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Advancing Pediatric Drug Development Using Simcyp PBPK

Case studies for neonate/child dosing, drugs for children's diseases, DDIs for pediatrics, and developing child-specific formulations

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After many years of encouragement and soft incentives, it is now a legal requirement for drug companies to develop medicines for children. Bolstering this regulatory initiative is an extra six months of patent protection provided to companies that develop and provide drugs for pediatric populations. In the US and EU, pediatric study (PSP) or investigation plans (PIP) need to be submitted to the regulators in early drug development, to indicate studies that will be conducted in this population. For drugs not likely to be used by children, deferrals or waivers can be requested.

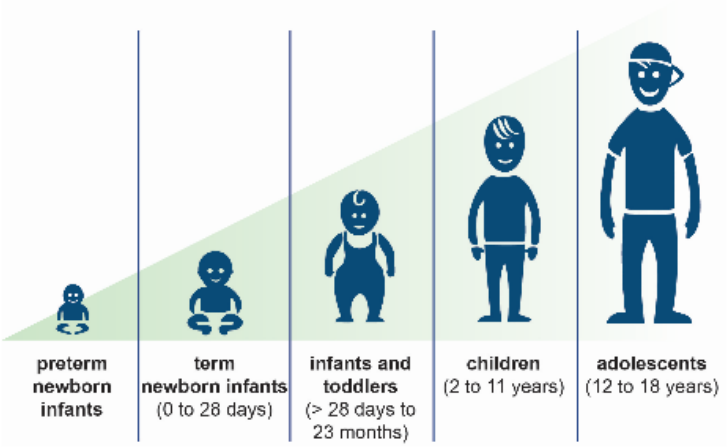
As part of the PSP and PIP, a suitable pediatric dose needs to be established. Dose selection and optimization is one of the major reasons for failures in pediatric drug development trials. While allometric scaling may be suitable in some cases for dose prediction, more mechanistic models are often needed to account for the complex interaction between the developmental physiological, biochemical and drug related factors in children. Model-informed drug development (MIDD), specifically physiologically based pharmacokinetics (PBPK) is an invaluable and proven tool that can help avoid unnecessary pediatric studies, ensure clinical trial dose selection is based on science and minimize clinical trial enrollment, while delivering relevant treatment data.

UNDERSTANDING DRUG EFFECTS IN CHILDREN

Children are not small adults, and not all children are the same. Children may need different doses of medicine, different sizes of devices, or different types of therapy at each stage of growth. Growth, maturation and environmental factors, along with disease and genetic factors directly affect drug performance in children, especially in those less than two years old.

For example, a premature baby's body is composed of 80% water and 5% fat, while at one year old that composition changes to 61% water and 20% fat. Factors such as kidney function, brain volume, blood flow, and absorption, distribution, metabolism, and excretion (ADME) are non-linear during the neonate to small child period. Finally, organ maturation has a significant effect on drug metabolism and excretion. Children have relatively larger livers, lower glomerular filtration rates, and less renal tubular absorption and excretion compared to adults. This distinct physiology means that traditional approaches such as allometry risk greatly over or under predicting drug clearance in pediatric patients, especially those that are less than one year old.

In short, developing and prescribing drugs to children is a scientific and logistical challenge.



Picture, courtesy of US NIH

Figure 1.

Children are not small adults, and not all children are the same.

CHALLENGES ABOUND IN PEDIATRIC DRUG DEVELOPMENT

The US FDA and other regulators have been encouraging pediatric drug development through legislation and guidance for almost 50 years. There has been progress, but the ethical, logistical and physiological issues remain significant, including:

- Enrollment and optimization of clinical trials
- Trial protocols for children, such as sampling frequency and placebo effect
- First-in-human dose prediction
- Impact of ontogeny and other age-dependent factors
- Disease-related changes
- Biomarkers and endpoints

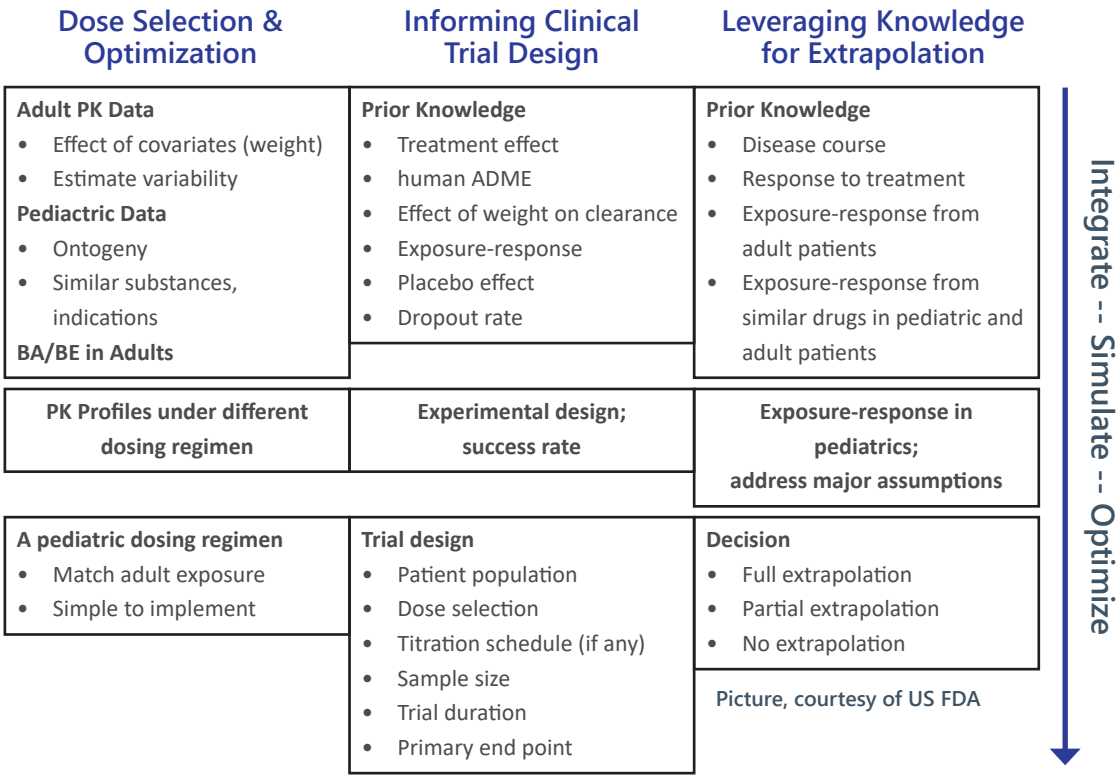
Pediatric drug development cannot be defined as one process; it is an expansive endeavor with much variation, especially for dosing recommendations. According to the regulatory guidance, neonates are from birth to one month, infants are from 1 month to less than 2 years of age, children are from two to eleven years old, and adolescents are from twelve to eighteen years old.

Pediatric drug–drug interactions (DDIs) can be life threatening, and a plan for assessing the potential interactions should form part of every pediatric drug development program, according to the FDA. DDI studies are rarely performed in this population for ethical and practical reasons. This is where MIDD, in particular PBPK modeling can be invaluable, for assessing the potentially age-dependent DDI liability across the pediatric groups.

FDA recently published a suggested “Integrate-Simulate-Optimize” workflow for applying MIDD (Figure 2). The understanding of the pathophysiology or the expression of the disease is the main driver for leveraging existing knowledge, as well as extrapolation of information from other populations (adults or other pediatric populations).

Figure 2.

Suggested workflow of applying MIDD in pediatric drug development: bioavailability; bioequivalence; pharmacokinetic, pharmacodynamic.



Picture, courtesy of US FDA

PBPK IS A POWERFUL TOOL FOR PEDIATRIC DRUG DEVELOPMENT

PBPK modeling enables extrapolation of relevant endpoints from in vitro and in vivo data and the answering of myriad 'what if' drug development questions. Simcyp PBPK models describe the drug concentration in different organs, behavior across different body tissues, and thus help to inform clinical trial design, first-in-human dosing, formulation design, dose differentiation for special populations, and predictions related to potential DDIs.

PBPK is increasingly applied in pediatric drug development, as evidenced by FDA's data (figures 3, 4). Used to propose initial dosing recommendations for clinical trials in the investigational new drug stage, pediatric PBPK modeling is a powerful tool in utilizing ontogeny data to predict drug PK in neonates and infants where ontogeny is an important determinant of a drug's ADME process. It can also be applied to investigate the mechanism that may cause different absorption behaviors in pediatric as compared to adult subjects. Even though published cases are slow to publication, both the FDA and EMA endorse the use of PBPK modeling for investigations in pediatric populations during drug development.

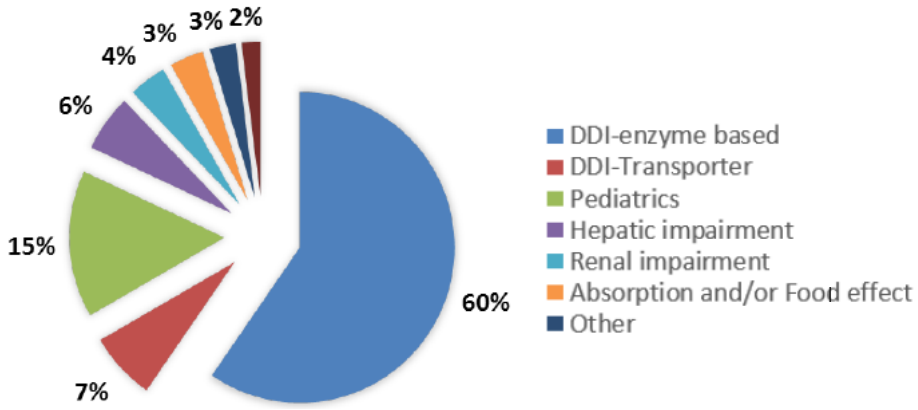


Figure 3.

FDA data on regulatory submissions using PBPK, through 2017

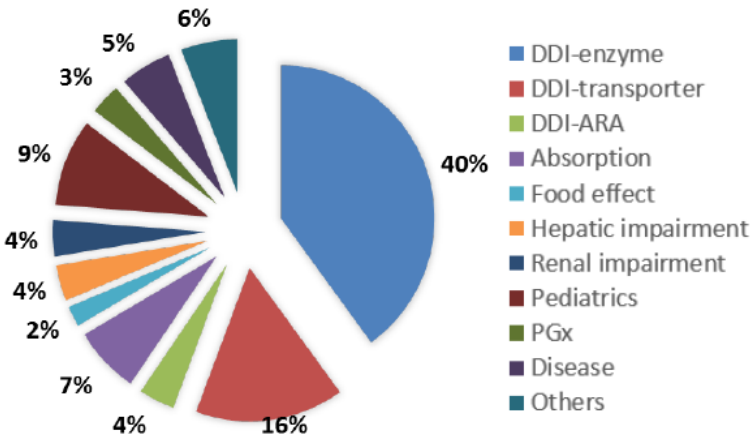


Figure 4.

FDA data on regulatory submissions using PBPK, 2018-19

Simcyp Pediatric™ is a module within the Simcyp Simulator that allows for the modeling of pharmacokinetic behavior in neonates, infants and children. This provides valuable information relevant to dosing decisions, analysis of DDI and other safety issues, design and formulation of drugs for children, and the design of pediatric clinical studies to minimize the number of required subjects.

With Simcyp Pediatric, researchers can:

- Determine and optimize dose selection for children, from neonates to age 2, 2-6 years, 6-12 years and adolescents;
- Predict pharmacokinetics based on in vitro drug data or from adult in vivo data by retrograde modeling;
- Quantify potential DDIs for any age range;
- Assess the impact of formulation changes for pediatric dosing;
- Simulate pharmacokinetic variability over any pediatric age range;
- Inform clinical trial design for pediatrics.

CASE STUDIES DEMONSTRATE SIMCYP PEDIATRIC APPLICATIONS

The Simcyp Simulator includes a full PBPK model together with extensive libraries on demographics, developmental physiology and the ontogeny of drug elimination pathways. It links in vitro data to in vivo ADME and pharmacokinetic/pharmacodynamic (PK/PD) outcomes to help explore potential clinical scenarios and support decision-making in drug development.

The adult and pediatric (neonate to age 2) versions of the Simcyp Simulator (Simcyp Pediatric) have been used in the seven applications in this paper, categorized as:

- Drugs developed specifically for children diseases or children's conditions as varied from adults;
- Dosing in children. In infants and neonates, PBPK models incorporating pediatric ontogeny can more accurately predict the drug PK as compared to allometry, when there is a sufficient understanding of the ADME process of the drug and the ontogeny is well-characterized for those processes;
- Formulation/bridging for children. Liquid versus oral, extended release, transdermal delivery, topicals and other options have been achieved via PBPK bridging analyses;
- DDI in children. Aligned with organ development, the DDI liability may vary widely from the adult data.

Case Study #1 – Regulatory Impact: Deflazacort—Rare Children's Disease

Duchenne Muscular Dystrophy (DMD) is a severe type of muscular dystrophy that primarily affects boys. Muscle weakness usually begins around the age of four, and worsens quickly. Muscle loss typically occurs first in the thighs and pelvis followed by the arms, which can result in trouble standing up. Scoliosis is also common. Females with a single copy of the defective gene may show mild symptoms.

Deflazacort (Emflaza®) was fast-tracked, given orphan status and approved by the US FDA in February 2017 for patients 5 years and older. Emflaza is a corticosteroid that works by decreasing inflammation and reducing the activity of the immune system. It is also a pro-drug, which undergoes conversion in the plasma by esterases, taken to the liver and metabolized by CYP3A4 enzymes. Not only did this raise a concern about the drug's DDI liability, but DMD patients typically take multiple other medicines to support the heart, breathing muscles, bone health, gastrointestinal symptoms, hormone levels, common antibiotics, and to manage pain.

Simcyp Pediatric Simulator was used to model exposure in children and adolescents, simulate DDI and provide dose recommendations. Dose adjustments for moderate to severe CYP3A4 inhibitors and inducers were determined using the PBPK modeling as shown in the label below.

FDA writes in a recently published paper, "*Approximately 60% of the intended uses of PBPK in regulatory decision making are related to drug-drug interaction. The PBPK predictions for the drug drug interaction in children and adolescents, such as the interaction with concomitant administration of CYP3A modulators, have been accepted as supportive evidence for the proposed dosing recommendations on the deflazacort label.*"

Moderate or Strong CYP3A4 Inhibitors:
The active metabolite of deflazacort, 21-desDFZ, is a substrate of CYP3A4 [*see Clinical Pharmacology (12.3)*]. Co-administration of deflazacort with clarithromycin, a strong CYP3A4 inhibitor, increased total exposure to 21-desDFZ by about 3-fold. Therefore, give one third the recommended dosage of EMFLAZA when moderate or strong CYP3A4 inhibitors (e.g., clarithromycin, fluconazole, diltiazem, verapamil, grapefruit juice) are used concomitantly with EMFLAZA *[see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)]*.

Moderate or Strong CYP3A4 Inducers:
Co-administration of deflazacort with rifampin, a strong CYP3A4 inducer, significantly decreased the exposure of 21-desDFZ. Avoid concomitant use of strong (e.g., efavirenz) or moderate (e.g., carbamazepine, phenytoin) CYP3A4 inducers with EMFLAZA *[see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)]*.

Figure 5.

Language from the drug label for Emflaza as determined by Simcyp PBPK simulations

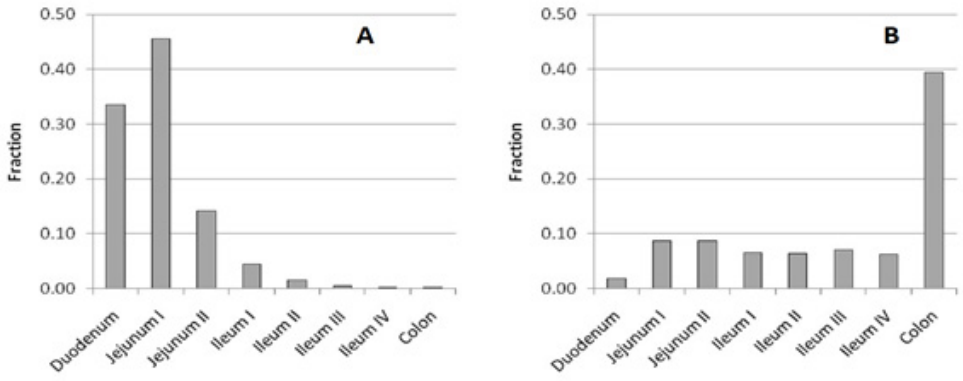
Case Study #2 – Regulatory Impact: Quetiapine—Formulation Bridging for Children

Early onset schizophrenia and bipolar disorder can occur in children as young as 12. As with many mental illnesses, adherence to drug regimen is a challenge, especially for teenagers. Quetiapine is an atypical antipsychotic for the treatment of schizophrenia, bipolar depression, bipolar mania that works by helping to restore the balance of certain natural substances (neurotransmitters) in the brain.

Originally approved as an immediate release (IR) formulation, given twice/day, changing the formulation to a daily extended release (XR) delivery to improve patient adherence was undertaken. The Simcyp ADAM module was used to compare exposure between the two formulations. The modeling showed differences in regional distribution, with most of drug in the IR formulation being absorbed in the duodenum and jejunim, while the XR formulation releasing further down the intestine and being absorbed in the colon (Figure 6). Although not relevant for quetiapine, using a modified release formulation, that avoids release in the proximal intestine is an approach that can be used for drugs with low bioavailability due to significant intestinal metabolism.

Figure 6.

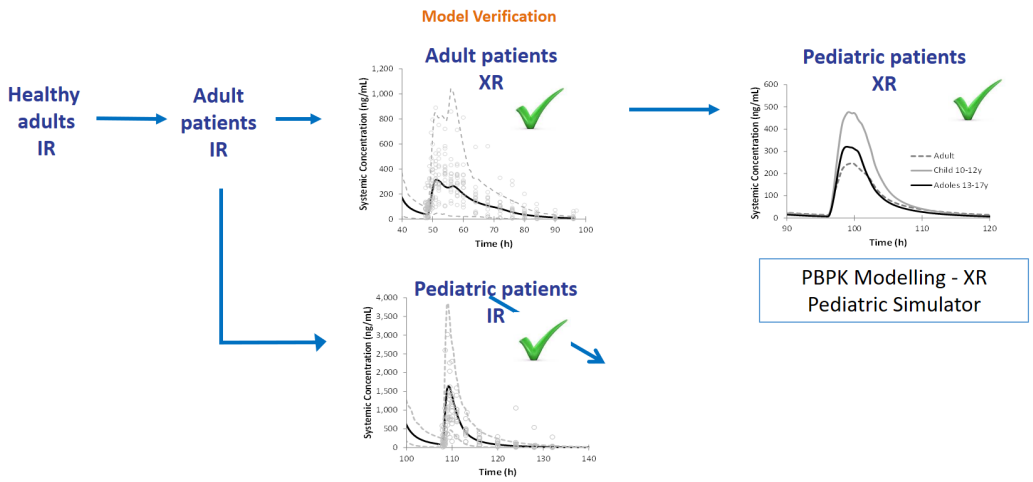
Simcyp's ADAM module shows the regional distribution of the predicted fraction of dose across the GI tract in IR (A) and XR (B) formulations of quetiapine



PBPK models using the Simcyp Simulator employing in vitro ADME and physicochemical data, clinical PK data of quetiapine IR/XR in adults and clinical PK data of quetiapine IR in children were developed. These models predicted the effects of CYP3A4 inhibition and induction on the PK of quetiapine, the PK profile of quetiapine IR in children and adults, and the PK profile of quetiapine XR in adults (Figure 7). Most important, the PBPK model predicted that children and adolescents are likely to achieve a similar exposure following administration of either the XR formulation once daily or the IR formulation twice daily at similar total daily doses. This was a high impact use of pediatric PBPK modelling in that a clinical study was avoided and approval was given for the pediatric labelling of Quetiapine XR.

Figure 7.

Strategy for application of Simcyp Pediatric module to assess differences in exposure after dosing of XR and IR formulations



Case Study #3: Voxelotor—Dosing for Children in a Complex Disease

Sickle Cell Disease (SCD) is a group of inherited red blood cell disorders in which there are not enough healthy red blood cells to carry oxygen throughout the body. In SCD, the red blood are shaped like sickles or crescent moons versus round blood cells. These cells can easily get stuck, and tend to die early, causing a shortage of red blood cells.

In November 2019, the US FDA granted accelerated approval for Voxelotor (Oxbryta®) tablets for the treatment of SCD in adults and children 12 years of age and older. A small molecule that binds to hemoglobin and increases the protein's affinity for oxygen, Voxelotor also inhibits hemoglobin polymerization, thus preventing red blood cells from becoming deformed.

The Simcyp Simulator was used to build and verify a model in healthy adults and integrate the disease-related factors (Figure 8). By incorporating binding changes and changes in hematocrit, we are able to capture that significant change in blood-plasma ratio and recover exposure we would expect to see in sickle cell adults. Next, we integrated age-related changes based data in children and adolescents with SCD.

In pediatrics, the physiological changes are significant. As this drug is highly protein bound, any change in ontogeny for albumin will have an impact on the binding of the drug, as well as hematocrit changes that will impact blood exposure of the drug. The simulations validated the dosing in older children and provide dosing recommendations for children 9 months to 12 years old. Further clinical studies and PBPK simulations are ongoing.

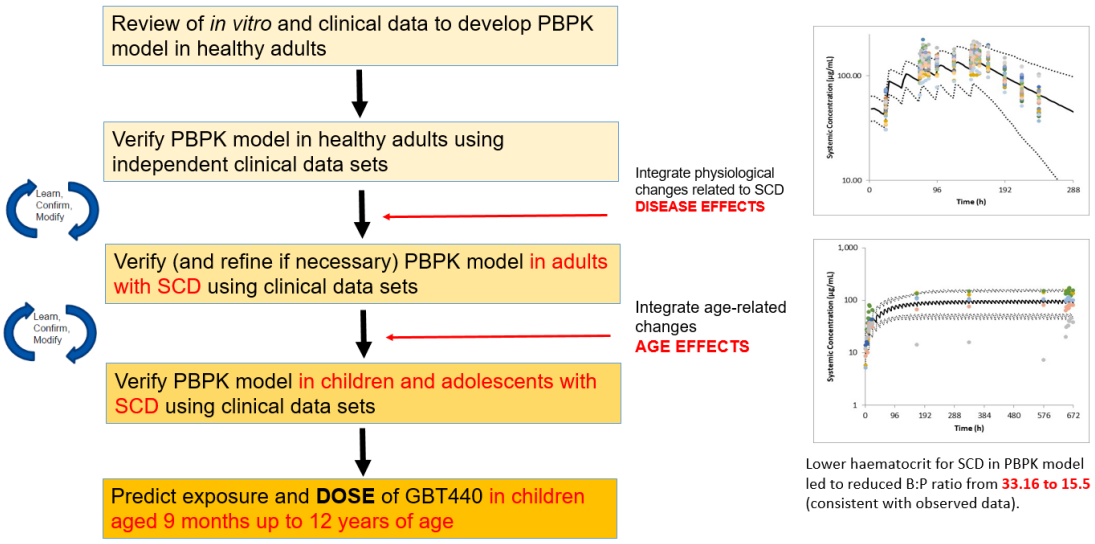


Figure 8.

Strategy to predict appropriate dose of Voxelotor in children with sickle cell disease

Case Study #4: Radiprodil—PBPK-PD Receptor Occupancy Model for Neonates

Infantile spasm syndrome, also called West syndrome is a rare type of epilepsy that affects babies. There is no cure for the disease and the standard of care has limited success in treating symptoms. The drug Radiprodil, originally developed for chronic neuropathic pain conditions was assessed as a potential treatment. Radiprodil is a selective allosteric modulator of the NR2B N-methyl-D-aspartate receptor GluN2B-NMDA.

Alongside clinical trials, a Radiprodil PBPK-PD model was built based on in vitro data in the Simcyp Simulator. The model was expanded to incorporate our understanding of the developmental physiology and ontogeny of elimination, to predict PK in the age-appropriate pediatric population for this disease (2 to 14 months). We then linked the PBPK model to a receptor occupancy (RO) PD model in the Simcyp Simulator.

In vitro experiment based on hepatocyte data was used to further assess our understanding of the ontogeny, first for CYP1A2/acetaminophen and then for Radiprodil. Based on those results, which strongly suggested a lack of ontogeny effect, a dosing decision tree was developed (Figure 9), recommending a low RO and low dose escalation approach. To our knowledge, this is the first time a PBPK model linked to RO has been used to guide dose selection and escalation in the live phase of a pediatric clinical trial.

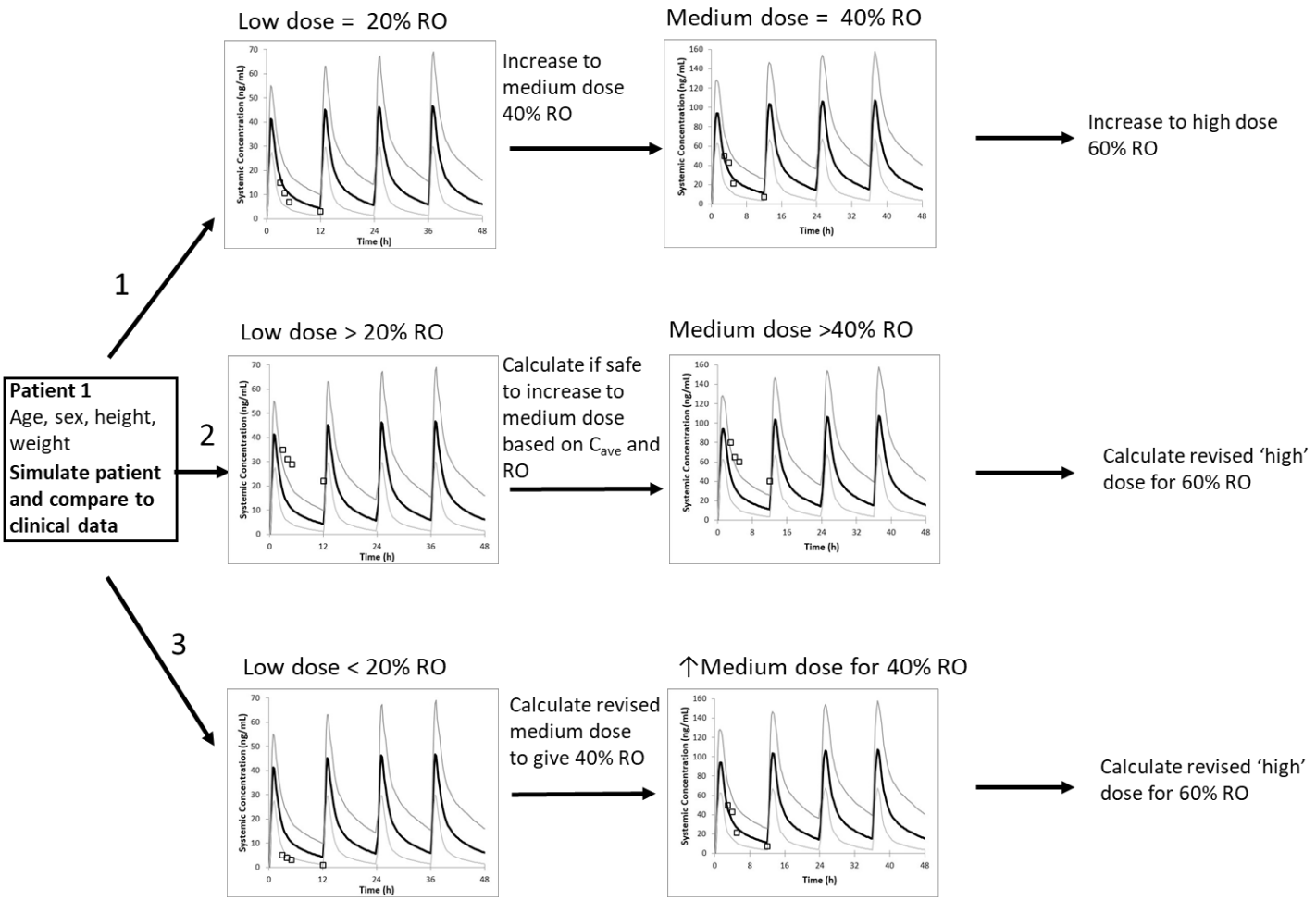
Because the disease is rare and potentially life threatening, there was the need for trial doses to be efficacious from the start, while paying attention to limiting the upper level of RO to avoid unwanted potential side effects associated with high levels of NMDA receptor antagonism. In this case, the use of a

PBPK-PD model allowed a potentially more robust dosing strategy to be developed compared to simple allometry alone, which tends to overestimate doses in neonates and infants. The final Simcyp model was used to determine initial doses with age and to guide dose escalation for three individual subjects in the live phase of a clinical trial, predicted and observed data was in close agreement.

Figure on next page

Figure 9.

Decision tree for Radiprodil dose escalation in clinical trial



Case Study #5: Everolimus—Simcyp's Age Defining Feature Facilitates Dosing in Neonates

Tuberous sclerosis complex (TSC) is a rare genetic disorder resulting in benign tumours in various organs, including the brain, eyes, heart, kidney, skin and lungs. The majority of patients with TSC develop epilepsy, and approximately two-thirds become refractory to antiepileptic drugs (AEDs). Everolimus (Afinitor®) was recently approved as adjunctive therapy for TSC-associated partial seizures in ages 2 and older. Unlike many other therapies for treating TSC-associated seizures, Everolimus addresses the underlying pathophysiology of TSC.

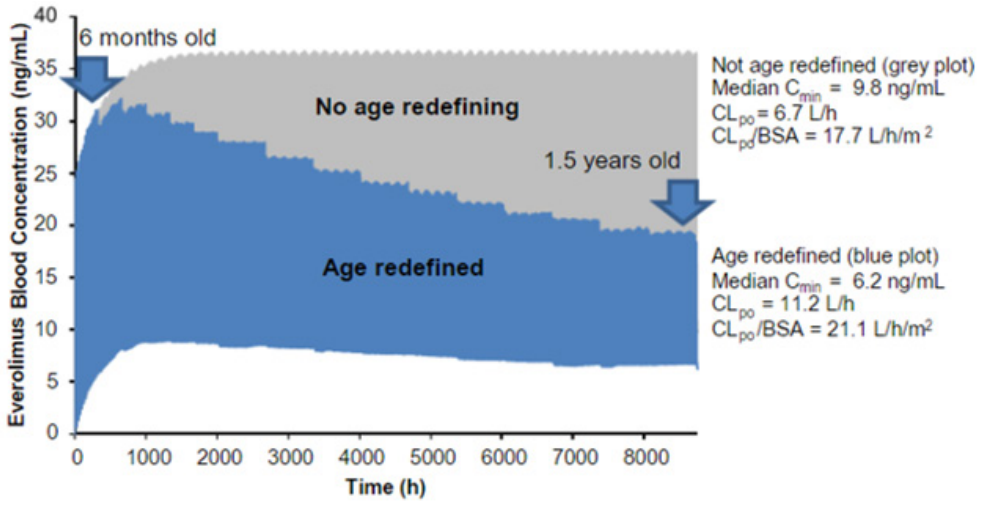
As TSC-associated seizures can also affect children aged between 6 months and 2 years, a modeling and simulation approach that incorporated Population PK, Population PD and PBPK was used to extrapolate exposure. The PBPK model, built and qualified in the Simcyp Simulator, predicted Everolimus exposure in 200 patients, ages 6 months to 1 year. The PBPK data was incorporated into a Population PD model to simulate the reduction in seizure frequency.

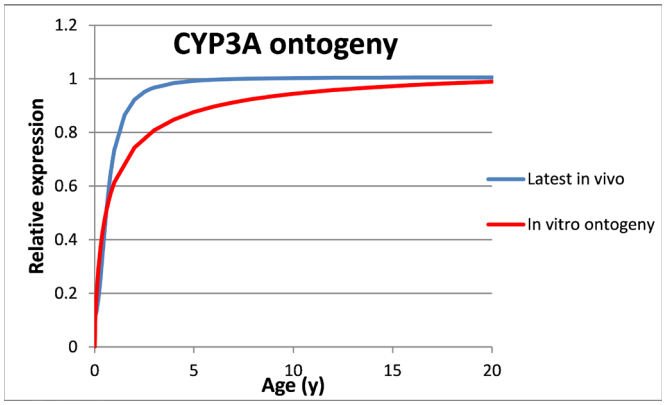
As certain enzymes, specifically CYP3A4, are ontogeny-specific, the unique 'age redefining feature' in the Simcyp Pediatric Simulator was used for this program. Everolimus is both a CYP3A4 and PgP substrate. This feature accounts for the time variance in very young subjects by simulating the aging elements over time (physical growth, non-linear organ development, age factors, blood flows, ontogeny kicking in). In short, Simcyp Pediatric can simulate the combination of changes resulting from both physiology and ontogeny factors as children age.

Final dosing determination required the prediction of the Cmin to stay within 5–15ng/mL for efficacy. By using the age defining feature in Simcyp, the model showed the dose recommendation of 6 mg/m2 is expected to be effective over the target range of 6 months to 2 years in both the short term (12 weeks of exposure) and long term (up to 2 years of exposure).

Figure 10,11.

PBPK predictions and ontogeny impacts using Simcyp's age redefining feature





Case Study #6 – Guanfacine – DDI liability in children

Attention deficit/hyperactivity disorder (ADHD) is a common childhood diagnosis. The average age of diagnosis for ADHD is 8 years old and 10 years for ADD. Guanfacine (Intuniv® XR) extended release (GXR) is an orally administered, selective alpha2A-adrenergic receptor agonist, non-stimulant treatment for children and adolescents with ADHD.

Guanfacine is primarily metabolized by the CYP3A4 enzyme, thus, it was important to evaluate the DDI liability perpetrated by strong inhibitors and inducers of CYP3A4. Using data from clinical PK studies in which GXR was administered as a monotherapy, or co-administered with strong CYP3A4 inhibitors or inducers, PBPK modeling using the Simcyp Simulator was employed for DDI evaluation. Based on these predictions, dosing recommendations for GXR were approved by the US FDA without the need to conduct further clinical studies.

The dosing recommendations on the label are to (1) decrease GXR to 50% of the usual target dose when it is co-administered with strong or moderate CYP3A4 inhibitors and (2) consider titrating GXR up to double the usual target dosage over 1–2 weeks when it is co-administered with strong or moderate CYP3A4 inducers. As pharmacological treatment of ADHD may be needed for extended periods, healthcare providers should periodically re-evaluate the long-term use of GXR and adjust weight-based dosage as needed. The majority of children and adolescents reach optimal doses in the 0.05-0.12 mg/kg/day range. Doses above 4 mg/day have not been evaluated in children (ages 6-12 years) and above 7 mg/day have not been evaluated in adolescents (ages 13-17 years).

Table 1: Recommended Target Dose Range for Therapy with INTUNIV®

Weight	Target dose range (0.05 - 0.12 mg/kg/day)
25-33.9 kg	2-3 mg/day
34-41.4 kg	2-4 mg/day
41.5-49.4 kg	3-5 mg/day
49.5-58.4 kg	3-6 mg/day
58.5-91 kg	4-7 mg/day
>91 kg	5-7 mg/day

Doses above 4 mg/day have not been evaluated in children (ages 6-12 years) and doses above 7 mg/day have not been evaluated in adolescents (ages 13-17 years)

Figure 12.

Dose selection for Guanfacine based on child's body weight

Case Study #7 – Trikafta – Combination therapy for Cystic Fibrosis

Cystic fibrosis is an inherited condition that causes sticky mucus to build up in the lungs and digestive system. This causes lung infections and problems with digesting food. Symptoms usually start in early childhood and vary from child to child, but the condition gets slowly worse over time, with the lungs and digestive system becoming increasingly damaged.

In 2012, FDA approved Ivacaftor (Kalydeco®) for treatment of the underlying cause of CF in a small subset of the patient population. In 2015, a combination treatment of Ivacaftor and Lumacaftor (Orkambi®), followed by a combination of Ivacaftor and Texacaftor (Symdeko®) in 2018. In 2019, the first triple combination of Elexacaftor/Texacaftor/Ivacaftor (Trikafta®) for patients 12 and up, accounting for about 90% of patients with CF was approved.

Many CF patients that take modulator regimens of the above dual combinations will need to transition to the triple combination. An assessment of whether adequate exposures to achieve clinical efficacy are maintained during this transition was needed, as this has not been directly addressed in clinical trials. PBPK modeling using Simcyp was used for this analysis, specifically to understand the CYP3A4 during the cystic fibrosis transmembrane conductance regulator process. Individual models for each drug were developed, followed by simulations of various combination to assess exposure.

The PBPK modeling demonstrated that immediate transfer from the three dual combinations to the triple combination resulted in sustained CFTR in patients 12 years and higher. Clinical trials on younger patients are ongoing.

Figure 13.

Dose adjustments for combination therapy

2.3 Dose Adjustment for Patients Taking Drugs that are CYP3A Inhibitors

Table 2 describes the recommended dosage modification for TRIKAFTA when co-administered with strong (e.g., ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, and clarithromycin) or moderate (e.g., fluconazole, erythromycin) CYP3A inhibitors. Avoid food or drink containing grapefruit during TRIKAFTA treatment *[see Warnings and Precautions (5.3), Drug Interactions (7.2), Clinical Pharmacology (12.3), and Patient Counseling Information (17)]*.

Table 2: Dosing Schedule for Concomitant Use of TRIKAFTA with Moderate and Strong CYP3A Inhibitors

Moderate CYP3A Inhibitors

	Day 1	Day 2	Day 3	Day 4*
Morning Dose	Two elexacaftor/tezacaftor/ivacaftor tablets	One ivacaftor tablet	Two elexacaftor/tezacaftor/ivacaftor tablets	One ivacaftor tablet
Evening Dose^	No dose			

* Continue dosing with two elexacaftor/tezacaftor/ivacaftor tablets and one ivacaftor tablet on alternate days.
^ The evening dose of ivacaftor should not be taken.

Strong CYP3A Inhibitors

	Day 1	Day 2	Day 3	Day 4#
Morning Dose	Two elexacaftor/tezacaftor/ivacaftor tablets	No dose	No dose	Two elexacaftor/tezacaftor/ivacaftor tablets
Evening Dose^	No dose			

Continue dosing with two elexacaftor/tezacaftor/ivacaftor tablets twice a week, approximately 3 to 4 days apart.
^ The evening dose of ivacaftor tablet should not be taken.

SUMMARY

One size does not fit all when it comes to pediatric drug development. The variation in disease type, drug characteristics, age and maturity of patients, ability to conduct clinical trials, and formulation/dosing options must drive the process. Fortunately, drug developers and regulators have recognized that while challenging, innovative approaches can greatly facilitate our ability to overcome the many ethical, logistical and physiological challenges inherent in pediatric drug development. PBPK is a proven approach to respond to this opportunity and the Simcyp Simulator has played a pivotal role in guiding that progress.

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Case Study Label Documentation

- **Emflaza:**
  https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/208684s000,208685s000lbl.pdf
- **Oxbryta:**
  https://www.accessdata.fda.gov/drugsatfda_docs/nda/2019/213137Orig1s000Multidiscipline.pdf
- **Guanfacine:**
  https://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022037s009lbl.pdf
- **Trikafta:**
  https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212273s000lbl.pdf

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Simcyp

Dr Karen Rowland Yeo is Senior Vice-President, Client & Regulatory Strategy at Certara UK Limited's Simcyp Division. Prior to this, she was the Head of PBPK Consultancy Services at Simcyp where she led a team of scientists engaged in Consultancy projects relating to the application of physiologically based pharmacokinetic (PBPK) modeling in the drug development process. This involved putting a framework in place for developing models used for both internal decision-making and regulatory submissions. Her work ranged across most therapeutic areas and included the development of models used for dosing of special populations, including organ impairment. She has worked directly with global regulators to gain acceptance of PBPK models, increasingly raising the bar in innovation and quality.

She received her BSc Honours degree in Physics at the University of Natal in South Africa in 1989 and her PhD in Drug Metabolism from the University of Sheffield in 1995. This was followed by a two-year position as a Postdoctoral Leukaemia Research Fund Fellow in the area of Childhood Acute Lymphoblastoid Leukaemia and then a 5-year lectureship in the Department of Clinical Pharmacology & Therapeutics at the University of Sheffield. Karen has been the author/co-author of more than 80 peer-reviewed articles, and is a frequently called as an invited speaker and session organiser/moderator at many international meetings in the field.

Trevor Johnson, PhD
Principal Scientist

Trevor Johnson is Principal Scientist at Certara UK Limited's Simcyp Division. He obtained his PhD in Paediatric Clinical Pharmacology from the University of Sheffield. Following a post doc in population pharmacokinetics he then joined the Simcyp team in 2003 as Senior Scientist responsible for specific populations (disease models, ethnicity and paediatrics). His current area of research focuses on development and clinical/ regulatory application of PBPK models particularly in relation to paediatric medicine. He has over 75 research publications and 7 book contributions in the areas of pharmacokinetics, drug metabolism, paediatric drug therapy and hospital Pharmacy.

About Certara

At Certara, we accelerate medicines to patients, partnering with life science innovators. Together we advance modern drug development with biosimulation, regulatory science, and market access solutions.

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