

**METHODS:** This is a retrospective cohort study analyzing mode of delivery in infants with initial neonatal HC measuring >35 cm from all deliveries at a single institution between July 2014 and December 2015. Of particular interest was whether cesarean was scheduled or labor was attempted. Secondary analysis involved analyzing those deliveries with prenatal ultrasound suggesting either fetal ventriculomegaly or hydrocephalus with a suspected HC >90th percentile for gestational age. A receiver operator curve (ROC) was then constructed to assess optimal head circumference by which to predict mode of delivery.

**RESULTS:** Our study included 527 cases with neonatal HC measuring >35 cm, including 252 cesareans and 275 vaginal deliveries. Of the cesarean deliveries, 136 were planned. 16 cases were identified with third trimester ultrasounds measuring HC >90th percentile for gestational age, 11 (68.75%) of which had ventriculomegaly. Of these, 9/16 (56.25%) were scheduled for cesarean without labor. The remaining 7/16 underwent trial of labor: 5/7 (71.43%) delivered via spontaneous vaginal delivery and 2/7 (28.57%) delivered via unanticipated cesarean due to failure to progress. 8 cases of neonatal HC  $\geq$ 40cm were identified; 7/8 (87.5%) received scheduled cesareans. Additional statistics are included in Table 1 below. ROC analysis demonstrated poor prediction of successful trial of labor at any specific HC between 36 and 40cm (Image 1).

**CONCLUSION:** These data suggest that a trial of labor should be offered to patients with known ventriculomegaly or an enlarged fetal HC measuring <40cm. Further research is needed to investigate patient profiles for predicting vaginal delivery when HC is >40cm, although vaginal delivery may still be considered in these cases.

*Image 1:* ROC analysis of successful trials of labor at various HC measurements.

*Table 1:* Characteristics of TOL participants with neonatal HC>35 cm.

*\*Figure(s) will be available online.*

### S-036

**Use of Uterine Electromyography to Evaluate Labor in Term Nulliparous Women.** Pin Li\*,<sup>2</sup> Le Le Wang†,<sup>2</sup> Huiping Hu†,<sup>2</sup> Robert E Garfield\*,<sup>2</sup> Huihu Liu\*.<sup>1,2</sup> <sup>1</sup>Guangzhou Medical University, Guangdong, Guangzhou, China; <sup>2</sup>Guangzhou Women & Children Medical Center, Guangzhou, China.

**INTRODUCTION:** The purpose of this study was to define the changes in uterine electrical signals recorded by electromyography (EMG) in relationship to progress in cervical dilation during the 1st stage of labor.

**METHODS:** Uterine EMG was recorded from the abdominal surface for 30 min. from one hundred and ninety five (total n=195) nulliparous women presenting at  $\geq$  37<sup>0/7</sup> weeks of gestation. Eight groups were defined: Group 1 (n=10), non-laboring patients with no cervical effacement; Group 2 (n=15), patients with cervical effacement; Groups 3 to 7, patients in 1<sup>st</sup> stage of labor with cervical dilation respectively at 1-2 cm (n=10), 2-3 cm (n=50), 3-5 cm (n=40), 5-7 cm (n=30) and 7-9 cm (n=25), and Group 8 (n=15) during 2<sup>nd</sup> stage of labor with cervix at 10 cm dilation (n=15). Uterine EMG bursts were characterized by analysis of various burst characteristics, including number of bursts, route mean squared, total power and power density spectrum of peak frequency.

**RESULTS:** The burst frequency increases progressively from no effacement to 2-3 cm of cervical dilation ( $P<0.05$ ) and then more steeply thereafter to a peak levels at about 3 to 5 cm ( $P<0.05$ ), then levels off thereafter ( $P>0.05$ ). The RMS values increase gradually throughout effacement with significantly higher levels at 10 cm cervical dilation ( $R=0.771$ ,  $P<0.025$ ). Similarly, burst power increases gradually and significantly ( $R=0.890$ ,  $P<0.001$ ) throughout the process of cervical dilation. Additionally, the PDS peak frequency increases progressively throughout cervical dilation ( $R=0.972$ ,  $P<0.001$ ). The relationship between the various components of bursts of uterine electrical activity, such as the power and power density peak frequency are demonstrated respectively in Figures.

**CONCLUSION:** Uterine EMG can effectively quantify the contribution of uterine muscle electrical activity to the advancement of cervical dilation and the progress of labor during the evolution of labor. This study

indicates that the dilation of the cervix is related to uterine EMG and contractions which suggests significant improvements in the diagnoses and the management of labor.

*\*Figure(s) will be available online.*

### S-037

**Effects of the Oral Prostaglandin F2 Alpha Receptor Antagonist Tocolytic OBE022 on Reproduction in Rats and Rabbits.** Oliver Pohl\*,<sup>1</sup> Roberta Sisti\*,<sup>2</sup> Jean-Pierre Gotteland\*.<sup>1</sup> <sup>1</sup>ObsEva, SA, Geneva, Switzerland; <sup>2</sup>Research Toxicology Centre, Pomezia, Italy.

**INTRODUCTION:** OBE022 is a novel, orally-active prostaglandin F2 alpha receptor antagonist under development for the treatment of preterm labor. The reproductive safety of OBE022 was evaluated in customized fetal development (FD) and pre/postnatal development (PPN) studies mimicking clinical exposure scenarios. The study investigated effects on pregnancy and fetal development in rats and rabbits. In addition, it provided information on pre- and post-natal development to sexual maturity in the rat and detected adverse effects on the pregnant female and on development of the conceptus and offspring.

**METHODS:** Oral OBE022 was administered at doses of 120, 360 and 1200 mg/kg/d to female rats throughout FD during a FD/PPN study. In the rabbit, OBE022 was dosed intravenously at 3, 6 and 9 mg/kg/d throughout the second half of pregnancy to assess fetal safety. Pharmacokinetic exposure assessments were performed on the last day of pregnancy.

**RESULTS:** No OBE022 effects were observed during the rat FD study. The rat PPN study did not result in adverse OBE022 effects in female rats allowed to litter, their offspring, and second-generation fetuses. At the highest dose, transient maternal toxicity (weight loss and reduced food intake) resulted in slightly reduced pup weights at birth which recovered within the first two weeks postpartum. The treatment of pregnant female rabbits with OBE022 during late stage gestation did not induce any signs of fetal toxicity. Dose levels of 6 and 9mg/kg/day were associated with maternal toxicity in the form of dose-dependent mortality and no effects on the fetuses. A dose level of 3mg/kg/day was not associated with any adverse effects.

**CONCLUSION:** OBE022 at up to 360 mg/kg/d had no adverse effects on FD and postnatal development of rats and none of the tested doses had any effect on rabbit fetuses. Exposures at No-Adverse-Effect doses were in excess of maximal clinical exposures. These results constitute an important step toward the development of OBE022 in preterm labor.

*\*Figure(s) will be available online.*

### S-038

**Safety and Pharmacokinetics of the Oral Prostaglandin F2a Receptor Antagonist Tocolytic OBE022: A First-in-Human Study in Healthy Women.** Oliver Pohl\*,<sup>1</sup> Ulrike Lorch\*,<sup>2</sup> Line Marchand\*,<sup>1</sup> Jean-Pierre Gotteland\*.<sup>1</sup> <sup>1</sup>ObsEva, SA, Geneva, Switzerland; <sup>2</sup>Richmond Pharmacology, London, United Kingdom.

**INTRODUCTION:** OBE022 is a novel, orally-active prostaglandin F2a (PGF2a) receptor antagonist under development for preterm labor and has previously been shown to delay delivery in animal models of preterm labor and to reduce the duration and strength of oxytocin and PGF2a-induced contractions in human myometrial strips. To enable future evaluation of OBE022 in preterm labor patients, we performed a Phase 1 single and multiple ascending dose study assessing the safety and pharmacokinetics (PK) of OBE022.

**METHODS:** This was a prospective, randomized, placebo-controlled, dose-escalating first-in-human Phase I study in 1 clinical site in the UK. A total of 36 healthy postmenopausal women were enrolled and treated orally with placebo or single doses (SAD) of 10, 30, 100, 300, 1000 or 1300 mg, or multiple doses (MAD) of 100, 300 or 1000mg/d during 7 days. In addition the food-effect was evaluated.

**RESULTS:** OBE022 was observed to be readily absorbed and converted into the active stable metabolite OBE002. Exposure to OBE002 increased with dose of OBE022 and reached anticipated clinically meaningful exposure levels within 1 hour after administration. In the MAD part, mean OBE002 half-lives were observed to be between 8-11 hours after a single dose and 22-29 hours after multiple doses. There was no clinically