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Safety and Efficacy of Sorfequiline (TBAJ-876) In Combination with Pretomanid and Linezolid – Week 8 Analysis Result of NC-009

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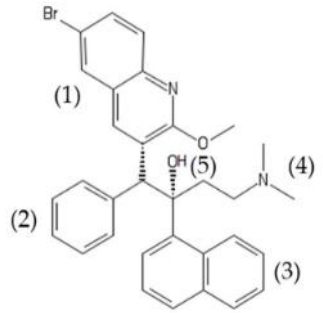
What is sorfequiline and why it is important?

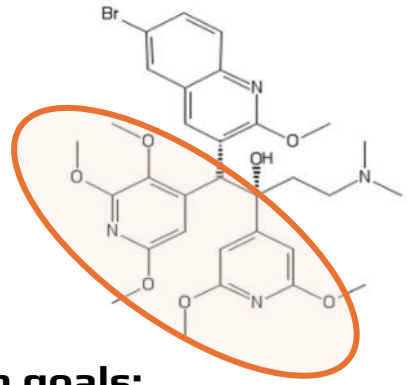
BDQ



Bedaquiline (BDQ)

- First-in-class diarylquinoline (DARQ)
- Novel mechanism of action
- QT prolongation

SFQ



Sorfequiline (SFQ) design goals:

- Increase potency
- Reduce/eliminate QT effect

10x greater potency compared with BDQ

- Potential to shorter treatment duration
- Lower likelihood of resistance emerging
- Activity against BDQ-resistant strains

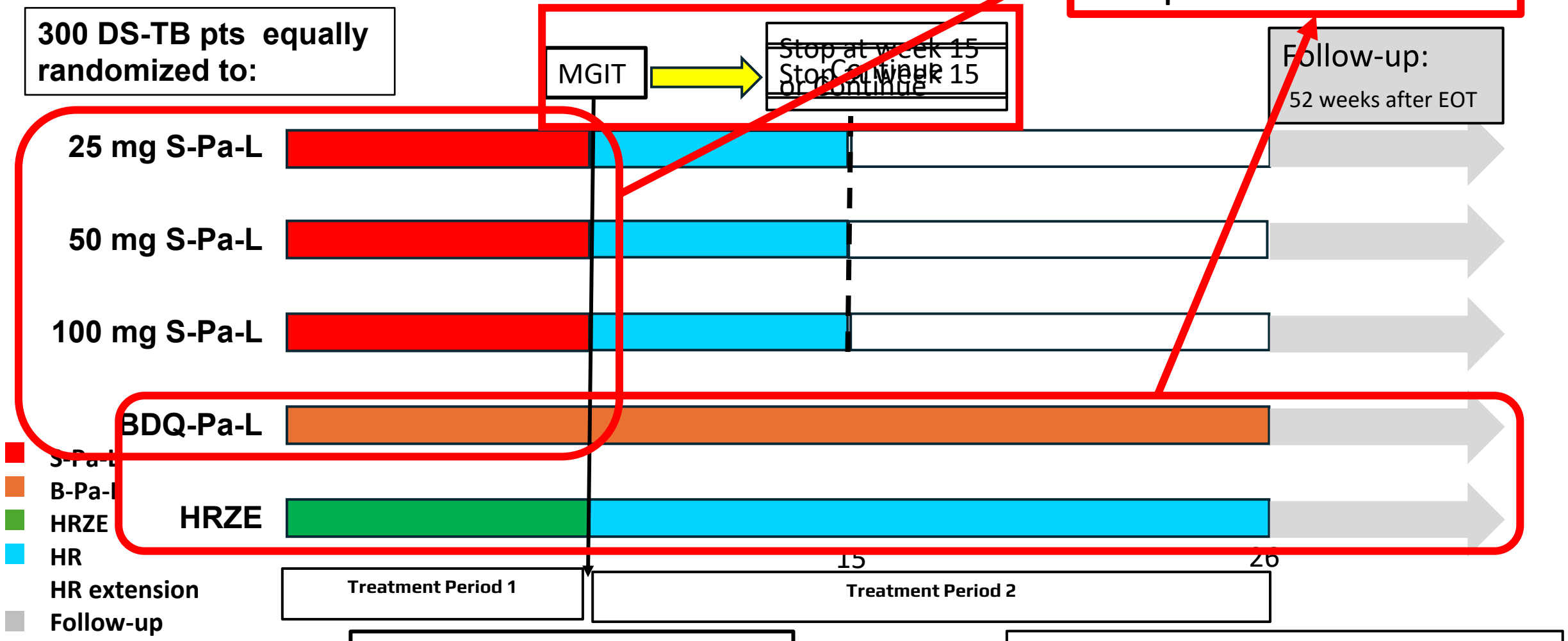
No QT prolongation observed in preclinical or clinical studies

NC009 Study Objectives

- **Objective:** Evaluate efficacy, safety, and tolerability of sorfequiline (3 dose levels) or bedaquiline in combination with pretomanid and linezolid in adult participants with newly diagnosed, smear-positive pulmonary DS-TB in comparison to SOC
- **Primary Endpoint:** Time to stable sputum culture conversion (TSCC) to negative status using results from weekly cultures through 8 weeks of treatment
- **Secondary Endpoint:** Proportion of participants with a favorable outcome at 26 weeks after the end of treatment

NC-009: Phase 2 Study Design for Sorfequiline

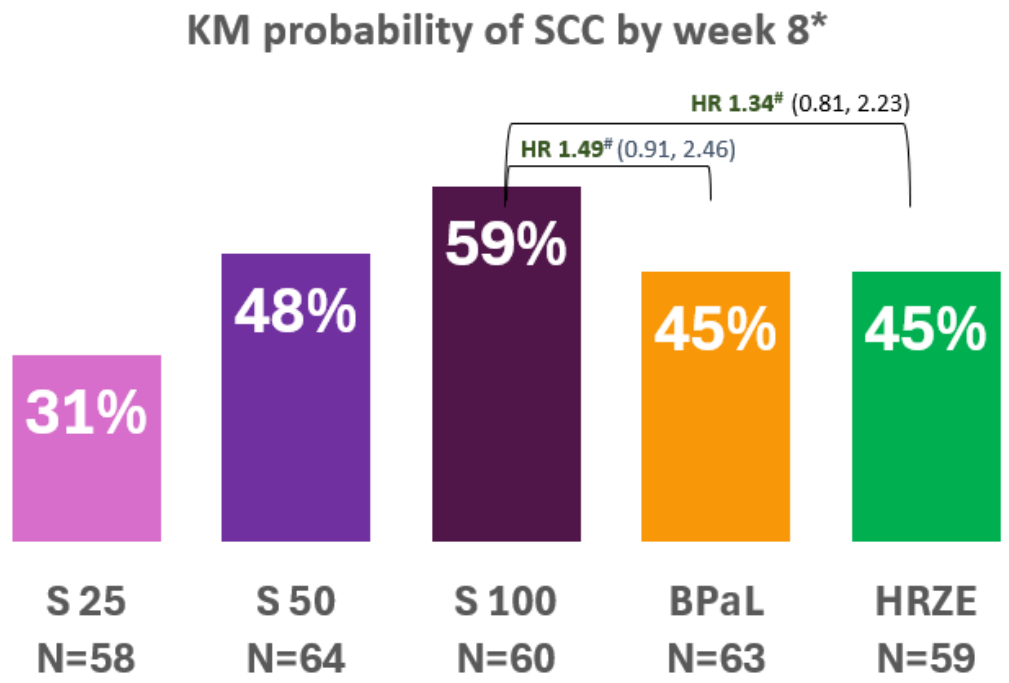
- Dose ranging S with Pa-L
- Option to stop at 15 weeks based on 8-week status
- First study of BPaL in DS-TB
- Comparison to HRZE SOC



Week 8 Primary endpoint: TSSC

Secondary endpoints: relapse free cure 6 and 12 months after actual end of treatment

NC-009 Efficacy at week 8 - mITT

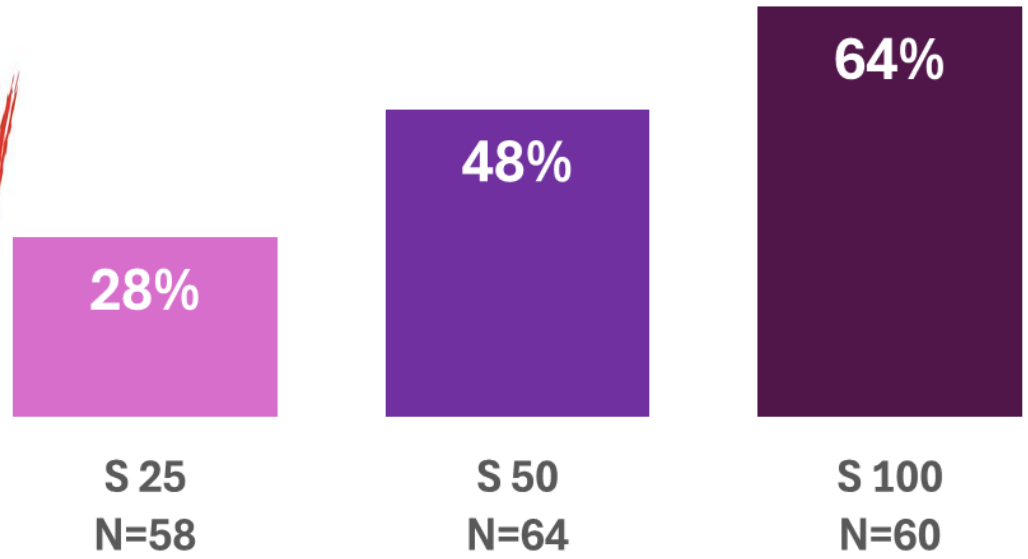


* Kaplan Meier method

\# Stratified Cox Proportional Hazard model

- Clear dose-response in sorfequiline arms
- 100 mg sorfequiline arm outperforms BPaL and HRZE

Proportion of pts who met criteria for 15-weeks total Rx duration - mITT



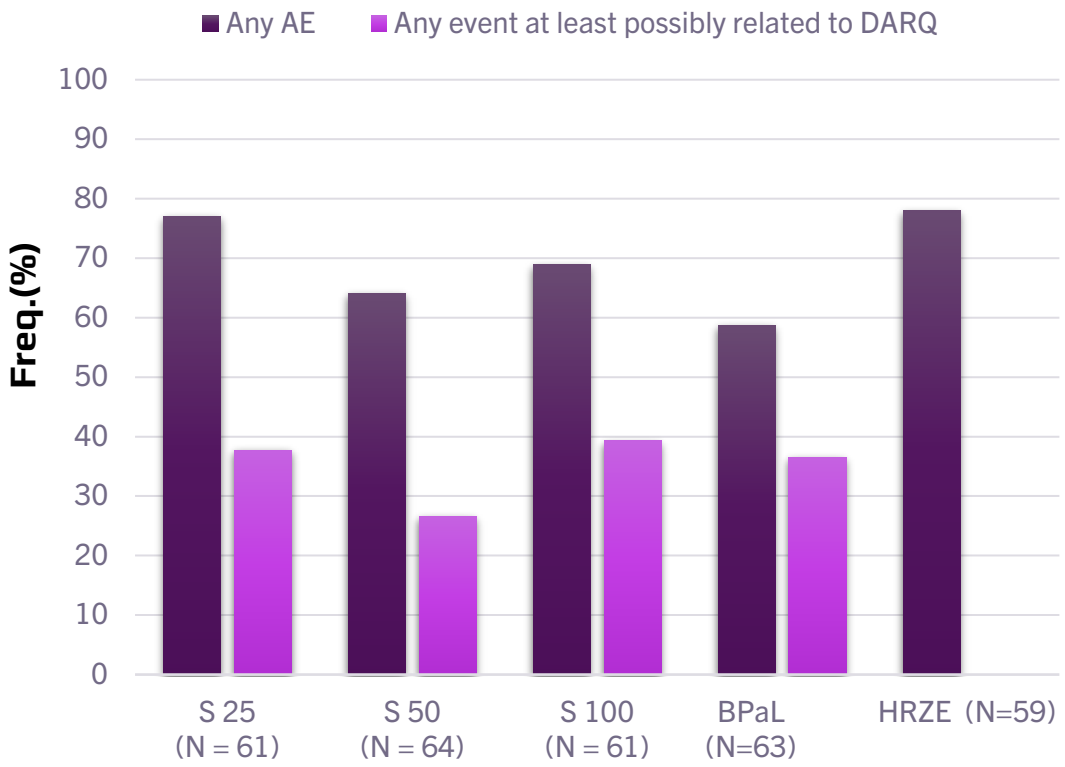
- Clear dose-response in sorfequiline arms
- At FUP Wk 26:
  - *1 relapse in 15 weeks 100 mg SPaL
  - 1 relapse in 26 weeks 100 mg SPaL
  - 1 relapse in BPaL
  - 1 relapse in HRZE

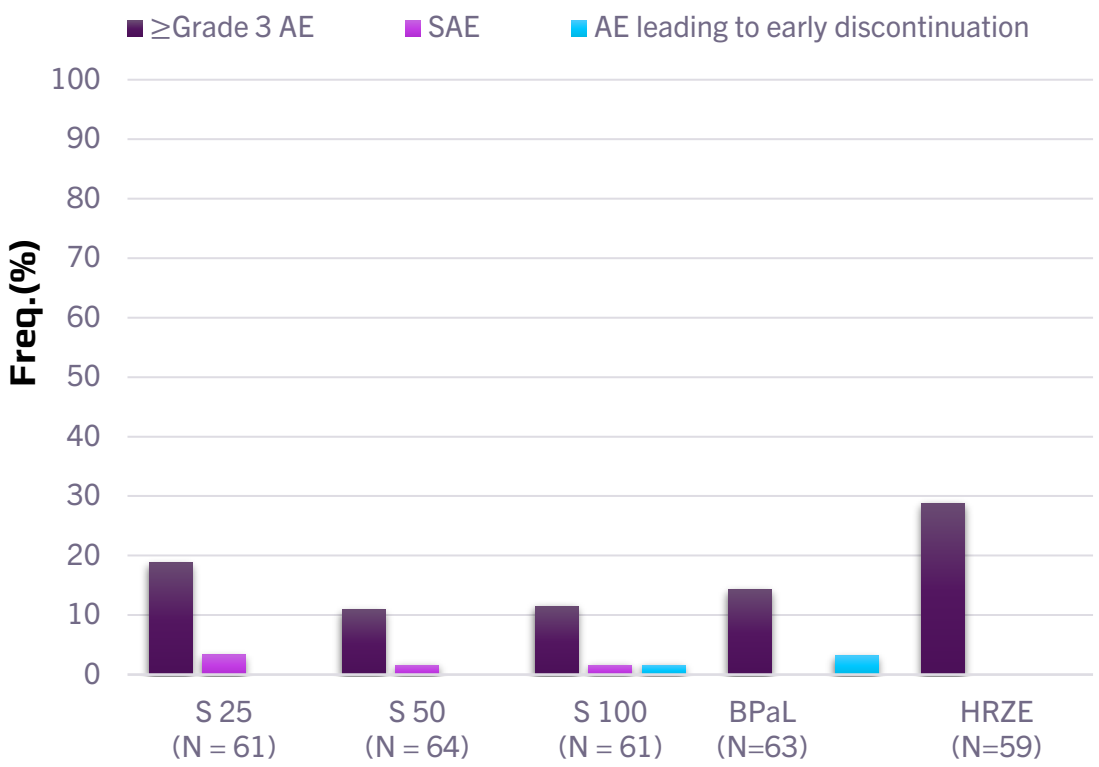
*early stable culture conversion (week 5), asymptomatic at recurrence, possible reinfection from infected untreated roommate

Relapse rate: 25 mg SPaL (15 week= 4; 26 week= 8). **50 mg SPaL** (15 week= 0; 26 week= 4).

FUP WK 52 Data to be presented at the UNION pending acceptance of abstract

NC-009 Safety Summary (Safety Population) – through 8 weeks





NC-009 Safety Summary: ECG Data Show SPaL effect on QTcF less than BPaL (Safety Population) – Through Week 8

	25 mg SPaL N = 61	50 mg SPaL N = 64	100 mg SPaL N = 61	BPaL N = 63	HRZE N = 59
Increase ≥30 ≤60 ms	30%	33%	34%	**59%**	17%
Increase ≥ 60 ms	2%	2%	3%	**5%**	3%
>500 ms	0%	0%	0%	**2%**	0%

SPaL effect is similar to what was seen with pretomanid monotherapy in an EBA study

Conclusion

- **Efficacy:**
  - Sorfequiline demonstrates efficacy dose response in combination with pretomanid (Pa) and linezolid (L)
  - 100 mg SPaL regimen has greater bactericidal activity than BPaL or HRZE
  - Low relapse incidence in 100 mg SPaL (including 15-week), BPaL and SoC treatment arms
  - SPaL regimen is a promising 4-month regimen
- **Safety:**
  - No apparent sorfequiline dose-related safety issues
  - SPaL effect on QTcF less than BPaL

Thank you!

We sincerely thank the trial participants, TB-affected community, partners, and funders for their dedication, support, and collaboration in driving forward the mission to end TB.