 10-year CV risk that had an ICCAE and only asingle event occurred in the low risk group. Additionally, throughout the DBTP and extension phase ICCAEs were uncommon and EAIR were similar across patients in all risk groups. This analysis helps provide more detail on the 10-year CV risk of patients in the erenumab clinical trial program. Further prospective evaluation is warranted to truly assess long-term exposure risk of anti-CGRP mAbs.

Funding: Amgen and Novartis

Table:
Exposure-adjusted Incidence Rate (EAIR) per 100 Patient-years for Treatment-emergent Ischemic Cardiovascular and Cerebrovascular Events through DBTP and Extension Phase

	Erenumab 70 mg/140 mg (N = 2499; 3482.2 patient-years)	
	Ischemic Cardiovascular Events n (EAIR) [95% CI of EAIR]	Ischemic Cerebrovascular Events n (EAIR) [95% CI of EAIR]
CV risk group (N [total PY])		
No Risk Factors (1805 [2581.1])	6 (0.2) [0.0, 0.4]	2 (<0.1) [0.0, 0.2]
Low Risk (492 [665.8])	1 (0.2) [0.0, 0.4]	1(0.2) [0.0, 0.4]
Moderate Risk (121 [143.3])	0	0
High Risk (81 [91.8])	0	1 (1.1) [0.0, 3.2]

MLR Id (128609)