Nurse Case Management
of Multi-drug Resistant Tuberculosis (MDR-TB)

Lisa True, RN, MS and Leslie Henry, BSN, RN, PHN
Multidrug-Resistant Tuberculosis Service
California Department of Public Health
Goal of TB Nurse Case Management

- Provide patient centered care that results in completion of treatment
- Stop the transmission of MDR-TB
Objectives

1. Identify the key components of nurse case management of MDR-TB

2. Become familiar with tools and resources that can be helpful in case managing an MDR-TB case

3. Describe 2 common side effects to MDR medications and how to manage them
Role of the TB Nurse Case Manager

- Team leader
- Provide patient-centered tuberculosis care
- Coordinate care with:
  - Treating physician and consultants
  - Other caregivers (primary provider)
  - Hospital staff
  - DOT worker
  - Social worker
  - Disease investigator
  - Providers treating contacts
  - Laboratory
- Treatment and medications
- Patient education
- Supporting adherence
- Respiratory isolation
- Monitoring clinical response
- Monitoring for toxicity and side effects
- Managing common side effects
- Contact investigation
Definitions

- **MDR-TB**: caused by bacteria that is resistant to at least isoniazid and rifampin

- **XDR-TB**: MDR + resistance to fluoroquinolone and 1 of the 3 injectable drugs (amikacin, kanamycin, capreomycin)

- **Poly-drug resistance**: resistance to more than one TB medication but not both INH and Rifampin (e.g. INH and PZA resistance)

- MDR and XDR-TB are diagnosed by molecular and phenotypic (growth based) drug susceptibility tests

For more information about lab tests for diagnosing drug resistant TB see the *Basics of MDR-TB Clinical Care Online Video Series* at: https://www.currytbcenter.ucsf.edu/products/basics-mdr-tb-clinical-care-online-video-series
Treatment and Medications
What the Nurse Case Manager Needs to Know

Treatment Principles

- New WHO guidelines released in 2018/19, new US MDR treatment guidelines anticipated by 2020
- Treatment regimen to include at least 4 medications initially (with no documented resistance)
- Regimen may be “all oral” or include an injectable agent for approximately 6 months
- Treatment duration is long: generally at least 18 months
What the Nurse Case Manager Needs to Know

- Become familiar with medication dosage and side effects
- Determine how/who will be ordering drugs
- Expect that medications may change depending on final drug susceptibility results and side effects

Second Line TB Medications

**BEDAQUILINE (BDQ)**

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Diarylquinolone</th>
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<tbody>
<tr>
<td>Trade name</td>
<td>Sirilu</td>
</tr>
<tr>
<td>Activity against TB</td>
<td>Bactericidal; has strong anti-TB activity. Inhibits adenosine 5'-diphosphosphate (ATP) synthase with in vitro activity against both replicating and nonreplicating bacilli.</td>
</tr>
<tr>
<td>Cross-resistance</td>
<td>Cross-resistance with doxazone has been demonstrated in both directions through efflux-based resistance.</td>
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</tbody>
</table>

**Dose**

- **Adults:** 400 mg daily for 14 days, followed by 200 mg 3 times weekly for 22 weeks. Has not been studied past 24 weeks of administration.
- **Missed doses:** After the first 2 weeks of treatment, the dose changes to the 200 mg three times per week, even if doses were missed during the first 2 weeks. Patients should not make up for missed doses during the first 2 weeks of treatment.
- **Concomitant medications:** Bedaquiline is metabolized by CYP3A4 and co-administration of rifampicin (e.g., rifampicin, rifapentine and rifabutin) or other strong CYP3A4 inducers may require dose adjustment. See Section 7 in [http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/204384s0008b1.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/204384s0008b1.pdf).
- **Children:** Has not been studied in children. Based strictly on weight, converting from the adult doses in a 70 kg patient, estimated pediatric doses would be 6 mg/kg daily for 14 days, followed by 3 mg/kg 3 times weekly for 22 weeks. However, these doses are not supported by clinical experience.
- **Renal failure/dialysis:** No dose adjustment needed for mild to moderate renal insufficiency, but should be used with caution in patients requiring renal dialysis.
### New Treatment Guidelines: WHO Reclassified MDR Medications

<table>
<thead>
<tr>
<th>Group</th>
<th>Medications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group A:</strong></td>
<td><strong>Include all three</strong></td>
</tr>
<tr>
<td></td>
<td>Levofloxacin <strong>OR</strong> Moxifloxacin</td>
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<tr>
<td></td>
<td>Bedaquiline</td>
</tr>
<tr>
<td></td>
<td>Linezolid</td>
</tr>
<tr>
<td><strong>Group B:</strong></td>
<td><strong>Add one or both</strong></td>
</tr>
<tr>
<td></td>
<td>Clofazimine</td>
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<tr>
<td></td>
<td>Cycloserine</td>
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<tr>
<td><strong>Group C:</strong></td>
<td><strong>Add to complete the regimen (ranked by relative balance of benefit to harm)</strong></td>
</tr>
<tr>
<td></td>
<td>Ethambutol</td>
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<tr>
<td></td>
<td>Delamanid</td>
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<tr>
<td></td>
<td>Pyrazinamide</td>
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<tr>
<td></td>
<td>Imipenem-cilastatin <strong>OR</strong> Meropenem</td>
</tr>
<tr>
<td></td>
<td>Amikacin <strong>OR</strong> Streptomycin)</td>
</tr>
<tr>
<td></td>
<td>Ethionamide</td>
</tr>
<tr>
<td></td>
<td>P-aminosalicylic acid</td>
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</tbody>
</table>

Adapted from the *WHO Consolidated Guidelines on drug-resistant tuberculosis treatment, 2019*: see resources slide for link.
## Newer Medications

<table>
<thead>
<tr>
<th>Medication Generic/Brand Name</th>
<th>Manufacturer/How to Order</th>
<th>Main Side Effects</th>
</tr>
</thead>
</table>
| Bedaquiline/Sirturo           | Janssen (member of Johnson & Johnson Pharmaceutical Companies) Contact Metro Medical: National specialty pharmaceutical distributor | • QTc prolongation  
• Hepatitis  
• Nausea |
| Clofazimine/Lamprene          | Novartis Pharmaceuticals Contact FDA for Single Patient Investigation New Drug approval and Novartis | • Skin discoloration  
• Gastrointestinal intolerance  
• QTc prolongation |
| Delamanid/Deltyba             | Otsuka Contact FDA for Single Patient Investigation New Drug approval and Otsuka for compassionate use | • Nausea/vomiting  
• Dizziness  
• Insomnia  
• QTc prolongation |
| Pretomanid                    | Mylan                      | • Peripheral neuropathy  
• Acne  
• Anemia  
• Nausea/vomiting |
Patient Education and Adherence
Patient Education Provided Initially

- Set up time and place that is comfortable and private
- Assess current knowledge of diagnosis and understanding of treatment plan
- Recognize and address the patient’s fears and concerns
- Share major concepts and tailor education
- Ask patient how they would like to receive education
- Share how to contact case manager and/or DOT worker if questions or side effects
- Anticipatory guidance: may feel worse before feeling better
Supporting Adherence

- Directly Observed Therapy (DOT) is essential
  - Allows DOT worker to assess if patient is tolerating the medications
- Identify and optimize management of other medical conditions
  - Mental health issues
  - Drug or alcohol use
  - Nutritional status
- Anticipate and address barriers
- Incentives & Enablers can help
Ongoing Patient Education

- Be responsive to patient’s concerns which may change over time
- Use analogies that the patient can relate to when describing the treatment plan

Goal is to gain/retain patient’s commitment to the treatment plan
Respiratory Isolation
Isolation

- Most transmission of TB occurs before treatment begins
- Transmissibility of MDR-TB is similar to susceptible TB
- Transmission of MDR-TB can have serious consequences
- Isolation is essential in minimizing transmission
- Settings should be assessed by the local health department prior to release from isolation
Criteria for Release from Isolation

HIGH RISK SETTINGS
- AFB smear negative x 3
- At least 14 days of appropriate MDR-TB treatment taken & tolerated by DOT
- Clinical improvement
- At least 2 consecutive negative sputum cultures

LOW RISK SETTINGS
- AFB smear negative x 3
- At least 14 doses of appropriate MDR-TB treatment taken and tolerated by DOT
- Clinical Improvement

Guideline for the Assessment of TB Patient Infectiousness and Placement into High and Lower Risk Settings, 2017: see resources slide
CA MDR-TB Service Recommendations

Clinical Evaluation
- At least monthly

TB Symptom Review
- Routinely note improvements/worsening of symptoms (cough, weight, fever, etc.)

Radiology
- Every 3 - 6 months throughout treatment and at completion of treatment

Bacteriology
- 3 sputa prior to MDR-TB treatment initiation
- Weekly sputum until smear negative
- Collect 2-3 sputa monthly until culture conversion
- At least 1 throughout treatment and at completion
- Document culture conversion date
## Monitoring for Drug Toxicity & Side Effects

<table>
<thead>
<tr>
<th><strong>TOXICITY</strong></th>
<th><strong>SIDE EFFECT</strong></th>
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<tbody>
<tr>
<td>Lab diagnosis</td>
<td>Unpleasant reaction</td>
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<tr>
<td>Serious reactions</td>
<td>Often expected</td>
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<tr>
<td>May require treatment and/or hospitalization</td>
<td>Not damaging to health</td>
</tr>
<tr>
<td>Can require change in dose or stopping drug</td>
<td>Usually does not require change in therapy</td>
</tr>
<tr>
<td>May be life threatening</td>
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</table>
Routine toxicity monitoring

Daily
- Monitor for treatment adherence and tolerance at every DOT encounter

Monthly
- LFTs, CBC, electrolytes, Creatinine
- Visual acuity & color discrimination
- Peripheral neuropathy
- Depression

Quarterly
- Thyroid function

Periodically depending on drugs
- EKG at 2, 12, 24 weeks when on bedaquiline (BDQ) alone
- More frequent EKG monitoring for pts on BDQ and other drugs that cause QTc interval prolongation (e.g. clofazimine, fluoroquinolone)
Monitoring for Relapse

Monitor for 2 years post-treatment at 6, 12, and 24 months

- Symptom review
- Medical evaluation
- Sputum collection
- CXR
Managing Common Side Effects
Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment
Possible offending medications

*Ethionamide, PAS, Bedaquiline*

Assess:
- For signs of hepatitis, GI bleeding, dehydration. Seek urgent medical attention if found.
- If vomiting is significant, check vital signs, serum electrolytes & creatinine

Counsel:
- Some nausea is expected early in MDR-TB treatment
- Encourage good hydration; small, frequent meals; ginger tea or hard candies

Consider:
- Anti-emetic, slow ramping up of suspect medication, change timing of dose, anti-anxiety medication
Peripheral Neuropathy

*Possible offending medications*

Linezolid, Isoniazid, Cycloserine

Is dose dependent & likely to appear later in treatment

**Assess:**
- Tingling, prickling, burning or numbness sensation in toes, balls of feet, fingers or hands

**Check:**
- HgbA1c; TSH, location/severity of peripheral neuropathy

**Counsel:**
- Importance of good nutrition, avoid alcohol & smoking, if diabetic, control blood sugar

**Consider:**
- More likely to occur in patients with HIV, diabetes, alcoholism, poor nutrition or pregnancy; should also take supplemental vitamin B6; report findings of peripheral neuropathy to treating physician
Use Case Management Tools

- Use drug-o-gram to follow:
  - Serial changes in drugs
  - Bacteriology
  - Chest x-rays
  - Drug toxicities

- Use MDR Monitoring Checklist
  - Track monitoring
## DRUG-O-GRAM

**Initial Contact Date:** XXXX/XXXXX  
**Name:** SAMPLE PATIENT  
**DOB:** XXXX/XXXXX  
**Health Department:** SAMPLE HEALTH DEPT  
**Treating Physician:** Dr. Marcus Wolfe  
**File No.:** XX-XXX

### TREATMENT REGIMEN

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<th>INH</th>
<th>Rif</th>
<th>PZA</th>
<th>EMB</th>
<th>BK</th>
<th>AK</th>
<th>BDQ</th>
<th>LFX</th>
<th>MFX</th>
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### BACTERIOLOGY

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<tr>
<th>Date</th>
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<td>2/25/19</td>
<td>Spol+</td>
<td>2+/+</td>
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</tbody>
</table>

### SUSCEPTIBILITY RESULTS

<p>| Date     | Spec | Lab     | INH | Rif | EMB | PZA | SM | Lzd | Ak | Cm | Pas | LFX | Mfx | Ofx | Cs | Rfb | Cpx | CFZ | Km | Reported |
|----------|------|---------|-----|-----|-----|-----|----|-----|----|----|-----|-----|-----|-----|-----|-----|----|---------|
| 1/24/19  | Smol | MDL-PSQ |     |     |     |     |    |     |    |    |     |     |     |     |     |     |    | 1/31/19 |
| 12/29/18 | Smol | CDC-MDR |     |     |     |     |    |     |    |    |     |     |     |     |     |     |    | 3/7/19  |
| 1/24/19  | Smin | OPCMH  |     |     |     |     |    |     |    |    |     |     |     |     |     |     |    | 3/11/19 |
| 12/20/18 | Snol | NI      |     |     |     |     |    |     |    |    |     |     |     |     |     |     |    | 3/13/19 |
| 12/20/18 | Smin | CDC     |     |     |     |     |    |     |    |    |     |     |     |     |     |     |    | 6/8/19  |</p>
<table>
<thead>
<tr>
<th>Activity</th>
<th>Month of Treatment</th>
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<tbody>
<tr>
<td>Date</td>
<td>1</td>
</tr>
<tr>
<td><strong>CLINICAL MONITORING</strong></td>
<td></td>
</tr>
<tr>
<td>Spectrum smear and culture</td>
<td></td>
</tr>
<tr>
<td>C/P</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
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<tr>
<td>Symptoms review</td>
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<tr>
<td>ESR</td>
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<tr>
<td><strong>LAB MONITORING FOR TOXICITY/CO-MORBIDITIES</strong></td>
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</tr>
<tr>
<td>CBC</td>
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<tr>
<td>Creatinine</td>
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<tr>
<td>LFTs</td>
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<tr>
<td>K+ Ca, Mg</td>
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<tr>
<td>Drug Level**</td>
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<tr>
<td>TSH</td>
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<tr>
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<td><strong>MONITORING PROCEDURES</strong></td>
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<td>Audiogram</td>
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<td>Vestibular exam</td>
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<td>Vision Exam**</td>
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<tr>
<td>Peripheral Neuropathy**</td>
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<tr>
<td>Arthralgies**</td>
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<tr>
<td>Depression**</td>
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<tr>
<td>EKG**</td>
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</table>

1. Collect three AFS smear and culture specimens every 2 weeks until smear or culture becomes negative. Once cultures have converted, obtain at least 1 smear or culture monthly throughout therapy.
2. Obtain baseline CBC and monitor q 3 months during the first year and q 6 months in the second year of treatment.
3. Check weight, height, and add medications as needed.
5. Obtain first and second line ESR results at baseline. Repeat if pimecrolimus (EMLA) or cortisone is used, prior to mDR therapy, and again if patient fails to convert culture after 3 months on treatment.
6. Obtain weekly for first month, then monthly for a month and weekly for the next 2 months.
7. Obtain creatinine at baseline and monthly while pt is on an injectable agent.
8. Obtain LFTs at baseline and monthly while pt is on an injectable agent.
9. Obtain K+ Ca, Mg at baseline and monthly while pt is on an injectable agent.
10. Three months after therapy (MDR) should be obtained for patients receiving statins after 2 weeks on therapy and every 4 months after that. TCAs may be obtained for patients to be used as inpatient medications.
11. Monitor TSH at baseline and every 3 months while pt is on an injectable agent or PEG, and more frequently if symptoms of adrenocortical failure.
12. Obtain baseline I&V.
13. Perform audiograms at baseline and monthly while pt is on an injectable agent.
14. Perform vestibular exam at baseline and monthly while pt is on an injectable agent.
15. Perform visual field exam at baseline and monthly while pt is on an injectable agent.
16. Monitor for peripheral neuropathy at baseline and monthly while pt is on an injectable and as clinically indicated for patients on fluoroquinolones.
17. Monitor for arthralgies at baseline and monthly while pt is on PEG or fluoroquinolones.
18. Monitor for depression at baseline and monthly while pt is on an injectable agent.
19. Obtain EKG at baseline and at least 2, 12, and 24 hours for pts on diabetes and at baseline and after treatment start for patients on fluoroquinolones as clinically indicated.
Contact Investigation

- Similar to contact investigation for drug-susceptible TB
  - Identify, locate, and evaluate contacts
  - Obtain expert consultation to help determine appropriate LTBI regimen
  - If no treatment available or accepted
    - Evaluate with clinical exam, symptom review every 3-6 months for 2 years
    - Chest x-rays and/or sputum collection as clinically indicated

- Clinical monitoring can be a reasonable alternative to treatment
Summary

- The main role of the nurse case manager is to provide patient centered care and support the patient toward completion of treatment.
- Individualized patient education messages and allowing patient to participate in decision making are important.
- Monitoring for clinical response to treatment and for toxicities to medications are key components of case management.
- Case managing MDR-TB requires good organization, attention to detail and time.
- Tools such as a drug-o-gram and Monitoring Checklist can help track patient’s clinical response to treatment.
- Prompt management of side-effects is important for adherence to treatment.
Pearl from your Peer

“Use your resources, do not feel like you are on your own. Ask for help, nobody expects you to know or have all the answers. Talk to your patient as much as you can. Develop a close relationship with him/her, spend time talking to them. If you do, they will tell you exactly how they are feeling -good or bad. And, always tell them the truth.”
Resources


- WHO Consolidated Guidelines on drug-resistant tuberculosis treatment 2019
  https://apps.who.int/iris/bitstream/handle/10665/311389/9789241550529-eng.pdf

- Nursing Guide for Managing Side Effects to Drug-resistant TB Treatment

- Guideline for the Assessment of TB Patient Infectiousness and Placement into High and Lower Risk Settings, 2017

- Guide for QTc monitoring and management of drug-resistant TB patients with QT-prolonging agents
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