TB outcome in people living with HIV: An integrative data analysis of Phase 3 trials

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BACKGROUND

- People with HIV (PWH) and tuberculosis (TB) have been historically at higher risk of unfavorable TB-related outcome than those without HIV.
- We want to understand the risk factors for unfavorable TB-related outcomes in PWH.

METHODS

- We performed an integrative data analysis of PWH in 4 recent Phase 3 TB trials (OFLOTUB[1], REMoxTB[2], RIFAQUIN[3], S31/A5349[4]) in which PWH received 9 unique TB regimens of 4- and 6-month duration.
- Primary endpoint was TB-related unfavorable outcomes, including TB treatment failure, relapse, or death. Risk factors included demographics and medical characteristics (**Table 1**). Data was analyzed through Cox proportional hazard controlled for treatment arm[5].

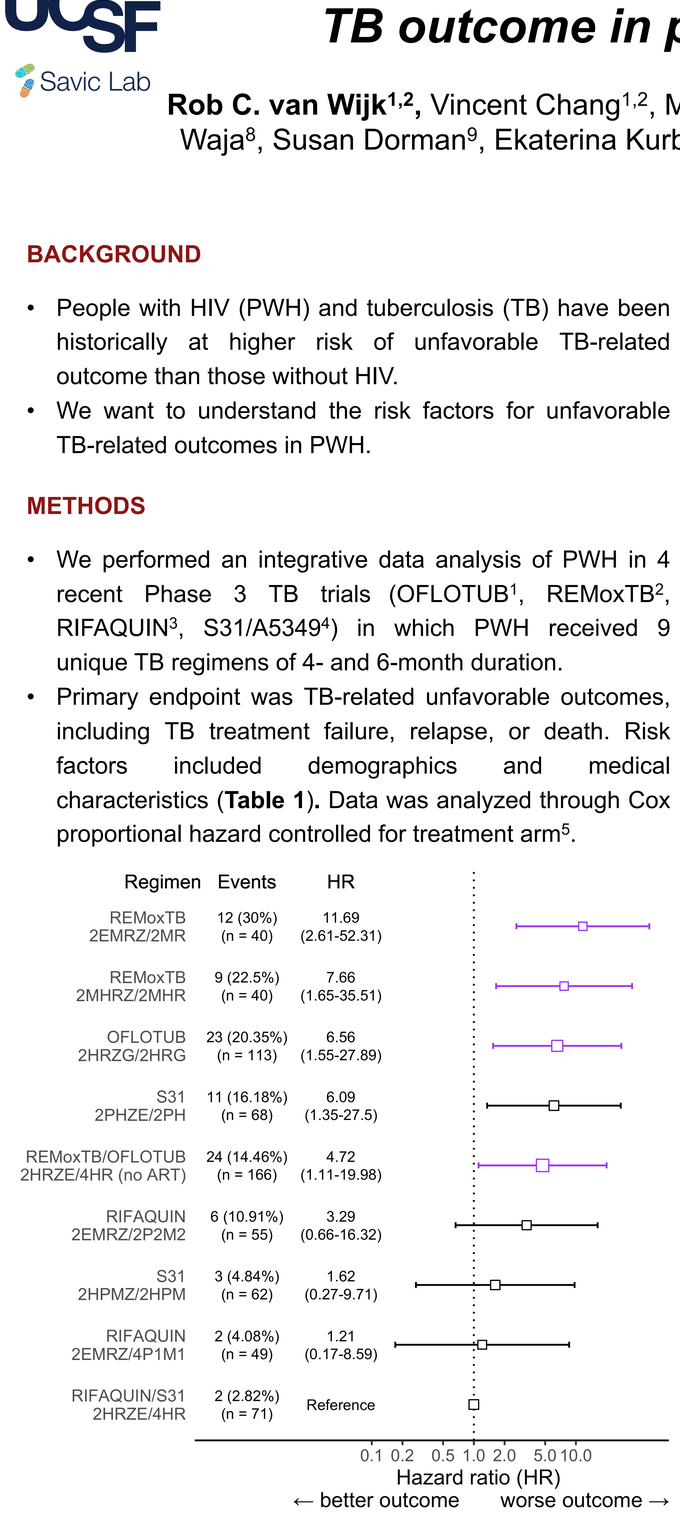


Figure 1. Hazard ratios (HR) with 95% confidence intervals for PWH receiving 9 regimens across 4 Phase 3 clinical trials. ART = antiretroviral therapy, purple indicates trials where no ART was used.

Among PWH, male individuals, those with baseline smear grade 2+ or 3+, and those with lower treatment adherence are at highest risk of unfavorable TB outcome

RESULTS

- 711 PWH had 93 unfavorable events.
- RIFAQUIN's 6-month moxifloxacin-, and S31's 4-month rifapentine-moxifloxacin regimens performed similarly to standard-of-care (**Figure 1**).
- PWH receiving ART had fewer TB-related unfavorable outcomes (7.9%) compared to PWH not receiving ART (18.9%).
- At high risk of TB-related unfavorable outcomes were male PWH, those with high baseline smear grade (2+ or 3+) and those with lower adherence (defined as % of total pills taken) (**Figure 2-3**).

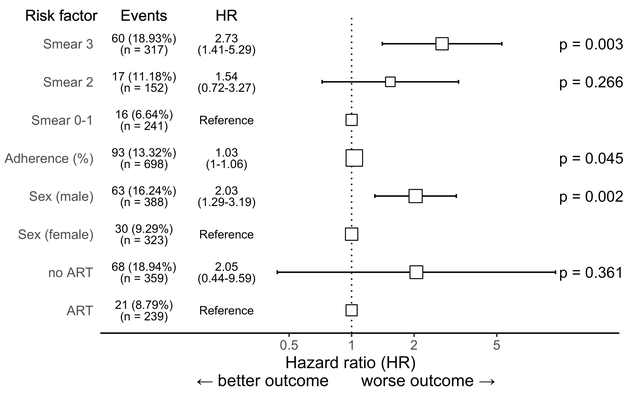


Figure 2. Multivariable analysis shows high risk for male PWH with high baseline smear grade and low adherence. Antiretroviral therapy (ART) correlated with study and was not statistically significant.

Table 1. Participant characteristics for the four Phase 3 clinical trials included in the integrative data analysis.

	RIFAQUIN	REMoxTB	OFLOTUB	S31/A5349	Total
Total patients	593	1674	1350	2331	5948
People with HIV	158 (26.6%)	123 (7.35%)	236 (17.5%)	194 (8.32%)	711 (12.0%)
Outcomes (TB)	10	26	42	15	93
Age (years)	32.5 (22.0-50.1)	33.0 (21.0-49.0)	31.5 (19.0-50.1)	35.0 (22.0-58.0)	33 (21.0-54.0)
Male sex	79 (50.0%)	70 (56.9%)	119 (50.4%)	120 (61.9%)	388 (54.6%)
Weight (kg)	51.8 (38.9-69.0)	54.9 (40.1-76.2)	53.3 (40.0-74.6)	54 (42.0-79.5)	54.0 (40.0-76.1)
Smear grade: 0-1	78 (49.4%)	32 (26.0%)	27 (11.4%)	104 (53.6%)	241 (33.9%)
2	26 (16.5%)	22 (17.9%)	59 (25.0%)	45 (23.2%)	152 (21.4%)
3	54 (34.2%)	69 (56.1%)	150 (63.6%)	44 (22.7%)	317 (44.6%)
Cavitation	79 (50.0%)	71 (57.7%)	151 (64.0%)	139 (71.6%)	440 (61.9%)
CD4 (cells/mm^3)	314 (205-896)	405 (253-952)	283 (42-737)	344 (118-777)	339 (98.8-856)
ART Yes	53 (33.5%)	0 (0%)	0 (0%)	186* (95.9%)	239 (33.6%)
No	-	123 (100%)	236 (100%)	-	359 (50.5%)
Missing	105 (66.5%)	-	-	8 (4.12%)	113 (15.9%)
Adherence (%)	69.7 (40.7-100)	100 (19.2-100)	79.1 (26.4-80.7)	100 (19.7-100)	80.7 (22.2-100)

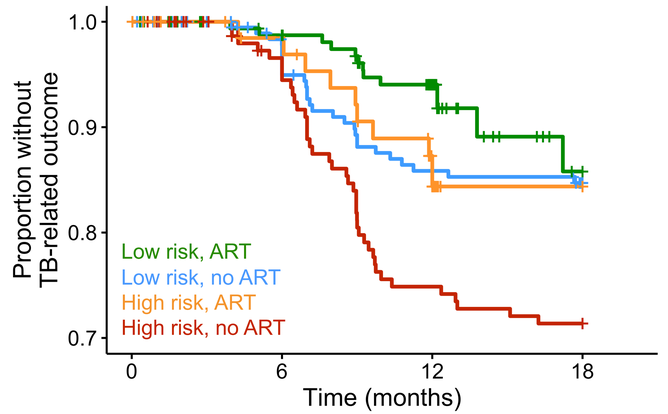


Figure 3. Proportion without TB-related outcome stratified by risk group and comedication of antiretroviral therapy (ART). High risk: Male PWH with smear grade 2+ or 3+; low risk: female PWH or male PWH with negative smear grade or 1+.

CONCLUSIONS

- Among PWH (as has separately been shown for people without HIV), higher sputum smear bacillary burden pretreatment, male sex, and lower adherence increase the risk of unfavorable TB-related outcome.
- Fewer TB-related unfavorable events are observed in PWH taking ART

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