Monoclonal anti-bodies towards CGRP and CGRP receptor will be first line treatment for the prevention of migraine.

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CGRP is a very potent vasodilator with distribution in all vascular regions with similar localization of CGRP receptors, however the detailed functional is incompletely known. CGRP has been shown to be released in primary headaches and blocking this peptide or its receptor reduces symptoms. The available prophylactic treatments rest on therapies that were originally not designed for migraine treatment. The molecular mechanisms of CGRP distribution, release and coupling to the pathophysiology is being elucidated. Blocking CGRP is useful both rapid and long-term in attack prevention. Can it be particularly useful in different subtypes of migraine? This has received novel interest because amazingly the phase II/III trials were positive without AEs. It is worth pointing out that (i) no patients developed hypertension related to the treatment during the trials. (ii) Males (age about 65 y) were exercised on treadmill until development of angina pectoris. They received the CGRP receptor anti-body Erenumab or its vehicle; interestingly there was no difference. (iii) It has been postulated that blocking the trigeminovascular reflex might exacerbate any cerebral ischemia or a stroke during CGRP blockade. Available trials have not supported this hypothesis BUT the CGRP trials have so far mainly been on subjects of middle age and thus not in a population of high risk for stroke or AMI. (iv) Studies on the CGRP anti-bodies show lack of passage of the blood-brain barrier hence this limits CNS side-effects.