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Title: OBE002, A PROSTAGLANDIN F2A ANTAGONIST FOR THE TREATMENT OF PRETERM LABOR, DOES NOT IMPAIR RENAL FUNCTION IN THE NEWBORN RABBIT

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Abstract:

Prostaglandins play an essential role in term and preterm labour. Tocolysis with non-steroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin synthesis, is an effective treatment for preterm labor (PTL). However, use of NSAIDs is limited to 48 hours because of neonatal acute renal failure or irreversible end-stage renal failure after maternal ingestion. OBE002 is a new, orally-active, selective prostaglandin F2 α (PGF2 α) receptor antagonist which is being developed to treat PTL.

This study was designed to investigate potential renal effects of OBE002 in newborn rabbits. Renal function and hemodynamic parameters were measured using inulin and para-aminohippuric acid clearances as markers of glomerular filtration rate (GFR) and renal blood flow, respectively. After a baseline period, 2 mg/kg indomethacin (IND), 10 mg/kg OBE002 (OBE) or vehicle (PEG) were given as intravenous boluses. While indomethacin treatment resulted in markedly increased median renal vascular resistance (IND:40%, OBE:-20%, and PEG:-37%) with a concomitant decrease in diuresis (IND:-50%, OBE:24%, and PEG:54%), GFR (IND:-51%, OBE:-13%, and PEG:47%), and renal blood flow (IND:-45%, OBE:34%, and PEG:71%), no significant effects were observed for OBE002 and vehicle, respectively. These results show that PGF2 α modulation does not interfere with neonatal renal function. Hence the future use of PGF2 α antagonists such as OBE002 may be devoid of the limitations of NSAIDs for the treatment of PTL.