

# Progress in the fight against Drug-Resistant Tuberculosis –

## World TB Day Update, March 24, 2024

The past year has seen progress in the fight to bring better treatment to people with DR-TB as well as identification of some new obstacles. This World TB Day Report for 2024 continues a RESIST-TB feature, an annual summary of progress towards shorter and less toxic treatment for all persons with DR-TB. These include advances in clinical trials, roll out of new drugs and regimens, regulatory approvals of new drugs, improved access to susceptibility testing for the new agents and lower diagnosis and treatment costs. We summarize these for the past year below:

### Published Clinical Trials of DR-TB

Four major clinical trials were completed in 2023 that have important implications for DR-TB: the TB-PRACTECAL trial, the endTB trial, the V-QUIN trial and the TB-CHAMP trial. However, only the first has been published in final form, with the other three having been published as abstracts only.

TB-PRACTECAL was a phase II/III clinical trial evaluating the efficacy of three 24-week, all oral regimens for rifampin-resistant tuberculosis. Preliminary results were published last year,[1] and the final results this year.[2]. The “BPaLM” regimen (Bedaquiline, Pretomanid, Linezolid and Moxifloxacin) was confirmed to be superior in efficacy to the standard of care, and participants receiving BPaLM had significantly fewer grade 3 or higher or serious adverse events than the local WHO-approved standard of care.

The endTB trial enrolled 754 participants with MDR-TB in Peru, Georgia, Palistan, Kyrgystan, Lesoth, Kazakhstan, South Africa and India to one of five 9-month experimental arms or the local WHO-approved Standard of Care (SOC). The control arm had 81% successful outcomes, while the table below shows the 5 experimental arms and their comparison with the SOC, with a 12% non-inferiority margin:

Experimental Arms:	B=Bedaquiline
	D=Delamanid
1. BLMZ - Non-inferior	L=Levofloxacin
2. BLLzCZ - Superior	M=Moxifloxacin
3. BDLLzZ - Non-inferior	Lz=Linezolid
4. DLLzCZ – <i>Not</i> non-inferior	C=Clofazimine
5. DMCZ - Non-inferior (MITT only)	Z=Pyrazinamide

Overall, only 2% of participants died. PZA was the most frequently stopped drug (16%) and Linezolid was the second most frequently stopped (11%).[3]

Both the V-QUIN trial and the TB-CHAMP trial examined the ability of a 6-month course of levofloxacin to prevent TB in household contacts of persons with pulmonary MDR-TB. V-QUIN ..took place in Vietnam and TB-CHAMP took place in South Africa. There was a prearranged plan to combine the results. Although neither trial by itself showed a statistically significant preventive effect, the individual patient database meta-analysis showed that levofloxacin was protective: HR=0.40 (0.17-0.90).[4,5]

### Other Important Publications

In November 2023 the new updated TAG TB Treatment Pipeline Report was published, providing an excellent summary of recent developments and clinical trials in progress.[3]. The TB Treatment report is an excellent source for details of the trials noted above, and others

2023 also saw the publication of a joint RESIST-TB/Union effort, “Clinical implications of

molecular drug resistance testing for Mycobacterium tuberculosis". After an extensive literature search, a multidisciplinary team of clinicians, microbiologists, and laboratory scientists reached consensus on critical questions about molecular prediction of susceptibility or resistance in *M. tuberculosis*. The consensus document aims to assist clinicians with management of TB patients by providing guidance on design of treatment regimen and optimizing outcomes.[6]

### **New WHO Guidelines in the past year**

This year the WHO released a Rapid Communication on Tuberculosis preventive treatment in November 2023. The statement indicates that WHO will release updated guidelines and an accompanying operational handbook on TPT in 2024. This will include TPT for individuals exposed to multidrug- or rifampicin-resistant TB (MDR/RR-TB). and will also incorporate current recommendations on screening strategies to rule out TB disease ahead of starting TPT, and the use of tests of TB infection. [7]

### **Around the corner...stay tuned!**

An exciting new clinical trial has been launched by the Gates Medical Research Institute that will study new shortened regimens of 2-4 months that will be applicable to MDR-TB. The drugs include Bedaquiline, Delamanid or Pretomanid, Quabodepistat and Sutezolid.[8] To hear the latest news, watch the RESIST-TB website ([www.resisttb.org](http://www.resisttb.org)) and/or visit the website and subscribe to our monthly e-newsletter!

### **References**

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