Treatment of Patients

Dosing of BPaL Regimen, Management of AEs, Treatment outcomes,data management and project monitoring

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Dosing of BPaL Regimen

Dosing

Table 5. Dosing of component drugs for adults and adolescents (aged 18 and over) based on a minimum of 26 weeks treatment

Drug (preparation)	Dose	Total number of tablets
Bdq (100 mg/tablet)	400 mg once daily for 2 weeks, then 200 mg 3 times per week for 24 weeks afterwards	200
Pa (200 mg/tablet)	200 mg once daily	182
Lzd (600 mg/tablet)	1200 mg once daily (adjustable) BPaL	264 to maximum of 364 (based on the Nix trial)

Duration Of Treatment

- **BPaL regimen is given for a duration of 6-9 months (26-39 weeks):**

❑ 6 months – standard treatment duration

❑ 9 months- treatment can be extended to 3 more months, If

- ❑ sputum culture at 4th Month of treatment is still positive, AND
- ❑ patient is clinically well and /or improving.

Patient Monitoring

- Weekly clinical monitoring by the OR site staff using :
  - face to face clinical assessment if necessary
  - video DOT or through a trained treatment supporter.
- Monthly monitoring of bacteriologic examination
  - to monitor sputum conversion which is an indicator of the effectiveness of the regimen.
  - Laboratory and diagnostic examinations are also done monthly to monitor possible acute drug reactions and ensure safety of the participants.

SCREENING AND TREATMENT

Based on a checklist of inclusion and exclusion criteria that will be provided to all TCs/STCs, patients who are potentially eligible to the BPaL OR will be referred to the OR sites for screening.

Table presents different scenarios of patients

	SCREENING	TREATMENT
Patient A **RR-TB patient registered and empirically started on a regimen, e.g., SSOR or SLOR for FQ-S, and turned out to have pre-XDR (Fq-resistant) on SL-LPA.** - **If started in a non-OR TC/STC, the patient is <u>transferred out</u> and referred to the OR site for screening.** - **If started in an OR site, the patient simply proceeds to screening.**	At the OR site, Form 1 (Screening, Annex 4) will be filled via the REDCap database and a Patient ID assigned. If there is no contraindication to BPaL, baseline tests will be conducted (Table 7). Note: In ITIS, the patient's classification as MDR-TB will remain, and the patient's original Patient code (TB Case No.) will be retained.	- If eligible, the patient will be enrolled on BPaL as Trans-in (if transferred out from the TC/STC) using the same patient code as before (with a "blue ink mark"). Form 2 (Enrolment, Annex 5) will be filled out. Treatment outcome will be recorded by the referring TC/STC (or by the OR site, if the patient started the original MDR-TB treatment in the OR site). - If not eligible, the patient is given the appropriate regimen using the same patient code (either referred back to the referring TC/STC or at the OR site where he started)

SCREENING AND TREATMENT

Patient B RR-TB patient registered and empirically enrolled on a regimen, e.g., SSOR, who turned out to have XDR (Fq- and second-line injectable-resistant) on SLD DST - If started in a non-OR TC/STC, the patient will be referred to the OR site for screening - If started in an OR site, the patient proceeds to screening	At the OR site, Form 1 (Screening, Annex 4) will be filled via the REDCap database and a Patient ID assigned. Note: In ITIS, the patient's MDR-TB classification will change to XDR-TB category, the patient's original Patient Card closed and the patient is marked excluded from the MDR-TB cohort in the DR-TB Register and in ITIS. The patient will be re-registered with a new Patient Code (TB Case No.)	- If eligible, patient will be enrolled on BPaL using the new patient code generated by the OR site (with a "blue ink mark"). Treatment outcome will be recorded by the referring TC/STC (or by the OR site if the patient started at the original MDR-TB treatment at the OR site). - If not eligible, patient is given the appropriate regimen using a new patient code and will be referred back to the TC/STC (if referred)

SCREENING AND TREATMENT

Patient C **RR-TB patient registered and enrolled on the shorter all-oral Bdq-containing regimen (SSOR) manifesting with non-response or intolerance and without additional resistance to Fq within 4 weeks from initiation of treatment**	**The same procedure follows as that in Patient A (MDR-TB category is unchanged).**	**If eligible, the patient will be enrolled as in Patient A.**
Patient D **RR-TB patient registered and enrolled on a longer MDR-TB regimen (non-Bdq/non-Lzd-containing) with known pre-XDR or XDR results at baseline manifesting with non-response, or intolerance to the regimen.**	The procedures will follow as above depending on whether there was a change in category (MDR to XDR) or not.	If eligible, the patient will be enrolled as in Patient A if there was no change in category (MDR) and as in Patient B (if there was a change in category (MDR to XDR)

Schedule of baseline, routine and post-treatment monitoring evaluations

Clinical Evaluation

	Baseline	2 weeks	Monthly	End of treatment	6- and 12-months after treatment
Clinical assessment*[1]	X	X	X	X	X
Psychosocial assessment*[2]	X	X	X	X	X
Performance status[3]	X				
Weight / BMI	X	X	X	X	X
Peripheral neuropathy screen[4]	X	X	X	X	X
Visual acuity and colour discrimination screen	X	X	X	X	X
Chest X-Ray	X		X, if no response to treatment	X	X
ECG	X	X	X	X	X, if indicated
Assessment and follow-up of AEs	X (X)	X (X)	X (X)	X (X)	X (X)
Treatment outcome assessment				X	X

Bacteriologic Evaluation

	Baseline	2 weeks	Monthly	End of treatment	6- and 12-months after treatment
GeneXpert	X				
Sputum smear	X		X	X	X
Sputum culture[5]	X (X)		X (X)	X (X)	X (X)
Sputum drug susceptibility testing[6]	X (X)		X, if culture-positive[7]		
Other sample smear	X		X, if no response to treatment		
Other sample culture	X (X)		X, if no response to treatment		
Other sample drug susceptibility testing	X		X, if culture-positive[7]		

Laboratory Examination

	Baseline	2 weeks	Monthly	End of treatment	6- and 12-months after treatment
Full blood count	X	X	X	X	X, if indicated
Liver function tests (AST, ALT, bilirubin)	X	X	X	X	X, if indicated
Thyroid stimulating hormone (TSH)	X		X, if indicated		
Serum electrolytes (Na, K, Ca, Mg)	X		X	X	X, if indicated
Serum amylase			X, if indicated		
Urea, creatinine	X		X, if indicated		
Baseline Sugar level (fasting or random) [8]	X		X, if indicated		
HIV / HBV / HCV tests (anti-HBs, anti-HCV)	X				
Pregnancy test[9]	X	X, if indicated	X, if indicated		

Examinations at baseline, during, and after treatment

- Laboratory and ECG monitoring should be continued at monthly intervals (where indicated) for the duration of treatment (i.e., up to 9 months in case of treatment prolongation).
- More frequent monitoring may be advisable in specific situations, including elderly people, patients infected with HIV, affected by HBV- or HCV, diabetes mellitus, or with moderate to severe hepatic or renal impairment.
- In case of electrolyte disturbances or ECG abnormalities, more frequent monitoring should be performed (refer to clinical guidelines).

Daily Treatment Delivery

- Provided through:

1**) In-patient treatment**(is not mandatory),

- but it should be ensured that the patient is well-informed of the study procedures, that baseline and follow-up tests are done on schedule and that patients can tolerate the regimen. The need for admission should, however, be considered when serious or severe AEs occur during treatment.

2**) Ambulatory Daily Treatment Services**

A) Facility Based – STC/RHU

- Referring sites or sites that will be involved in treatment must be informed of the patient's enrolment to the BPaL OR and the agreed **daily treatment arrangements**.

Daily Treatment Delivery

B) **Home or community-based**

- A patient's home,
- At a designated community area,
- Workplace

- Daily treatment will be administered by a **trained** treatment supporter who is either:
  - a trained health worker,
  - community volunteer or
  - family member with a **health background**

Responsibilities of a Treatment Supporter

1) Strictly administer daily treatment
   - visits the patient daily (7 days) for drug administration (or *vice versa*) through the entire duration of treatment

2) Ensure that the patient attends all scheduled follow ups and examination on time and ad hoc

3) Monitor AEs closely and address AEs in a timely manner either by giving advice or relief and informing the clinical staff

4) Update the patient Treatment card daily

5) Initiate contacting the patient if the patient fails to return for treatment as scheduled.

Treatment Follow Up

1. The OR site physician will evaluate the patient during follow up visits. The OR site can refer to TBMAC as necessary. Any management done should be relayed to STC/TC involved in providing treatment support.
2. Follow up tests are requested and done through designated laboratories of each OR site. Results should be made available prior to the patient's scheduled visit.
3. For Urgent evaluation, the STC/TC physician where the patient is registered will evaluate the patient and decide whether the patient needs to visit the OR site. All findings and interventions done should be relayed to the OR site within 24 hours.
4. AEs noted during the Follow up visits (scheduled or urgent) should be noted in Form 6 in REDCap.

Completion and Assigning of Treatment Outcome

- The OR site will assess the patient and declare the treatment outcome
- Outcome of **Cure** cannot be given to patients with Culture Negative at baseline. An Outcome Completed is the most that can be assigned to them. They cannot be included in the analysis for Culture Conversion.
- Any sputum sample obtained up to 90 days before starting treatment may be used as Baseline Culture if the patient has not received any treatment during this period.

Post Treatment Follow Up

- Done at 6th and 12th month after end of treatment
- Clinical evaluation will be done by the OR site physician
- DSSM, TBC and Chest Xay are requested
- Treatment outcome Assessment
- Assessment and follow ups of AEs
- Other tests like ECG and other diagnostic laboratory tests are requested if indicated
- The patient and family of possible recurrence hence the reason for follow up

Discontinuation of treatment due to toxicity or treatment failure

- **The most common situations in which the regimen may be discontinued include:**

1) Intolerable toxicity.

- Bdq and/or Pa need to be suspended permanently
- . Lzd, the drug may be suspended permanently only after completing a total of **four weeks** of Lzd treatment with 1200 mg daily dose,
  - with the patient remaining in the BPaL cohort at the discretion of the TB MAC, considering the clinical response to treatment and the adequacy /duration of Lzd dosing in the patient's regimen.

Discontinuation of treatment due to toxicity or treatment failure

2) Treatment failure

- Poor clinical and bacteriological responses to treatment ,
- DST should be repeated if culture is still positive at month 4, whether or not the treatment regimen is changed, in order to inform future management decision.

3) Resistance to Drugs in the BPaL Regimen

- if resistance to any of the BPaL component drug is discovered after initiating treatment, the patient should be switched to another regimen.

❖ *The study regimen will be discontinued after an evaluation by the TB MAC and switched to an individualized regimen, based on the WHO and country guidelines for regimen design.*

Detection and Management of AEs

- Adverse Events (AEs) are:
  - Untoward medical occurrences
  - Screening of AEs is two weeks after start of treatment, monthly during treatment and at 6th and 12th month post treatment
  - May be present during treatment with a pharmaceutical product, BUT
  - Does not necessarily have a causal relationship with this treatment
  - May be mild, moderate or severe or life threatening
    - Mild to Moderate AEs- managed by:
      - Using ancillary medications
      - Reducing the dose of Lzd
      - Temporary stopping of the regimen
    - Severe or refractory Aes
      - May entail discontinuation of one of the BPaL component drugs

Safety Reporting

aDSM is an essential part in treating DRTB

- The following are routine aDSM activities in the OR:
  - 1) Report all SAE or AESI through the prescribed reporting form or system
  - 2) Complete the report through the Pharmacovigilance Monitoring System (PViMs)
  - 3) The FDA Suspected Adverse Reaction Form can be used in case PViMS is not accessible. This paper form will be submitted to the Regional NTP coordinator and National Drug Policy Compliance Officer (NDPCO).
  - 4) Submit the report within 2 working days from the occurrence of the AE or immediately upon receipt of the information.
  - 5)Manage all AEs accordingly

Serious Adverse Event (SAE)

any untoward medical occurrence that results in:

1. death or is life-threatening
2. hospitalization is required
3. persistent disability or incapacity
4. congenital anomaly/birth defect
5. AEs that do not immediately result in any of the above but needs intervention to prevent serious outcome

Adverse Event of Special Interests (AESI)

- AE documented to have occurred in the clinical trial
- Need to be reported regardless of seriousness, severity or causal relationship to the TB treatment
- AESI considered in BPaL OR
- The OR site physician must assess first whether the AE is an SAE or AESI in this OR

Modification, Interruptions and Discontinuation of the BPaL regimen

- Safe management of AEs may warrant modification of the regimen.
- However, the BPaL regimen has been studied as a standardized course of treatment.
- Modification of the regimen through replacement of any of the component drugs or early discontinuation may result to poor outcomes.
- Favorable results within 24 months relapse free follow up were achieved in BPaL patients who received 4-6months of LZD as part of the BPaL Regimen
- Patients who had a 1200mg total daily dose of Lzd for 4 weeks were included in the final trial analysis following the protocol.

Acceptable modifications in the management of AEs for BPaL regimen:

1)LINEZOLID can be temporarily or permanently interrupted or the dosage can be reduced.

2) Permanent discontinuation of Lzd while Bdq and Pa are continued, is only allowed for patients with toxicity issues that prohibit further treatment with Lzd,

- ❖Response to treatment must always be closely monitored.
- ❖Interruptions/reductions to Lzd without clinical improvement should be regarded with additional caution.
- ❖Permanent discontinuation with a total exposure of less than 4 weeks should be discussed with the TB MAC.

Discontinuation of BPaL regimen due to AEs Related to Bdq and Pa:

- 1) ***Neither Bdq nor Pa may be interrupted or discontinued alone any time during the treatment.***
- 2)***The doses of Bdq and Pa are fixed***

  dose modification of neither medicine is allowed at any time during treatment with the BPaL regimen

Modification, Interruptions and Discontinuation of the BPaL regimen

- INTERRUPTION OF THE FULL BPaL REGIMEN is allowed wthin 4 weeks of treatment and only for 14days
- Any treatment interruptions should be discussed within preferably 1-2 days with the TB MAC (including external experts whenever necessary), and optimally *prior to the interruption of treatment.*
- If a patient is failing treatment, he should be referred to the tb mac for review and design of *a new individualized regi*men.

Outcome Measurement

Outcomes for BPaL Treatment

1**) Cured-** treatment completed w/o evidence of failure AND 2 or more NEGATIVE cultures taken 30 days apart within the last 3 mo of treatment.

2) **Treatment Completed-** treatment completed w/o evidence of failure BUT with no record of 2 or more NEGATIVE cultures within the last 3 mo of treatment

3) **Treatment Stopped due to Baseline Drug Resistance-** resistance to any of the BPaL component drugs noted in the Culture based DST done several months after starting the BPaL Regimen. Patients should be shifted to ITR

Outcomes for BPaL Treatment

4) **Treatment Failed**

- Lack of Culture conversion by the 6th mo of treatment
- Culture Reversion after conversion to Negative at 5th mo or later
- Decision to terminate treatment early because
  - Poor clinical/radiologic response or ADRs as decided by the TBMAC
  - Permanent discontinuation of Bdq or Pa at any time or Lzd if with less than 1 full month of full dosage (1200mg) or if with 1 month full dosage but with no smear conversion or clinical improvement.

- Conversion – two consecutive cultures taken at least 30 days apart are NEGATIVE after an initial culture POSITIVE
- Reversion- After an initial Conversion, two consecutive cultures at least 30days apart are POSITIVE at 5th month of treatment or later.

Outcomes for BPaL Treatment

5) **Died** –A patient who dies for any reason during the course of treatment.

6) **Lost to Follow Up-** A patient with treatment interruption for 2 consecutive months or more

7) **Not Evaluated-** No treatment outcome is assigned

- Transferred out to another treatment unit
- Treatment outcome is unknown

8) **Treatment Success-** sum of Cured and Treatment Completed

Recurrent TB

Occurs anytime after cure or completion of treatment is declared:

1) Two consecutive positive cultures at least 30 days apart, even without clinical signs and symptoms or radiographic deterioration, or

2) One positive culture with clinical signs and symptoms or radiographic deterioration (an isolated positive smear or culture without clinical or radiographic deterioration after treatment completion provides insufficient evidence to define recurrent TB).

Recurrent TB may be further classified as relapse, reinfection, or undetermined as defined below:

- **Relapse**: isolates of the recurrent episode share the same genotype pattern with isolates taken at baseline of the most recent episode of MDR-TB.
- **Reinfection**: isolates of the recurrent episode and isolates taken at baseline of the most recent episode of MDR-TB have different genotype patterns.
- **Undetermined**: there is insufficient information to determine whether the recurrent episode is due to relapse or reinfection.

Data Management

Data Collection

- All implementing sites shall maintain the regular PMDT records and reports. However, special records will be maintained, and reports submitted specific for the BPaL OR
- Patients data will be recorded on standard NTP forms as listed below and electronically in the NTP's Integrated TB Information System (ITIS).
- The regular PMDT reports will be submitted thru channels to NTP per MOP 6th ed.[4] guidelines. REDCap is the official software that will be used for electronic data collection. The Research Team shall ensure the accuracy and completeness of the electronic OR data recording forms.

Data Collection

REDCap Database for the BPaL Study

- It is study-designed and password-protected REDCap database**.**
- It is user friendly, cost-effective, and secure platform to capture and manage research study data.
- It is not open source or freeware,
- It cannot be downloaded by individuals
- The OR data will be collected using the specially designed standardized data collection forms according to primary document forms
- Patients will be informed that there will be soft and hard copies of their data, as well as the data management system, such as storage location and duration, security measures, and data sharing plans.
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Data Collection Forms

- **Existing NTP Forms for PMDT**

1) Presumptive TB Masterlist
2) DR-TB Register
3) DR-TB Treatment Card
4) PPRF- Patient Progress Report Form

- **Individual Patient Study Case Report Forms (CRF) for BPaL**

1) Form 1. Screening
2) Form 2. Enrolment
3) Form 3. Evaluation
4) Form 4. Treatment Completion
5) Form 5. After Treatment Follow-up
6) Form 6. Adverse Event

- All forms are in English, which is the standard language used for the medical records and reporting in the Philippines as patients' informed consent, and hard copies of data collection tools will be retained safely in a secured area inside a locked filing cabinet or drawer in a room, and accessible only by the study investigators and designated staff.
- All paper documents received by the Data Manager will be stored or archived for **ten years** from the submission of the final report or following program requirements. These guidelines also apply to electronically stored data and data that have been printed out for some reason.
- The research team should make sure paper and printouts are not left where unauthorized people could see them. Data printouts should be shredded and disposed of securely when no longer needed including but not limited to, the OR protocol, printouts of all patient data, list of patients and contacts, etc.

Data Analysis

- This operational research will estimate the effectiveness and safety of the BPaL regimen among patients with resistance to at least rifampicin and fluoroquinolone, and patients with MDR-TB with documented treatment non-response or intolerance.

- Data analysis shall apply the methods prescribed in the protocol.

Report writing and dissemination

- Results of the Philippine BPaL protocol will be analyzed as part of the multi-country data led by KNCV.
- Country-specific analysis and publications, if decided, will be discussed in the future with other stakeholders but the NTP will be the first author.
- The final technical report will be subject for review and approval by the Laboratory and Treatment sub-Technical Working Group or sub-TWG (refer to Section III.A. for composition).
- Thereafter, it will be submitted to the Oversight Committee (refer to Section III.A. for composition) for approval. Once finalized, it will be converted for publication and will be disseminated in a stakeholders' meeting.

Data Management

- The Research Team shall consolidate the data on a quarterly basis using the prescribed indicators for monitoring and evaluation as per protocol. ITRC, as the overall project coordinating organization for the Philippines in partnership with the TDF as the local partner organization will perform of the overall project implementation monitoring jointly with the Research Team and other stakeholders or independently.

Monitoring and Evaluation

Methodology	Frequency	Person/s responsible
1. Online data validation	weekly	Research Team
2. Online remote monitoring	monthly	Research Team, ITRC, LIFT-TB consultant, TDF
3. Review of PMDT reports	quarterly	Research Team
4. Review of quarterly progress of patients on treatment	quarterly	Laboratory and Treatment sub-TWG, NTP, Research Team, NTRL, ITRC, LIFT-TB consultant, TDF
5. Monitoring visit to study sites and laboratory facilities (if feasible)	as allowable	Joint monitoring team (Research Team, NTP, NTRL, LIFT-TB consultant, TDF, ITRC, KNCV, members of Laboratory and Treatment sub-TWG , members of Oversight Committee)
6. End-of-research evaluation	2022	NTP, KNCV, ITRC, LIFT-TB consultant, TDF, sub-TWG and Oversight Committee

Description of risks to the operational research participants and methods to minimize risks

- The risks to operational research participants will include

a) the possible intolerance and adverse events that may or may not be related to the component medicines of the BPaL regimen,

b) possible non-response or failure to the regimen in case of poor adherence or underlying patient factors and undetected resistance, which can lead to amplification of resistance,

c) possible breech of data privacy and confidentiality and,

- d) possible stigmatization of study participants.

Description of risks to the operational research participants and methods to minimize risks

- the protocol of this OR ensures active safety monitoring and management of patients started on the regimen, including the clinical and laboratory identification of AEs, timely and appropriate management, and a referral mechanism to a hospital in case of moderate to severe AEs.
- Patient support will be provided to facilitate adherence and clinical management of AEs. Staff will be trained, and project monitoring will be done for early identification of AEs and signs of non-response.
- Staff will observe confidentiality of data to protect patient's privacy at all times throughout the duration of the study in compliance to Republic Act 10173 – Data Privacy Act of 2012. accessing and processing patient's personal and sensitive information will enter into data sharing agreement.

Description of risks to the operational research participants and methods to minimize risks

- All data forms and the password-protected database will only be accessible to the researchers.
- To prevent stigmatization, staff will always maintain privacy and confidentiality of patients and their household contacts or close contacts as part of the contact investigation,
- OR site staff will provide accurate information on DR-TB disease to patients and their families and avoid using languages that can cause stigma,
- research team will ensure that all study related-forms will contain non-stigmatizing language, and patients will be informed where to seek support in case they have experienced stigma.

Description of anticipated benefits to the operational research participants

- The anticipated benefits to patients include treatment success from pre-/XDR-TB attributable to the BPaL regimen as demonstrated in the Nix-TB trial, and good quality of life while on this much shorter, all-oral and three-drug regimen.

- With no injection, patients can receive daily treatment easily on a community-based approach rather than facility-based, thereby eliminating frequent transport to the facility and allowing them to continue uninterrupted work and domestic duties.

Incentive for research participants

- The BPaL OR patients will be given the same support and amount to patients enrolled under PMDT through NTP with support from Global Fund Access TB Project.
- No compensation for study related injuries with be provided to the participants. However, in case of severe or serious adverse events (may or may not be directly related to the treatment regimen), patients will be promptly referred to a specialist and/or to a hospital.

Provision of psychosocial support

Includes:

- 1) Health education and counseling to patients and their family members upon enrolment will be conducted by the staff.

- 2) Psychosocial assessment including mental health status will be done at baseline, repeated regularly while patient is on treatment, and during the post-treatment follow-up visits.

- 3) Individual and/or group counselling session through focus group discussions either face to face (with strict observance of minimum heath standards) or through online platform will be organized by the staff.

Provision of psychosocial support

- 4) Patients will be informed of available support from peer group.
- 5) Prompt and proper referral of patients to a specialist (psychologist or psychiatrist) will be done , if necessary.
- 6) Patients will also be linked or referred to relevant government or non-government programs (with strict observance of data privacy and confidentiality) for financial or social support, if needed.

Data Protection of participants during the follow-up visits amid the pandemic Analysis

- All facilities, providers, and staff involved in patient's care should observe the minimum public health standards such as hand hygiene, physical distancing, and use of appropriate personal protective equipment and comply with infection prevention and control guidelines.
- Before entry to any health facility, patients and their companions will be instructed to wear mask (without filter) and face shield and perform hand hygiene with 70% ethyl alcohol or hand wash by soap and water whichever is available.
- Body temperature will be measured by non-contact digital thermo-sensor at least from 3 cm away from the forehead of the client.
- Patients and companions will fill-out the facility's health declaration form and all those considered as suspect or probable COVID-19 will be segregated immediately from non-COVID-19 patients.
- Staff must require all suspect or probable COVID-19 to wear medical mask. If the patient does not have a medical mask, study site will provide one to the patient.

Data Protection of participants during the follow-up visits amid the pandemic Analysis

- The number of patients and companions gathering will be limited by assigning time slots considering the size/space of the waiting area at the health facility, and at the laboratory and diagnostic facility.
- Schedule (date and time) will be pre-coordinated with the laboratory and diagnostic facility.
- Physical distancing at least 1 meter apart will be observed among patients and companions as well as patients and the staff except during procedures requiring close contact (e.g., blood extraction, placement of ECG leads, etc.).
- Proper disinfection of equipment and surfaces will be done after every patient encounter. emphasized As much as possible, all required monitoring evaluations will be done at one visit.
- Compliance to minimum public health standards will be to the patients and their companions during the follow-up visits.

Description of the potential risks vs anticipated benefit ratio

- The potential benefits are perceived to outweigh the risks considering the high likelihood of treatment success encountered in 90% of very difficult cases in the Nix-TB trial.

Response to new or unexpected findings

- Should there be new and unexpected findings, the study will raise these among the technical committees involved in the study, e.g., the sub-TWG, KNCV, ITRC and TBA which will collectively respond appropriately.

Confidentiality

- All site staff and research team will preserve the confidentiality of all Participants taking part in the study in accordance with International Good Clinical Practice (GCP), and applicable local legislation/regulations.
- Permission from participants will be asked in relation to the required source data verification by the study site staff
- Patients will be given a unique Study Patient Identification
- The written informed consent will contain a clause granting permission for review of the Participants' source data.
- We based our principles on the WMA Declaration of Helsinki and Republic Act 10173 or the Data Privacy Act.

Human subject's protection

- The study will follow the principles of the Declaration of Helsinki. The study protocol will be submitted to the relevant ethics review committee for approval prior to initiation of the study.
- No patient will be enrolled into this study until the investigator has obtained the patient's informed consent.

Ethical considerations:

- As part of the community consultation and preparation, the research team together with NTP, KNCV, TDF, NTRL, PBSP and other stakeholders, conducted a needs assessment to know the challenges in the OR sites and to address this before the commencement of the enrollment of patients.
- There is anticipated direct benefit to the patients enrolled in this study.
- Confidentiality and privacy will be guaranteed, and informed consent obtained from all patients that will be included.
- OR site staff will initially contact patients to ask if they agree to be included in the study. If they agree, full informed consent will be obtained.

Ethical considerations:

- Participants will not receive additional compensation for participation in the study,
- All project staff will ensure that the confidentiality of participants is protected.
- Data access and security rules will be in place for all study personnel, and training will be provided to the health staff prior to the study.
- The project will ensure compliance with the Data Privacy Act of 2012, also known as the Republic Act 10173, an.
- All efforts should be made to conduct interviews and physical examinations in a space where people cannot overhear or see the patient.

NEXT STEPS ON THE BPaL OR

- Review patients recently enrolled (<3-4 weeks) on treatment with intolerance to the current regimen
- Review the RR TB patients for SL LPA and send the specimens at once to TDF
- Send word to STCs (within the zone catchment) regarding patients who can be screened for eligibility to BPaL OR

THANK YOU

PBSP

Philippine Business for Social Progress

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VECTORS