Comment:
Monoclonal antibodies in chronic migraine—Are early effects meaningful?

Chronic migraine affects approximately 1% of the adult population and is defined as headache on ≥15 d/mo with ≥8 days of migraine-type headache. Since treatment often remains frustrating for both the patient and physician, new treatment strategies are highly welcome.

No doubt, monoclonal antibodies (mAbs) against calcitonin gene-related peptide (CGRP) for the preventive treatment of episodic and chronic migraine deserve to be called a breakthrough—not because they cure headache, but rather because they are effective for relatively refractory headaches and were developed based on the pathophysiologic concept that the trigeminovascular system and CGRP have a key role in the development of migraine pain; this was not a serendipitous discovery.

Recently, the authors presented convincing evidence that TEV-48125 reduced headache hours over 9 to 12 weeks.[1] Here, they present data on early effects, suggesting a reduction of headache hours within the first few weeks.[2] But statistical significance notwithstanding—how clinically meaningful is a reduction of a few headache hours per week? A valid answer to this question is not given here and would require multiple measurements and evidence to determine the benefit for patients' lives.

Are these data still important? Most definitely: first, there is a biological effect with relatively quick onset, whether clinically meaningful or not. Second, unlike with many established drugs, we do not see the early onset of adverse events and later onset of clinical benefit, which often challenges patient adherence. Third, mAbs do not cross the blood–brain barrier, hence the critical therapeutic target is, rather, located peripherally and not in the brain.[3] This reasoning, together with the demonstrated rapid onset, strongly supports an important concept toward improved understanding of migraine mechanisms and guidance of future drug discovery. Finally, this study reinvigorates an attractive objective, namely, to treat other chronic-refractory craniofacial pain syndromes with CGRP-neutralizing mAbs, such as trigeminal neuropathic pain, chronic temporomandibular joint pain, and, certainly, cluster headaches.

1. Bigal ME, Edvinsson L, Rapoport AM, et al. Safety, tolerability, and efficacy of TEV-48125 for preventive treatment of chronic migraine: a multicentre, randomised, double-blind, placebo-controlled, phase 2b study. Lancet Neurol 2015;14:1091–1100.
2. Bigal ME, Dodick DW, Krymchantowski AV, et al. TEV-48125 for the preventive treatment of chronic migraine: efficacy at early time points. Neurology 2016;87:41–48.
3. Pietrobon D, Moskowitz MA. Pathophysiology of migraine. Annu Rev Physiol 2013; 75:365–391.

Volker Limmroth, MD, PhD

From the Klinik für Neurologie und Palliativmedizin Köln-Merheim, Cologne, Germany.

Study funding: No targeted funding reported.
Disclosure: The author reports no relevant disclosures. Go to Neurology.org for full disclosures.