rGLC report format

TECHNICAL ASSITANCE REPORT – Operational Research on BPaL and all-oral shorter regimen

Country:	Thailand
Dates of TA provision:	4 May 2021
Consultant(s):	1. Corinne Simone Collette Merle, TDR/WHO HQ 2. Fraser Wares, KNCV 3. Medea Gegia, GTB/WHO HQ. 4. Padma Chandrasekharan, NIRT 5. Salah Foraida, Sr Director Medical Affairs, TB Alliance. 6. Sandeep Juneja, Head Market Access, TB Alliance
Clearance of the report	The content of the report has been shared with the National Tuberculosis Program through WHO country office.
Sharing of the report	1. The report is being shared with The Global Fund Portfolio Manager, Thailand. 2. In-country circulation of the report done via WHO Country office
TA coordination	rGLC/SEAR Secretariat and WHO Country Office, Thailand.
Summary of the TA provided	The following activities were covered during the webinar: • Overview of the pre- and XDR-TB situation and current gaps in Thailand • Current recommendations and guidance from WHO on use of BPaL (and other oral shorter regimen) • Designing OR protocol for shorter regimen like BPaL (and other oral shorter regimen) • BPaL clinical updates • BPaL Implementation updates (including LIFT-TB projects) • Possible support during the implementation of BPaL OR, on monitoring and data collection The presentations were followed by discussions on implementation of WHO guidelines, country capacity, designing of OR protocol and implementation preparations including drugs availablity. Summary of discussions: The current eligibility criteria for BPaL is those who have had prior exposure of 2 weeks or less for Bdq and Lzd. Other considerations can be taken into account while designing the Operational Research (OR) regimen at the country level. A patient who has been exposed to Bdq and Lzd earlier, but reliable DST results show susceptibility, maybe eligible for BPaL but other eligibility criteria should be also taken into consideration (refer to WHO Operational Handbook, Module 4). It was emphasized by participants that during patient follow-up, a mental health check-up is also important. The need for psycho-social support should be evaluated and provisions made as per the country guidelines. A mental health evaluation is integral part of the clinical examination. When you are doing the baseline clinical examination and are looking at the clinical parameters, a mental health evaluation should be included. If you want to add this into the tools, it can be adapted in the REDCAP database. Regarding the burden of pre-XDR-TB (as per new WHO definition), it was clarified that the number of patients who may have MDR-TB with additional FQ resistance and those who

	have intolerance to their MDR-TB treatment could be more than 90, in Thailand. Hence, there is sufficient numbers to constitute a cohort for the intended OR. In-country capacity to undertake quinoline and linezolid DST: In Thailand, 2 labs have the capacity to do quinolone and linezolid DST. The NRL has started functioning, but there is some delay at the Chest Hospital lab because of the COVID-19 situation. There are 20 laboratories capable to perform first-line and second-line LPA testing. Adverse events during the BPaL regimen: It was clarified that any regimen, shorter or longer, has some side effects and the real difference is how well the side effects can be managed. The current BPaL regimen is for the patient who are resistant to FQ in addition to MDR-/RR-TB irrespective of resistance to an second-line injectable agent. For the moment, we don't have any specific recommendation for any regimen for patients who have side effects. Side effects for the shorter Bdq-containing regimen are less, but if other options have been exhausted already and the clinician has no other treatment option, BPaL can be considered. The WHO's Operational Handbook has some answers on what modifications to the BPaL regimen are permitted. AE management was also discussed during the TB Alliance presentation, including linezolid dose adjustment and duration. The current recommendation is based on the NIX-TB study and in the handbook, there is the 1200 mg dosage can be adjusted. This year, WHO will be reviewing data from the ZeNix trial to check the optimal dose and duration of linezolid. More details will be available on WHO website in Quarter 4 2021. BPaL regimen duration: If the culture is positive around the fourth month of treatment, then the duration of treatment should be extended to 9 months. The median time for culture conversion is however 6 weeks and therefore, the results should be available before the end of treatment at 6 months. If culture results are not available, then sputum smear results along with clinical progress may be an indicator for extension of the treatment. The definition of the failure of BPaL regimen: The definition TDR is proposing in the ShORRT research user package is applicable for whatever regimen is being tried. Standard definitions as per WHO guidelines may be used for any individual regimen. Data analysis and management: TDR can support data data collection and analysis, in coordination with the Global TB Programme. Country specific variables for which data needs to be collected can be defined on paper first and then adapted for software like REDCAP. If this is chosen for the data collection purposes, administrator and user rights can be assigned to country colleagues based on who needs to use it for what purpose. It was clarified during the meeting that for OR protocol and methodology, TDR unit may be contacted while regimen specific questions may be posed to Global TB Programme or the Regional Office.
Summary of the recommendations to follow up	• Adoption/adaptation of BPaL OR protocol. There is a generic OR protocol for modified oral shorter regimen "ShORRT" developed by TDR/WHO-HQ and a generic BPaL OR protocol developed by KNCV. • Adoption of updated WHO definitions for pre-XDR-TB and XDR-TB • Implementation considerations – experience sharing from other countries • Organize capacity building for management of AEs, treatment monitoring, specific for BPaL regimen • Plan for access to drugs, specifically pretomanid • Streamline data collection, recording and management, to be in alignment with expectations.

	• Set up systems for long term support from international experts. The Regional office, through country office has linked NTP with relevant experts. Discussions are ongoing on start of the OR and need-based support will be provided.

Agenda of the meeting

	Session	Speaker	Time
1	Overview of the pre- and XDR-TB situation and current gaps in Thailand	Dr Phalin Kamolwat/ NTP Thailand	15 mins
2	Current recommendations and guidance from WHO on use of BPaL (and other oral shorter regimen)	Dr Fuad Mirzayev/ Dr Medea Gegia, GTB/WHO HQ.	15 mins
3	Designing OR protocol for shorter regimen like BPaL (and other oral shorter regimen)	Dr Corinne Simone Collette Merle/ Dr Debora Pedrazzoli, TDR/WHO HQ.	50 mins
4	BPaL clinical updates	Dr Salah Foraida, Sr Director Medical Affairs, TB Alliance.	15 mis
5	BPaL Implementation updates (including LIFT-TB projects)	Dr Sandeep Juneja, Head Market Access, TB Alliance	15 mins
6	Possible support during the implementation of BPaL OR, on monitoring and data collection	Dr Fraser Wares, KNCV and Dr Padma Chandrasekharan, NIRT	15 mins
7	Discussions and Way Forward	Plenary	15 mins

List of participants:

Department of Disease control and Division of Tuberculosis

7. Dr.Phalin Kamolwat: NTP manager, acting director of Division of Tuberculosis
8. Dr.Petchawan Pungrassami : Senior consultant on Disease Control
9. Miss Saijai Smithikan:Chief of Laboratory
10. Dr.Napas Petsuntad : Physician
11. Dr.Thidaporn Jirawattanapisal: Chief of Epidemiology & Emergency, PMDT, International collaboration
12. Dr.Juntima Jaronnasri: Chief of OPD and Research demonstration
13. Miss Piriya (Pharmacist): Chief of Pharmacy
14. Miss Walaya Sitti: TB global fund manager
15. Other staff of Division of Tuberculosis (3)

Country experts:

16. Dr.Charoen Chuchotaworn
17. Dr.Piamlarp Sangsayunh
18. Prof.Wipa Reechaipichitkul
19. Ass.Prof.Angkana
20. Dr.Surakameth Mahasirimongkol

Other participants/ facilitators

21. Aastha Gupta, TB Alliance
22. Aung, Damien Foundation/Bangladesh
23. Corinne Simone Collette Merle TDR/WHO HQ
24. Debora Pedrazzoli, TDR/WHO HQ.
25. Fraser Wares, KNCV
26. Fuad Mirzayev GTB/WHO HQ
27. Ghodousi Arash, SRL Milan
28. Medea Gegia, GTB/WHO HQ.
29. Morounfolu Olugbosi, TB Alliance
30. Muhammed Asif, Senior advisor, USAID
31. Nimalan Arinaminpathy, Imperial college
32. Padma Chandrasekharan, NIRT
33. Paran Sarimita Winarni, PoP-TB
34. Philippe Creac'H, Global Fund
35. Salah Foraida, Sr Director Medical Affairs, TB Alliance.
36. Sandeep Juneja, Head Market Access, TB Alliance
37. Regional office and country office staff (6)