Experimental research

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A PHASE II RANDOMISED CONTROL TRIAL ASSESSING THE SAFETY, TOLERABILITY AND EFFICACY OF AN 11B-HYDROXYSTEROID DEHYDROGENASE TYPE 1 INHIBITOR IN IDIOPATHIC INTRACRANIAL HYPERTENSION: IIH:DT.

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Introduction: Pharmacological therapies in idiopathic intracranial hypertension (IIH) are limited and can be poorly tolerated. Novel treatments have not been assessed previously in early phase clinical trials.

Objectives: We investigated the safety, tolerability and efficacy of a novel drug, an 11β-hydroxysteroid dehydrogenase type-1 inhibitor (AZD4017), in a phase 2 multicentre randomised, double-blind, placebo-controlled trial.

Methods: Thirty females aged between 18-55 years with active IIH (lumbar puncture (LP) pressure >25cmCSF and papilloedema) were to be randomised 1:1 to receive either 400mg twice daily oral AZD4017 or matching placebo for 12 weeks. The primary outcome was the difference in LP pressure at week 12. Secondary outcomes included: headache frequency, severity and analgesic use, HIT-6 scores, papilloedema grading, Logmar visual acuity and visual field mean deviation.

Results: LP pressure decreased from 33.7(6.3) to 29.7(5.2) cmH_2O at 12 weeks for AZD4017 and from 32.7(4.8) to 31.3(6.7) cmH_2O for placebo (mean difference:-2.8, 95%CI:-7.1 to 1.5; p=0.2). Visual field mean deviation (MD) (worst eye) changed from -6.1dB (5.4) to -3.4dB (3.2) at 12 weeks for AZD4017 and from -3.4dB (6.8) to -2.2dB (3.1) for placebo (mean difference: 0.3, 95%CI:-2.0 to 2.7, p=0.8). There was no difference in headache outcomes, HIT-6 scores, visual acuity and papilloedema between AZD4017 and placebo at week 12. Only 9 adverse events were deemed to be drug-related and no patients withdrew. One unrelated serious adverse event was recorded two days post-randomisation.

Conclusion: This is the first ever phase 2 trial in IIH to assess a novel agent, AZD4017. The treatment was safe and tolerable over the 12 week study period. We noted a trend for improvement which would be interesting to evaluate in a larger phase 2B or 3 randomised controlled trial.

Disclosure of Interest: None Declared

Keywords: None