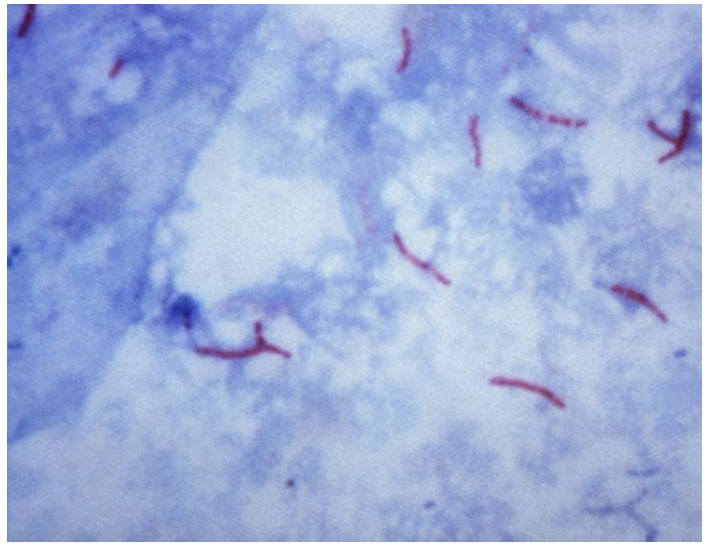
Introduction to BPaL/M



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Questions

- **Have you ever cared for a patient on the BPaL/M regimen?**
- **Have you ever had an MDR pt?**

DR-TB Care = team sport

Objectives

- Identify drugs of the BPaL/M regimen
- Describe who can be treated with the BPaL/M regimen
- Identify common adverse reactions to medications
- Learn how to monitor for side effects
- Become familiar with resources to assist patients on BPaL/M

The 5 Ws of BPaL/M

What is it?

Who is it for?

Why is it being used?

When is it being used?

Where is it being used?

What is the BPaL/M regimen?

6 months
(26 weeks)
given 7days/week with food

Bedaquiline
400mg PO daily x 14 days followed by
200mg PO 3x/week

Pretomanid
200mg PO daily

Linezolid
600mg PO daily
can be dose adjusted or changed to TIW

Moxifloxacin
400mg PO daily
if FQ sensitive / no contra-indication

Can be extended to 9 months (cavitary disease or culture conversion longer than 2 months)

Bedaquiline

- **Activity against TB**: bactericidal activity (similar to INH); in vitro activity against replicating and nonreplicating bacilli.
- **Class**: Diarylquiniolone
- **Dose**: 400 mg qd load x 2 wk, then 200mg tiw
- **Adverse Reactions**
  - **Hepatoxicity**
  - **QTc Prolongation**
- Long-half life –5.5 months (!!)

Who is BPaL/M for?

Adults (> 15)

With pulmonary TB that is:

- CDC (1): drug resistant (XDR), treatment-intolerant, or nonresponsive multidrug-resistant (MDR) tuberculosis
- WHO(2): MDR (BPaLM); Fluoroquinolone resistant MDR (BPaL)

Not approved for:

- **Patients <15yo**

Excluded from studies/no data

- Severe extrapulmonary (CNS, bone)
- Pregnancy/breastfeeding
- LFTs > 3x uln
- Cardiac disease (arrhythmia risks)

- (1)Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease
- https://www.cdc.gov/tb/hcp/treatment/bpal.html?CDC_AAref_Val=https://www.cdc.gov/tb/topic/drtb/bpal/default.htm
- (2) WHO consolidated guidelines on tuberculosis https://iris.who.int/bitstream/handle/10665/365308/9789240063129-eng.pdf?sequence=1

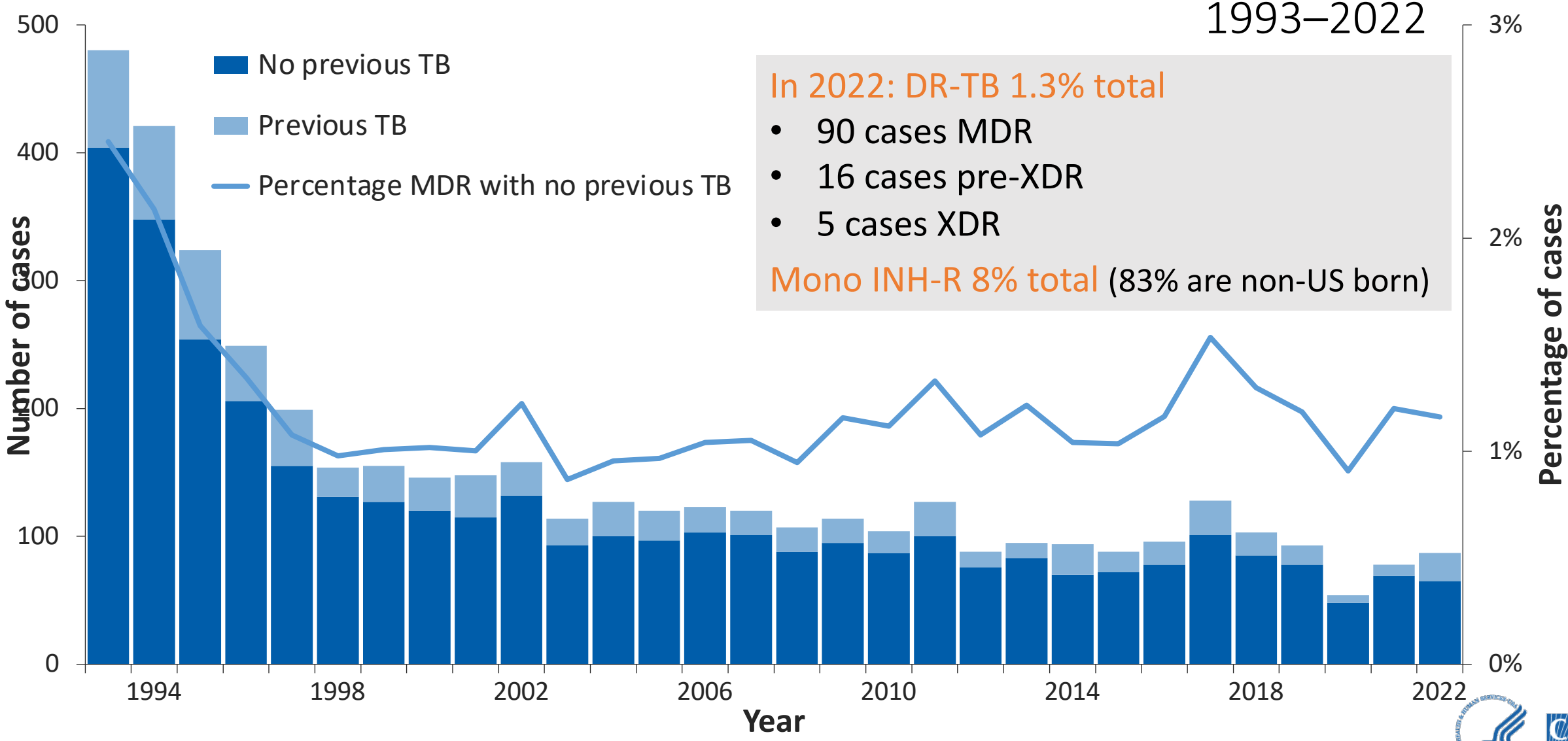
Drug-Resistant TB: Definitions

- **Mono-resistant:** Resistance to a single drug
- **Poly-resistant:** Resistance to more than one drug, (not isoniazid and rifampin)
- **Multidrug-resistant (MDR):** Resistance to at least isoniazid and rifampin
- **Pre-extensively drug-resistant (Pre-XDR):** MDR plus resistance to
  - Fluoroquinolones WHO 1/2021
  - Fluoroquinolones or 2nd-line injectable CDC 1/2022 surveillance

- **Extensively drug-resistant (XDR):** MDR plus resistance to
  - Fluoroquinolones and bedaquiline or linezolid WHO 1/2021
  - Fluoroquinolones + 2nd-line injectable OR bedaquiline or linezolid CDC 1/2022 surveillance

U.S. Cases and Percentages of MDR TB by history of TB

1993–2022



In 2022: DR-TB 1.3% total

- 90 cases MDR
- 16 cases pre-XDR
- 5 cases XDR

Mono INH-R 8% total (83% are non-US born)

*Persons with isolates resistant to at least isoniazid and rifampin among persons with isolates tested with at least isoniazid and rifampin

†Excludes persons with unknown origin of birth

Why Use BPaL/M?

SHORTER REGIMEN

NO INJECTION!!

STUDIES HAVE SHOWN GOOD OUTCOMES

Key trials: BPaL & BPaLM

NIX-TB trial (Conradie et al, NEJM 2020); n=109, XDR/MDR intolerant or non-responsive, 51% HIV+

- LZD 1200mg dose (min. x1mo) then could hold/decr./stop -> only 15% completed full 6mo on this dose; 30% stopped LZD completely
- 100% AE (17% serious), most associated with LZD (81% neuropathy, 48% myelosuppression); no QTc >480 msec, 17 incr. LFT; majority of neuropathy resolved at 24m f/u

ZeNIX-TB trial (Conradie et al, NEJM 2022); n=181, randomized 4 arms, MDR/preXDR/XDR, 20% HIV+

- LZD dose optimization: 600mg qd, 90% favorable outcomes (all similar), less AE/dose changes

TB Practecal trial (Nyangwa et al, NEJM 2023; early data 2021); n= 549; RR/MDR,+/- FQ-R

- Stage 1: BPaLM vs BPaLC vs BPaL vs WHO SoC/control -> not powered as head-to-head comparison; BPaLM most effective/safe -> moved to Stage 2 BPaLM vs WHO Soc/control
- Stopped early: BPaLM 89% cure, 20% AE, 0 deaths (control 52% cure, 59% AE, 2 deaths); difference primary due to withdrawal due to AE

Multi-Drug Resistant TB Treatment is Evolving

Slide curtesy of Sundari Mase

Year	Drugs	Total Duration
1980s-2000	Fluoroquinolones, injectables, cycloserine, ethionamide, PAS, clofazimine (4-6 drugs)	18- 24 months post culture conversion
2000-2012	Linezolid use	18- 24 months post culture conversion
2012	Bedaquiline FDA approved (when an effective regimen cannot otherwise be provided)	18-24 months post culture conversion
2018/2019	All-oral regimens recommended	15-24 months post culture conversion
2019	FDA: BPaL approved	6-9 months
2022	CDC Provisional Guidelines WHO: BPaLM for Fluoroquinolone susceptible MDR and BPaL for Fluoroquinolone resistant MDR	6-9 months

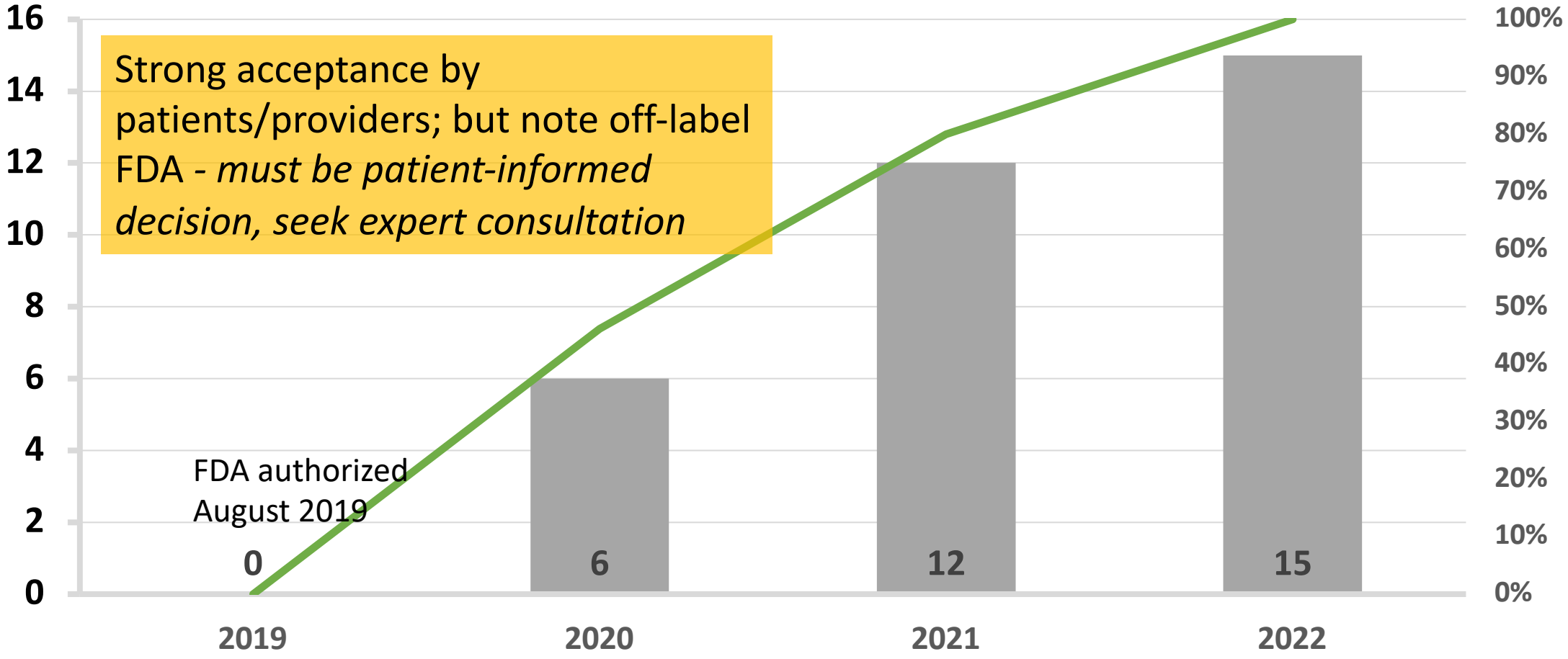
When can it Be Used?

- 2019: FDA approved the drug Pa for use as part of the new 6- month (26 weeks) BPaL
- 2022: CDC issued provisional guidance for the use of BPaL
- 2022: WHO guidelines recommend BPaLM for Fluoroquinolone susceptible MDR and BPaL for Fluoroquinolone resistant MDR
- 2024: CDC issued updated provisional guidance

https://www.cdc.gov/tb/hcp/treatment/bpal.html?CDC_AAref_Val=https://www.cdc.gov/tb/topic/drtb/bpal/default.htm

We are using BPaL/BPaLM in CA

Pretomanid use by year in California – MDR & RIF-intolerant



Known pretomanid use among MDR cases in California as of 10/12/22; courtesy of P. Barry

BPaL/M use for drug intolerant TB

Some patients cannot tolerate first line TB medications

When RIF cannot be used in the regimen, the duration of treatment extends to 12- 18 months (compared to 6 months)

With increased familiarity and comfort, clinicians are starting to use BPaL/M for drug intolerant patients

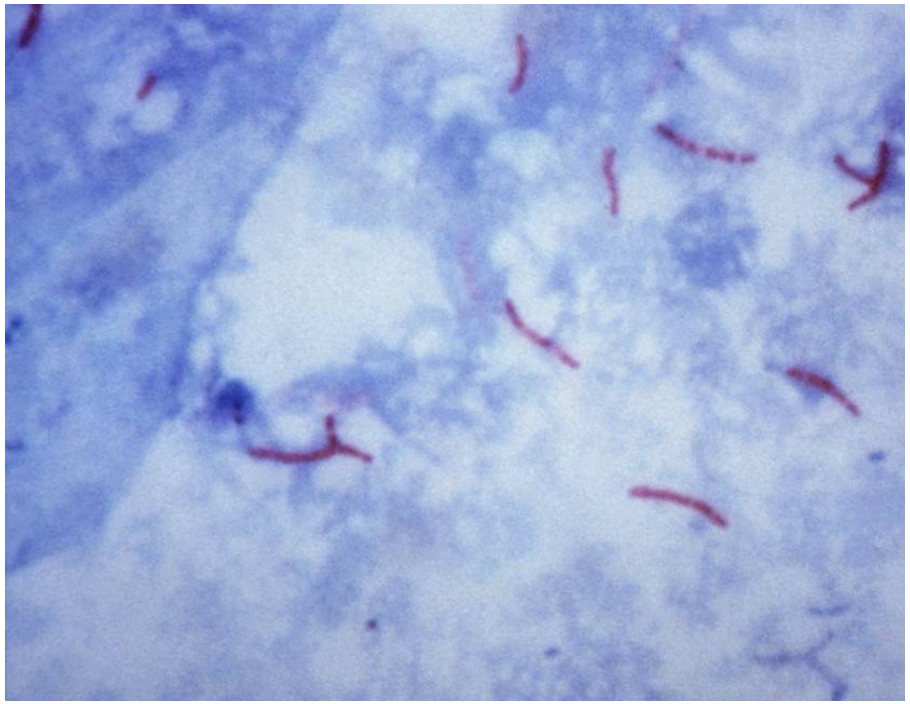
BPaL/M Experiences from the Field

Interviews with nurses in Texas, California and Washington:

- Generally, well tolerated (no more injections!)
- Patients benefit from shorter course of treatment
- Drug procurement more complicated
- Can take 1-3 weeks before treatment initiated after initial diagnosis resulting in longer time in isolation
- Obtaining drug levels requires careful attention
- Treatment interruptions a concern due to long half-life of BDQ

BPaL/M Regimen: Nurse Management

Colleen Hoehn, BSN, MPH
UCSF Curry International TB Center



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BPaLM

- Medications: dosing and procurement
- Drug Susceptibility results
- Patient Education
- Monitoring: drug levels, response to treatment, adverse events
- Resources

Case Presentation

Patient
80+F US born (rural state), TB exposure to father 70 yrs ago (PPD neg, no tx)
No travel/residence in high-incidence country; lives in Las Vegas 3 mo/yr

Presentation
6/12/24 with hemoptysis and 13lb weight loss over 7 months
No fever / N / V / CP / SOB

Imaging
6/13/24 CT Angio: Multiple cavitary and non cavitary nodules in bilat lungs.

Sputum
Bronchoscopy 6/21/24 with BAL AFB 3+/culture pos, Xpert +MTBC/Rif-R

What is the patient's risk for drug-resistant TB

High

Medium

Low

What would be thinking at this point?

- Start first line drug therapy because Rif-R is likely an error based on the patient's risk for MDR
- Review GeneXpert results – which probe has mutation?
- Send sputum for additional phenotypic / molecular testing (many weeks)
- Start a bridging regimen (with which drugs?)
- Start procuring medications for BPaLM

Available U.S. Lab Services

Lab	Tests
CDPH MDL Laboratory	Molecular testing for BDQ, LZD
CDC DTBE Laboratory	Molecular testing for BDQ, LZD
New York Wadsworth Mycobacteriology Laboratory	Molecular testing for BDQ, LZD, Pa Phenotypic testing for BDQ, LZD, Pa
Johns Hopkins Mycobacteriology Research Laboratory	Molecular testing for BDQ, LZD Phenotypic testing for BDQ, LZD, Pa
Florida Department of Health State Laboratory	Molecular testing for BDQ, LZD Phenotypic testing for BDQ, LZD

CDC does not endorse testing that has not undergone regulatory approvals

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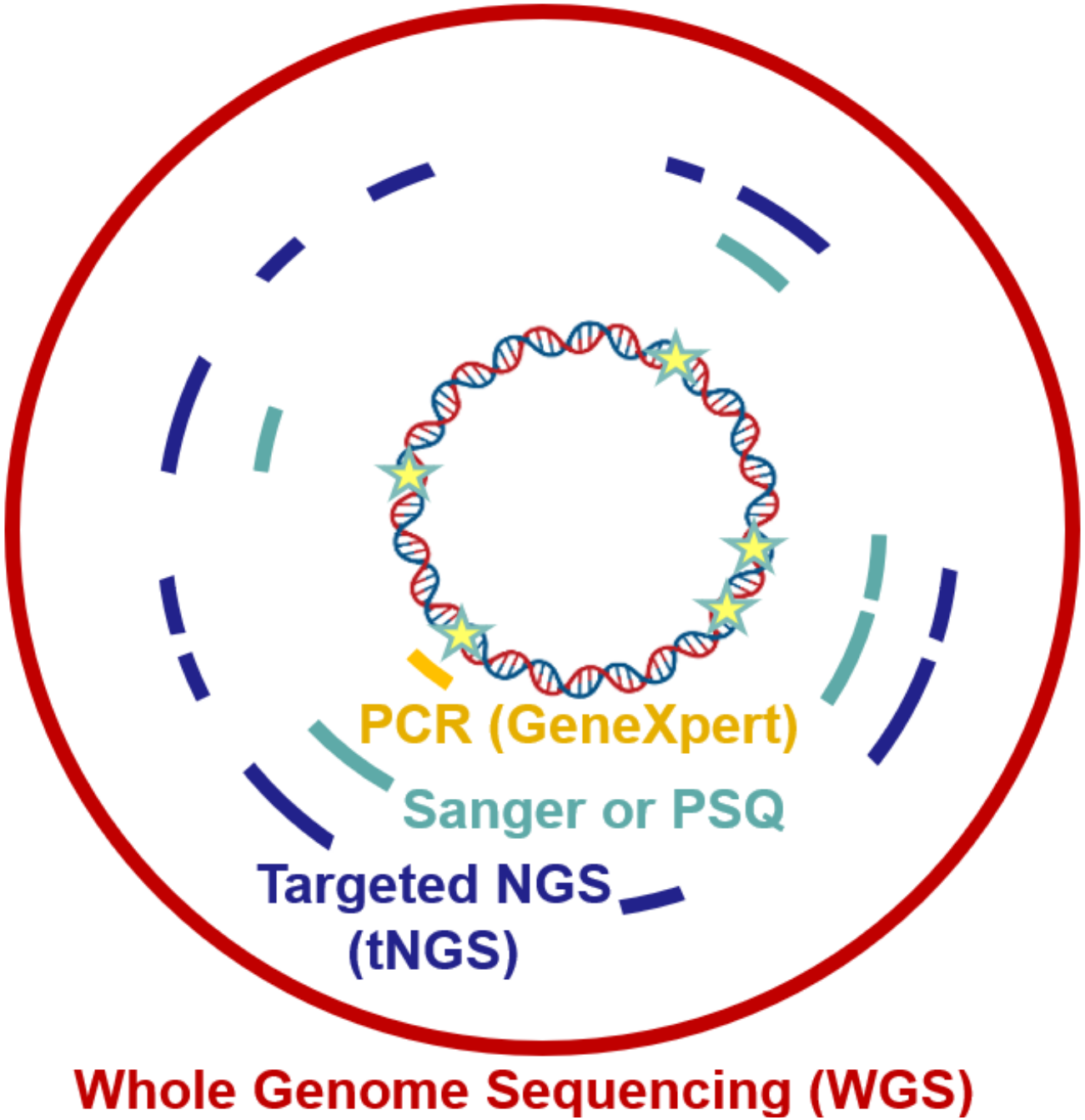
MAYO CLINIC

Southeastern National Tuberculosis Center

Slide courtesy of
Neela Goswami, CDC

Molecular methods of resistance detection



Credit: Varvara Kozyreva
October 2024

DSTs: 6/21/24 BAL: AFB 3+ / Culture +

MOLECULAR	MUTATION	NO MUTATION
Local State Lab Xpert	RIF	
CDPH tNGS (7/16/24)	**RIF, INH, EMB, PZA, KM, AK**	**ETA, CM, MFX, LFX, BDQ, CFZ, LZD**
CDC MDDR (8/2/24)	**RIF, INH, EMB, PZA, KM**	**FQ, BDQ, CFZ, LZD**
CDPH WGS	RIF, INH , EMB, PZA, KM, AK	ETA, CM, MFX, LFX, BDQ, CFZ, LZD
Wadsworth WGS	RIF, INH, KM, AK, SM	FQ, ETA

PHENOTYPIC	RESISTANT	SUSCEPTIBLE
CDPH Mgit	RIF, INH, EMB, RFB, KM	MFX, AK, CM, ETA
CDC Agar	RIF, INH, RFB	EMB, Cipro, ETA, PAS, OFX, AK
Wadsworth Mgit		BDQ, CFZ, LZD
FL State Lab Sensititre	RIF, INH, SM	RFB, AK, MFX, CS, CM, LZD

CDC MDDR

Rifampin (RIF)	Result	Interpretation
RIF interpretation		RIF resistant
rpoB*	Ser450Leu	

Comments and Disclaimers

* DTBE Reference Laboratory has transitioned from the E. coli to the M. tuberculosis numbering system for reporting rpoB gene mutations.

Isoniazid (INH)	Result	Interpretation
INH interpretation		INH resistant
inhA	No mutation	
fabG1	No mutation	
katG	Ser315Thr	

Ethambutol (EMB)	Result	Interpretation
EMB interpretation		Effect of mutation unknown. Cannot rule ou EMB resistance.
embB	Glu405Asp	

Pyrazinamide (PZA)	Result	Interpretation
PZA interpretation		PZA resistant
pncA	His51Arg	

Fluoroquinolones (FQ)	Result	Interpretation
FQ interpretation		Cannot rule out FQ resistance.
gyrA	No mutation	
gyrB	No mutation	

Amikacin, Capreomycin, and Kanamycin (AMK, CAP, and KAN)	Result	Interpretation
AMK CAP and KAN interpretation		KAN resistant
rrs	No mutation	
eis	G-10A	

Bedaquiline (BDQ)	Result	Interpretation
BDQ interpretation		Cannot rule out BDQ resistance.
atpE	No mutation	
rv0678	No mutation	
pepQ	No mutation	

Clofazimine (CFZ)	Result	Interpretation
CFZ interpretation		Cannot rule out CFZ resistance.
pepQ	No mutation	
rv0678	No mutation	

Linezolid (LZD)	Result	Interpretation
LZD interpretation		Cannot rule out LZD resistance.
rplC	No mutation	
rrl	No mutation	

INH/RIF-resistant: What kind of TB is this?

Pan-Sensitive TB

Multidrug-resistant (MDR) TB

Pre-extensively drug-resistant (Pre-XDR) TB

2022 WHO consolidated guidelines on tuberculosis

https://iris.who.int/bitstream/handle/10665/365308/9789240063129-eng.pdf?sequence=1

WHO suggests the use of a 6-month treatment regimen composed of ***bedaquiline, pretomanid, linezolid (600 mg) and moxifloxacin (BPaLM)*** for MDR/RR-TB

BPaLM

6 months (26 weeks)

Bedaquiline
400mg PO daily x 14 days followed by
200mg PO 3x/week

Pretomanid
200mg PO daily

Linezolid
600mg PO daily
can be dose adjusted or changed to TIW

Moxifloxacin
400mg PO daily
if FQ sensitive / no contra-indication

Can be extended to 9 months (cavitary disease or culture conversion longer than 2 months)

Drug Procurement

1. Know your resources:
   - ***WA State BPaL Guidance***
   - ***NTCA Bedaquline Access***
2. Know your patient's insurance information / utilize a navigator
3. Details matter:
   Complete forms completely or there can be delays

It can take 1-3 weeks to procure medications.
The patient will remain in isolation while waiting or may be started on a bridging regimen.

Bedaquiline (BDQ)

400mg QD x 2 weeks followed by
200 mg 3x/week given 48 hours apart

- **Adverse Reactions**:
  - Hepatotoxicity
  - QT prolongation
- Long half-life – 5.5 months!!!
- Take with food

Pretomanid (PMD)

200mg once daily

- **Adverse Reactions**:
  - Peripheral neuropathy
  - Anemia
  - GI upset
  - Elevated liver enzymes

Linezolid (LZD)

600mg daily
May be dose adjusted based on drug levels or adverse events

- **Adverse Reactions**:
  - Myelosuppression
  - Peripheral neuropathy
  - Optic neuropathy

Avoid tyramine containing foods, SSRIs, trycyclic antidepressant and OTC meds containing pseudoephedrine and pheylpropanolamine

Moxifloxacin (MFX)

400mg daily
May require 600-800mg daily based on serum concentrations

- **Adverse Reactions**:
  - Nausea and diarrhea
  - Headache and dizziness
  - Rare tendon rupture, arthralgias
  - Rare hepatotoxicity
  - QTc prolongation
  - Hypo/hyperglycemia

Patient Education

- Provide nursing care and support
- Take medications with food.
- Use daily DOT throughout entire treatment.
- Prepare the patient for weekly, monthly, and post-treatment monitoring
- Manage underlying medical conditions and nutritional status (i.e. diabetes control)
- Report adverse reactions to your care team

Case: Start of Treatment

Concerns:

- 80+ years old
- Didn’t tolerate levofloxacin previously
- Had diverticulitis and had recently changed her diet
- Privacy with DOT
- Coordinating care with all stakeholders (PCP, specialists, PHNs) to communicate side effects and plan for labs / drug levels

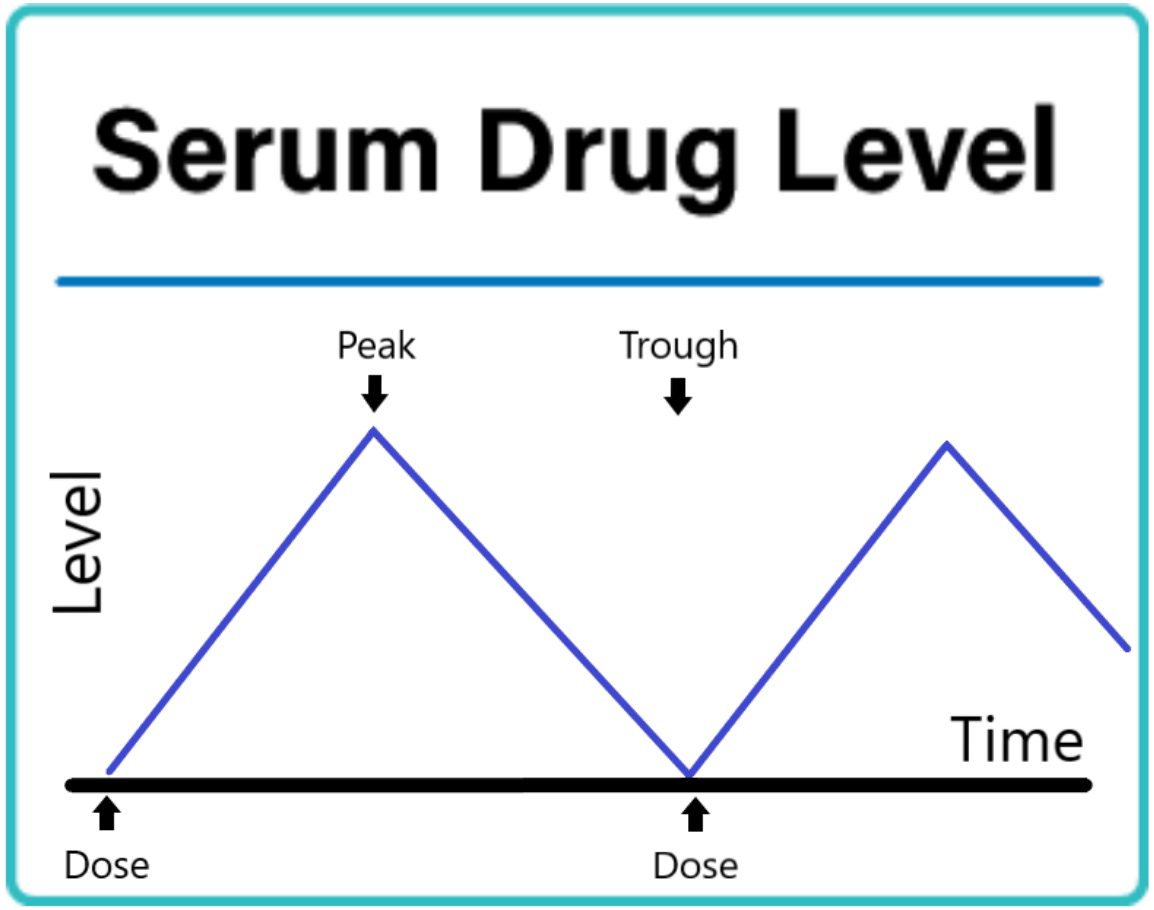
Once the patient started medications she had vomiting / diarrhea and was prescribed Imodium, which was an added concern for prolonged QTc

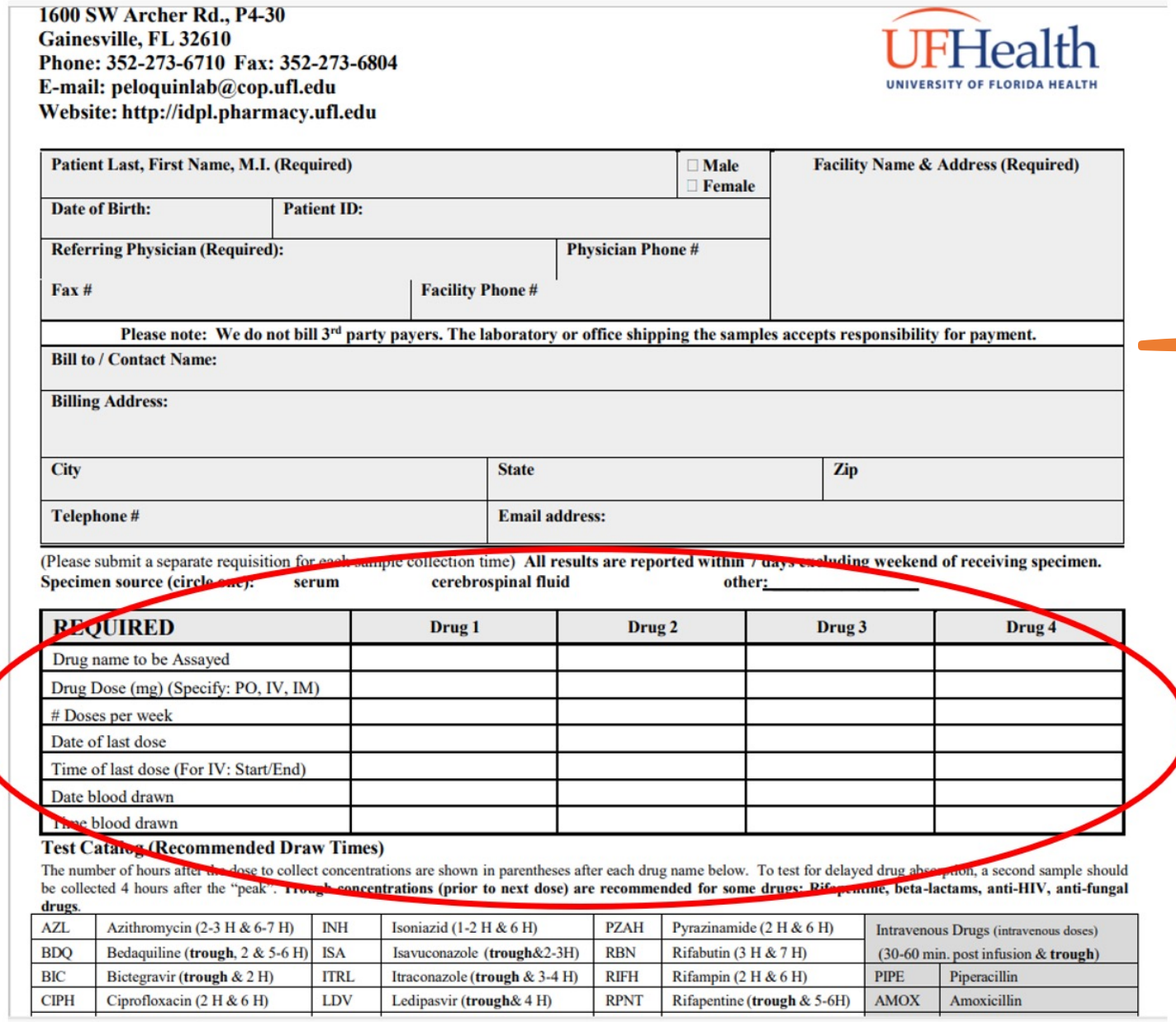
		TREATMENT REGIMEN				BACTERIOLOGY				Labs	TDM	Symptoms
Date:	**WT (kg)**	**BDQ**	**Pa**	**LZD**	**MFX**	**DATE**	**SPEC**	**NAAT**	**S/C**			
6/13/24	48 kg					6/21/24	BAL	**+MTBC/Rif-R**	**3+/+**			
8/1/24						7/12/24 7/13/24 7/14/24	sputum sputum sputum	**+NAAT** **neg** **neg**	**-/+** **-/+** **-/-**	**Baseline** WBC: 8.1 **RBC 3.84 L** Hgb: 12 Hct: 36.9 Plt: 242		
8/5/24		**BDQ 400mg QD**	**Pa 200mg QD**	**LZD 600mg QD**	**MFX 400mg QD**							

Therapeutic Drug Monitoring (TDM)

Therapeutic Drug Monitoring (TDM) tests the amount of certain medicines in a patient's blood to determine dose amounts that are safe and effective.

- **Trough**: A medication *trough* indicates the lowest concentration of medication in the blood and, for some medications, high levels can be a sign of toxicity. A trough level is drawn right before the next dose of a medication.
- **Peak**: A *peak* level is the highest level of medication in the blood and can tell if the medication is reaching concentrations high enough to be effective in killing TB.





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UFHealth
UNIVERSITY OF FLORIDA HEALTH

Patient Last, First Name, M.I. (Required)	☐ Male ☐ Female	Facility Name & Address (Required)
Date of Birth:	Patient ID:	
Referring Physician (Required):	Physician Phone #	
Fax #	Facility Phone #	

Please note: We do not bill 3rd party payers. The laboratory or office shipping the samples accepts responsibility for payment.

Bill to / Contact Name:		
Billing Address:		
City	State	Zip
Telephone #	Email address:	

(Please submit a separate requisition for each sample collection time) All results are reported within 7 days excluding weekend of receiving specimen.
Specimen source (circle one): serum cerebrospinal fluid other:_____

REQUIRED	Drug 1	Drug 2	Drug 3	Drug 4
Drug name to be Assayed				
Drug Dose (mg) (Specify: PO, IV, IM)				
# Doses per week				
Date of last dose				
Time of last dose (For IV: Start/End)				
Date blood drawn				
Time blood drawn				

Test Catalog (Recommended Draw Times)

The number of hours after the dose to collect concentrations are shown in parentheses after each drug name below. To test for delayed drug absorption, a second sample should be collected 4 hours after the "peak". **Trough concentrations (prior to next dose) are recommended for some drugs: Rifapentine, beta-lactams, anti-HIV, anti-fungal drugs.**

AZL	Azithromycin (2-3 H & 6-7 H)	INH	Isoniazid (1-2 H & 6 H)	PZAH	Pyrazinamide (2 H & 6 H)	Intravenous Drugs (intravenous doses) (30-60 min. post infusion & **trough**)	
BDQ	Bedaquiline (**trough**, 2 & 5-6 H)	ISA	Isavuconazole (**trough**&2-3H)	RBN	Rifabutin (3 H & 7 H)		
BIC	Bictegravir (**trough** & 2 H)	ITRL	Itraconazole (**trough** & 3-4 H)	RIFH	Rifampin (2 H & 6 H)	PIPE	Piperacillin
CIPH	Ciprofloxacin (2 H & 6 H)	LDV	Ledipasvir (**trough**& 4 H)	RPNT	Rifapentine (**trough** & 5-6H)	AMOX	Amoxicillin

Complete requisition forms:

- **date/time of last med dose**
- **date/time of blood draw**

Linezolid levels

Trough: <2

Shows that the body is clearing LZD so that it doesn't build up in toxic levels to cause problems. Often we can see LZD problems after a few months on treatment, so it's always important to monitor labs and adverse events.

Peak: 12-26

Shows that LZD is reaching therapeutic level in the blood so it can kill the TB

		TREATMENT REGIMEN				BACTERIOLOGY				Labs	TDM	Symptoms
Date:	**WT (kg)**	**BDQ**	**Pa**	**LZD**	**MFX**	**DATE**	**SPEC**	**NAAT**	**S/C**			
6/13/24	48 kg					6/21/24	BAL	**+MTBC/Rif-R**	**3+/+**			
8/1/24						7/12/24 7/13/24 7/14/24	sputum sputum sputum	**+NAAT** **neg** **neg**	**-/+** **-/+** **-/-**	**Baseline** WBC: 8.1 **RBC 3.84 L** Hgb: 12 Hct: 36.9 Plt: 242		
8/5/24		**BDQ 400mg QD**	**Pa 200mg QD**	**LZD 600mg QD**	**MFX 400mg QD**							
8/19/24		**200 mg TIW**				8/20/24 8/20/24 8/20/24	sputum sputum sputum		-/- -/- -/-	**2 weeks** WBC: 6.6 **RBC 3.64 L** **Hgb: 11.5 L** **Hct: 34.9 L** **Plt: 110 L**	**LZD levels** Trough: none 2-hr: 21.42 6-hr: 16.47	Exhaustion weakness

		TREATMENT REGIMEN				BACTERIOLOGY				Labs	TDM	Symptoms
Date:	**WT (kg)**	**BDQ**	**Pa**	**LZD**	**MFX**	**DATE**	**SPEC**	**NAAT**	**S/C**			
6/13/24	48 kg					6/21/24	BAL	**+MTBC/Rif-R**	**3+/+**			
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8/5/24		**BDQ 400mg QD**	**Pa 200mg QD**	**LZD 600mg QD**	**MFX 400mg QD**							
8/19/24		**200 mg TIW**				8/20/24 8/20/24 8/20/24	sputum sputum sputum		-/- -/- -/-	**2 weeks** WBC: 6.6 **RBC 3.64 L** **Hgb: 11.5 L** **Hct: 34.9 L** **Plt: 110 L**	**LZD levels** Trough: none 2-hr: 21.42 6-hr: 16.47	Exhaustion weakness
9/6/24	48 kg			**Change to 600mg TIW**		9/3/24 9/3/24 9/3/24	sputum sputum sputum		-/- -/- -/-			Exhaustion weakness

MDR Monitoring Checklist*

Patient Name: Treatment Start Date: Treatment Regimen:

Activity	Baseline	Month of Treatment									Post-treatment Monitoring[17]				
		1	2	3	4	5	6	7	8	9	3	6	12	18	24
Date															
CLINICAL MONITORING															
Sputum smear and culture[1]															
Imaging[2] (CXR, CT, other)															
Weight[3]															
Symptom review[4]															
DST[5]															
LAB MONITORING FOR TOXICITY / CO-MORBIDITIES															
CBC[6]															
Creatinine[7]															
LFTs[8]															
K+, Ca++, Mg++, bicarbonate[9]															
Drug Level[10]															
HIV[11]															
Pregnancy[12]															
MONITORING PROCEDURES															
EKG[13]															
Vision Exam[14]															
Peripheral Neuropathy[15]															
Arthralgias[16]															

***Important**: **Monitoring recommendations may change if treatment regimen or patient status changes. A box indicates monitoring activity is recommended. Months 7-9 (i.e., weeks 27-39) are as needed. Check box when activity is completed.**

[1] Collect three AFB smear and culture specimens every 2 weeks until smear conversion, and then 2-3 specimens monthly until cultures have converted to negative. Once cultures have converted, obtain at least 1 specimen monthly throughout therapy
[2] Obtain baseline imaging and monitor q 3 months until end of treatment
[3] Monitor weight monthly and adjust medications as needed
4 Monitor for symptoms monthly and document when symptoms resolve
[5] Obtain 1st and 2nd-line DSTs at baseline. Repeat if on RIPE and culture remains positive prior to MDR Rx, and again if failure to convert culture after 3 months on treatment
[6] Obtain CBC every 1-2 weeks for the first 6-8 weeks, then monthly while on LZD
[7] Obtain serum creatinine at baseline and monthly while on BPaL(+)
[8] Obtain LFTs at baseline and then monthly while on BDQ and Pa
[9] Obtain K+, Ca++, Mg++, and bicarbonate at baseline and monthly while on BDQ
[10] Obtain therapeutic drug monitoring (TDM) of LZD after 1-2 weeks on therapy & if signs of toxicity develop. Recommend collecting a LZD trough and peak (2-hr and 6-hr) if resources allow. TDM may be obtained for other drugs as clinically indicated.
[11] Obtain baseline HIV
[12] Obtain baseline and monthly pregnancy test for patients capable of becoming pregnant who decline long-acting forms of birth control (e.g., intrauterine devices or implantable contraception)
[13] Obtain EKG (check QTcF) at baseline, 2, 12, and 24 weeks while on BDQ. Consider checking monthly if taking additional QT-prolonging agents (e.g., MFX, CFZ, other)
[14] Perform visual acuity (Snellen) + color discrimination (Ishihara) exams at baseline and monthly while on LZD
[15] Monitor for peripheral neuropathy at baseline and monthly while on LZD
[16] Monitor for arthralgias at baseline and monthly while patient on a FQ
[17] Recommend MD visit (including physical exam and symptom review), sputum collection (2-3 specimens), and chest imaging at 3, 6, 12, 18, and 24-months post-treatment completion
NOTE: The CDC provisional guidance for use of BPaL recommends amylase, lipase, and TSH at baseline. These may not be necessary for all patients. Consider checking amylase and lipase if underlying concerns for pancreatitis or if symptoms develop. Consider checking TSH if there are concerns for prolonged QT interval on baseline EKG.

Monitoring

Response to treatment

Adverse events

MDR Monitoring Checklist*

Patient Name: Treatment Start Date: Treatment Regimen:

Activity	Baseline	Month of Treatment									Post-treatment Monitoring[17]				
		1	2	3	4	5	6	7	8	9	3	6	12	18	24
Date															
CLINICAL MONITORING															
Sputum smear and culture[1]															
Imaging[2] (CXR, CT, other)															
Weight[3]															
Symptom review[4]															
DST[5]															
LAB MONITORING FOR TOXICITY / CO-MORBIDITIES															
CBC[6]															
Creatinine[7]															
LFTs[8]															
K+, Ca++, Mg++, bicarbonate[9]															
Drug Level[10]															
HIV[11]															
Pregnancy[12]															
MONITORING PROCEDURES															
EKG[13]															
Vision Exam[14]															
Peripheral Neuropathy[15]															
Arthralgias[16]															

***Important**: Monitoring recommendations may change if treatment regimen or patient status changes. A box indicates monitoring activity is recommended. Months 7-9 (i.e., weeks 27-39) are as needed. Check box when activity is completed.

[1] Collect three AFB smear and culture specimens every 2 weeks until smear conversion, and then 2-3 specimens monthly until cultures have converted to negative. Once cultures have converted, obtain at least 1 specimen monthly throughout therapy
[2] Obtain baseline imaging and monitor q 3 months until end of treatment
[3] Monitor weight monthly and adjust medications as needed
4 Monitor for symptoms monthly and document when symptoms resolve
[5] Obtain 1st and 2nd-line DSTs at baseline. Repeat if on RIPE and culture remains positive prior to MDR Rx, and again if failure to convert culture after 3 months on treatment
[6] Obtain CBC every 1-2 weeks for the first 6-8 weeks, then monthly while on LZD
[7] Obtain serum creatinine at baseline and monthly while on BPaL(+)
[8] Obtain LFTs at baseline and then monthly while on BDQ and Pa
[9] Obtain K+, Ca++, Mg++, and bicarbonate at baseline and monthly while on BDQ
[10] Obtain therapeutic drug monitoring (TDM) of LZD after 1-2 weeks on therapy & if signs of toxicity develop. Recommend collecting a LZD trough and peak (2-hr and 6-hr) if resources allow. TDM may be obtained for other drugs as clinically indicated.
[11] Obtain baseline HIV
[12] Obtain baseline and monthly pregnancy test for patients capable of becoming pregnant who decline long-acting forms of birth control (e.g., intrauterine devices or implantable contraception)
[13] Obtain EKG (check QTcF) at baseline, 2, 12, and 24 weeks while on BDQ. Consider checking monthly if taking additional QT-prolonging agents (e.g., MFX, CFZ, other)
[14] Perform visual acuity (Snellen) + color discrimination (Ishihara) exams at baseline and monthly while on LZD
[15] Monitor for peripheral neuropathy at baseline and monthly while on LZD
[16] Monitor for arthralgias at baseline and monthly while patient on a FQ
[17] Recommend MD visit (including physical exam and symptom review), sputum collection (2-3 specimens), and chest imaging at 3, 6, 12, 18, and 24-months post-treatment completion
NOTE: The CDC provisional guidance for use of BPaL recommends amylase, lipase, and TSH at baseline. These may not be necessary for all patients. Consider checking amylase and lipase if underlying concerns for pancreatitis or if symptoms develop. Consider checking TSH if there are concerns for prolonged QT interval on baseline EKG.

Monitoring Response to Treatment

- Sputum smear/culture
- Imaging
- Weight
- Symptom screen

		TREATMENT REGIMEN				BACTERIOLOGY				Labs	TDM	Symptoms
Date:	**WT (kg)**	**BDQ**	**Pa**	**LZD**	**MFX**	**DATE**	**SPEC**	**NAAT**	**S/C**			
6/13/24	48 kg					6/21/24	BAL	**+MTBC/Rif-R**	**3+/+**			
8/1/24						7/12/24 7/13/24 7/14/24	sputum sputum sputum	**+NAAT** **neg** **neg**	**-/+** **-/+** **-/-**	**Baseline** WBC: 8.1 **RBC 3.84 L** Hgb: 12 Hct: 36.9 Plt: 242		
8/5/24		**BDQ 400mg QD**	**Pa 200mg QD**	**LZD 600mg QD**	**MFX 400mg QD**							
8/19/24		**200 mg TIW**				8/20/24 8/20/24 8/20/24	sputum sputum sputum		**-/-** **-/-** **-/-**	**2 weeks** WBC: 6.6 **RBC 3.64 L** **Hgb: 11.5 L** **Hct: 34.9 L** **Plt: 110 L**	**LZD levels** Trough: none 2-hr: 21.42 6-hr: 16.47	Exhaustion weakness **8/20/24: Culture conversion**
9/6/24	48 kg			**Change to 600mg TIW**		9/3/24 9/3/24 9/3/24	sputum sputum sputum		-/- -/- -/-			Exhaustion weakness

MONITORING RESPONSE TO TREATMENT

Sputum: Culture converted 2 weeks after starting meds

Imaging: Baseline done in August; next due in November

Weight: Stable (no gain or loss)

TB Symptoms: Hemoptysis resolved

MDR Monitoring Checklist*

Patient Name: Treatment Start Date: Treatment Regimen:

Activity	Baseline	Month of Treatment									Post-treatment Monitoring[17]				
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[12] Obtain baseline and monthly pregnancy test for patients capable of becoming pregnant who decline long-acting forms of birth control (e.g., intrauterine devices or implantable contraception)
[13] Obtain EKG (check QTcF) at baseline, 2, 12, and 24 weeks while on BDQ. Consider checking monthly if taking additional QT-prolonging agents (e.g., MFX, CFZ, other)
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NOTE: The CDC provisional guidance for use of BPaL recommends amylase, lipase, and TSH at baseline. These may not be necessary for all patients. Consider checking amylase and lipase if underlying concerns for pancreatitis or if symptoms develop. Consider checking TSH if there are concerns for prolonged QT interval on baseline EKG.

Monitoring Adverse Events

- Labs
- Drug Levels
- EKG
- Vision
- Peripheral Neuropathy
- Arthralgias

Common Side Effects & Assessments

Symptoms	Med	Blood test	Tool
Bone marrow suppression (myelosuppression)	LZD	CBC w/ platelets	
Altered renal (kidney) function	BDQ Pa LZD MFX	Creatinine	
Hepatotoxicity	BDQ Pa MFX	LFTs	
Electrolyte imbalance	BDQ	Potassium (K+) Calcium (Ca++) Magnesium (Mg++)	
Visual Changes	LZD		Snellen Ishihara
QTc prolongation	BDQ MFX		EKG
Peripheral neuropathy	LZD		Peripheral neuropathy assessment
Arthralgias (joint pain)	MFX		Arthralgia assessment

		TREATMENT REGIMEN				BACTERIOLOGY				Labs	TDM	Symptoms
Date:	**WT (kg)**	**BDQ**	**Pa**	**LZD**	**MFX**	**DATE**	**SPEC**	**NAAT**	**S/C**			
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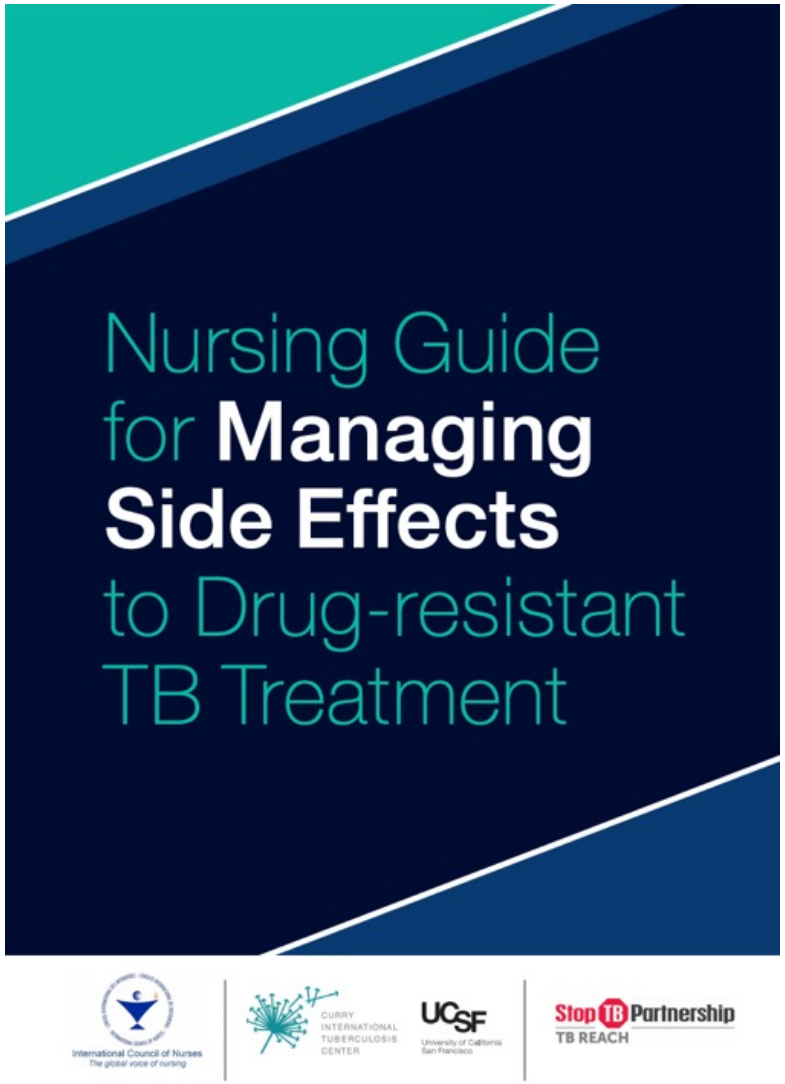
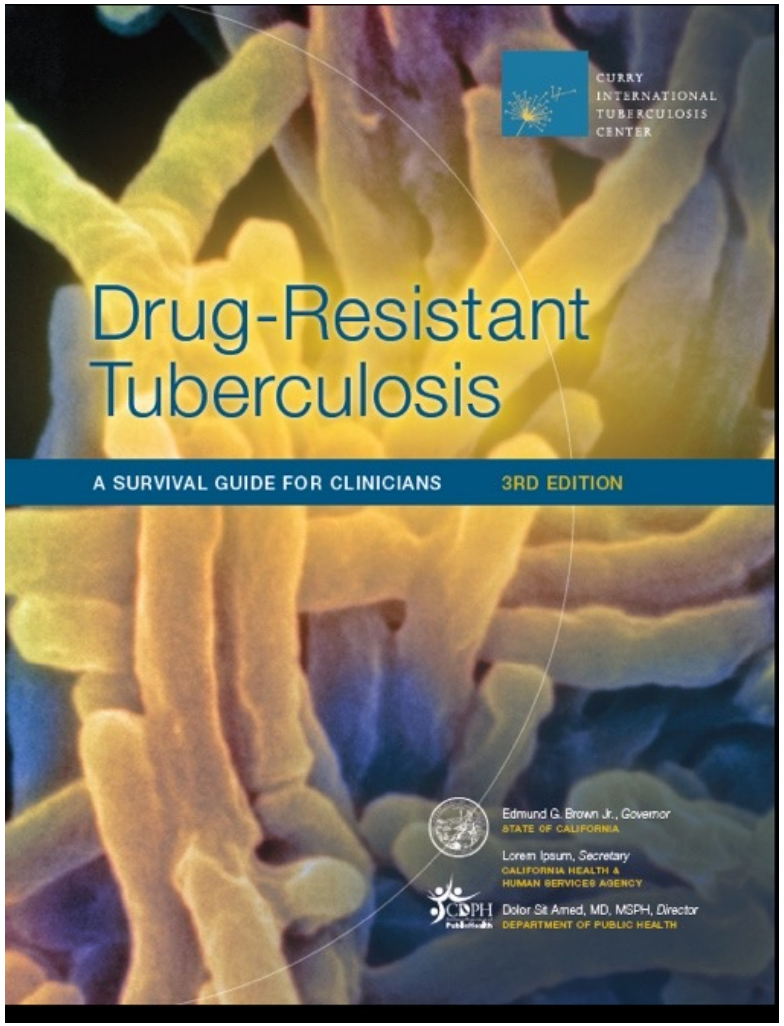
8/19/24		**200 mg TIW**				8/20/24 8/20/24 8/20/24	sputum sputum sputum		-/- -/- -/-	**2 weeks** WBC: 6.6 **RBC 3.64 L** **Hgb: 11.5 L** **Hct: 34.9 L** **Plt: 110 L**	**LZD levels** Trough: none 2-hr: 21.42 6-hr: 16.47	Exhaustion weakness
9/6/24	48 kg			**Change to 600mg TIW**		9/3/24 9/3/24 9/3/24	sputum sputum sputum		-/- -/- -/-			Exhaustion weakness
9/11/24										**5d LZD TIW** WBC: 6.1 **RBC 2.81 L** **Hgb: 8.9 L** **Hct: 26.3 L** Plt: 144		
9/24/24										**WBC 4.3 L** **RBC 3.08 L** **Hgb 10.1 L** **Hct 31.2 L** Plt 210		
10/9/24									-/pend -/pend	WBC 8.5 **RBC 3.10 L** **Hgb 10.9 L** **Hct 33.1 L** Plt 195	**LZD levels::** Trough: pend	Mild symptom improvement Report that patient has not gained weight


Nursing Guide
for Managing
Side Effects
to Drug-resistant
TB Treatment
International Council of Nurses
The global voice of nursing
CURRY INTERNATIONAL TUBERCULOSIS CENTER
UCSF
University of California San Francisco
Stop TB Partnership
TB REACH


CURRY INTERNATIONAL TUBERCULOSIS CENTER
Drug-Resistant Tuberculosis
A SURVIVAL GUIDE FOR CLINICIANS
3RD EDITION
Edmund G. Brown Jr., Governor
STATE OF CALIFORNIA
Lorem Ipsum, Secretary
CALIFORNIA HEALTH & HUMAN SERVICES AGENCY
CDPH
Dolor Sit Amed, MD, MSPH, Director
DEPARTMENT OF PUBLIC HEALTH

Resources

Request a Consultation

Who can request a consultation?
Anyone working with a TB patient who has questions

When to request a consultation?

- Clinical questions
- Programmatic questions
- Reassurance

Warmline Consultation Service

https://www.currytbcenter.ucsf.edu/consultation

- **ID Crowd**: CITC.idcrowd.org
- **Email**: currytbcenter@ucsf.edu
- **Call**: 877-390-6682 / 415-502-4700

Resources

- Drug-Resistant TB Survival Guide: https://www.currytbcenter.ucsf.edu/products/cover-pages/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition
- Nursing Side Effect Guide: https://www.currytbcenter.ucsf.edu/products/view/nursing-guide-managing-side-effects-drug-resistant-tb-treatment
- BPaLM monitoring tool
- WA State BPaL Guidance
- NTCA Bedaquiline Access: https://www.tbcontrollers.org/resources/bdq-access/
- Therapeutic Drug Monitoring (TDM) aka Drug Levels
  - https://idpl.pharmacy.ufl.edu/forms-and-catalog/
  - https://idpl.pharmacy.ufl.edu/wordpress/files/2022/08/Instructions-sample-handling-UFShands-v-08.22.pdf
- CDC Provisional Guidance: https://www.cdc.gov/tb/hcp/treatment/bpal.html
- WHO BPaLM Guidance: https://iris.who.int/bitstream/handle/10665/365308/9789240063129-eng.pdf?sequence=1