Long-term safety and tolerability of erenumab in episodic migraine: A pooled analysis from two clinical trials and their extension phases

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Background and objective: To assess the long-term safety of erenumab using pooled data from the double-blind treatment phases (DBTP) and open-label extension phases (OLEP) of two clinical trials in episodic migraine (NCT03096834, NCT01952574).

Methods: The incidence of adverse events (AEs) were summarized as exposure-adjusted patient incidence rates per 100 patient-years (r). Anti-erenumab antibodies were detected using a validated bridging electrochemiluminescence immunoassay.

Results: Of 729 patients randomized across both studies, 502 received erenumab (70 or 140 mg) or placebo in the 12-week DBTP and 623 received erenumab (70 or 140 mg) in the 3- or 5-year OLEP. The cumulative duration of exposure to erenumab during the DBTP and OLEP was 54.3 and 1899.5 patient-years, respectively. Overall exposure-adjusted AE incidence rates were similar in the DBTP and OLEP; no new AEs emerged over time (**Table**). The most common AE for the erenumab treatment groups (presented as n [r], whereby n = number of subjects reporting ≥1 AE) was nasopharyngitis (DBTP, 11 [20.9]; OLEP, 224 [24.0]). The incidence of constipation (DBTP: 4 [7.5]; OLEP: 40 [3.2]) and hypertension (DBTP: 3 [5.6]; OLEP: 46 [3.7]) remained low over time. The occurrence of anti-erenumab antibodies was 5.8% in the DBTP and 10.3% in the OLEP, with a respective 0.4% and 1.4% developing neutralizing antibodies.

Conclusions: Erenumab demonstrated a consistent favorable safety and tolerability profile with long-term exposure.

Exposure-adjusted incidence rates of AEs in the short-term DBTP and long-term OLEP

	DBTP (12 weeks)				OLEP (Up to 5 years)		
	Placebo	Erenumab			Erenumab		
	(N=277) n (r)	70 mg (N=106) n (r)	140 mg (N=119) n (r)	All (N=225) n (r)	70 mg (N=383)* n (r)	140 mg (N=490)* n (r)	All (N=623) n (r)
Any AE	149 (357.5)	57 (326.2)	65 (363.7)	122 (345.1)	323 (141.7)	431 (136.6)	555 (171.6)
Grade ≥3	3 (4.5)	3 (11.5)	3 (10.9)	6 (11.2)	55 (8.7)	66 (5.6)	109 (9.3)
Serious AEs	1 (1.5)	1 (3.8)	2 (7.3)	3 (5.6)	30 (4.5)	59 (4.9)	83 (7.0)
AEs leading to discontinuation	3 (4.5)	3 (11.5)	0 (0.0)	3 (5.6)	16 (2.3)	14 (1.1)	30 (2.4)
Fatal AEs	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.1)	1 (0.1)	2 (0.2)
Most frequent AEs (r>15 in any treatment arm in any treatment phase)							
Nasopharyngitis	24 (38.2)	6 (23.3)	5 (18.6)	11 (20.9)	82 (14.1)	172 (18.0)	224 (24.0)
Injection site pain	9 (13.8)	2 (7.7)	7 (26.3)	9 (17.1)	10 (1.5)	26 (2.1)	34 (2.8)
Fatigue	5 (7.6)	4 (15.6)	3 (11.1)	7 (13.3)	19 (2.8)	26 (2.1)	44 (3.6)
Back pain	6 (9.1)	1 (3.8)	5 (18.6)	6 (11.2)	30 (4.6)	54 (4.5)	81 (6.9)
AEs of interest							
Constipation	2 (3.0)	3 (11.6)	1 (3.6)	4 (7.5)	9 (1.3)	31 (2.5)	40 (3.2)
Hypertension	2 (3.0)	2 (7.6)	1 (3.6)	3 (5.6)	14 (2.1)	32 (2.6)	46 (3.7)

AE, adverse event
N, number of patients who received at least one dose of erenumab or placebo
n, number of patients reporting at least one occurrence of an adverse events
r, exposure-adjusted patient incidence rate per 100 patient-years (n/total time at risk * 100)
*N=250 patients switched from 70 mg to 140 mg during the OLEP and were included in both 70 mg and 140 mg columns

Abstract Topic: Migraine preventive therapy

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