APAP should therefore be preferred for acute pain management.
Disclosure(s) Nothing to disclose

P53 EXPOSURE OF INFANTS TO BROMINATED FLAME RETARDANTS THROUGH BREAST-MILK

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Introduction Polybrominated Diphenyl Ethers (PBDEs) are non-biodegradable flame retardants, accumulated in biological systems and acting as endocrine disruptors. Breast feeding is a major route of exposure in infancy. Taken together with the critical development of this age and the potential adverse effects of PBDEs, it is important to monitor these contaminants in breastmilk.
Objective To evaluate the exposure of infants to PBDEs
Methods 343 families were recruited during 2013–2016 in Assaf Harofeh and Ichilov to create the AHI-EHF cohort. Maternal blood and urine, cord blood, breast milk and meconium were collected. Participants filled out questionnaires about socio-demographic status, medical history, exposures and life habits. Colostrum samples were collected from women at the maternity department. PBDEs in colostrum and Infant formulas levels were analyzed using GC-MS
Results and discussion Out of 183 serum samples, only 11 (6%) detectable levels of PBDEs. PBDEs were found in all colostrum samples. The average concentration of total PBDEs in breastmilk was 714ng/L. PBDEs levels were also measured in three infant formulas. Unlike breastmilk, infant formulas had of only 3 congeners and levels were relatively low. The average concentration of total PBDEs in infant formulas was 153ng/L. PBDEs, were found to be negatively correlated to anno-penile index (API) which serve as a marker for endocrine disruption.
Conclusions PBDEs levels in breast milk are higher than levels in some European countries, but lower than in North America. PBDEs might have negative influence on AGD in boys. Maternal exposure to PBDEs and the significance of it should be further investigated.
Disclosure(s) Nothing to disclose

P54 KIDS-STEP: A SWISS MULTI-CENTRE RCT ON EFFECTIVENESS OF ADJUNCT BETAMETHASONE THERAPY IN HOSPITALISED CHILDREN WITH COMMUNITY ACQUIRED PNEUMONIA

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Background The incidence of community-acquired pneumonia (CAP) in young children is high (20- 30/1000 child-years) and is associated with a high rate of hospitalisation (around 10/1000 child-years). In adults, a benefit of adjunct corticosteroids on time to clinical stability and hospital discharge has been observed and confirmed in systematic reviews and meta-analyses. In contrast, only few small trials have addressed the potential impact of oral steroid treatment in CAP during childhood. The purpose of this study is to concurrently evaluate whether adjunct treatment with corticosteroids in children hospitalised with CAP is more effective in terms of the proportion of children reaching clinical stability and whether such adjunct treatment is no worse in terms of CAP relapse.
Methods Children in KIDS-STEP[1] receive either oral betamethasone or oral placebo dosed once daily for two consecutive days. We include 700 children from age 1 weighing at least 7 kilograms and up to a body weight of 35 kilograms and age below 10 years hospitalised for CAP using a clinical diagnosis.
Co-primary outcomes are (a) The proportion of children clinically stable at 48 hours after randomisation. (b) The proportion of children with CAP-related readmission within 28 days after randomization. Secondary outcomes will be captured to further evaluate the efficacy and safety of adjunct oral steroids in the management of childhood CAP, including proportion of children experiencing solicited side effects of the trial treatment and/or serious adverse events, time to hospital discharge after index hospitalisation in days, time away from routine child care and away from work (for parents) in days up to 28 days after randomisation and total antibiotic exposure in days up to 28 days after randomisation.
Results Enrolment started in November 2018 and is currently proceeding at approximately 1 participant per participating hospital per week.

REFERENCES
1. Study registration: BASEC - EKNZ 2018–00563

Disclosure(s) Nothing to disclose

P55 PREVENTING INAPPROPRIATE HYDROXYUREA DOSING IN CHILDREN BY INTRODUCING A CHILD-APPROPRIATE PREPARATION

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Background Hydroxyurea (HU) is the only FDA- approved disease- modifying drug for sickle cell disease, by inducing the production of fetal hemoglobin and thus decreasing the sickling of red blood cells. Till recently HU was available only in adult doses of 1000 mg. This meant that to aim at the standard dose of 20 mg/kg/d, most young children had to be overdosed, or the dose had to be fluctuated daily to achieve the aimed mean dose. Because adherence improves with unchanged daily dose, and due to the more than 10 fold variability in HU pharmacokinetics in children, there was an urgent need for a pediatric formulation of HU.
Methods and results This issue has been solved with the FDA approval of the French-originated orphan HU, Siklos, a preparation of 50 and 100 mg, which prevents the risk of inappropriate dosing in children.

Studies show that the child appropriate dose preparation much more closely allow young children to receive

appropriate dose of Hydroxyurea, and increase adherence with this critical drug.

Conclusions In summary, FDA approval of the French-originated orphan HU, Siklos in preparations of 50, 100 mg, prevents the risk of inappropriate dosing of the drug in children. This should encourage all involved in pediatric medicine, from health care physicians and pharmacists, to the pharmaceutical industry and regulators to act similarly in other therapeutic areas where inappropriate pediatric dose schedules are endangering the health and wellbeing of children.

Disclosure(s) G Koren has been a consultant for Medunik USA.

P56 BREAKTHROUGH IN THE TREATMENT OF NAUSEA AND VOMITING OF PREGNANCY; THE FIRST DUAL RELEASE COMBINATION OF DOXYLAMINE-PYRIDOXINE

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Background Nausea and vomiting of pregnancy (NVP) affect almost pregnancies. The only agent approved by the FDA and other countries for the management of NVP symptoms has been the delayed release combination of doxylamine and pyridoxine. This combination, formulated as a 10 mg/10 mg delayed release tablet, was approved by the FDA for the treatment of NVP in 2013 (Diclegis®).

Due to its delayed release properties, Diclegis® begins to exert its antiemetic properties 6–8 hours after ingestion, and hence symptom relief may be delayed and necessitate the use of an immediate release medication.

Methods In 2016 the FDA approved Bonjesta®, a novel, dual-release combination of doxylamine and pyridoxine, whereby a rapid release phase is followed by a delayed release phase, thus overcoming the time delay in action of Diclegis®. Bonjesta®, is a multilayer, extended-release tablet consisting of an enteric-coated core containing 10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride, and an immediate-release coating of 10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride, delivering a total of 20 mg doxylamine succinate and 20 mg pyridoxine hydrochloride

Results In a single-and multiple dose study in 48 healthy, premenopausal women, one Bonjesta® (20 mg doxylamine succinate and 20 mg pyridoxine) was bioequivalent to two combination tablets of 10 mg doxylamine succinate and 10 mg pyridoxine hydrochloride

Bonjesta has shown an immediate peak concentrations, followed by a delayed release phase.

Conclusions The combination of the immediate release with a delayed action is unique to Bonjesta® as it allows for the bedtime dose to be effective immediately and also provide with sustained control of NVP symptoms throughout the day.

Disclosure(s) G Koren has been a consultant for Duchesnay Inc.

P57 FILLING THE GAP FOR CHILDREN WITH HEART FAILURE: THE EU-FUNDED DRUG DEVELOPMENT PROGRAM LENA (LABELING OF ENALAPRIL FROM NEONATES UP TO ADOLESCENTS)

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Background ACE-inhibitors are first choice treatment for adult and paediatric patients with heart failure. Since there are no systematic data on pharmacokinetics and safety in the young heart failure population, the EU funded a drug development program[1] to fill those gaps for the ACE-inhibitor enalapril. An age appropriate paediatric formulation was also required.

Methods A paediatric patient cohort with heart failure was recruited to fulfil the paediatric investigation plan (PIP) requirements. The PIP required a total of 85 evaluable patients from birth to less than 12 years of age with a subset cohort of 25 patients with heart failure due to dilated cardiomyopathy and a subset of 60 heart failure patients of congenital heart disease. Out of these, 54% of patients must be aged below 12 months to provide a substantial amount of young patients.

Results The LENA consortium recruited 102 children from birth to 12 years. Out of those, 89 patients fulfilled relevant protocol criteria and could be regarded as evaluable. Of these, 26 demonstrated heart failure due to cardiomyopathy and 63 due to congenital heart disease. Sixty five patients (73%) were below 12 months of age. Moreover, 22 patients were below 3 months of age, 26 patients from 3 months to less than 6 months and 17 patients from 6 months up to 12 months of age.

Conclusions The LENA consortium had recruited the PDCO required number of paediatric patients for the drug development program LENA. As more than 2/3 of patients belong to the most vulnerable patient population below the age of 12 months, relevant data can be generated to fill gaps for the safe and reliable treatment with ACE-inhibitors of children with heart failure.

REFERENCES

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