Conclusion

Robust treatment effects were observed for both 70 mg and 140 mg erenumab in subjects who had previously failed preventive migraine treatments. For 140 mg, effects were numerically greater in this subgroup than in the overall trial population, and as in the overall population, erenumab 140 mg showed numerically greater efficacy than erenumab 70 mg. These results suggest that erenumab may have particular utility in this subgroup of patients.

O2

GLP-1 Reduces Cerebrospinal Fluid Secretion And Intracranial Pressure: A Novel Treatment For Idiopathic Intracranial Hypertension?

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Background

Current therapies for reducing raised intracranial pressure (ICP) in conditions such as idiopathic intracranial hypertension have limited efficacy and tolerability. As such, there is a pressing need to identify novel drugs. Glucagon-like peptide-1 receptor (GLP-1R) agonists are used to treat diabetes and promote weight loss but have also been shown to affect fluid homeostasis in the kidney. Here, we investigate whether exendin-4, a GLP-1R agonist, is able to modulate cerebrospinal fluid (CSF) secretion at the choroid plexus and subsequently reduce ICP.

Methods

GLP-1R mRNA and protein was assessed by quantitative PCR, immunohistochemistry and fluorescently tagged exendin-4 in human and rat choroid plexus. The effect of exendin-4 on GLP-1R activation and CSF secretion was evaluated in cultured rat choroid plexus epithelial cells using cAMP assays and a Na+/K+ ATPase activity assay. The effect of Exendin-4 on ICP was assessed in adult female rats with normal and raised ICP.

Results

We demonstrated that the GLP-1R is present in human and rat choroid plexus. Exendin-4 significantly increased cAMP levels (2.14 ± 0.61 fold, P<0.01) part of the GLP-1R signalling pathway, in a concentration-dependent manner and this response could be inhibited by the addition of the GLP-1R antagonist exendin 9-39. Exendin-4 also significantly reduced Na+/K+ ATPase activity, a marker of CSF secretion (39.3±9.4% of control; P<0.05). Finally, in vivo ICP recording in female adult rats demonstrated that subcutaneous administration of 20μg/kg exendin-4 significantly reduced ICP in normal (65.2 ± 6.6% of baseline; P<0.01) and raised ICP rats (56.6 ± 5.7% of baseline; P<0.0001).

Conclusion

We demonstrate that exendin-4 reduces CSF secretion by the choroid plexus, and ICP in normal rats and rats with raised ICP. Repurposing existing GLP-1 drugs may represent a novel therapeutic strategy for conditions of raised ICP such as idiopathic intracranial hypertension. Additionally, GLP-1R agonist therapy promotes weight loss, which would be advantageous in idiopathic intracranial hypertension.

O3

Phase 3, randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of erenumab (AMG 334) in migraine prevention: Primary results of the STRIVE trial

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Background

Efficacy and safety/tolerability of erenumab, a human anti-CGRP receptor monoclonal antibody, were evaluated in episodic migraine (EM) subjects in a multinational, phase 3 trial (NCT02456740).

Methods

Adults with EM (n=955) were randomised 1:1:1 to subcutaneous monthly placebo or erenumab 70 mg or 140 mg for 24 weeks. The primary endpoint was change from baseline in mean monthly migraine days (MMDs) over weeks 13-24. Secondary endpoints were ≥50% reduction in MMDs; change in acute migraine-specific medication days; change in Physical Impairment (PI) and Impact on Every-day Activities (EA) (as measured by the Migraine Physical Function Impact Diary (MPFID)). P-values are for pairwise comparisons of each erenumab dose with placebo, statistical significance determined after multiplicity adjustment.

Results

Subjects reported 8.3 MMDs at baseline and experienced -3.2, -3.7, and -1.8-day reductions in the 70 mg, 140 mg, and placebo groups, respectively (p<0.001). A ≥50% reduction in MMDs was achieved by 43%, 50%, and 27% in the 70 mg, 140 mg, and placebo groups (p<0.001), and monthly acute migraine-specific medication was reduced by -1.1, -1.6, and -0.2 days (p<0.001). Subjects had improved PI scores (-4.2, -4.8, -2.4 points in the 70 mg, 140 mg, and placebo groups; p<0.001) and EA scores (-5.5, -5.9, and -3.3 points; p<0.001). The safety/tolerability profile of erenumab was similar to placebo; subjects most frequently reported nasopharyngitis, upper-respiratory-tract infection, and sinusitis.

Conclusion

Erenumab 70 mg and 140 mg significantly reduced migraine frequency and use of migraine-specific medications, reducing migraine’s impact on physical impairment and everyday activities in this EM trial. Numerically greater efficacy was observed for the 140 mg dose consistently across endpoints.

Trial registration

Clinicaltrials.gov NCT02456740.

O4

Modelling cortical spreading depression by a computational agent of distributed neural excitability: correlation with clinical features in single migraine with aura patients

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Background
Cortical spreading depression (SD) is thought to underlie migraine aura but mechanisms of triggering SD and propagation in the structurally normal cortex of migraine patients is still unknown. Some studies showed that the sensory predominance of migraine aura is likely due to a greater susceptibility of primary sensory cortex to SD probably for their structural complexity [1]. We used MRI imaging in migraine with aura patients to elaborate a CSD propagation algorithm that takes into account the morphology of the various cortical areas involved.

Materials and methods
We process the data sets with the Freesurfer software to obtain the geometry and labelling for the different brain regions (Desikan-Killiani Atlas or Brodman areas 1, 2, 3, 4, 44, 45, 17, 18) in five migraine with aura patients. According to the map of the disturbed areas suggested by the aura symptoms, we then initialize the region first affected in the respective hemisphere. Starting the propagation of the CSD in this region we recorded the arrival time in each point of the brain cortex.

Results
We obtained the different brain geometries and the Brodman areas 1, 2, 3, 4, 44, 45, 17 and 18 of the five subjects. In order to run a simulation of the CSD propagating on the cortex we need to identify an initial region as a starting point for the wave. We take a bearing on the map of the disturbed regions provided along with the MRI data from the patients. For the simulation of the CSD we started the wave in these regions and recorded the propagation. In each point we recorded the arrival time of the wave. We visualize the arrival times of the wave in the Fig. 1. This was in accord with the reported evolution of the clinical symptoms.

Conclusions
The way CSD propagates can change in relation to brain morphology. The specific algorithm was able to provide for a simulation of the electrical phenomenon, explaining the progressive evolution of clinical symptoms. Further tests in larger series, could give an aid in understanding the pathophysiological peculiarities of migraine-with-aura brain.

References

Fig. 1 (abstract O4). Simulation of CSD progression in a single patient with reported scotomas in the right visual hemifield, followed by bilateral brachial paresthesia and speech disturbances. The time of progressive cortical areas involvement in the simulation model, was in accord with the reported clinical evolution of aura symptoms.

O5
Interventional management in refractory headache disorders; Tertiary Center Based Experiences supported by application videos and a model for interactive practice of attenders
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Interventional treatment is an important but underevaluated issue for neurologist. However peripheral nerve blocks have been used for both acute and preventive treatment of headaches for decades and are safe and effective therapeutic options for many patients with headache disorders. They can cause a long lasting (several weeks to months) pain relief. This long lasting effect is thought to be due to central pain modulation. Nerve blocks may be an option for the patients who have failed their home medications or who doesn’t want to use drugs. Blocks may also be used to treat patients who need relief between the attacks of migraine or tension type headache and in medication overuse headache during their acute therapy. Nerve blocks are safe and can be appropriate for children and pregnant patients, and also in patients with kidney-liver diseases. In pregnancy, lidocaine is considered a category B drug. Greater occipital nerve blockade is the most common procedure in peripheral nerve blocks. But lesser occipital nerve blockades, sphenopalatine ganglion blockades, supratrochlear, auriculotemporal, supraorbital, infraorbital and mental nerve blockades, cervical root blockades, their combinations can be used in patients with headache disorders. Local anesthetics and steroids are being used for nerve blockades. Botulinum toxin injections are also approved effective methods for migraine all over the World. There is some other indications under search and experiences increases the applications in every day.

We want to show the injection techniques and efficacy by sharing our cases. Deepending on the time, after the presentation some audience keep a chance to applicate tehmselves on the model provided by authors.

O6
A phase 3 placebo-controlled study of galcanezumab in patients with chronic migraine: results from the 3-month double-blind treatment phase of the REGAIN study
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Background
A study was conducted to determine if galcanezumab (120 or 240 mg monthly), a humanized monoclonal antibody that selectively binds to calcitonin gene-related peptide, was superior to placebo in the prevention of chronic migraine.

Materials and methods
Eligible patients 18-65 years of age with chronic migraine (≥15 headache-days per month, of which at least 8 met criteria for migraine) were randomized 2:1:1 to subcutaneous monthly injections of placebo (N=558), galcanezumab 120 mg (N=278) or 240 mg (N=277). The primary endpoint was the overall mean change-from-baseline in the number of monthly migraine headache days (MHD) during the 3-month double-blind treatment period. Key secondary measures included rates of ≥50%, ≥75%, and 100% reduction in monthly MHD, as well as the changes in monthly MHD with acute migraine treatments, the Role Function-Restrictive domain score of the Migraine-Specific Quality of Life Questionnaire (MSQ-RFR), and the Patient Global Impression-Severity of Illness (PGI-S).