

## Everolimus use in kidney transplant recipients during pregnancy: case report and literature review.

**Dr Hannah Blakey<sup>1</sup>**, Dr Ellen Knox<sup>2</sup>, Dr Graham Lipkin<sup>1</sup>

<sup>1</sup>Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom, <sup>2</sup>Birmingham Women's Hospital, Birmingham, United Kingdom

### Introduction:

Everolimus is an mTOR (mammalian target of rapamycin) inhibitor and is sometimes used as maintenance immunosuppression for kidney transplant (KT) recipients. mTOR inhibitors are not licensed for use in pregnancy due to associations with prematurity, low birth weight and pregnancy loss in rats, although human data is lacking (1). There are only 5 reported cases of everolimus use throughout pregnancy in KT recipients (1-3) (Table 1). No fetal malformations have been reported although adverse pregnancy outcomes are common, in keeping with the general KT population (4). The evidence base requires expansion to better guide treatment decision-making. We report a pregnancy in a KT recipient treated with everolimus.

### Case:

27-year-old nulliparous female with a background of IgA nephropathy who received a living donor KT in 2011. Immunosuppression initially comprised tacrolimus, prednisolone and mycophenolate, but the latter was discontinued due to leucopenia. An antibody-mediated rejection episode was treated in 2016 and Azathioprine temporarily added to immunosuppression but with no impact on donor-specific antibody (DSA) levels. DSA levels were only successfully suppressed following introduction of everolimus (Certican®). She was referred to a specialist renal-obstetric clinic in the first trimester of an unplanned pregnancy in 2019. Given previous rejection on dual immunosuppression and lack of suitable alternative agents, everolimus was continued after detailed discussion around the risks of potential teratogenesis.

Early pregnancy creatinine fell to 105µmol/l (pre-pregnancy baseline 126µmol/L, eGFR 44ml/min). Tacrolimus and everolimus doses were reviewed monthly, aiming for 12-hour trough levels of 3-7µg/l. Rising blood pressure, transaminitis and deteriorating graft function prompted hospital admission at 34+6 weeks for obstetric cholestasis and superimposed pre-eclampsia. She delivered a female weighing 2765g at 35+6 weeks by vaginal delivery following induction of labour. The baby required 7 days of neonatal care for phototherapy and establishing feeding. Data regarding breastmilk transfer of everolimus is lacking, and therefore bottle feeding was advised. The mother was treated postnatally for respiratory tract infection. Creatinine at 2 months postpartum was 148µmol/l, and GFR 36ml/min.

### Discussion:

Caution is required when continuing everolimus in pregnancy for KT recipients. There are no existing reports of fetal malformation with everolimus use, although the evidence base is small. Furthermore, the majority of reported cases used low or unmonitored everolimus trough levels. Adverse pregnancy outcomes including pre-eclampsia, low birth weight, and requirement for neonatal care are common, in keeping with the general KT cohort (4).

In highly selected cases with oversight from renal and obstetric specialists, everolimus may be continued where there is significant risk to graft survival in switching immunosuppression regime and where the patient has been counselled regarding potential risks to the fetus.