Methods This retrospective analysis included a cohort of patients < 30 years (y) on chronic HD treatment since childhood, having received thrice-weekly HD between 2004 and 2016 in outpatient DaVita dialysis centers. Survival while on HD (death from any cause) was investigated using Kaplan-Meier analysis stratified by age at start of HD (0–2, >2–6, >6–12, and >12–18 y), and three mean delivered dialysis dose levels (spKt/V < 1.4, 1.4–1.6, >1.6). Survival curves between subgroups were compared using the Log-rank test.

Results 1773 patients were included in the analysis, among n=34 having started HD at age of 0–2y, n=57 at >2–6y, n=244 at >6–12y, and n=1438 at >12–18y. Median follow-up on HD ranged between 1.5 (>2–6y) to 4.7 years (>6–12y) with maximal follow-up of 23 years. Death while on HD occurred in 1/34, 6/57, 26/244, and 101/1438 patients during recorded follow-up (p=0.075, n.s.). Patients with mean spKt/V < 1.4 had lower survival on HD than those with spKt/V >1.4–1.6 (p=0.019) and those with spKt/V >1.6 (p=0.035), with 10-year survival estimated to 75% (65.2–86.2%) versus 84.5% (78.5–90.9%) and 85.0% (80.8–89.5%), respectively.

Conclusions This is the first study to report long term survival and its relationship with delivered HD dose in patients starting HD in childhood. Our results support targeting spKt/V (urea)>1.4 in children on chronic HD treatment.

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CHARACTERISING THE PHARMACOKINETICS OF PHENOBARBITONE IN NEONATES TO FACILITATE FUTURE INDIVIDUALISED DOSING

¹A Williams*, ²T Donovan, ¹B Charles, ³C Staatz. ¹School of Pharmacy, The University of Queensland; ²Grantley Stable Neonatal Unit, Royal Brisbane and Women's Hospital, Brisbane; ³School of Pharmacy, The University of Queensland, Woollangabba, QLD, Australia

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Background Phenobarbitone is commonly used as a first-line drug in the treatment of neonatal seizures. Previous studies, with small subject numbers, have identified covariates that may influence the pharmacokinetics of phenobarbitone but results have been inconsistent. In particular, oral bioavailability is poorly described with doses reported as being identical for intravenous and oral administration, however, 2 recent studies have reported oral bioavailability of 49% and 59% respectively.^{1,2}

Methods A population pharmacokinetic model was built based on routine therapeutic drug monitoring data from 112 infants at the Royal Brisbane and Women's Hospital Neonatal Intensive Care Unit. Population modelling was performed using NONMEM 7.3 and PsN 4.7 with assistance from R studio and the packages Xpose and VPC. Body weight with

allometric scaling on Clearance (CL) and Volume of Distribution (V) were included *a priori* in the structural model. Covariates tested included age (post-menstrual, gestational and post-natal), Apgar scores, concomitant phenytoin treatment, infection and method of nutrition.

Results A one-compartment model provided an adequate fit to the data. Typical clearance increased with patient post-natal age (PNA) and was best modelled using the equation $CL = 5.1 * WT^{0.75} * (PNA/6.25)^{0.43}$ (mL/h) where weight is in kg, PNA in days and 6.25 is the median post-natal age. Volume of distribution (V) was best modelled using the equation $V = 799 * WT^{1.0}$ (mL). Oral bioavailability (F) was 85%. Between-subject variability was 25% and 30% respectively for CL and V.

Conclusion This study describes the largest population pharmacokinetic model of phenobarbitone developed to date with estimates of CL and V similar to previously published models. Estimated F is higher than previously reported but still lower than the implied F of 100% in most recommended dosing regimens. The model could be used to assist with future individualisation of dosing in this cohort.

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CIRCULATING CONCENTRATIONS OF BROAD-SPECTRUM BETA-LACTAMS IN CHILDREN WITH CANCER: BEWARE OF GLOMERULAR HYPERFILTRATION!

¹P André*, ¹L Diezi, ¹LA Decosterd, ²PA Crisinel, ¹K Dao, ³M Diezi, ²S Asner, ¹T Budin. ¹Service of Clinical Pharmacology; ²Pediatric Infectious Diseases and Vaccinology unit, Service of Pediatrics; ³Pediatric Hemato-Oncology Unit, Service of Pediatrics, University Hospital Center, University of Lausanne, Lausanne, Switzerland

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Background Broad-spectrum beta-lactams such as meropenem (MER) and piperacillin-tazobactam (PIP) are commonly prescribed in children with cancer having febrile neutropenia. They are introduced at intensive dosage, unless decreased renal function calls for dose reduction. Recently, glomerular hyperfiltration (HF) was recognized to be frequent among children with cancer during initial cycles of chemotherapy.¹ We evaluated the impact of HF on therapeutic exposure to MER and PIP.

Methods We retrieved retrospectively all MER and PIP plasma levels measured in children with cancer in our hospital between 2012 and 2018. We compared trough levels with usual therapeutic ranges (derived from reference values of minimum inhibitory concentrations). We classified the children according to plasma creatinine and estimated glomerular filtration rate (Schwartz formula) as either altered-normal (< 160 mL/min/1.73 m²) or increased (i.e. HF, ≥160). Neutropenia was defined as absolute neutrophil count < 500 cells/μL.

Results We collected 120 concentration values (53 MER, 67 PIP) measured in 50 children with cancer. Among them, 74 (62%) had concomitant creatinine values suggestive of HF, and 80 (67%) were neutropenic. Overall, 67% of trough