ultrasound on Day 38 and Day 70. Primary efficacy endpoint was clinical pregnancy on Day 38. Secondary outcomes included lH-hCG levels (Day 18, Day 38) and implantation rate (N implanted embryos/N embryos transferred) on Day 38 and Day 70.

Main results and the role of chance: For the primary end-point, non-inferiority of progesterone pessary versus progesterone gel was met in the full analysis set (FAS) but could not be formally shown for the per protocol set (PPS) based on the pre-defined 9% non-inferiority margin (actual value: 9.5%). Pregnancy rates on Day 38 were 38.3% for progesterone pessaries and 39.9% for progesterone gel (FAS). These rates were higher than anticipated in sample size calculations (assumed a reference rate: 30%) leading to an increased variability, thus to wider confidence intervals than expected and explaining the marginal violation of the non-inferiority criterion for the PPS. Pregnancy rates on Day 70 were 34.5% (progesterone pessary) and 37.6% (progesterone gel). In the progesterone pessary group, the pregnancy rate was higher in younger patients (<35 years: 41.4%; >35 years: 33.8%) and transfer of two or three embryos led to a higher rate (42.1%) compared to single embryo transfer (31.1%). Pregnancy rates on Day 38 were 21.1%, 38.9%, 37.9%, 38.3%, and 42.4% in Belgium, Bulgaria, Czech Republic, Hungary, and Serbia, respectively. Implantation rates for progesterone pessaries compared to progesterone gel on Day 38 were 24.6% and 26.5% and on Day 70, 22.5% and 24.5% respectively. Both treatments were safe and well tolerated.

Limitations, reasons for caution: A logistic regression analysis was applied to investigate potential country effects. The test for any interaction between country and treatment (p = 0.13) indicated a tendency for country specific differences between treatments. However, since this test is not statistically significant, treatment comparisons over all countries are considered valid and reliable.

Wider implications of the findings: Progesterone pessary, shown to be non-inferior to progesterone gel in regards to clinical pregnancy rates in this study, can be regarded as a reasonable alternative to current treatment options for LPS in ART cycles. Additional available options allow an increasing role for patient centered decision making in LPS.

Trial registration number: EudraCT number 2013-001105-81

O-119 Combination tolcolytics on the inhibition of OT-induced contractions of human pregnant myometrium in vitro

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Study question: Can OBE002, a novel FP receptor antagonist, which inhibits PGF2α- and OT-induced myometrial contractions enhance inhibitory effects of existing tolcolytics on OT-induced myometrial contractions in-vitro?

Summary answer: The combination of OBE002 with existing tolcolytics, atosiban and nifedipine, enhanced their inhibitory effect on OT-induced contractility.

What is known already: Preterm labour (PTL) is a major cause of neonatal morbidity and mortality. Currently, management of PTL aims to reduce uterine contractions. Since most tolcolytics have been developed specifically for the inhibition of uterine contractions, tolcolytics are not urotensin specific and thus have dose-dependent multi-organ side effects. It is suggested that combined use of tolcolytics with drugs interfering with different signalling pathways lead to additive inhibitory effects allowing lower doses with reduced side effects and increased efficacy.

Study design, size, duration: The inhibitory effects of OBE002 in combination with either atosiban or nifedipine, in OT-induced myometrial contractions, were investigated in human pregnant myometrial strips. For each combination tolcolytics experiment, six non-labouring human myometrial biopsies were used from six different patients undergoing elective caesarean section at term. All experiments were performed within 24 hours from tissue collection to ensure myometrial viability and optimal contractility performance.

Participants/materials, setting, methods: Myometrial strips from the same patient were mounted on a DMT Myograph 800 MS. Regular baseline contractions were recorded for 20 mins prior to treatment with OBE002 at 60 and 600 nM alone or with atosiban or nifedipine (6 nM) and effects on spontaneous contractility were measured in the next 10 min. The effect of the tolcolytics upon OT stimulation was measured with increasing OT concentrations (1, 10, and 100 nM) at 10 min intervals.

Main results and the role of chance: Atosiban reduced OT-induced myometrial contractility at 6 nM and this effect was enhanced in a dose-dependent manner when combined with OBE002 (p < 0.01 vs Ato 6 nM, ANOVA). Concurrent administration of OBE002 and atosiban, at maximum concentration of 600 nM, reduced the contractility to basal level. Nifedipine and OBE002 alone inhibited the OT-induced contractions, and their inhibitory effects were increased further when the two drugs were used together. The combination of OBE002 and nifedipine was more effective than OBE002 alone (p < 0.01 OBE002 60 nM vs Nif+OBE002 60 nM, ANOVA).

Limitations, reasons for caution: Synergistic effects of OBE002 and atosiban/nifedipine were observed but further dose-response treatments could strengthen our findings. This study was carried out using term, non-labouring samples, but preterm or labouring samples will be useful to be examined in the future.

Wider implications of the findings: Targeting the FP receptors with OBE002 in combination with the existing tolcolytics may therefore be a more effective strategy for preventing or delaying preterm delivery.

Trial registration number: N/A.

O-120 Melatonin in assisted reproductive technology: the MIART trial - A pilot double-blind randomised placebo-controlled clinical trial

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Study question: Does oral melatonin, when given during ovarian stimulation, improve clinical pregnancy rate after IVF?

Summary answer: When given at the doses tested, melatonin does not improve clinical pregnancy rate after ART.

What is known already: Melatonin is a potent oxygen scavenger and for this reason, it is thought to protect the oocyte and embryo from oxidative damage during the ART process. Previous uncontrolled and non-randomised studies have indicated that melatonin may improve ART outcomes, including the total number and quality of oocytes and embryos as well as pregnancy rate. Based on this, melatonin is currently used by many infertility specialists as an adjunct to ovarian stimulation with the intention of improving IVF success rates.

Study design, size, duration: A pilot double-blind, dose-finding, randomised placebo-controlled clinical trial of 160 women recruited between September 2014 and September 2016.

Participants/materials, setting, methods: Women undergoing their first cycle of IVF or ICSI were randomised to receive one of four different regimes of trial medication (placebo, n = 40; melatonin 2 mg, n = 41; melatonin 4 mg, n = 39; melatonin 8 mg, n = 40) twice per day from Day 2 of their cycle until the night before oocyte retrieval. Primary outcome was clinical pregnancy rate (presence of a live intrauterine fetus at 7-week ultrasound). Secondary outcome measures included oocyte number and maturity and embryo number and quality.

Main results and the role of chance: Compared with placebo, the geometric mean concentrations for melatonin in the highest dose group (8 mg bd) on the day of oocyte retrieval were 2-fold (P < 0.03) and 8-fold (P < 0.001) higher in serum and follicular fluid respectively. Despite these significant changes in serum and follicular fluid concentrations, there was no statistically significant difference in clinical pregnancy rates between the four groups. There were no