

MDR TB
IN OTTAWA COUNTY
PATTY FEENSTRA RN

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BACKGROUND

- 27 year old female from India
- Arrived in U.S. on student visa in 2016
- Had history of positive TST and declined LTBI treatment at that time
- Currently employed full time at local company as a contract worker

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BACKGROUND CONT...

- Developed enlarged cervical lymph node in July 2018
- Seen in urgent care on 8/24/18, 4 weeks after onset
- Diagnosed with right cervical lymphadenitis
- Started on Keflex



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BACKGROUND CONTINUED

- 9/4/18 Follow-up visit with ENT – CT of neck ordered and Keflex changed to Clindamycin due to rash
- 9/11/18 Follow up visit with minimal improvement
 - IGRA ordered and collected on 9/12/18
 - Biopsy of lymph node 9/17/18 – AFB/Culture ordered
- 9/17/18 IGRA positive
- 9/18/18 CXR negative for TB

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MORE BACKGROUND STUFF

- 9/19/18 AFB smear positive and MTB complex by PCR positive
- 9/19/18 Referred to LHD by ENT
- 9/20/18 Sputum collection attempted but unable to produce
- 9/24/2018 started on 4 drug TB therapy
- 10/24/18 Culture positive for MTB
- Not considered contagious, although roommate/boyfriend tested with IGRA and negative

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EVERYTHING WAS SMOOTH SAILING UNTIL...



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MDR TB DIAGNOSIS

- 10/29/18 Voicemail from MDHHS BOL indicating drug resistance to INH, RIF and PZA.
- 10/30/18 LHD contacted MDHHS TB consultant
 - All treatment d/c until all susceptibility results available
 - Consulted with Rutgers Global Tuberculosis Institute
 - CDC contacted to order molecular detection of drug resistance

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RESISTANCE

- 11/7/18 CDC molecular testing showed resistance to – INH, RIF, EMB, PZA, Streptomycin, Rifabutin, and low level resistance to Moxifloxacin
- 11/9/18 Patient evaluated by Infectious Disease and ENT at Spectrum Hospital due to lymph node drainage. Admitted to Spectrum for I and D and debridement
- 1/13/19 concern for secondary lymph node rupture. Admitted to Spectrum again for I and D and debridement

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INITIAL MDR TREATMENT REGIMEN

- 11/9/18 - MDR Treatment started during inpatient stay
- Anticipated length of treatment – 18 mo.
- **Amikacin IV**
 - PICC line placed while inpatient
 - Home Health managing dosages
 - Fiancé administers infusions
- **Linezolid**
- **Moxifloxacin**
- **B6**
- **Bedaquiline** – added 12/13/18
- **Ethionamide** – added 12/19/18

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MDR MONTHLY DRUG COSTS

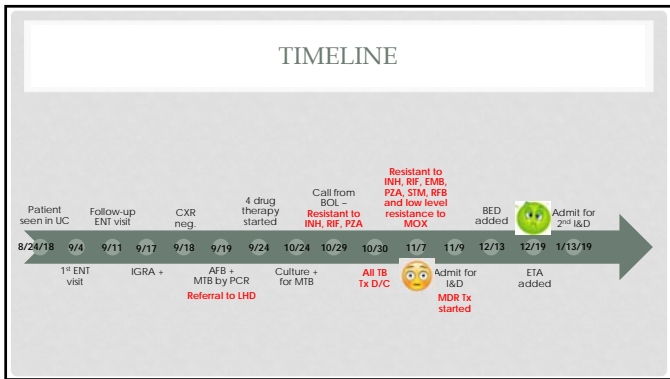
Drug	Pharmacy	Wholesale	Retail	Copay
Bedaquiline*	Metron Medical	\$30,000.00	\$23,000.00	\$30.00
Ethionamide	Meijer Specialty Pharmacy	NA	\$354.00	\$30.00
Linezolid	Walgreens	NA	\$5300.00	\$10.00
Moxifloxacin	Walgreens	NA	\$496.00	\$10.00
Amikacin	Spectrum Home Health	NA	\$550.00	UNK**

*treatment for 6 mo.
**no bill has been received

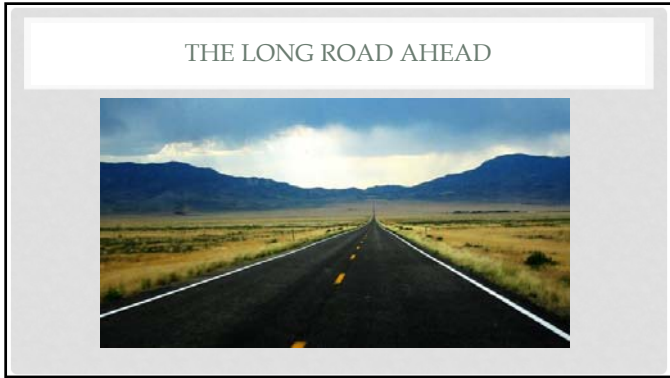
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- ### REQUIRED SCREENINGS
- EKG every 2 weeks (Bedaquiline)
 - Monthly CBC/CMP
 - TSH every 2 months (Ethionamide)
 - Audiogram every 2 months (Amikacin)
 - Amikacin peak every week (Amikacin)

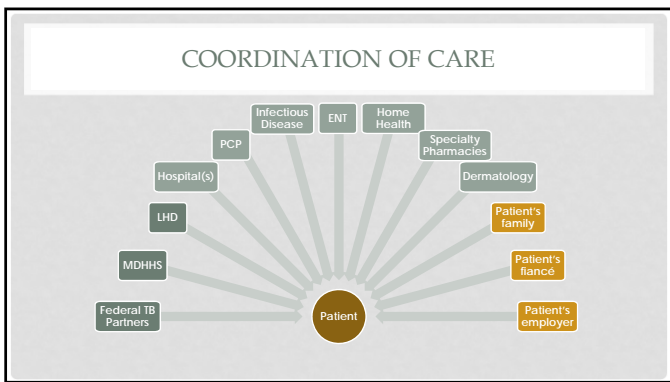
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-
- PATIENT'S PERSONAL CHALLENGES - SIDE EFFECTS
- Nausea/Vomiting
 - Vistaril
 - Zofran
 - Ativan
 - Dizziness
 - Acne
 - Fatigue
 - Depression
 - Suicidal ideation
 - Phobia of medication
 - Letting family and employer down

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PERSONAL CHALLENGES CONT...

- Compliance with treatment
 - DOT compliance (video, timeliness, no-shows)
 - Work pressures
 - Family/cultural pressures
 - Multiple providers and screenings (no-shows)
 - Denial of seriousness of MDR TB
- Desire to return to India...or not
 - Misses family
 - Recently engaged
 - Will she lose job/insurance if she leaves?
 - Challenges to public health in attempting to coordinate care and change to all oral regimen
- Stress on fiancé

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NURSING CHALLENGES



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NURSING CHALLENGES

- Uncharted territory
 - Finding and understanding new TB meds
 - Working with home health
 - Ordering new tests and procedures
 - Coordinating with other providers
- Late night, holiday and weekend texts
- Lack of follow through by patient
- Patience
 - Waiting for answers
 - Wanting to be able to provide answers to patient

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THE FEELS...

- Frustrated
- Loss of confidence in self
- Empathy
- Discouraged
- Overwhelmed
- Anger
- Repeat...

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ITS NOT ALL SUNSHINE AND RAINBOWS, BUT...

- The learning curve
- Teamwork
- State and Federal support
- Patient appreciation...
- Humor



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QUESTIONS?


THANK YOU!

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Lessons learned from a case of multidrug-resistant tuberculosis

Bob Dickson
 March 21, 2019
 2019 MDHHS World TB Day Conference



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A 29 year-old woman from South Africa develops swelling in her neck.

It waxes and wanes. She denies fevers, chills, sweats, cough, or weight loss.

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January 2018 March 2019

Evaluated by ENT: CT and FNA
 Onset of symptoms: swelling in neck

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Component
FNA SAMPLE TO CYTOLOGY
 CYTOPATHOLOGY NON-GYNECOLOGIC / FNA REPORT

Order Number: CN-18-1652 Date Received: 2/21/2018 2:19 PM
 Date Completed: 2/22/2018 11:20 AM Date Collected: 2/21/2018 11:40 AM

Diagnosis:
 Negative for carcinoma.
 Lymphocytes and focal granulomatous inflammation present. See comment.

Notes Recorded by [REDACTED] MD on 2/22/2018 at 11:52 AM EST
 Please call with results. No cancer, I will see her back in 1-2 weeks for repeat Biopsy and possible core needle biopsy.

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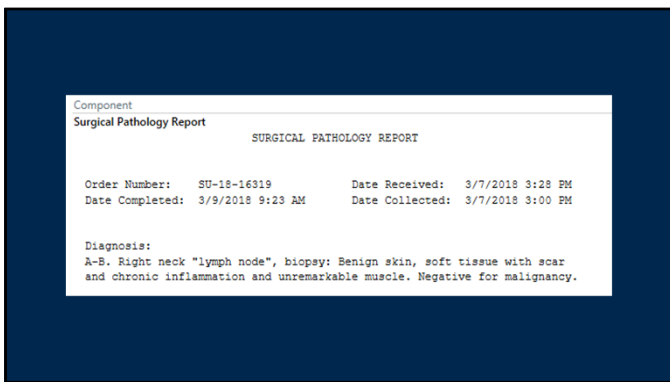
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Lessons learned:

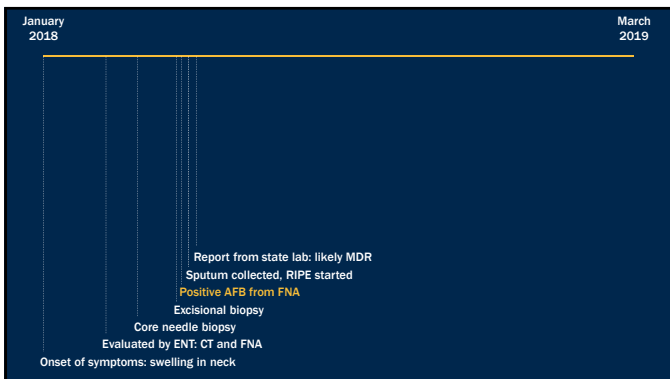
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- 2) Extrapulmonary TB is not an immediate public health threat.
- 3) MDR susceptibility testing take *time*.

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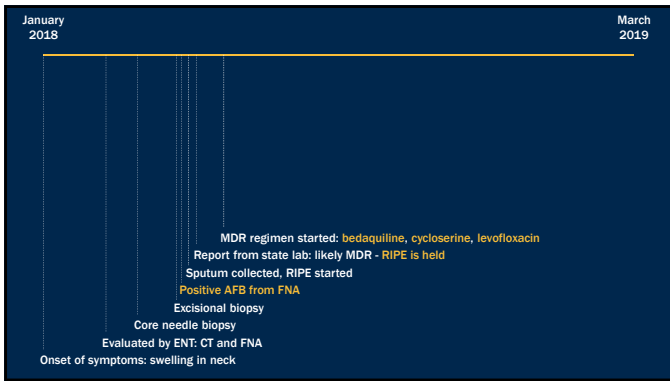
January 2018 March 2019

Report from state lab: likely MDR - RIPE is held
 Sputum collected, RIPE started
 Positive AFB from FNA
 Excisional biopsy
 Core needle biopsy
 Evaluated by ENT: CT and FNA
 Onset of symptoms: swelling in neck

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Susceptibility	Mycobacterium tuberculosis H ₂ O
Amikacin 6.0 mcg/mL	Resistant
Capreomycin 10 mcg/ml	Resistant
Ciprofloxacin 2.0 mcg/mL	Sensitive
Cycloserine 20 mcg/mL	Sensitive
Ethambutol 10 mcg/ml	Sensitive
Ethambutol 5.0 mcg/ml	Sensitive
Ethionamide 5.0 mcg/mL	Resistant
Isoniazid 0.1 mcg/mL	Resistant
Isoniazid 0.2 mcg/ml	Resistant
Isoniazid 1.0 mcg/mL	Resistant
Kanamycin 6.0 mcg/ml	Resistant
Ofloxacin 2.0 mcg/mL	Sensitive
P-aminosalicylate 10 mcg/mL	Sensitive
P-aminosalicylate 2.0 mcg/mL	Sensitive
Pyrazinamide 100 mcg/ml	Sensitive
Rifampin 1.0 mcg/mL	Resistant
Streptomycin 10 mcg/mL	Resistant
Streptomycin 2.0 mcg/mL	Resistant

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Multidrug-Resistant Tuberculosis and Culture Conversion with Bedaquiline

ABSTRACT

BACKGROUND: Tuberculosis (Tb) is a global health problem. It is a leading cause of death and disability, but has been associated with unexplained spontaneous remissions in patients with multidrug-resistant tuberculosis, who started a parenteral background regimen for 8 weeks.

OBJECTIVE: In this phase 2b trial, we randomly assigned 80 patients with newly diagnosed, culture-positive, multidrug-resistant tuberculosis to receive either 8 weeks of bedaquiline, 800 mg, daily, in combination with a parenteral background regimen, or placebo, both in combination with a parenteral background regimen. The primary end point was culture conversion by 24 weeks in the bedaquiline group.

DESIGN: Randomized clinical trial.

SETTING: The trial was conducted in 10 sites in the United States and 10 sites in South Africa.

RESULTS: Bedaquiline reduced the median time to culture conversion, as compared with placebo, from 22.5 weeks to 17.5 weeks (based on the bedaquiline group, 100.0% culture conversion at 24 weeks; 95.0% at 20 weeks; 80.0% at 16 weeks; 60.0% at 12 weeks; 40.0% at 8 weeks; 20.0% at 4 weeks). The median time to culture conversion in the placebo group was 22.5 weeks (100.0% at 24 weeks; 95.0% at 20 weeks; 80.0% at 16 weeks; 60.0% at 12 weeks; 40.0% at 8 weeks; 20.0% at 4 weeks). The median time to culture conversion in the bedaquiline group was 17.5 weeks (100.0% at 24 weeks; 95.0% at 20 weeks; 80.0% at 16 weeks; 60.0% at 12 weeks; 40.0% at 8 weeks; 20.0% at 4 weeks). The median time to culture conversion in the placebo group was 22.5 weeks (100.0% at 24 weeks; 95.0% at 20 weeks; 80.0% at 16 weeks; 60.0% at 12 weeks; 40.0% at 8 weeks; 20.0% at 4 weeks).

CONCLUSIONS: The addition of bedaquiline to a parenteral background regimen for 8 weeks in addition to 8 weeks of a parenteral background regimen significantly improved culture conversion in patients with multidrug-resistant tuberculosis. These results support the use of bedaquiline in combination with a parenteral background regimen for 8 weeks in patients with multidrug-resistant tuberculosis.

Time to Culture Conversion

Weeks	0	4	8	12	16	20	24
Placebo	100	95	80	60	40	20	10
Bedaquiline	100	80	60	40	20	10	5

No. at Risk

Weeks	0	4	8	12	16	20	24
Placebo	58	37	25	12	7	3	3
Bedaquiline	61	53	40	30	22	5	5

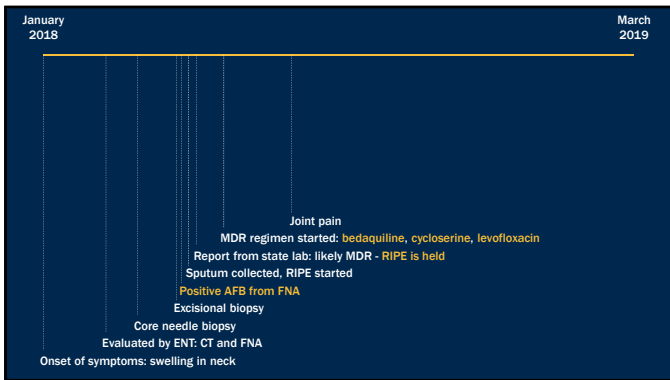
N Engl J Med 2014; 371:723-732

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- 2) Extrapulmonary TB is not an immediate public health threat.
- 3) MDR susceptibility testing take *time*.
- 4) Bedaquiline is a viable oral option for MDR TB.
- 5) Bedaquiline is *expensive*.
- 6) Help is available: local, state, national.

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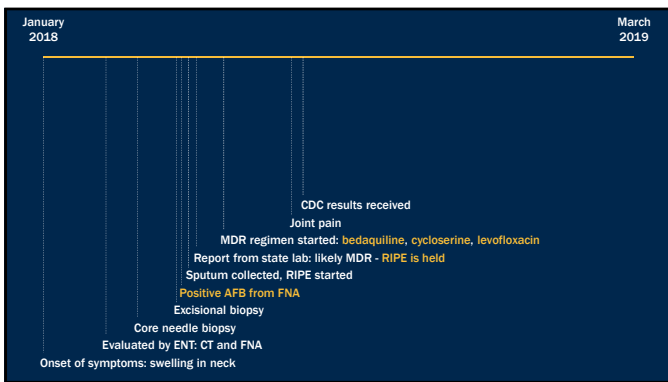
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Table 2. Adverse Events during 120 Weeks in the Intention-to-Treat Population.*

Variable	Bedaquiline (N=79)	Placebo (N=81)
Median duration of overall treatment phase (range) — wk	91.7 (2.0–120.0)	94.1 (2.0–137.3)
Adverse event — no. (%)		
Any	78 (99)	79 (98)
Related to treatment	55 (70)	56 (69)
Grade 3 or 4†	34 (43)	29 (36)
Leading to discontinuation of treatment	4 (5)	5 (6)
Serious adverse events — no. (%)‡	18 (23)	15 (19)
Adverse event occurring in ≥20% of patients — no. (%)		
Nausea	32 (41)	30 (37)
Arthralgia	29 (37)	22 (27)
Vomiting	23 (29)	22 (27)
Headache	23 (29)	18 (22)
Hyperuricemia	20 (25)	27 (33)
Hemoptysis	16 (20)	14 (17)

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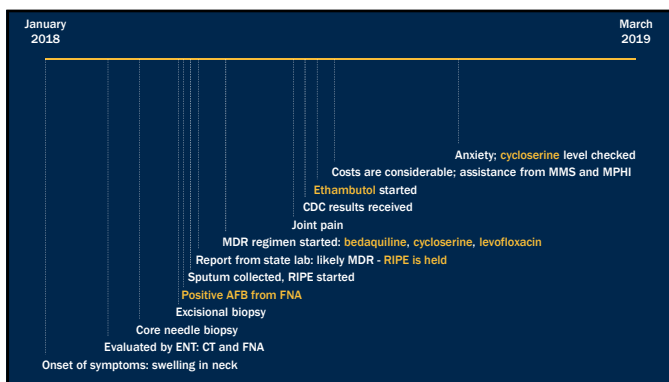
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- 9) Cycloserine can cause neuropsychiatric toxicity and has a narrow therapeutic range.

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Drug Level	Conc.	Unit	Flags
Colorimetric Cycloserine Level	38.84	mcg/mL	Critical

Expected sample type received.

Test Name: Cycloserine Level
Cycloserine Level: 38.84 mcg/mL

Interpretation:
This test report is for cycloserine.

Cycloserine (cycloSERINE) may be confused with cyclosporine (cycloSPORINE). These two drugs sound alike and look alike.

The target range for mycobacterial infections is 20 to 35 mcg/mL 2 hours after oral dose. Samples drawn later than two hours after the dose may display concentrations below the stated range.

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January 2018 March 2019

Levofloxacin → rifabutin
Bedaquiline → linezolid

Anxiety; cycloserine level checked

Costs are considerable; assistance from MMS and MPH

Ethambutol started
CDC results received

Joint pain

MDR regimen started: bedaquiline, cycloserine, levofloxacin

Report from state lab: likely MDR - RIPE is held

Sputum collected, RIPE started

Positive AFB from FNA

Excisional biopsy

Core needle biopsy

Evaluated by ENT: CT and FNA

Onset of symptoms: swelling in neck

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241-26-2018 10:23AM No. 0302 P. 3

Centers for Disease Control & Prevention
Medical Tuberculosis Reference Laboratory

Patient Name: Eric Fenech April 23 Year

Public Health / International Submission Site

Drug	Percent Resistance	Interpretation	Drug	Percent Resistance	Interpretation
Isoniazid 0.2 ug/ml	100%	R	Kanamycin 5.0 ug/ml	50%	R
Isoniazid 1.0 ug/ml	100%	R	Rifloxamide 10.0 ug/ml	0%	S
Isoniazid 5.0 ug/ml	100%	R	Capreomycin 10.0 ug/ml	25%	R
Rifampin 1.0 ug/ml	100%	R	PAS 2.0 ug/ml	0%	S
Ethambutol 5.0 ug/ml	0%	S	Ofloxacin 2.0 ug/ml	0%	S
Streptomycin 2.0 ug/ml	100%	R	Amikacin 4.0 ug/ml	100%	R
Streptomycin 10.0 ug/ml	100%	R			
Rifabutin 2.0 ug/ml	0%	S			
Ciprofloxacin 2.0 ug/ml	0%	S			

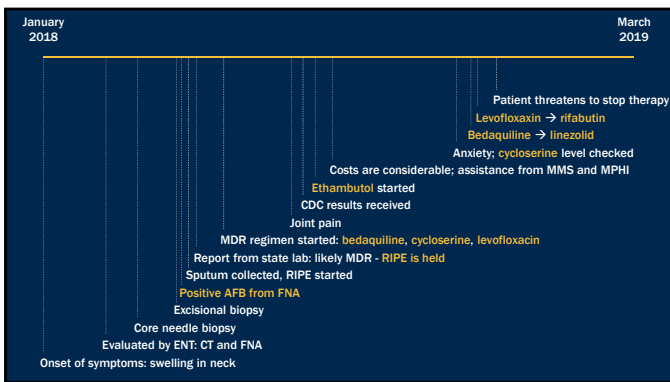
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- 10) Not all rifampin-resistant strains are rifabutin-resistant.

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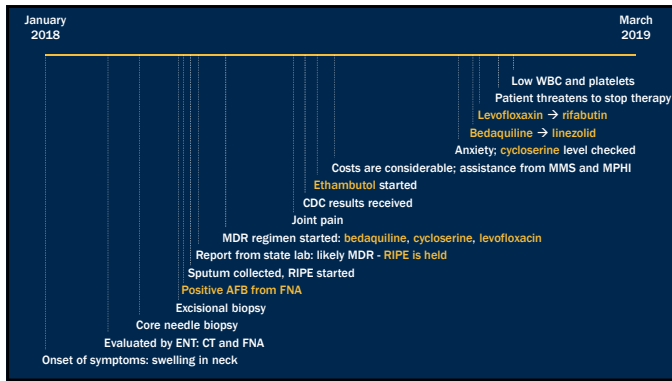


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- 11) Compelling a patient to take treatment – even for MDR-TB – is challenging.

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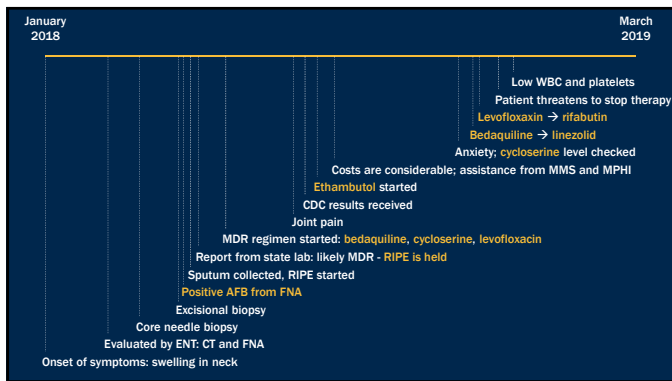


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- 11) Compelling a patient to take treatment - even for MDR - is challenging.
- 12) Duration of therapy is based on expert opinion, not data.

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Thank you!

Bob Dickson
rodickso@med.umich.edu



