

[S-002] Effect of OBE022, an Oral and Selective Non-Prostanoid PGF2 α Receptor Antagonist in Combination with Nifedipine for Preterm Labor: A Study on RU486-Induced Pregnant Mice.

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INTRODUCTION: Management of preterm labor remains an unmet medical need. Pan-prostaglandin inhibition with non-steroidal anti-inflammatory drugs (NSAID) is an effective treatment for preterm labor, but is limited due to adverse effects on the fetus. PGF2 α is a naturally occurring prostaglandin that acts to induce labor in pregnant women. Through specific antagonism of the PGF2 α (FP) receptor, OBE022 is designed to control preterm labor by reducing inflammation, decreasing uterine contractions and preventing cervical changes and membrane ruptures while being safe for the fetus. The FP receptor antagonist OBE022 has shown not to have safety limitations of the NSAID indomethacin. The induction of labor by the antiprogesterin RU486 activates endocrine pathways and a drop in progesterone level characterized by the up-regulation of labor-associated proteins as seen in the case of idiopathic preterm labor.

There is also evidence that FP antagonists when combined with tocolytics acting through a different pathway may result in synergic effects on parturition as described for the beta-mimetic ritodrine, an agent acting through cyclic adenosine monophosphate elevation. Currently, though not approved, one of the most recommended preterm labor treatments is the oral calcium channel blocker nifedipine. Therefore, targeting the FP receptor in combination with the nifedipine may be an optimized strategy for preventing or delaying preterm delivery.

METHODS: To demonstrate the effect of OBE022 alone or in combination with calcium channel blocker nifedipine on parturition in a RU486-induced pregnant mouse model.

Pregnant CD-1 mice were induced with RU486 on gestation day 17; time to delivery was measured.

RESULTS: Compared to the vehicle control, nifedipine (5mg/kg, p.o.) or OBE022 (100mg/kg, p.o.) alone significantly delayed RU486-induced preterm labor. Combination treatment of OBE022 and nifedipine demonstrated a clear synergic effect on the delay of delivery when compared to vehicle, nifedipine or OBE022 alone ($p < 0.001$, $p < 0.001$ and $p < 0.01$, respectively).

CONCLUSIONS: This study confirms the effect of the FP antagonist OBE022 on parturition and establishes a rationale for the usage of combined FP and calcium channel antagonism in the prevention of preterm birth.

Session: Poster Session: Basic Parturition (9:00 AM-10:30 AM)

Date/Time: Saturday, March 18, 2017 - 9:00 am

Room: Bonnet Creek I - IX

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