UBROGEPANT –A REVIEW

ABSTRACT:

Introduction: Migraine is a mysterious disorder characterized by pulsating head ache which last for 3-48 hours. Inspite of many other causative factors for migraine, Calcitonin Gene-related peptide also plays an integral role in migraine attacks. Though previous CGRP antagonist drugs like Telcagepant was discontinued due to its hepatotoxicity, a newer CGRP – Ubrogepant is a promising and more potent drug with reduced risk of hepatotoxicity. **Methods:** Participants were re-randomized to 1:1:1 to usual care, ubrogepant 50mg and ubrogepant 100mg. Randomization for the ubrogepant dose was blinded. The primary outcomes were safety and tolerability.**Results:** On long duration with intermittent usuage of Ubrogepant 50mg and 100mg when administered as 1 or 2 doses per attack for the acute treatment of migraine was safe and better tolerated, with lower incidence of treatment related Treatment-emergent adverse effects and serious adverse events. **Conclusion:**A new drug Ubrogepant, CGRP receptor antagonist useful in the treatment of acute migraine with lower risks of hepatotoxicity compared to the previous ones.

Keywords:*Ubrogepant; Migraine; Hepatotxicity*. [1]

Introduction: Migraine is a mysterious disorder characterized by pulsating head ache, which is usually restricted to one side, which comes in attacks lasting for nearly 3-48 hours and associated with nausea,vomiting,sensitivity to light and sound,flashes of light,vertigo,and loose stools. Inspite of many other causative factors for migraine, Calcitonin Gene-related peptide also plays an integral role in migraine attacks. Though previous CGRP antagonist drugs like Telcagepant was discontinued due to its hepatotoxicity, a newer CGRP – Ubrogepant was approved by the FDA on 23rd December 2019 by the ALLERGAN COMPANY, is a promising and more potent drug with reduced risk of hepatotoxicity[1].

Clinical trial[2]:A phase III, multicentric, randomized,open label with 52 weeks extension trial was conducted. Adults patients having Migraine with or without aura have been enrolled for the trial after completing one of 2 phase 3 lead-in trials. Participants were re-randomized to 1:1:1 to usual care, ubrogepant 50mg and ubrogepant 100mg. Randomization for the ubrogepant dose was blinded. The primary outcomes were safety and tolerability. The study population included 1230 paticipants (404 for Ubrogepant 50mg, 409 for Ubrogepant 100mg and 419 for usual care). Throughout the study, 21454 migraine attacks were treated with 31968 doses of ubrogepant. On long duration with intermittent usuage of Ubrogepant 50mg and 100mg when administered as 1 or 2 doses per attack for the acute treatment of migraine was safe and better tolerated, with lower incidence of treatment related Treatment-emergent adverse effects and serious adverse events[2].

Pharmacokinetics: After oral administration, ubrogepant is absorbed with maximum plasma levels reaching in 1.5 hours approximately.High fat meal delays and reduces absorption. It has 87% of plasma protein binding capacity. Mainly metabolized by CYP3A4.The elimination half life is 5-7 hours. Most of the drug is eliminated via feces and renal elimination is only a minor pathway[1].

Dosage: Oral tablets – 50mg or 100mg of Ubrogepant

Mechanism of action: It's a Calcitonin gene related peptide receptor antagonists.

Use in specific population:Renal impairment – Dose alteration is recommended in patients with severe renal impairment due to the possibilities of increased levels of Ubrogepant[1].

Hepatic impairment: Patients with hepatic impairment or disorders requires dose adjustments.

Pregnancy: There is no adequate information on the developmental risks with the use of Ubrogepant in pregnant women. Adverse effects on embryofetal developments were observed in the animals following administration of Ubrogepant[3]. In lactating rats, oral dosing with ubrogepant resulted in levels of ubrogepant in milk comparable to peak plasma concentrations.

Geriatric: Elderly patients dosages has to be altered and cautious and to be started with the lower doses.

Adverse effects: Nausea, dry mouth and somnolence.

Nonclinical toxicology: Carcinogenicity – There is no evidence for any drug related tumours in animals or humans.

Indication: It is indicated only in the treatment of acute migraine attack and not for preventive therapy.

Drug interactions: Ubrogepant should not be given along with CYP3A4 inhibitor which will increase the drug exposure. Coadministration with CYP3A4 inducers leads to loss of efficacy of ubrogepant and leads to significant reduction in the drug exposure. Use of BCRP/P-gp inhibitors will lead to increased drug levels since ubrogepant is substrate for BCRP/P-gp[4].

Conclusion:A new drug Ubrogepant, CGRP receptor antagonist useful in the treatment of acute migraine with lower risks of hepatotoxicity compared to the previous ones.

Ethical clearance: Ethical Clearance for this study was got approved from the Institutional Human Ethical Committee (IHEC).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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