Monoclonal antibodies to CGRP will not become first line treatment fort he prevention of migraine

C. Lampl
Headache Medical Center
Ordensklinikum Linz, Barmherzige Schwestern

Migraine is a very disabling disorder with severe impact on patients' lives and substantiale costs to society in terms of healthcare costs and lost productivity. Prevention is a key component of migraine therapy. Numerous preventive options exist, however not been adequately applied to patient´s needed. In the 2015 Global Burden of Disease Study, migraine was the seventh leading cause of disability globally and the leading neurological cause of disability, accounting for over half of the years lost to disability from all neurological disorders. These may indicate that there is a need for improved preventive treatments for migraine. Monoclonal antibodies against CGRP or its receptor are new promising therapies. They have a long half-life that makes them suitable for therapies requiring chronic activity such as migraine prevention and allows for less frequent dosing, e.g., once or twice monthly. Four monoclonal antibodies are currently in development for migraine prevention: three against CGRP itself: galcanezumab (LY2951742), eptinezumab (ALD403), and fremanezumab (TEV-48215) and one against the CGRP receptor erenumab (AMG-334). Initial safety and tolerability data from phase II trials appears excellent for the anti-CGRP monoclonal antibodies. However, there are some unknown facts to be discussed: Their long-term safety is entirely unknown at this time. The full range of CGRP's physiologic functions is complex. CGRP is a potent vasodilator, and thus, a theoretical risk exists that CGRP blockade could hinder vasodilation in physiologically appropriate situations such as cardiac or cerebrovascular ischemia. Additionally, since antibodies have a relatively long half-life, any untoward effects could not be quickly reversed. CGRP receptors are found outside of the nervous and vascular systems, including in the adrenal glands, kidneys, pancreas, and bone. The effect of chronic CGRP antagonism on other organs is unknown. Their site of action in migraine prevention is unclear. The cost of treatment, once the monoclonal antibodies become commercially available, will certainly be high. In a healthcare system of limited resources, this cost will need to be balanced with the magnitude of benefit. An important group of patients, those that failed more than two preventive categories, was largely excluded from the trials, and thus, it is unknown what benefit this population would derive.