

Association of anti-tuberculosis drugs serum concentrations with drug-related adverse events in TB/HIV co-infected patients in Uganda

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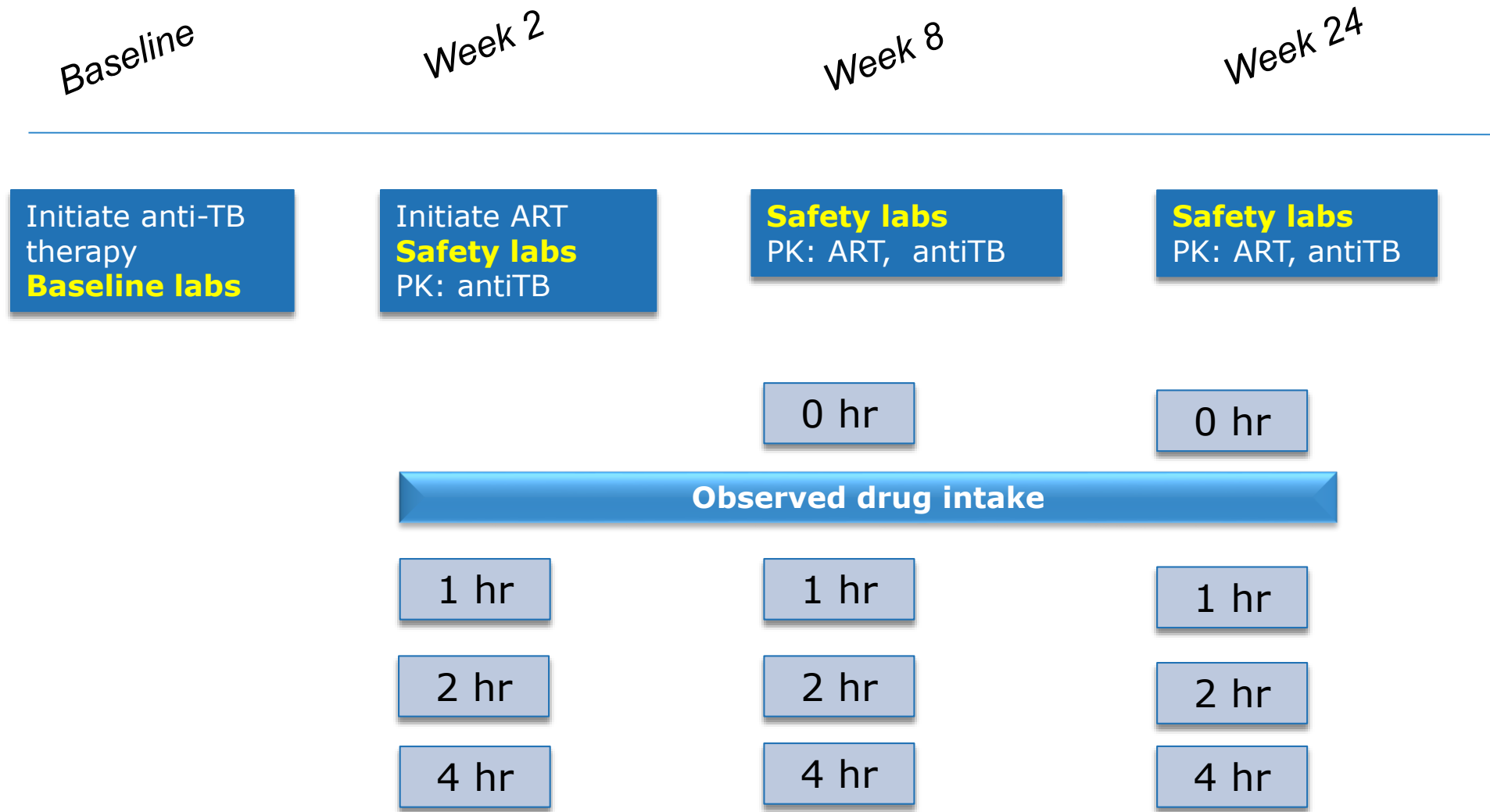
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Investing In The Future – Impacting Real Lives



Anti-TB Drugs and Toxicities

- Antituberculosis (Anti-TB) drugs are generally well tolerated
- Side effects may occur (mild, mod, severe, fatal)
- Implications on adherence, treatment interruption and treatment outcome
(Lorent N et al, PloS one 2011, Smith C et al, Thorax, 2014)
- Side effects include: neuropathy (isoniazid), arthralgia (pyrazinamide), hepatotoxicity (all)
- Limited data correlating toxicities with pharmacokinetic (PK) parameters of antituberculous drugs.

SOUTH Study Visit Procedures



Assessment of Toxicities

- Peripheral neuropathy
 - Self report
 - Vibration sensation (worsening score over time)
 - Assessment of reflexes

- Arthralgia
 - Self report

- Liver toxicity
 - DAIDS (ALT 41 – 119 mild/grade 1, 120 -199 moderate/grade 2, >200 severe/grade 3)

Baseline Characteristics (1)

Characteristics	N=268
Gender (males)	155 (57.8%)
Age (median, in years)	33.9 (IQR: 28.6 , 39.6)
BMI (median, in kg/m ²)	19.2 (IQR: 17.7, 21.7)
• BMI <18	74 (27.6%)
Time since HIV diagnosis (median, months)	6.0 (IQR: 0.5, 11.0)
WHO stage III	233 (86.9%)
WHO stage IV	22 (8.2%)
CD4 count (median, in cells/ μ L)	172(IQR: 47, 334)
CD4 count <200 cells/μL	120 (44.8%)
CD4 count <50 cells/μL	55 (20.5%)
First line ART	56 (20.9%)
Second line ART	3 (1.11%)

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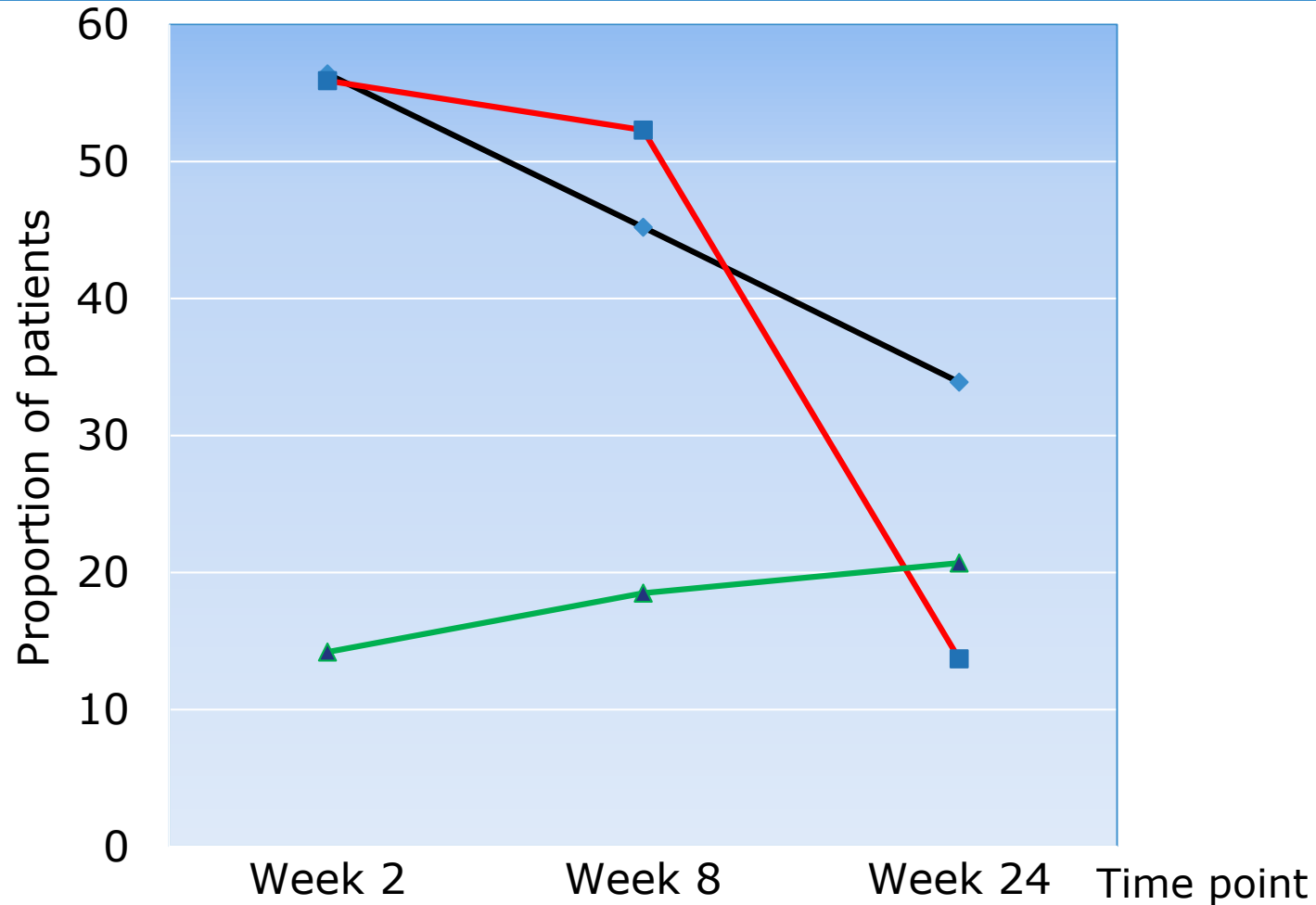
Baseline Characteristics (2)

Characteristic	With toxicities	Without toxicities	P-value
Male (%)	129 (57.1)	26 (61.9)	>0.6
Female (%)	97 (42.9)	16 (38.1)	
Age (median, years)	34	33.5	0.639
BMI (median, kg/m ²)	19.2	18.5	0.354
CD4 cell count (median, cells/ μ l)	189	120	0.04

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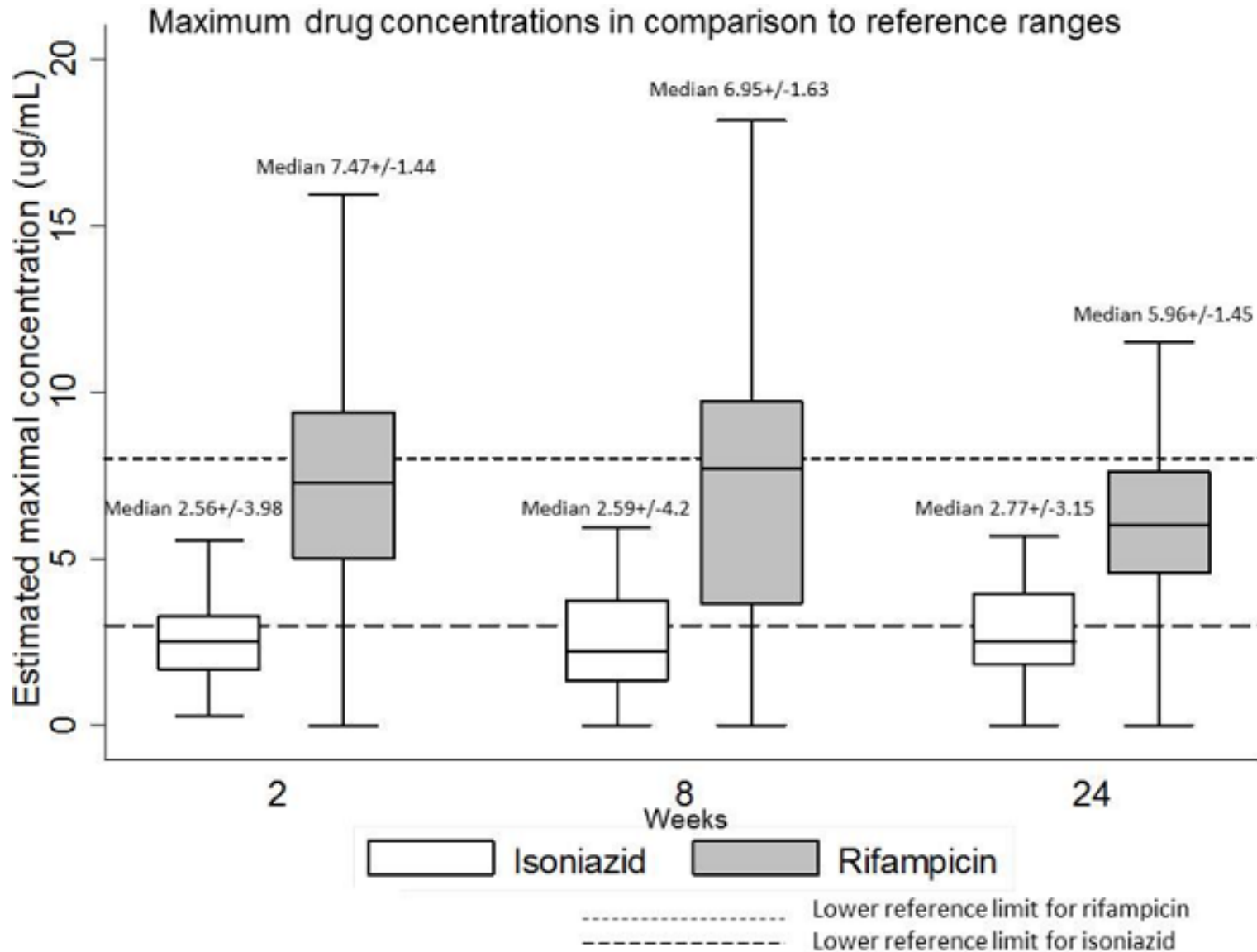
Proportion of Patients with Toxicity by Visit



- ◆ Peripheral Neuropathy
- Arthralgia
- ▲ Hepatotoxicity (Grade 1)

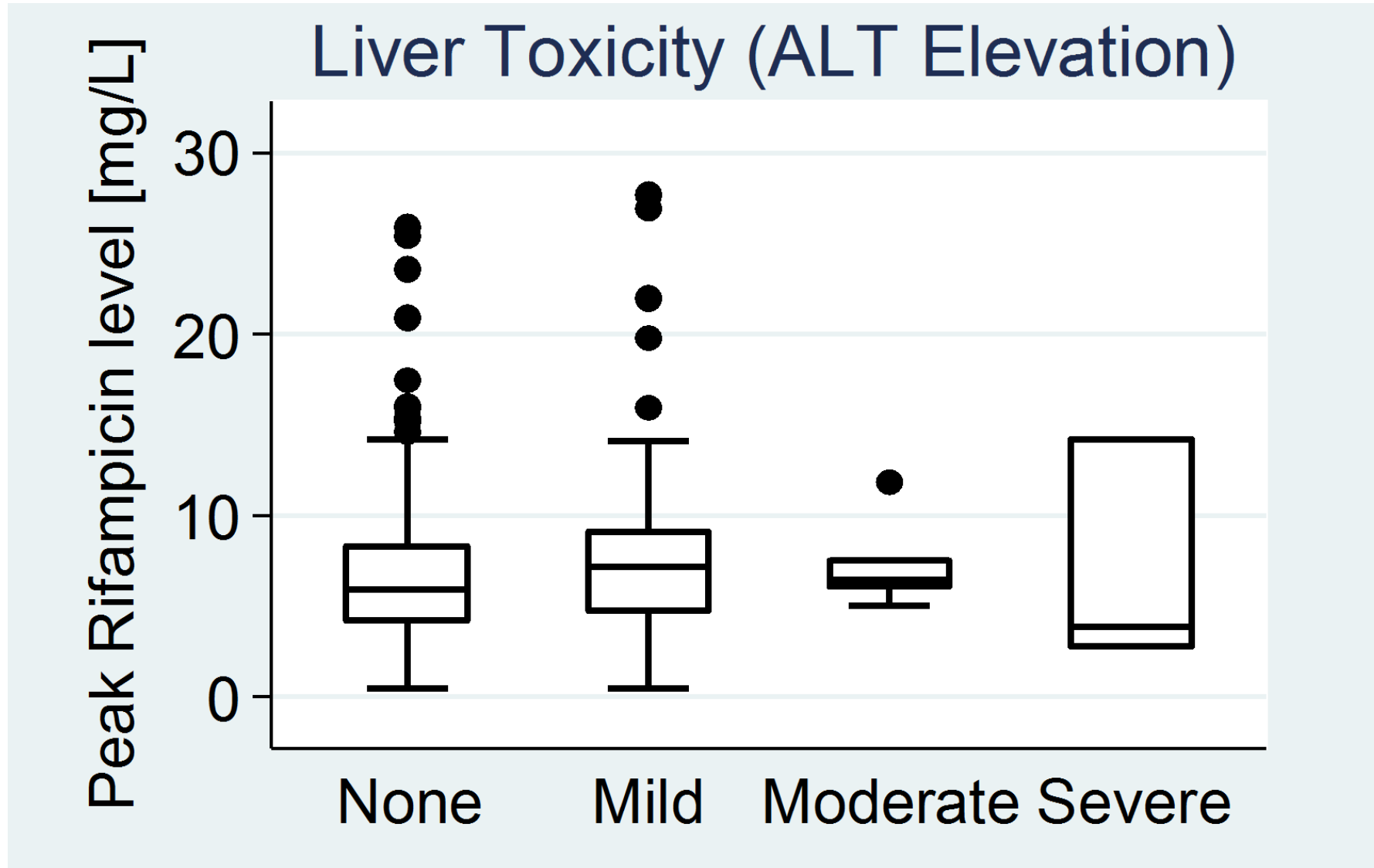
Week 2	Week 8	Week 24
56,4	45,2	33,9
55,9	52,3	13,7
14,2	18,5	20,7

Table of anti-TB concentrations

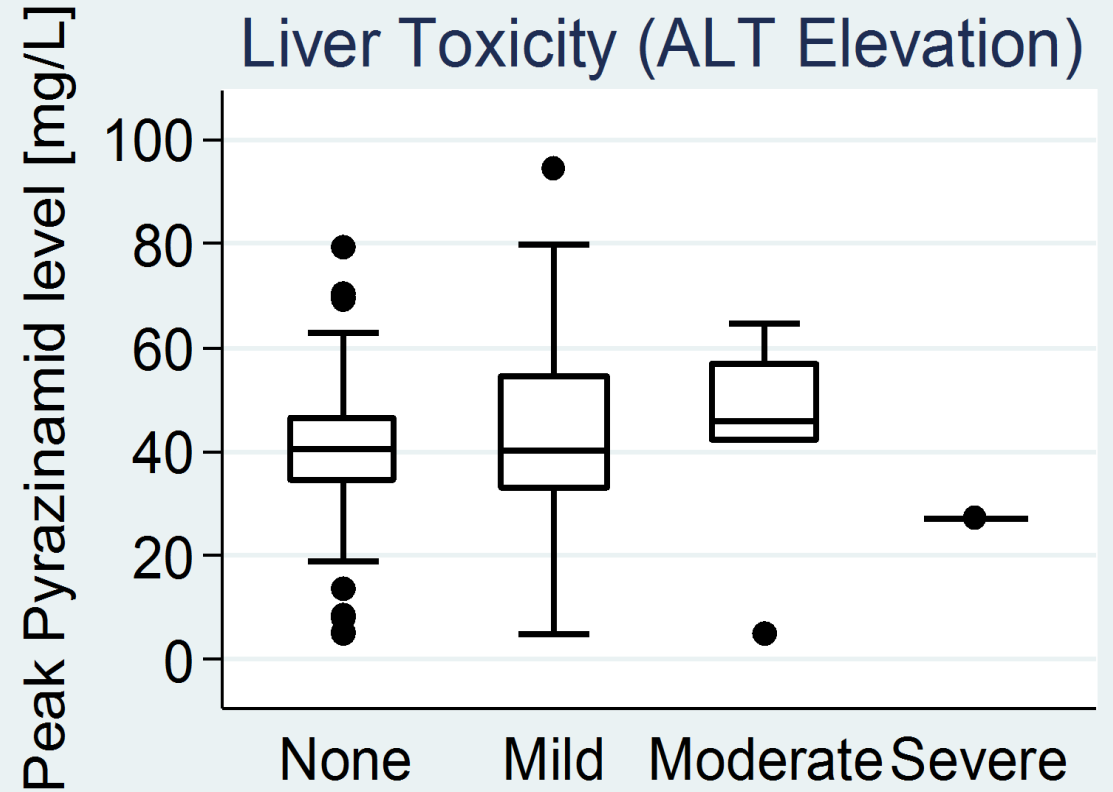
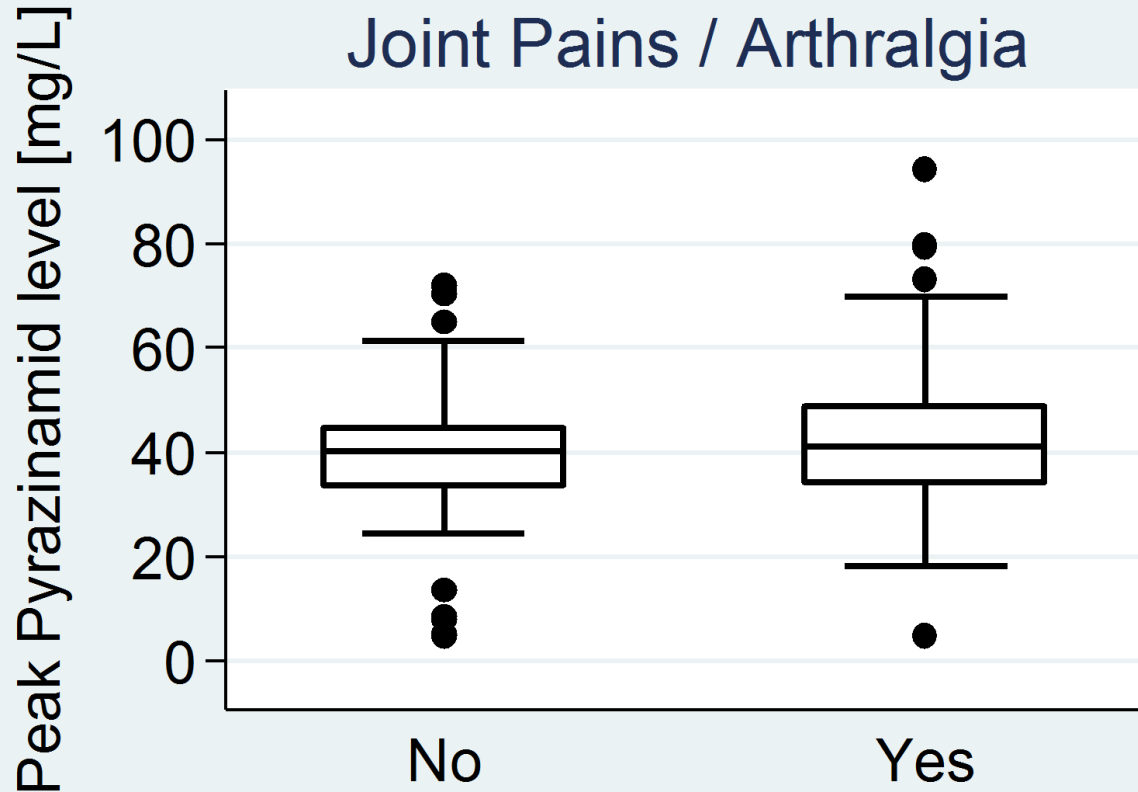


Pyrazinamide Mean C_{max}
 $41.6 \pm SD 13.1 \mu\text{g/mL}$

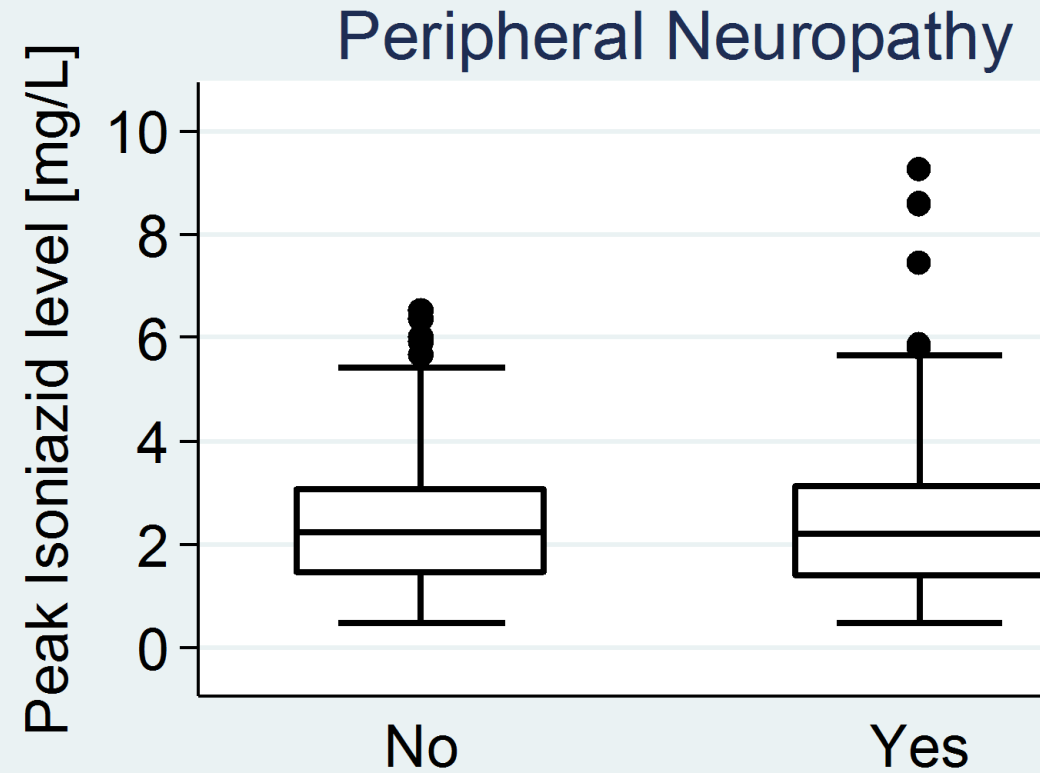
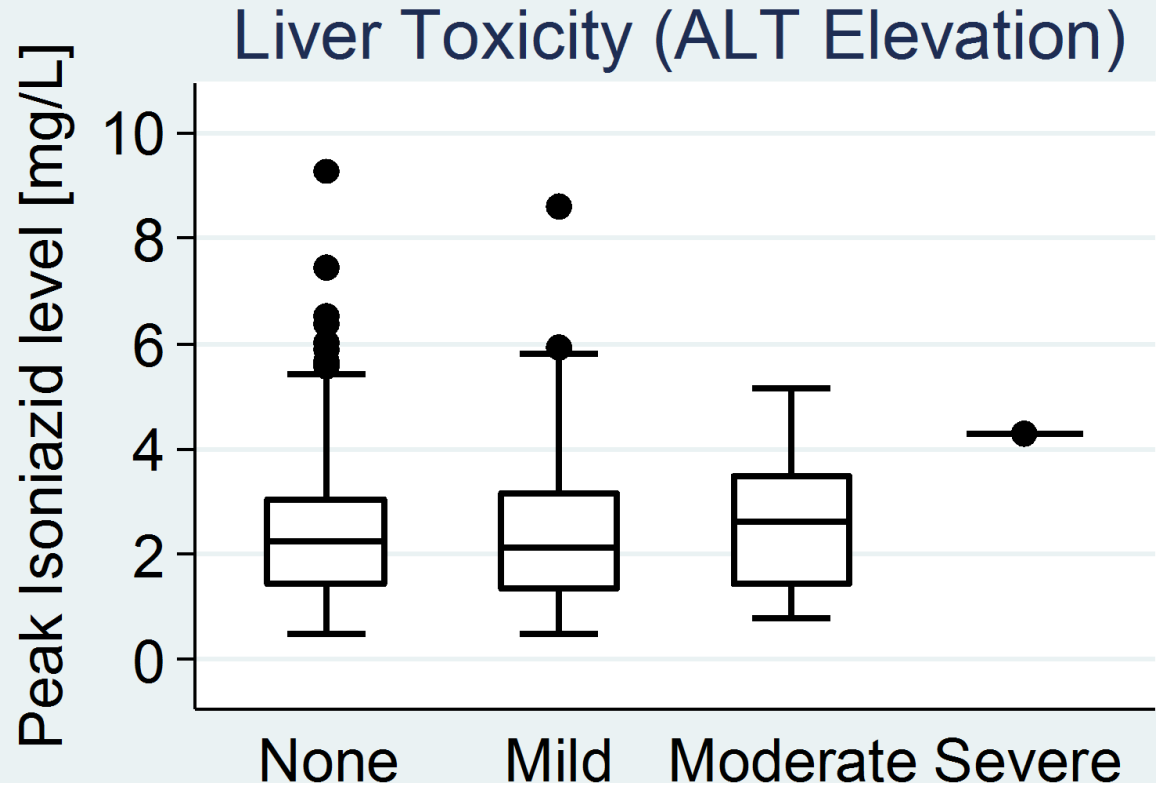
Rifampicin Concentrations: Correlation with Liver Toxicity



Pyrazinamide Concentrations: Correlation with Toxicities



Isoniazid concentrations: Correlation with Toxicities



Conclusion

- We found **no association** between anti-TB drug serum concentrations and occurrence of toxicities (arthralgia, neuropathy and hepatotoxicity)
- Peripheral neuropathy and arthralgia significantly improved over subsequent visits.



University of
Zurich ^{UZH}

Rainer Weber
Jan Fehr
Alexandra Scherrer
Bruno Ledergerber
Nataschia Corti
Daniel Müller
Ursula Gutteck

Thank you



University Hospital
Zurich



Andrew Kambugu
Barbara Castelnovo
Mohammed Lamorde
Amrei von Braun
Allan Buzibye
Moses Kanya
TB clinic team

