Invention ID:	**D21-0030**
Title:	**Model-informed sirolimus precision dosing for the Treatment of Vascular Anomalies.**
Technology ID:	**2021-0608**
Submitted By:	**Matt Wortman**
Original Submitted Date:	**6/28/2021**
Stage:	**Approved**
Type:	**Invention Disclosure (with Proof of Concept)**
Updated Date:	**6/28/2021**
Last Submitted Date:	**6/28/2021**
Status:	**3. Disclosure Accepted**

Description

This invention is (category)
List of categories

Software

Short Description
Please provide 3-5 sentences to describe your innovation. Please attach any figures, legends, or additional supporting data in the documents section below.

Background: Sirolimus has recently been shown to be efficacious and tolerable in pediatric patients with complicated vascular anomalies. Nevertheless, dosing information remains very limited especially for neonates and infants. The purpose of this study was to develop an age appropriate sirolimus starting dosing regimen based on the developmental changes in drug elimination capacity using data collected in neonates and infants.

Procedure: A recently developed sirolimus maturation model [Emoto et al. CPT Pharmacometrics Syst Pharmacol, 2016] was used to simulate clearance estimates using realistic age and weight covariates for age cohorts aged 0–24 months. Next, predose concentrations at steady state were generated for each age cohort of neonates and infants. Dose requirements to attain predefined target trough concentration ranges (10–15 and 5–10 ng/ml) were simulated across the different age groups. Starting doses were chosen to maximize the likelihood of achieving sirolimus-targeted concentrations.

Results: The trajectory of simulated sirolimus clearances increased with age and was in agreement with the previous findings in the Phase 2 study. The proposed dosing regimens covered eight age cohorts and resulted in target attainment of more than 75–95% across selected regimens.

Conclusions: This study identified age-appropriate sirolimus dosing regimens for neonates and infants. The algorithm in combination with therapeutic drug management will facilitate sirolimus precision dosing in young children with vascular anomalies. A prospective evaluation is being planned.

Inventors

Inventors

First Name	MI	Last Name	Email	Significance	Contribution	Role Type	Working For Company	Working For Department
Alexander	A	Vinks	sander.vinks@cchmc.org	1	0.00 %		Cincinnati Children's Hospital Medical Center	Clinical Pharmacology
Denise		Adams	Denise.Adams@cchmc.org	2	0.00 %		Cincinnati Children's Hospital Medical Center	Hematology/Oncology

Innovation Funding Applicants

Is this the result of an Innovation Fund?

No

Public Discl.

Have there been any abstracts, posters, presentations or publications (online or in print)? (Please attach if possible)

Yes

If previous public disclosure, enter the date

12/28/2016

Non-Inventor Publication Co-Authors
If co-authors on the above publication did not contribute to the invention as described, please list the non-inventors here. (Co-inventors will be listed below under "Inventors" section)

Tomoyuki Mizuno, Tsuyoshi Fukuda, Chie Emoto,
Paula S. Mobberley-Schuman, Adrienne M. Hammill

Description

Novel and unusual features
Please enter a short description of the expected novel and useful features.

A method for creating a patient-specific precision dosing plan to optimize therapeutic response while minimizing side effects.

Funding

Is there federal funding tied to this technology ? (REQUIRED FIELD)

No

If federally funded give a short description of what the funds were used for. IF NO FUNDING PUT N/A. (REQUIRED FIELD)

R01FD003712 was used by can't find any info on it.

3rd Party IP Assessment

Were 3rd Party Materials Utilized in the invention? (REQUIRED FIELD)
Please let us know if you used any 3rd Party Materials in the invention.

No

"Please indicate whether this invention incorporates or used any materials received or acquired from outside your lab or immediate collaborators. This could include plasmids, mouse models, images, text, open-source software, etc." (REQUIRED FIELD)

Yes

If yes, please describe the materials and their source?

Pfizer

Were all inventors employees of CHMC at the time of invention?

Yes, All Inventors are CHMC Employees

Is this an improvement or modification to a previously developed research tool ? (i.e. cell line, mouse model, software) (REQUIRED FIELD)

No

Is this an improvement or modification on a previously disclosed technology? (REQUIRED FIELD)

No

Dual appointments

Do you have a lab at/or are employed by a non-CCHMC institution? (REQUIRED FIELD)

No

Documents

Documents

File Name	Created By	Date Created
Developmental pharmacokinetics of sirolimus- Implications for precision dosing in neonates and infants with complicated vascular anomalies.pdf	Matt Wortman	6/28/2021

Technology

Technology

Tech ID	Title	Manager	Status	Disclosure Date	Status Date
2021-0608	Model-informed sirolimus precision dosing for the Treatment of Vascular Anomalies.	Justin Levy		6/28/2021	

Patents

Agreements

Remarks

Remarks

By	Comment	Date Added
Matt Wortman	Grant info in paper acknowledgements	6/28/2021

Alexander A Vinks (0.00 %) Date

Denise Adams (0.00 %) Date

Witness Signature Date

Witness Signature Date