Rimegepant oral disintegrating tablet for migraine

In *The Lancet*, Robert Croop and colleagues[1] present a carefully designed phase 3 trial on an oral disintegrating tablet (ODT) of rimegepant for the acute treatment of migraine among 1375 patients (85% female, mean age 40·2 years [SD 12·0]). The trial was positive, showing an increase in relief from headache pain among the group receiving rimegepant at 2 h after dosing (10% over placebo) and improvement in the most bothersome symptoms, which included photophobia and nausea (8% over placebo). The onset was reported to be slightly faster than that of other gepants (first positive effect at 1 h for rimegepant *vs* 2 h for telcagepant) and the effect on the lower side (10% for rimegepant *vs* a mean of 17% in four trials on telcagepant), but the duration was up to 48 h. Adverse events were not different from placebo.

This trial is part of an emerging wave of novel migraine treatments targeted toward calcitonin gene-related peptide (CGRP) mechanisms, now considered a key player in the pathogenesis of migraine.[2] Clinical studies have shown CGRP concentrations increase with migraine attacks, and effective migraine therapies decrease concentrations of this neuropeptide[3] or block its receptors.[4] The approval of three monoclonal antibodies, two against CGRP and one against the CGRP receptor, has been a major breakthrough in preventive drug therapy that is specific for migraine.[2]

The success of the CGRP-related antibodies has rekindled interest in traditional antagonists of the CGRP receptor, small molecules known as the gepants. Early research on CGRP receptor structure, function, and localisation led to the initial characterisation of compounds that block the CGRP receptor 15 years ago.[2] The first-generation gepants showed positive efficacy for acute migraine, but enthusiasm for these drugs was tempered by safety findings, and further development was discontinued.[5] Now, however, a second generation of gepants is being greeted with promise. Clinical trials, such as the one reported by Croop and colleagues, support the development of gepants: rimegepant and ubrogepant for acute therapy, and atogepant for migraine prophylaxis.[2]

Gepants are well suited for acute use in management of a migraine attack. The present study concerns an ODT formulation of rimegepant, developed to optimise patient convenience and response time to effect. Previous studies using oral tablets of rimegepant (75 mg) have shown this compound significantly reduces headache during a migraine attack.[6–8] With a profile of fairly early and sustained therapeutic action, a 75 mg dose of rimegepant in an ODT formulation should be a clinically useful addition for the acute treatment of migraine. This therapy might offer advantages for certain patients—eg, an effect that is early and long lasting, potentially from only a single dose. The limitation would be that the effect is less than that reported with older gepants (telcagepant) and triptans.[9]

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Published **Online**
July 13, 2019
http://dx.doi.org/10.1016/S0140-6736(19)31611-3

See **Online/Articles**
http://dx.doi.org/10.1016/S0140-6736(19)31606-X

Lars Edvinsson
Department of Medicine, Lund University, Lund 22185, Sweden
lars.edvinsson@med.lu.se

I declare no competing interests.

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