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Pragmatic Dosing Recommendations of Rifapentine-containing Regimens for Latent Tuberculosis Infection

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BACKGROUND: Rifapentine-containing short-course regimens for latent tuberculosis infection are not optimized in children and adults.

GOALS
- Evidence-driven optimization of P dosing in adults for 1HP and 3HP regimens
- Align H and P weight bands for child dosing of 3HP with current formulations

METHODS
1. Rifapentine population pharmacokinetic model was built from 9 clinical studies (n=863 adults). The effect of weight, HIV, food, and others were evaluated
2. Pharmacokinetic simulations for P-containing regimens were performed with developed model (P, adults) and published models from literature (H, adults[1]; P, child[2]; H, child[3])
3. Optimized doses were determined based on matching child to adult exposures and adults to the typical adult

RESULTS
- Weight-based dosing of P results in low exposure in low weight individuals
- HIV+ adults require 30% higher doses to achieve equal exposure as HIV-
- Aligned weight bands in children delivered equal exposure to adults

IMPACT: 3HP dosing can be simplified to improve implementation without compromising efficacy

REFERENCES: (1) Wilkins et al. (2011) pmid 21320152; (2) Weiner et al. (2014) pmid 2662522366; (3) Guiatrennec et al. (2018) pmid 29247506

The revised dosing algorithm is pragmatic and simplifies 3HP dosing for adults and children

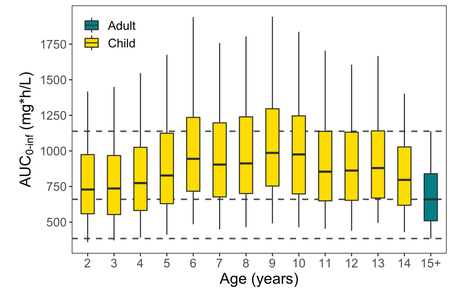
	Rifapentine (P)		Isoniazid (H)	
	Number of tablets	Dose	Number of tablets	Dose
Children aged 2-14 years:				
10-15 kg	2	300 mg	3	300 mg
16-23 kg	3	450 mg	5	500 mg
24-30 kg	4	600 mg	6	600 mg
≥31 kg	5	750 mg	7	700 mg
Adults and children 15 years and older:				
<50 kg	6	900 mg	2	600 mg
≥ 50 kg	6	900 mg	3	900 mg

Tablet sizes are 150 mg (P) and 100 mg (H, child) or 300 mg (H, adult).

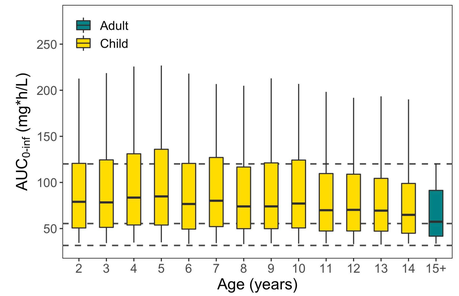
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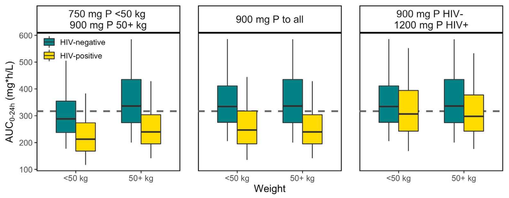
Rifapentine exposure with revised **3HP** dosing



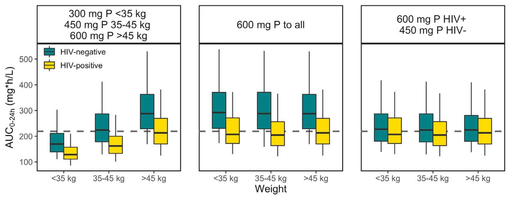
Isoniazid exposure with revised **3HP** dosing



Simulated **adult** rifapentine exposure with **3HP**



Simulated **adult** rifapentine exposure with **1HP**



Adult rifapentine population pharmacokinetic model

