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Independent scientific evidence review of baloxavir marboxil use in pregnancy

Baloxavir marboxil is a Cap-dependent endonuclease inhibitor; a single-dose antiviral, licensed in the UK for post-exposure prophylaxis of influenza and in the treatment of uncomplicated influenza in patients aged 12 years or older[1]. Baloxavir exerts its antiviral activity through inhibiting viral genome transcription by inhibition of Cap-dependent endonuclease, an influenza virus-specific enzyme in the polymerase acidic subunit of the viral RNA polymerase complex, thereby preventing viral replication[1].

Influenza in pregnancy

Natural physiological and immunological adaptations that occur during pregnancy result in pregnant women being at increased risk of severe influenza infection in comparison to the general population[2]. Influenza infection in pregnancy carries increased risks of intensive care admission, preterm delivery, low birth weight, congenital anomalies, fetal demise and maternal death[2].

Efficacy and general safety of balxoavir

Clinical trials in non-pregnant participants have demonstrated that single dose baloxavir results in a similar time to alleviation of influenza symptoms as five days of oseltamivir treatment, greater reduction in viral load and fewer adverse events[3]. However, decreased influenza susceptibility to baloxavir after treatment has also been described[4].

Pregnancy safety data

Preclinical safety data

Baloxavir has been administered to pregnant rats and rabbits without adverse embryo-fetal effects at doses up to five (1,000 mg/kg/day) and seven (100 mg/kg/day) times the human therapeutic dose respectively (equivalence based on AUC concentrations)[5]. Maternal toxicity occurred in rabbit models following the administration of doses 17-times (1,000 mg/kg/day) the human therapeutic dose (equivalence based on AUC concentration[1]), and two of the 19 pregnancies resulted in abortion. Skeletal variations (cervical rib reabsorption during the growing process of adjacent cervical vertebra[1]) were also described among the rabbit kits exposed to maternally toxic doses[5].

Human data

There are no human pregnancy exposure data for baloxavir. As such, the manufacturer states that it is preferable to avoid the use of baloxavir during pregnancy on a precautionary basis[1].

Conclusion

Although the manufacturer states that it is preferable to avoid the use of baloxavir during pregnancy[1], randomised controlled trials have shown single dose baloxavir treatment to have a similar efficacy as five days of oseltamivir treatment and to be associated with greater reductions in viral load and fewer adverse events[3]. Baloxavir treatment may be of particular benefit to pregnant women with influenza, as they are at increased risk of developing severe disease[2]. Preclinical animal models of exposure in pregnancy do not provide evidence of adverse embryo-fetal effects at doses up to five and seven times the human therapeutic dose respectively[1,5]. The risk of harm from baloxavir in pregnancy is likely to be low given the animal model data, together with the therapeutic target for baloxavir being a virus specific enzyme. However, given that no human data are available, it is recommended that a cautious approach is taken and baloxavir use in pregnancy be reserved to clinical trial settings with careful collation of pregnancy outcome data.

References

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