0.018). Gestational age at delivery was much shorter in high risk group than intermediate (35w vs 37w p = 0.003) and low risk group (35w vs 39w p = 0.002).

Discussion: sFlt-1/PlGF at late weeks of gestation can be useful on predicting late onset PE. Further clinical research is needed to make this biomarker established.

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200. Clinical trial of metformin to treat preterm preeclampsia: pharmacokinetics and biomarker studies

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Introduction: Metformin is a potential therapeutic for preeclampsia as it decreases sFlt-1 and soluble endoglin and rescues endothelial dysfunction. Metformin pharmacokinetics in preeclampsia, where there is increased renal clearance and proteinuria, has not been established.

Objective/Hypothesis: To evaluate metformin XR (extended release) pharmacokinetics in preterm preeclampsia, obtain data on pregnancy prolongation and circulating levels of biomarkers associated with endothelial dysfunction.

Methods: 15 women with preterm preeclampsia were treated with 1.5 g metformin XR twice daily. Pharmacokinetic sampling was performed on day 1 at 2,4,5,6,7,8,24 h, and concentrations measured using liquid chromatography-tandem mass spectrometry. Given steady state is reached at 24–48 h, trough concentrations were measured at day 1 and 5 to assess the increase in Cmin over time. Plasma was taken twice weekly and biomarkers of endothelial dysfunction measured.

Results: Gestation at recruitment ranged from 27 to 31 weeks, and median prolongation was 11.5 days [IQR 5.8–23.8].

Pharmacokinetic studies confirmed excellent circulating levels at 0–12 h exposure, with Cmax [median (IQR)] 1.6 (1.3–1.9) mg/l, AUC 0–12 11.7 (8.9–13.5) mg.h/l and AUC 0-infinity 17.0 (10.7–36.6) mg.h/l.

Day 1 and 5 trough concentrations were 0.55 (0.34–1.22) mg/l and 0.01 (0.01–0.70) mg/l suggesting steady state exposure is similar to day 1. Umbilical cord blood:plasma ratios taken 4 (3–9.5) hours after dosing were 0.67 (0.2–0.86).

None of the following circulating biomarkers increased across pregnancy among those who remain undelivered: sFlt1, soluble endoglin, Vascular Cell Adhesion Molecule 1, Endothelin-1 and placental growth factor.

Discussion: 1.5 g of metformin XL twice daily in preterm preeclampsia resulted in at least the same exposure as 2 g daily in healthy controls, despite pregnancy and preeclampsia related changes. Metformin potentially stabilised levels of circulating biomarkers of endothelial dysfunction. Randomised trials to treat preterm preeclampsia should be performed.

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201. Higher levels of memory T-cell subsets in decidua parietalis compared to basalis tissue of uncomplicated term pregnancies

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Introduction: During pregnancy, tolerance towards the fetus is induced by adaptations in the maternal immune system. Maladaptation of the maternal immune system is associated with pregnancy complications like preeclampsia and fetal growth restriction. Memory T-cells might play an important role in fetal-maternal tolerance. It is at the fetal-maternal interface where the maternal immune system especially needs to create tolerance towards the fetus. Decidua basalis is the maternal part of the basal plate whereas decidua parietalis is the maternal part of the fetal membranes. Decidual distribution pattern of memory T-cells during pregnancy is not known.

Objective: Since it is unknown how memory T-cells are distributed in decidual tissue, memory T-cells in decidua basalis and decidua parietalis were evaluated.

Methods: Lymphocytes were isolated from decidua basalis and decidua parietalis from uncomplicated term pregnancies. Using flowcytometry, subsets of memory T-cells (central, effector, regulatory, and tissue resident) of uncomplicated term pregnancies were analysed (n = 27). To compare different subsets of memory T-cells between decidual tissues, a student's t-test ($p < 0{,}05$) was used.

Results: Levels of memory T-cells (CD45RO+) were higher in decidua parietalis compared to decidua basalis in both CD4+ and CD8+ cells. Moreover, CD8+ central memory cells (CD45RO+CCR7+) and CD8+ tissue resident cells (CD45RO+CD103+) were higher in decidua parietalis compared to decidua basalis. Lastly, activation status (CD69+) was higher for all memory subsets (except for CD4+ effector memory T-cells) in decidua parietalis compared to decidua basalis.

Discussion: This study shows that memory T-cell subsets are differently distributed in decidua parietalis and basalis, with higher percentages of memory T-cell subsets as well as more activated memory T-cell subsets found in decidua parietalis compared to decidua basalis. Since memory T-cells are found to be present at higher percentages in decidua parietalis, this could suggest that these cells are especially important for creating tolerance to the fetal membranes.

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202. Joint exposure to antiangiogenesis and inflammation in pregnant mice results in sex specific growth restriction patterns

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Introduction: Preeclampsia is a multifactorial pregnancy disorder presented with angiogenic imbalance and low-grade systemic inflammation. However, animal models which represent these variety of pathophysiological conditions are missing.

Objective/hypothesis: We aimed to establish a novel double hit preeclampsia animal model in order to mimic the complex multifactorial conditions that are present during preeclampsia and to investigate the early consequences to the fetus.

Methods: C57Bl/6 mice on gestational day GD 8.5 were injected with adenovirus overexpressing sFlt-1 (1×10^9 PFU in 100 ml) or empty adenovirus. On GD 10, a second hit was introduced with a low dose of lipopolysaccharide (LPS, 25 μg/kg, i.p.) or PBS. Between GD 16.5 and 17.5, 24-h urine was collected. Blood pressure and blood analysis were performed on GD 18.5. Fetuses and placentas were collected at GD 18.5.

Results: Animals exposed to sFlt-1 and LPS showed increased blood pressure and albumins in 24-h urine. sFlt-1 concentrations were 2×higher in the double hit preeclampsia group. Blood pressure values were positively correlated with the sFlt-1 concentrations. Fetuses were growth restricted and subclassification based on sex showed that females have symmetrical growth restriction