



Pilot study to estimate the effectiveness and safety of the BPaL treatment regimen in Philippines

Irene A. Flores, MD



- Data Collection Forms version 9
- Informed Consent Forms ver 9
- BPaL OR Protocol PHL ver 9.pdf 🚢
- BPaL OR TOT Program of Activities.pdf 🚢
- DRAFT BPaL IP Ver 3.pdf 🚢

- TOT Program Of Activities
- BPaL Protocol





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"PILOT STUDY TO TEST THE EFFECTIVENESS AND SAFETY OF THE BEDAQUILINE, PRETOMANID, LINEZOLID (BPAL) TREATMENT REGIMEN IN THE PHILIPPINES"

TRAINING OF TRAINERS

May 19-21, 2021 1:00 PM - 5:00 PM

| | SESSION 4 /May 10 | Annual Control of the | |
|-----------------------------------|--|--|--|
| SESSION 1 (May 19, 2021) | | | |
| | 1:00-5:00 PM | | |
| 12:30-1:00 PM Online Registration | | | |
| 1:00-1:15 PM | Opening Ceremonies | Moderator: | |
| | Prayer | Ms. Ma. Cristina Brigaste | |
| | Introduction of facilitators, participants, and guests | Asst Moderator: | |
| | | Ms. Patrice Jamie Cabasis | |
| | Welcome Remarks | Dr. Anna Marie Celina Garfin | |
| | 100 a 70 mar (100 a 70 mar) and (100 a 100 a | (DPCB-NTP) | |
| 1:15-1:20 PM | Course Overview | Dr. Marietta Solante | |
| | | (LCP-PMO) | |
| 1:20-1:50 PM | Rationale for the BPaL Regimen | Dr. Maria Imelda Quelapio | |
| | | (KNCV) | |
| 1:50-2:10 PM | Updates on PMDT and the Role of | Dr. Rem Paul S. Bautista | |
| | BPaL Regimen in the Philippines | (DPCB-NTP) | |
| 2:10-2:20 PM | Q&A (or poll questions) | Moderator/s | |
| 2:20-3:05 PM | BPaL OR Country Protocol Part 1 | Dr. Irene Flores | |
| | 989 | (BPaL OR PI) | |
| 3:05-3:15 PM | BREAK | | |
| 3:15-3:35 PM | Q&A (or poll questions) | Moderator/s | |
| 3:35-4:05 PM | BPaL OR Country Protocol Part 2 | Dr. Irene Flores | |
| | | (BPaL OR PI) | |
| 4:05-4:20 PM | Q&A (or poll questions) | Moderator/s | |
| 4:20-4:30 PM | Implementing Structure | Dr. Anna Marie Celina Garfin | |
| | | (DPCB-NTP) | |
| 4:30-4:50 PM | Updates on Laboratory | Mr. Earl Mantes | |
| | | (NTRL-FOM) | |

Philippine protocol for BPaL introduction and scale-up under operational research ver9

Pilot study to estimate the effectiveness and safety of the BPaL treatment regimen in Philippines

March 2021

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Informed **Concent Forms** (ICF)





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Unang Bahagi. Ang Impormasyon ng BPaL Regimen para sa Pasyente

Mungyaring basahing mahuri ang mga sumusuncel na Impormasyon at kong mais ay ng usapan ngo ng mga kasansik kabilapan at myong didoktor. Tamungin ang mga bagay nahindi namanawan o humingi ng karagdagang impormasyon kung kinakailangan. Pag-isipang mabuti kung nais ninyong lumahuh. Pagkatapon mananwan ng mabuti at nasagot ang lahat ng katanungan at ayon. Ang pagsali sa pamandiksik na ito ay kusang koob. Bo ay nangangahuhugan na ang inyong pakkitalabok ay inyong sariting pagpapasyo. Manaring umanggi sa pagsali sa pag-arari na ito at na inyong naisin. Manari pa ring magkaroon ng benepisyong medikal o pangkalusugan kahit na turnanggi so bawiin nang pakkitalabok sa pas-arari na ito at na inyong naisin. Manari pa ring magkaroon ng benepisyong medikal o pangkalusugan kahit na turnanggi so bawiin nang pakkitalabok sa pag-arari na ito at

Fara as inyong kashuman, ang TB ay isang sakit na dulor ng isang bakterya na kadalasang nakakaapeko sa baga at masaring kumalar sa hangin mula sa isang taong may TB sa pamamagitan ng nag ubo, pagbahing. Nagagamot ang TB; ngunit may mga bakterya ng TB na hindi tinatablam ng dalawa sa mga pinaka-epoktibong gamot (*chonichid in Khimpichi* ni karaniwang ginagamit sa mga dalawa sa mga pinaka-epoktibong amot (*chonichid in Khimpichi* ni karaniwang ginagamit sa ring hindi malanasan ng ba pang gamot katulad ng Fhuoroquinolone. In ay tinatawag na pre-extensively drug resistant ne extensively drug resistant ne extensively drug resistant ne RUMR TB).

Ang kasalukuyang gamutan sa pre/XDR TB ay gumagamit ng mga di pangkarinawang mga gamut sa TB (kilala bilang Second line drugg) na umaubut sa 20 bawang gamutan at mas masuming sida



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friends, and your doctor, if you wish. Ask us if there is anything that is not clear, or if you would like more information. Take time to decide whether or not you wish to participate. After you are properly satisfied that you understand this study, and all your queries/questions have been satisfactorily answered, and that you wish to participate. you must sign an informed consent form attached with this information sheet. Your participation in this study is object from attached with this information sheet. Your participation in this study is object in the study if you want to or decide to do so out of your own choice. You do not have to be in this study if you do not work to. Even if you decide to participate in this study, you may withdraw (take shock your decision to participate) from this study at any time during the course of the study. Your crusal to participate or withdrawal will not affect any medical or health

What is the purpose of this study?

What is the purpose of this study?

As you may know, To Is a disease caused by bacteria usually affecting the lungs and As you may know, To Is a disease caused by bacteria usually affecting the lungs and the stream of the cought of the stream of the stre XDR) or extensively drug-resistant tuberculosis (XDR-TB).

Current treatment of pre-/XDR-TR involves the use of less common anti-TR drugs (also Current treatment of pre-JXDR-TB involves the use of less common anti-TB drugs (also years and with more side effects and less chance of cure. Therefore, new TB drugs and novel regimens are urgently required to enable faster, safer and more effective treatment for persons with drug-resistant TB. A new regimen that is now available in the properties of the properties these patient groups. It has been found effective and side effects were manage



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| l | (parent's/guardian's name), give permission for the participant, |
|-------------------|---|
| | (name of 15-17 year old individual) to participate in this operational resear |
| entitled "Pilot s | tudy to estimate the effectiveness and safety of the BPaL treatment regimen in the |
| Philippines." Th | e study has been explained to me and my questions answered to my satisfaction. I |
| understand that | t my child's right to withdraw from participating or to refuse to participate will be |
| respected and t | hat his/her responses and identity will be kept confidential. I give this consent |
| voluntarily. | |
| | |
| | |

Parent/Guardian's Printed Name ____

Signature or thumbprint of Parent/Guardian

Date (MM/DD/YYYY)

If the Parent or Guardian is illiterate, a literate witness must sign, (If possible, this person should be selected by the Parent or Guardian of the participant and should no connection to the care providers). Patients/Guardians who are illiterate should include their thumbprint.

I have minessed the accurate reading of the consent form to the Parent or Guardian of the potential recipient of the BPAL regimen, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.



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Bahagi III: Nabatid na Pahayag ng Pahintulot mula sa magulang o tagapag-alaga ng isang 15-17

Ako, (pangalan ng magulang/tagapag-alaga), maghibigay ng pahintulot para sa kalahok, pangalan ng 15-17 taong gulang na indibidwai) upang lumahok sa pananalikuik na ito "Pilot study to estimate the effectiveness and safety of the IPpa I treatment regimen in the Philippines." Ang pag-aaral ay naipaliwanag sa akin ng aking anak na umalis mula sa paglahok o tumanggi na lumahok ay igagalang at ang kanyang ma tugon at pagkakakitanlan ay panatilihing kumpidensyal. Boluntaryong nagbibigay ako ng pahintulot na ito.

Pangalan ng Magulang/tagapag-alaga

Lagda o thumborint ng magulang/tagapag-alaga

Petsa (MM/DD/YYYY)

kung ang magulang o tagapag-alaga ay hindi marunong magbasa at magsulat, kang sakki na marunang magbasa at magsulat ang masarimg humagda. (kung posibk, ang taong ito ay dapat napili ng Magulang o Tagapangalaga, ang kalahok at dapat walang koneksyon sa mga tagapagbigay ng pangangalaga). Ang mga pasyenter / Tagapangalaga

Nasaksihan ko ang tamang pagbabasa ng consent form sa Magulang o Tagapangalaga ng ng kalahok sa RPal. Recimen. at naskaroon ng paskakataons mastanons. Kinukumpirma



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BPaL OR KIT Implementation Plan (IP)

Implementation Plan for BPaL Operational Research, Philippines Ver 1

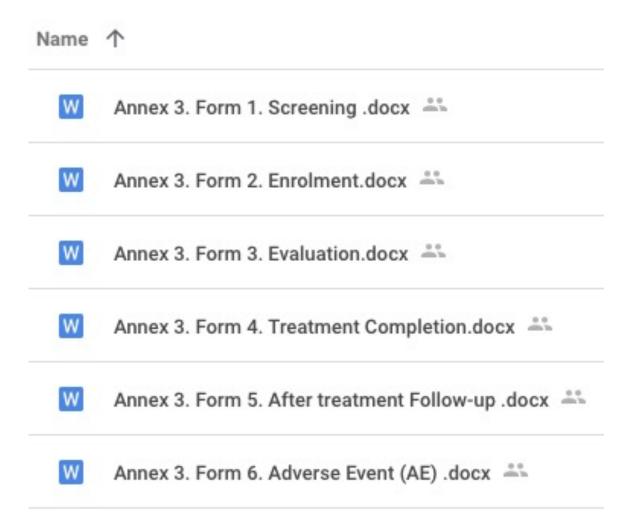
12 May 2021

IMPLEMENTATION PLAN FOR THE BEDAQUILINE-PRETOMANID-LINEZOLID OPERATIONAL RESEARCH (BPAL OR), PHILIPPINES

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REDCap Data
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Objectives of the Study

Primary objectives:

- To estimate the effectiveness of the BPaL regimen by assessing the end of treatment outcome
- To estimate the safety of the BPaL regimen by determining the rates of serious adverse events (SAE)

Secondary objectives:

- To determine the time to sputum culture conversion
- To determine the rate of recurrence at 6 and 12mo after the successful treatment with the BPaL regimen.
- To determine the rate of occurrence of AESIs (QT-prolongation, peripheral neuropathy, myelosuppression, optic neuritis and hepatotoxicity)

Objectives of the Study

 The goal is to enrol 100 patients over a period of 2 years in 12 sites in the Philippines based on the inclusion and exclusion criteria after informed consent.

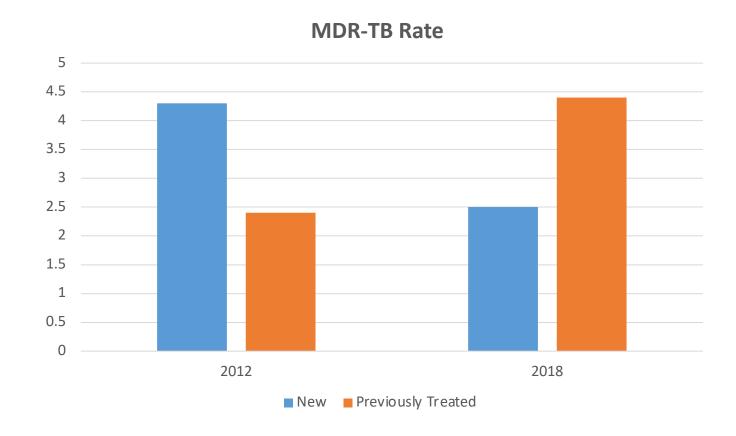
The OR study, will strengthen the NTP to implement the BPaL regimen, and the results of the OR will be used to support national scale-up of the regimen.

DRTB in the Philippines

■ The Philippines is among the world's high burden countries for TB and MDR-TB with an MDR-/RR-TB incidence of 21,000 (10,000-34,000) and 19/100,000 (9.6-32).

DRS in the Philippines, 2012 and 2018

The Philippines has had two drug resistance surveys (DRS) of nationwide scale:



DRS in the Philippines

■ The Global TB Report, 2020, showed that MDR-/RR-TB was 1.8% (1.3–2.6) among new, and 28% (27–29) among previously treated TB cases.

 Only 1 patient had XDR among 2,107 with MDR-TB; pre-XDR was 2%

Patient recruitment and selection

- The study site staff or the focal point persons, either the PMDT doctor or nurse, will recruit BPaL patients from the DR-TB patients who are assessed using a triage approach.
- All detected TB patients are tested for both FL and SL resistance, using rapid molecular methods (including Xpert MTB/XDR cartridge, once available).

Patient recruitment and selection

If this is not feasible, FL and SL DST could be limited to only those TB patients who have detected R resistance.

They can also recruit patients who are on programmatic treatment regimens who need to be shifted to another regimen due to intolerance or failure.

DR-TB treatment regimens in the country

| Regimen | Composition | Duration | | | |
|--|--|--------------|--|--|--|
| A. UNDER PROGRAMMATIC CONDITIONS | | | | | |
| Shorter Regimen | | | | | |
| Standard short all-oral regimen (SSOR) | 4-6 Lfx-Bdq (6)-Cfz-Pto-E-Z-Hhd/ 5 Lfx- Cfz-Z-E | 9-11 months | | | |
| Longer Regimen ** | | | | | |
| Standard long all-oral regimen (SLOR) for FQ- susceptible (FQ-S) | 6 Lfx-Bdq-Lzd-Cfz/12-14 Lfx-Lzd-Cfz | 18-20 months | | | |
| 2. Standard long all-oral regimen (SLOR) | 6 Bdq-Lzd-Cs-Cfz-Dlm/12-14 Lzd-Cs-Cfz | _ | | | |
| for FQ-resistant (FQ-R) | | 18-20 months | | | |
| Individualized Regimen | | | | | |
| Individualized Treatment Regimen (ITR) | Composed of at least 4 likely effective | 20.months | | | |
| | drugs as approved by the Medical | | | | |
| | Advisory Committee (MAC) | | | | |
| B. UNDER OPERATIONAL RESEARCH CONDITIONS*** | | | | | |
| BPaL regimen | Bdq-Pa-Lzd | 6-9 months | | | |

Component Drugs in the Study

Bedaquiline Pretomanid Linezolid

Evidence on the drugs proposed in this study: BDQ

Study is limited for Bedaquiline

- regarding the safest and most effective dose,
- the dose response relative to TB outcomes,
- the singular contribution of Bdq when added to other active drugs in a regimen, and
- the use of Bdq together with other new anti-TB drugs

Evidence on the drugs proposed in this study: BDQ

Safety and Tolerability

- QTC Prolongation
- Transaminitis or elevated liver enzymes
- Drug to Drug Interaction with EFAVIRENZ
- No adequate and well-controlled studies in pregnant women.

Evidence on the drugs proposed in this study: Linezolid

Dosing

- 600 mg daily and given for the entire course of therapy
 - Current recommendation in PMDT
 - Can either be decreased to 300 mg daily or stopped if limiting toxicity develops.

- 1200 mg daily was used for Lzd (NIX trial)
 - with the option to reduce or stop after one month of treatment in case of toxicity

Evidence on the drugs proposed in this study: Linezolid

Efficacy

- increase culture conversion and treatment success in DR-TB patients.
 - demonstrated in two randomized controlled trials and in observational studies
- It is an effective agent, but its use is <u>limited by</u> safety concerns.

Evidence on the drugs proposed in this study: Linezolid

Safety and Tolerability

- myelosuppression, optic neuritis, neuropathy, and lactic acidosis,
 - >discontinuation of Lzd use can occur in as many as 18% of persons who receive treatment with Lzd.

- Adverse events (AE) more frequent at more than 600 mg a day
 - > can be identified early with routine monitoring
 - > often reversible upon discontinuation of the drug or lowering of the dose.

- Effect on pregnancy and breastfeeding
 - **►**limited; <u>Caution is advised</u>

Evidence on the drugs proposed in this study: Pretomanid

Safety and Effectiveness

- has M.tb bactericidal activity as a single drug based on Phase 2 Early Bactericidal Activity studies
- Its safety and effectiveness for its use is established ONLY in combination with Bdq and Lzd as part of the recommended dosing regimen.
- Tested for use among DR-TB patients co-infected with HIV- including those receiving ARVs.

Evidence on the drugs proposed in this study: Pretomanid

Safety and Effectiveness

- Cause <u>testicular atrophy and impaired fertility in</u> male rats but not in monkeys.
 - -potential effects on human male fertility have not yet been adequately evaluated

There are no data available on the use of Pa in pregnant women.

- 1. MTB patient with a laboratory-confirmed (rapid and/or phenotypic DST) resistance to at least rifampicin and fluoroquinolone(s) within the last three months* of the screening date;
- 2. Patient has strong clinical and radiological evidence of active TB AND has been a close household contact of an index patient with:
 - a. active laboratory-confirmed resistant TB to at least rifampicin and FQs within the last 3 months of screening date AND
 - b. no documented resistance to any of the BPaL component drugs (Bdq, Pa, Lzd) within the last three months * of the screening date; or

3. has been treated for MDR-/RR-TB and has documented non-response to treatment, has bacteriologically active TB ** within the last three months* of the screening date, and a decision has been made by the TB Medical Advisory Committee (TB MAC) to shift the patient to the BPaL regimen; or

4.has been treated for MDR-/RR-TB, has documented intolerance, to treatment, has bacteriologically confirmed active TB** within the last three months* of the screening date, and a decision has been made by the TB MAC to shift the patient to the BPaL regimen; and

Any of the above AND

- Patient is willing and able to give informed assent or consent (signed or witnessed consent, if illiterate) to be enrolled in the OR and adhere to the OR procedures and the follow-up schedule; and
- Patient is at least 18 years old at the time of enrolment

**Non-response is defined as: a) two consecutive positive cultures of sputum samples collected after the end of the 2nd month (separated by at least 30 days) of treatment with lack of clinical improvement or deterioration; or b) treatment outcome of failure according to the WHO definition

***Intolerance is defined as: Inability to continue the second-line MDR-/RR-TB regimen due to a documented adverse event to any of the component drugs.

- Patients for BPaL must have:
- * Documented proof of active TB (LPA or culture) within the last 3 months before deciding that a patient is eligible for the BPaL regimen, regardless of history of previous TB treatment.
- If the patient has not been on treatment during the previous 3 months, a repeat LPA, culture, and pDST are needed.

 Patient who developed Intolerance or Non response to Treatment are shifted to BPaL Regimen irrespective of Resistance to Flouroquinolone

Relative indications needing TB MAC recommendation

- is 15-17 years old at the time of enrolment with recommendation for inclusion in BPaL by the TB MAC
- has mild form of extrapulmonary TB with or without pulmonary TB with recommendation for inclusion in BPaL by the TB MAC

Exclusion Criteria

1. Known severe allergy to any of the BPaL component drugs (Bdq, Pa, Lzd); or

2. DST showing resistance to any of the component drugs; or

3. Previous exposure to any of the component drugs or Delamanid (Dlm) for >4 weeks; or

4. Known severe adverse event associated to any of the BPaL component drugs, or

Exclusion Criteria

- 5. Extrapulmonary TB that would require treatment longer than would be usual for pulmonary TB (e.g., TB meningitis, other central nervous system TB, or TB osteomyelitis); or
- 6. Inability to take oral medications; or

7. Body weight of <35 kg

8. Pregnant; or plan to conceive within the next year; or

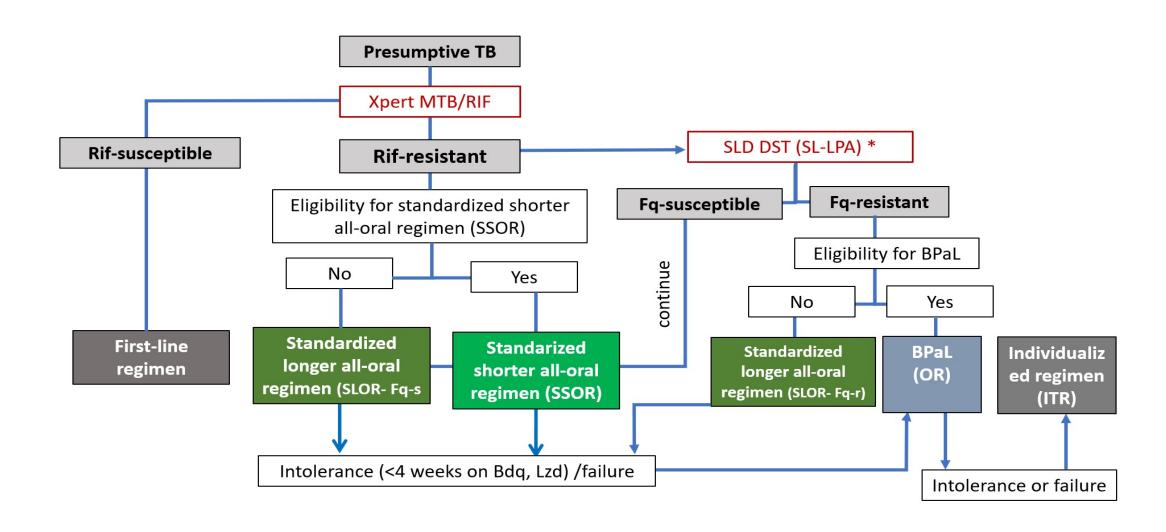
Exclusion Criteria

9. Childbearing ability and is reluctant to use effective contraception while on the BPaL treatment;

10. Breastfeeding; or

11. The TB MAC decides that it is not in the best interest of the patient to be enrolled on the BPaL OR due to the need of an individualized treatment regimen.

Algorithm showing eligibility to BPaL



Selected relative contraindications to the use of the BPaL patients with MDR-/RR-TB

| High risk of cardiac arrhythmia | Baseline QTcF > 500ms | |
|---------------------------------|--|--|
| | History of syncopal episodes, ventricular arrhythmias, heart failure or severe coronary artery disease | |
| | Family history of long-QT syndrome | |
| | | |
| | | |
| Severe anaemia | Haemoglobin level < 8.0 g/dL | |
| Moderate thrombocytopaenia | Platelet count <75,000/mm ³ | |
| Moderate neutropaenia | Absolute neutrophil count < 1000/ mm ³ | |
| | | |
| | | |

Selected relative contraindications to the use of the BPaL patients with MDR-/RR-TB

| Severe peripheral neuropathy | Grade 3 or Grade 4, according to the Division of Microbiology and Infectious Diseases (DMID) | |
|------------------------------|--|--|
| | | |
| | | |

¹ Paresthesia grade 3: severe discomfort; narcotic analgesia required with symptomatic improvement; and /or BPNS subjective sensory neuropathy score 7-10 on any side. Grade 4: incapacitating; or not responsive to narcotic analgesia.

Selected relative contraindications to the use of the BPaL patients with MDR-/RR-TB

AST/ALT > 3.0 x upper limit of normal (ULN)Evidence of hepatic impairment Total bilirubin > 2.0 x ULN Albumin < 32 g/L Significant renal insufficiency Serum creatinine > 3.0 x UI N No dose adjustment, other than an interruption for an AE, should be made for Bdq or Pa. Lzd dose reductions, interruptions or discontinuations are allowed. Primary metabolites of Lzd accumulate in renal impairment and the clinical significance of this is unknown. Due to limited experience, caution should be exercised in patients with significant renal impairment.

Selected relative contraindications to the use of the BPaL patients with MDR-/RR-TB

Concurrent use of medications that have known interactions or **overlapping** toxicities with BPaL component drugs

Inducers of CYP450 enzymes:

- Efavirenz
- Rifamycin
- Antiepileptics

Inhibitors of CYP450 enzymes:

- Fluconazole/itraconazole
- Clarithromycin/erythromycin

First-line TB drugs (HRZE)

Drugs that prolong the QT interval (see list in clinical guide)

Drugs that increase serotonin levels (see list in clinical guide)

Selected relative contraindications to the use of the BPaL patients with MDR-/RR-TB

In case of relative contraindications, the clinician judges that the potential benefits outweigh the potential risks (also taking into account alternative treatment options), treatment may proceed with caution as part of the OR study. In these situations, advice needs to be sought from the TB MAC.

Adolescents 15 years -17 years may be included for treatment with the BPaL regimen on the decision of the TB MAC (as noted in the inclusion criteria).

Adolescents

Note: Bdq is recommended for use in patients aged 6 and over by the WHO, and Lzd for all ages. There is no recommendation for Pa (Dlm is recommended in those aged 3 and over).

Extrapulmonary TB

Patients with "minor" forms of extrapulmonary TB can be included for treatment with BPaL on the decision of the TB MAC (as noted in the inclusion criteria). Consideration should be given to the planned duration of treatment, and any planned strategies for monitoring treatment response in the absence of sputum testing.

HIV Infection

People living with HIV may be included for treatment with the BPaL regimen. In the Nix-TB study, 50% of participants were HIV-positive and treatment outcomes were similar between groups.

There are two important drug-drug interactions between antiretroviral drugs and Bdq, also mentioned above:

- Efavirenz: induces metabolism of Bdq, reducing drug levels
- Ritonavir: inhibits metabolism of Bdq, increasing drug levels

HIV Infection

ARV regimens including the above drugs should be modified at least one week before commencing an HIV-positive patient on treatment with BPaL.

ARV therapy including zidovudine should be used with special caution as zidovudine and Lzd may both cause peripheral nerve toxicity and are known to have myelosuppression cross-toxicity.

Informed Consent

Patients who are eligible for inclusion in the study will be given information about MDR/XDR-TB and the BPaL treatment regimen. Patients will be provided with information in a language that understandable to them. Consent for enrolment should be based on the Patient Information Sheet (Annex 1). Patients should have the opportunity to discuss the consent form with the medical officer/treatment supporter. The patients will be assured that their decision to participate in the study or not will not affect the quality of care they will receive.

Informed Consent

■ The patient will be given a copy of the Informed Consent Form (ICF) and if needed, the patient is given at least 1-2 days to discuss his or her decision to family and significant others. Once the patient agrees to participate in the study, the patient will be asked to sign the consent form.

• All patients who are not eligible for the study, or refuse to be enrolled, or withdraw after enrolment, will be managed with a DR-TB treatment regimen according to the national guidelines.

The total number of patients to be enrolled on the BPaL regimen during the first 2 years is 100.

The site selection criteria for the BPaL OR include the following characteristics of the site.

The site:

- has been implementing PMDT for 1 year or more.
- has a strategic location providing access to other referring facilities.
- has a strategic location with access to private and public facilities for the identification and management of AEs and comorbidities.
- has access to diagnostic and monitoring laboratories.
- has >30 MDR/RR-TB patients enrolled in 2019.
- has a designated physician trained in PMDT.

 No statistical sampling will be done as all eligible patients will be offered the BPaL regimen.

The number of patients to be treated under this protocol was estimated based on the following assumptions:

1) Patients will be recruited from all study sites over the span of 2 years to reach the target of 100 patients. Non-study sites may refer potential patients to the study sites guided by the zoning mechanism.

| GION | FACILITY/ADDRESS | PHYSICIAN/NURSE | Curren t # of ongoin g patient s | Enrolled cases 2019 | Rapid TB Diagnostic Laboratory (Xpert site) | TBC laboratory | DST laboratory | LPA laboratory | Access to lab/dxtics services | ZONING of patients |
|------|--|--|---|---------------------|---|-------------------|-------------------|-------------------|-------------------------------|--------------------|
| :R | Lung Center of the Philippines PMDT TC NCPR Bldg, Quezon Ave., Quezon City | Dr. Joan Tuy/09278020796 joantuymd@gmail.com John Alfred Caparos/09178736713 john.alfred.caparros@gmail.com Paula Carmelli Fulgencio/09275345860 paulacarmeli@gmail.com Joanna Kristine Espena/091569332 jespena@gmail.com Ma Jhoanna De Gracia/09329141332 jhoannagascon@gmail.com | 108 | 126 | LCP | LCP | NTRL | NTRL | YES | NCR |

| NCR | Dr. Jose N. Rodriguez Memorial Hospital (DJNRMH) - PMDT TC Administration Site, St. joseph, 187 Tala, Caloocan city | Dr. Chiqui Villegas/09175333780 chiqs126@gmail.com Kristine Marie Pulanco/09255458560 kmtpulanco@gmail.com | 50 | 93 | DJNRMH | LCP | NTRL | NTRL | YES | NCR |
|-----|--|---|----|----|--|--|------|------|-----|---|
| | Medical Center Mc Arthur Hiway San Fernado La Union | Dr. Chester Directo/ 09209481584 chesterdirecto@gmail.com Lovely Ducusin/09399393024 Ilducusin.pbsp@gmail.com Amor Santiago/09167760011 amorsantiago@gmail.com | 20 | 36 | La Union Medical (LUMC) | Dagupan Doctors Villaflor Memorial Hospital (DDVMH) | NTRL | NTRL | YES | Region I CAR Region II (Cagayan Valley) |
| | Region I Medical Center Arellano St., Dagupan City | Dr. Arthur Sy | 48 | 54 | Pangasinan Provincial Hospital (PPH) | DDVMH | NTRL | NTRL | YES | Region I |

| III | Jose B. Lingad Memorial Regional Hospital (JBLMRH) Mc Arthur Hiway Dolores St., San Fernando, Pampanga | Dr. Sheryll Magayanes / 09176771677 shexy716@yahoo.com Mary Joy Chavez / 09273953871 | 24 | 41 | JBLMRH | Central Luzon CHD TBC Laborator y (CL CHD TBC Lab) | NTRL | NTRL | YES | Central Luzon |
|------|---|--|----|----|--|---|---------|------|-----|------------------------|
| IV A | Batangas Medical Center (BatMC) Kumintang Ibaba, Batangas City | Dr. Luisa Elena L. Ticsay/ 09237358076 ellenlipatticsay@gmail.com Marvin Catilo / 09175617098: mvcatilo@gmail.com | 23 | 61 | BatMC | Philippine Tuberculo sis Society, Inc. (PTSI QI) | PTSI QI | NTRL | YES | CALABARZON MIMAROPA |
| V | Sorsogon Medical Mission Group Hospital and Health Services (SMMGHHSC) Pangpang, Sorsogon City, Sorsogon | Dr. Nancy Rose Labarete/09175590422 nflabarete@gmail.com Carlo Ryan Estopace/09175878905 crestopace@gmail.com | 39 | 40 | SMMGHHSC (all patients screened in SMMGHHSC only); the rest of the zoned specimens are temporarily routed to Gubat and Pilar | SMMGHH SC | NTRL | NTRL | YES | Bicol Region |

| V | /1 | Western Visayas Medical Center (WVMC) Q. Abeto St., Mandurriao, Iloilo City | Dr. Leonie Estoce/09228432749 learidel@gmail.com Kristy Corazon Cabanalan/0936-9950195 kgcabanalan.pbsp@gmail.com Elena Belican/09184190667 enbelivano.pbsp@gmail.com Marian Rose Calawigan/09089326161 macalawigan.pbsp@gmail.com | 74 | 77 | WVMC | WVMC | WVMC | NTRL | YES | Region VI (Western Visayas) |
|---|-----|---|---|----|----|------|---------|--|------|-----|---------------------------------------|
| V | /11 | Eversly Child Sanitarium (ECS) | Dr. Alimer Nassale/ 09177798804 | 39 | 98 | ECS | PTSI-QI | PTSI-QI | NTRL | YES | Region VII (Central Visayas) |
| | | Jagobiao, Mandaue City | ainassaie.pbsp@gmail.com | | | | | | | | Region VIII (Eastern Visayas) |
| | X | Zamboanga City Medical Center (ZCMC) Dr.Evamgelista St., Sta. Catalina, Zamboanga City | Dr. Marcelino Medina/09279759575 sanmarcelinoclinic@gmail.com Shermain Labrador/09175106300 sheirn23@gmail.com | 36 | 38 | ZCMC | ZCMC | Davao TB Referenc e Laborato ry (DTRL) | NTRL | YES | Region IX (Zamboanga Peninsula) |

| X | Northern Mindanao Medical Center (NMMC) Capitol Road, Cagayan de Oro City | Dr. Leslie Christine B. Magsayo-Salon/ leschristinemagsalon@g mail.com Doris F. Apit/09173635761 dfapit.pbsp@gmail.com Marie Fe Chiu/09985512745 mmchiu.pbsp@gmail.com | 38 | 49 | NMMC | CDO Polymedic Plaza (CDOPMP) | DTRL | NTRL | YES | Region X (Northern Mindanao) BARMM CARAGA SOCCSKSARGEN |
|----|---|---|----|----|------|------------------------------|------|------|-----|--|
| XI | Southern Philippines Medical Center (SPMC) JP Laurel Ave., Bjada, Davao City | Dr. Virgilio Dave Cania/09228207147 deyvcania@gmail.com deyv_cania_cania@yahoo .com David Glen Olimba/09339476136 olimbadavidglen@gmail.c om | 86 | 67 | SPMC | DTRL | DTRL | NTRL | YES | Region XI (Davao Region) CARAGA Region XIII (SOCCSKSARGEN) |

2) Data on the average enrolment of patients with XDR-TB nationwide from 2017-2019 was 48 patients per year.

3) Trend on final treatment outcome of patients under PMDT from 1999-2018 showed <1% had failed outcome equivalent to an average of 27 patients from 2016-2018.

4) ≥75 patients nationwide may be eligible to receive the BPaL regimen.

5) It is estimated that around 50 patients per year is feasible to be enrolled under the study considering the inclusion and exclusion criteria as well as the access of patients from non-study sites

OR Sites for BPaL OR in the Philippines

National Capital Region (NCR):

- Lung Center of the Philippines, Quezon City
- Dr. Jose N. Rodriguez Memorial Hospital, Caloocan City

Region 1:

- Ilocos Training and Regional Medical Center, La Union
- Region I Medical Center, Pangasinan
- Region III: Jose B. Lingad Regional Memorial Hospital, Pampanga
- Region IV-A: Batangas Medical Center, Batangas

OR Sites for BPaL OR in the Philippines

- Region V: Sorsogon Medical Mission Group HHSC, Sorsogon
- Region VI: Western Visayas Medical Center, Iloilo City
- Region VII: Eversley Childs Sanitarium and General Hospital, Cebu
- Region IX: Zamboanga City Medical Center,
 Zamboanga City
- Region X: Northern Mindanao Medical Center,
 Cagayan de Oro City
- Region XI: Southern Philippines Medical Center,
 Davao City

THANK YOU



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