levels were below usual therapeutic ranges (MER: 2–8 mg/L, PIP 8–30 mg/L). This was more often the case in presence of concomitant HF (MER: 92%, PIP: 83%), often associated with neutropenia. Low exposure was observed not only at initial intensive dosage (MER: 120 mg/kg/day, PIP: 400 mg/kg/day) but tended to persist despite dosage readjustment based on concentration monitoring. Moreover, bacteremia was diagnosed in 38 cases.

Conclusion Current recommended doses of MER and PIP do not provide optimal concentration coverage throughout the dosing interval in a large fraction of children with cancer and febrile neutropenia as a result of HF. Monitoring of beta-lactams should be offered to all children with cancer to ensure best therapeutic success and avoid the development of resistance.

REFERENCES

Disclosure(s) Nothing to disclose

013 IMPROVED EARLY VANCOMYCIN EXPOSURE IN NEONATES USING A POPULATION PHARMACOKINETIC MODEL-BASED VANCOMYCIN DOSING REGIMEN
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Background We previously documented that 2 published vancomycin dosing regimens resulted in subtherapeutic exposure in 66.3 and 76.2% of neonates.1 A new dosing regimen derived from a population pharmacokinetic (PK) analysis and using a loading dose, was implemented in our unit.2 We aimed to investigate if the new regimen results in improved vancomycin exposure (target trough 10–15 mg/L).

Methods Clinical data and early (24 h after start) vancomycin therapeutic drug monitoring (TDM) in neonates receiving vancomycin for medical reasons, were retrospectively collected and pooled with 2 historical cohorts [cohort 1 (2011, n=193 observations), dosing based on postmenstrual age (PMA) and pooled with 2 historical cohorts [cohort 1 (2011, n=193 observations), dosing based on PMA and postnatal age (PNA)]. The new regimen was implemented in our unit (target trough 10–15 mg/L). We found no increased risk of spontaneous abortions and major malformation exposure and the risk of spontaneous abortions and the association to major malformation. Data were obtained from the Medical Birth Registry and the National Hospital Registry. All fathers exposed to acitretin were identified by the Danish National Prescription Registry.

Results We identified in total 1,477,252 registered pregnancies with known father identity. Of these 244 pregnancies and 205 children were exposed to paternal acitretin treatment between one year prior to conception to the end of first trimester. The adjusted hazard risk (HR) of spontaneous abortion was 0.71 (95% CI: 0.43–1.17). When analysing exposure three months prior to conception and during first trimester only, the adjusted HR was 0.76 (95% CI:0.38–1.51) and 1.06 (95% CI:0.55–2.04), respectively. As for the association between major malformation and paternal acitretin exposure between one year prior to conception to the end of first trimester the adjusted odds ratio (OR) was 1.15 (95% CI: 0.57–2.34). When stratifying for the period of acitretin exposure the same insignificant trend was detected. In addition, both spontaneous abortions and major malformation were independent of dosage.

Conclusion We found no increased risk of spontaneous abortions or major malformation in pregnancies exposed to paternal acitretin one year before to three months after conception. This was persistent when sub-analysing exposure period and dosage. These data are an important contribute to the sparse evidence suggesting that paternal acitretin exposure during fertility is safe.

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014 PATERNAL ACITRETIN EXPOSURE AND PREGNANCY RISKS
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