P1797 Results from a phase II proof of concept trial of VSN16R to treat multiple sclerosis related spasticity

R. Farrell[1], D. Selwood[2], D. Baker[3], Canbex VSN16R Spasticity Study Group

[1]UCL, Institute of Neurology | Neuroinflammation, National Hospital for Neurology and Neurosurgery,

[2]Wolfson Institute for Biomedical Research, University College London,

[3]Neuroscience, Queen Mary University London, London, United Kingdom

Background: VSN16R is an opener of neural, big-conductance, calcium-activated, potassium channels. We report the results of a phase 2a trial of twice daily oral tablet therapy in people with spasticity due to multiple sclerosis (MS).

Methods: Subjects had confirmed diagnosis of MS, spasticity reported as 4 on the spasticity numerical rating scale (NRS) and modified Ashworth scale 2 in 2 or more lower limb muscle groups.

Participants entered (i) a hospital-based, placebo-controlled, single ascending dose (SAD) group (100mg, 200mg, 400mg and 800mg) to assess pharmacokinetics (n=10), safety and drug tolerability (n=53) and (ii) a second group (Total n=156) to receive either a maximum-tolerated dose or up to 400mg BID of VSN16R capsules or matching placebo. The primary end-point was reduction of spasticity as measured by the NRS, with secondary-outcomes including reduction of modified Ashworth and Tardieu Spasticity Scales, Penn spasm scale and 10m walk following treatment.

Results: Pharmacokinetics and relative lack of adverse events in the SAD safety phase were consistent with phase I safety studies in healthy individuals and all people tolerated the single 800mg dose. Therefore, all people were assigned to 400mg BID during the efficacy arm. Among the people who received VSN16R (n=77) the change in the NRS was -0.9 ± 1.50 in the VSN16R 400mg BID group and -1.1 ± 1.52 in the placebo group (n=79), giving a non-significant treatment difference of +0.20 (95% CI: -0.2 to +0.7, p=0.3434). There was no significant effect on the secondary endpoints. However, post-hoc analysis of people who responded (>30% inhibition of the NRS) to the 800mg dose in the SAD phase (n=10) demonstrated a significant ($p< 0.02$) inhibition in the NRS compared those receiving placebo during the multiple dosing arm. The drug was not associated with any sedation. Reported adverse effects were inconsistent and generally mild.

Conclusions: VSN16R at the dose 400mg BID did not show activity in reducing spasticity in MS patients. The single dose of 800 mg showed activity in comparison to placebo in the dose escalation phase. VSN16R has a very good safety profile. Due to a short halflife of VSN16R further studies with higher doses and slow-release formulation may be warranted. (ClinicalTrials.gov number NCT02542787. EU trials register Number: 2014-004412-11).

Disclosure Source of Funding: The trial was supported by Canbex Therapeutics, a semi-virtual spin-out company from University College London, using: existing Canbex assets, UCL ventures and a donation by Ipsen Pharmaceuticals as part of a pre-licencing agreement.

Potential Conflicts of Interest: Rachel A. Farrell: Principal Investigator of Trial received consultancy fees from Canbex therapeutics, GW Pharma, TEVA, Biogen Idec, Merck, Allergan PLC. David L. Selwood: Founder, shareholder, recipient of research funds and consultant to Canbex therapeutics.Others are irrelevant. David Baker: Founder, shareholder, recipient of research funds and consultant to Canbex therapeutics. Others are irrelevant but has received honoraria or research funds from Japan Tobacco, Merck, Sanofi-Genzyme,Takeda.