



# **BPaL + Moxifloxacin Regimen Implementations and Outcomes in Texas**

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Webcast

**Barbara Seaworth, MD, FIDSA** has the following disclosures to make:

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- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity





# Implementation of BPaL and BPaLM In Texas

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# Characteristics of Drug Resistant TB on BPaL and BPaLM

## Diagnosis

Pulmonary TB (PTB)	23
PTB + Extra Pulmonary TB*	9

**First Case 8/3/2021**

## # starting treatment

2021 (5)

2022 (16)

2023 (11)-

*who finished treatment in 2023*

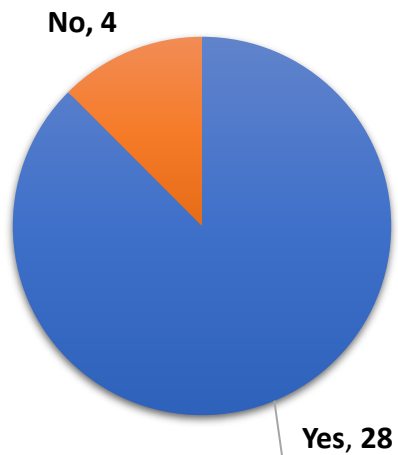
## Age at Diagnosis

0 – 17	1
18 – 39	14
40 – 59	6
60 – 70	5
70 or greater	6

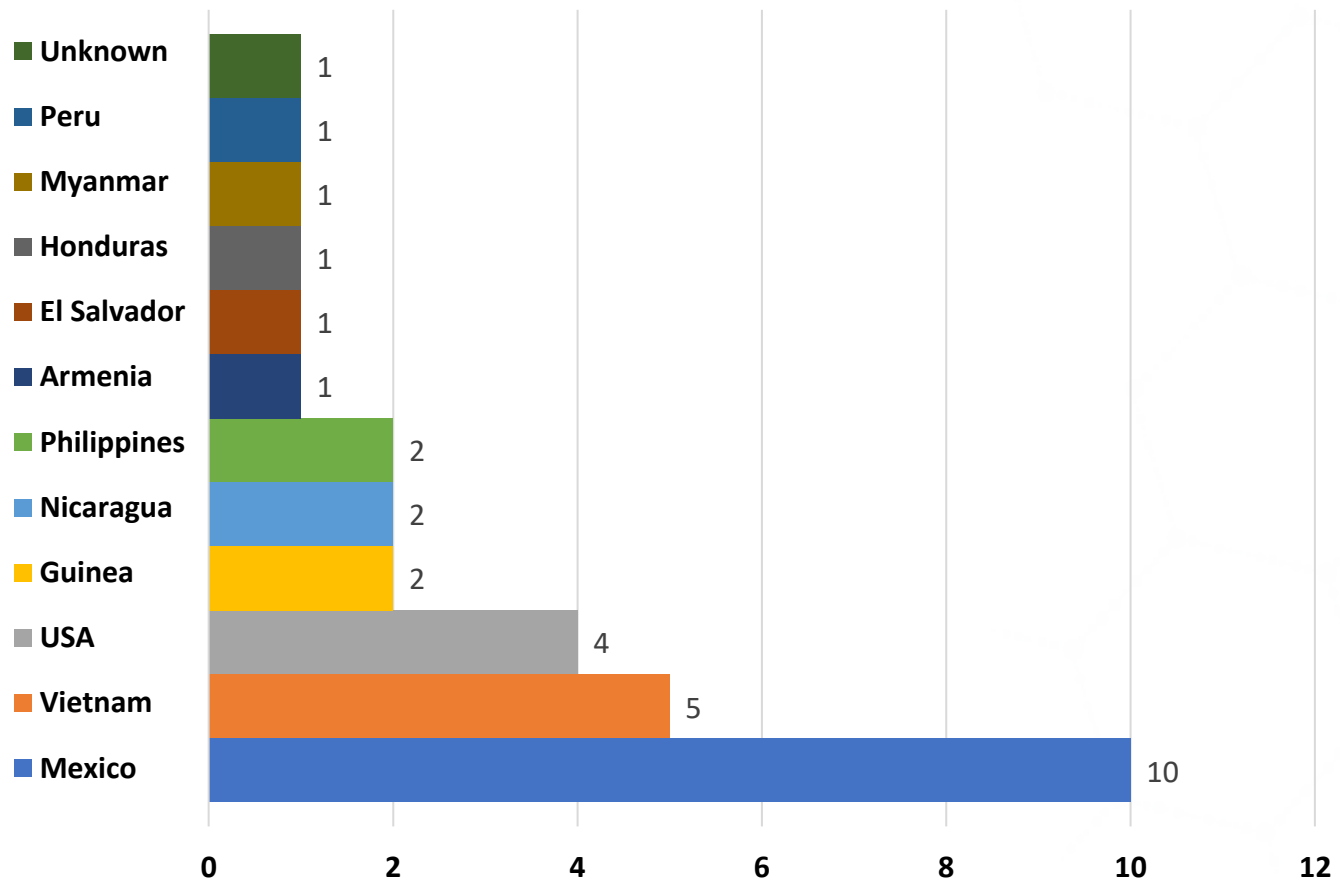




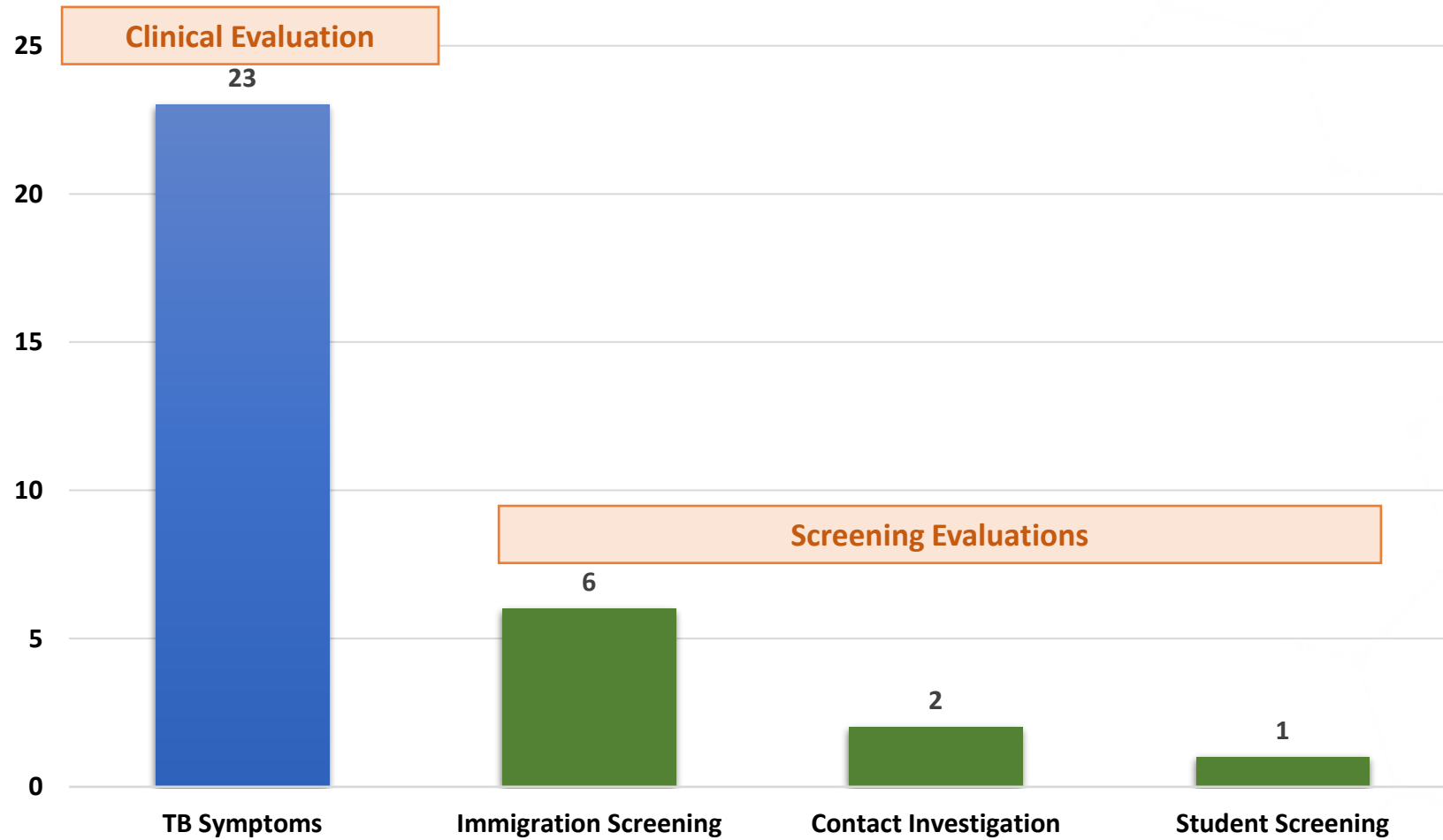
## Foreign Born



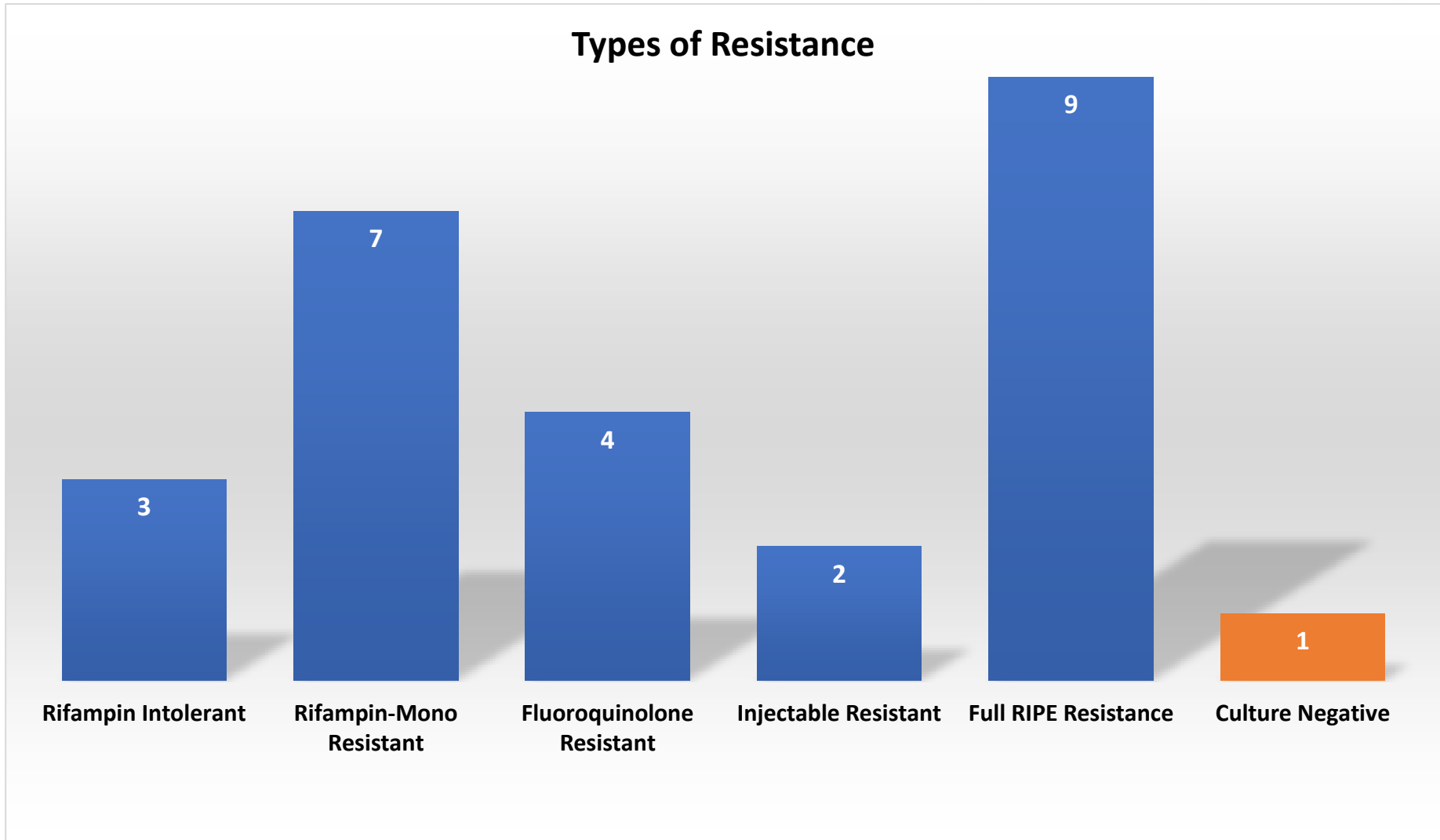
## Countries of Birth



## How was the TB discovered?



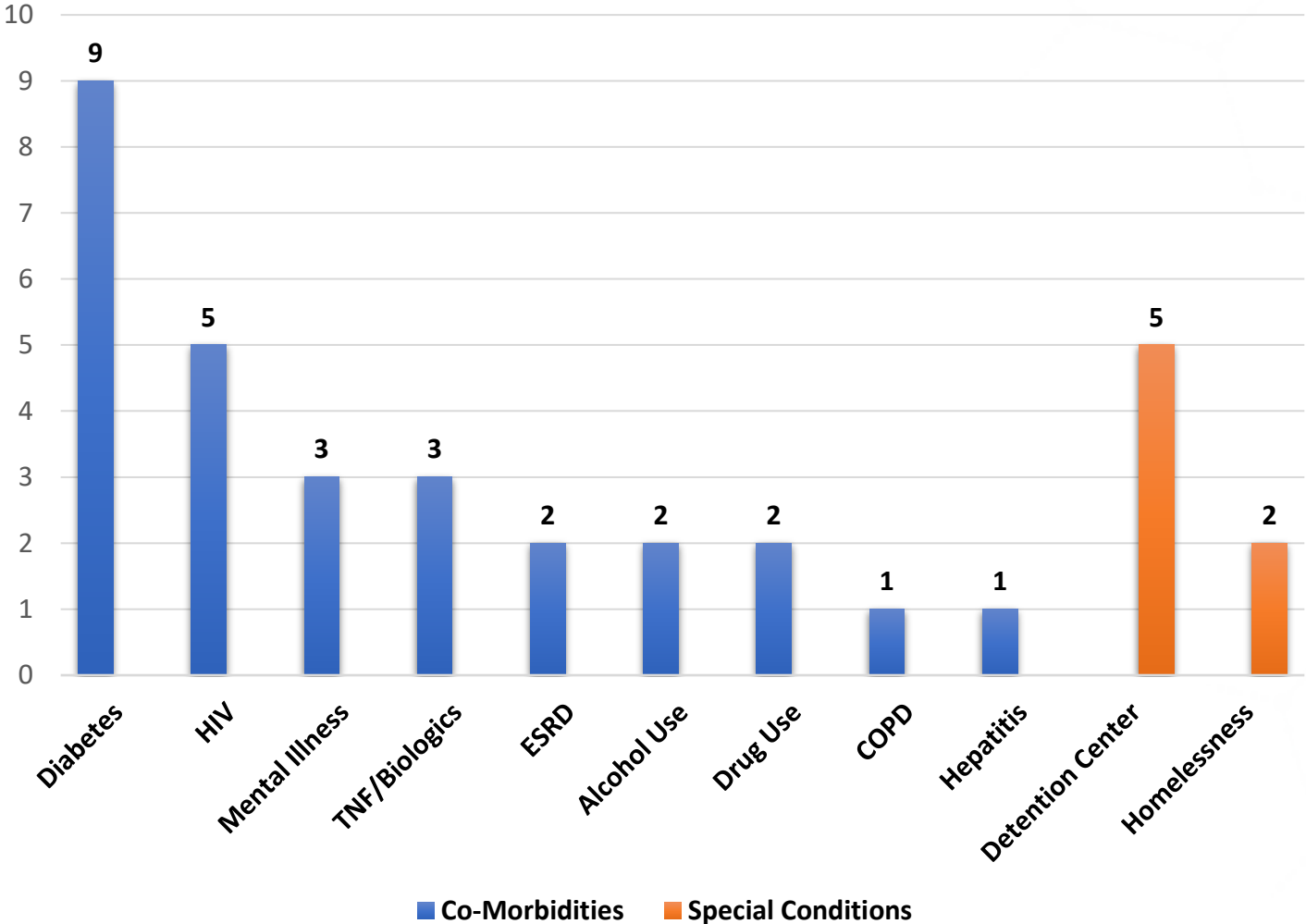
## Types of Resistance



Culture negative patient - mother of individual with severe disease  
who responded to MDR treatment clinically and radiographically



# Co-Morbidities and Special Conditions

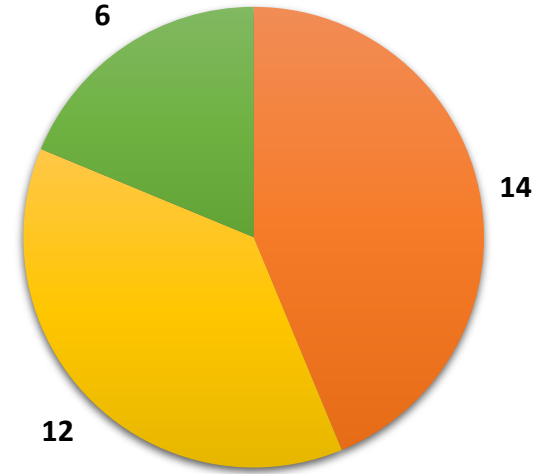
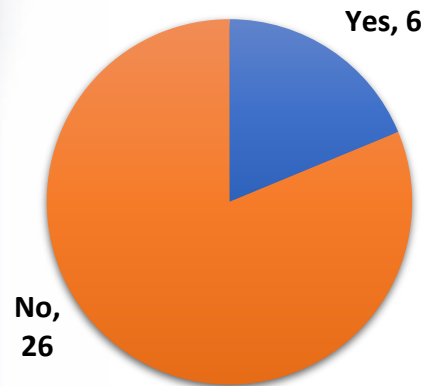




## Timeframe to Appropriate Treatment

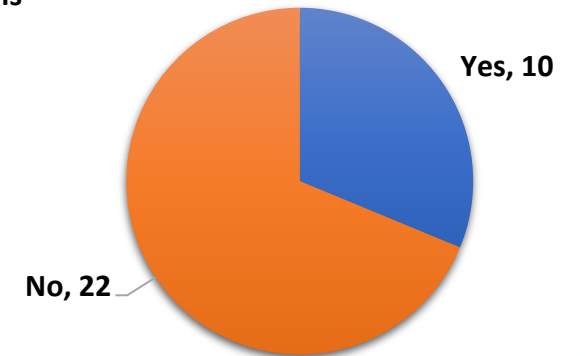


Prior Treatment for Drug Resistance



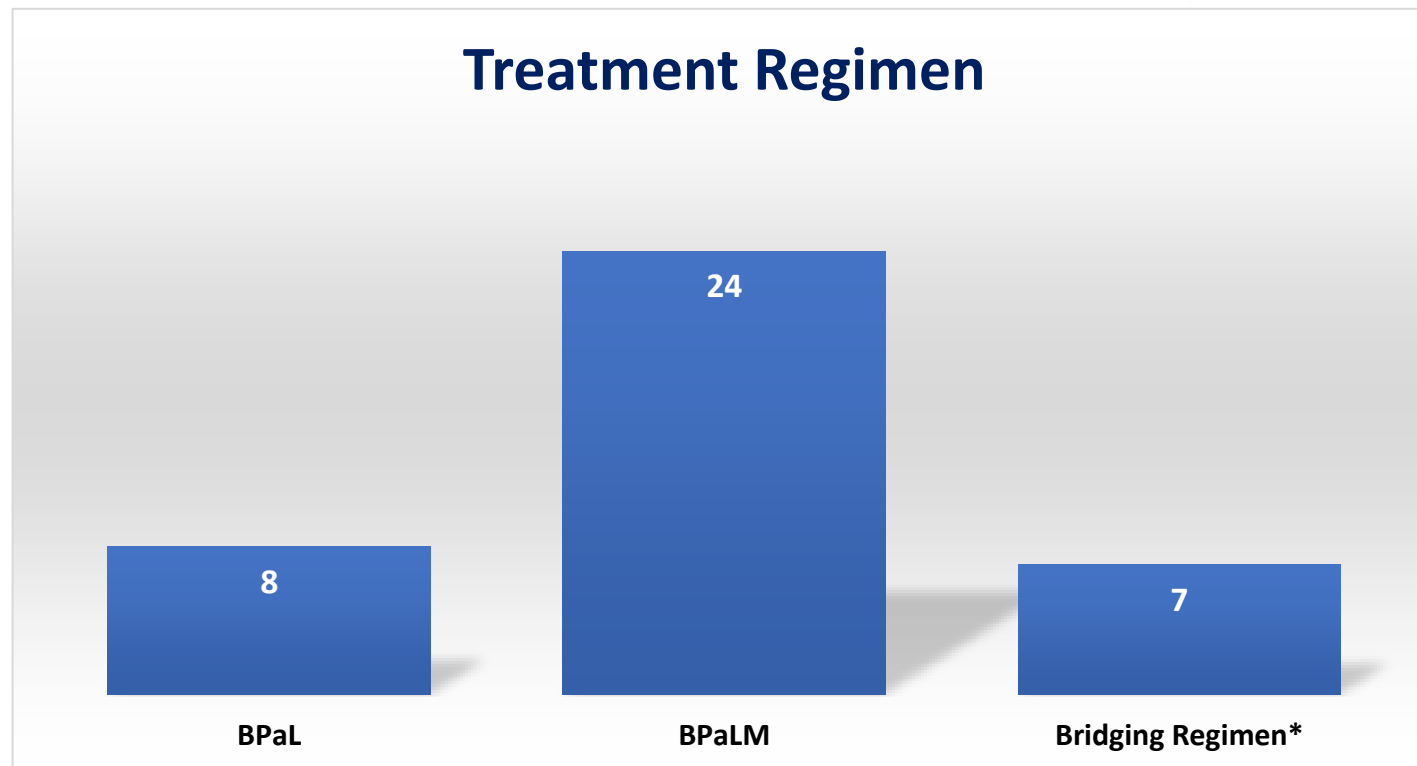
Legend for Timeframe to Appropriate Treatment:  
■ < 1 Month    ■ 1 - 3 Months    ■ > 3 Months

Prior Treatment with RIPE ( $\geq 1$  month)



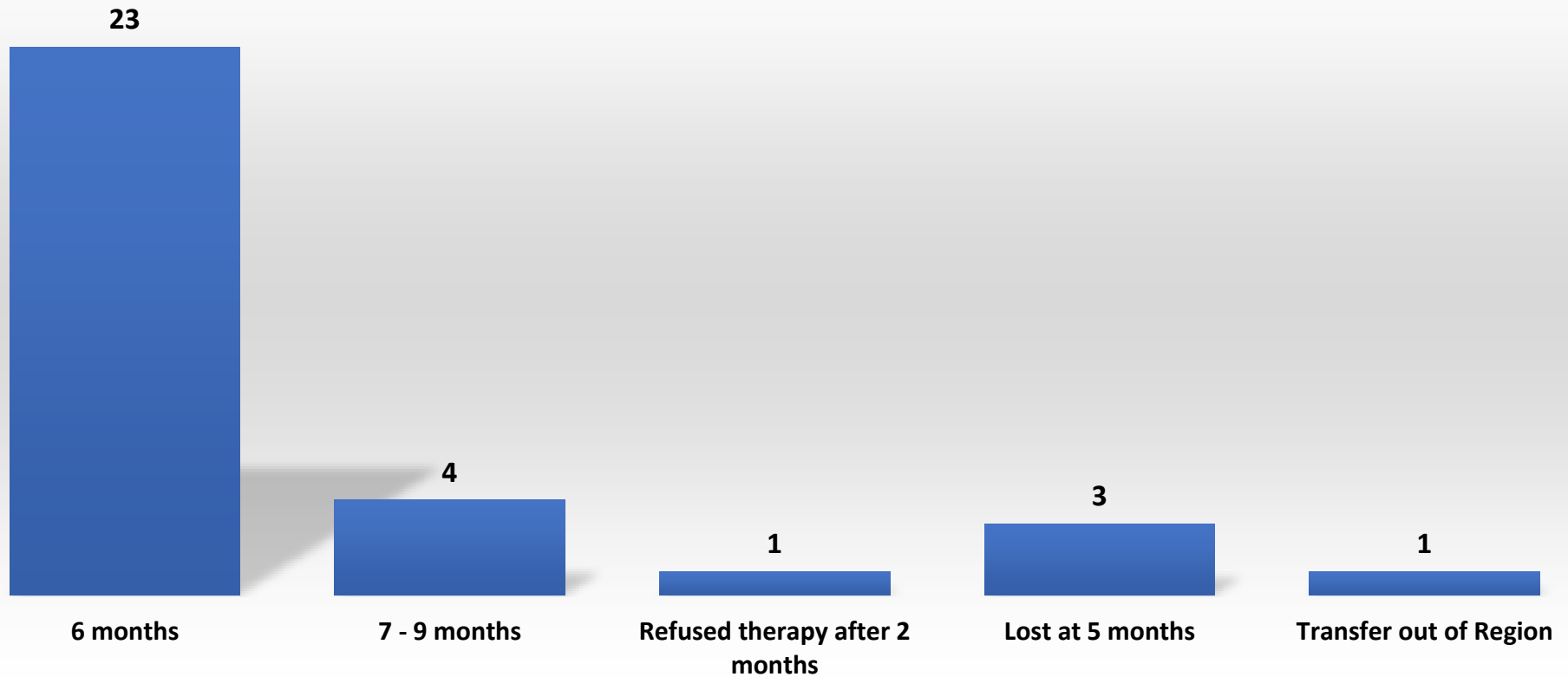


## Treatment Regimen



- **Bridging regimen** – Adequate treatment regimen for RR or MDR/pre-XDR or XDR TB prior to start of BPaL or BPaLM
- **BPaLM** (Bedaquiline, Pretomanid, Linezolid and Moxifloxacin)
- **BPaL** (Bedaquiline, Pretomanid, Linezolid)

## Duration of Treatment



# Time to Culture Conversion with BPaLM & BPaL

- Prior to start of BPaLM or BPaL 7
- < 1 month after start of BPaLM or BPaL 7
- < 2 months after start of BPaLM or BPaL 3
- 3 months after start of BPaLM or BPaL 1
- Not determinable
  - 2 patients diagnosed with + Xpert showing rifampin resistant
  - 1 clinical case
  - 6 missing date of culture conversion



# Medication Toxicities

Peripheral Neuropathy Linezolid stopped after month 4; early in treatment high peak/trough levels, DM with baseline neuropathy which worsened	1
EKG/QTc – No arrhythmia, no symptoms, all continued with normalization of QTc 3 with QTc > 500 on single reading 1 with > 60 increase from baseline	4
Vision	0
Hematology Decreased WBC in first month, LZD held and successfully rechallenged	1
Hepatotoxicity	0
Dermatology Rash with pretomanid Brown tongue	2

Monthly toxicity assessment performed to include:  
Visual acuity, Ishihara, EKG, Peripheral Neuropathy screen, CBC, CMP, Medical Assessment



## Preserved Efficacy and Reduced Toxicity with Intermittent Linezolid Dosing in Combination with Bedaquiline and Pretomanid in a Murine Tuberculosis Model

Bigelow et al : Antimicrobial Agents and Chemotherapy Oct 2020

- Compared C3HeB/FeJ and BALBC mouse models of TB
- Daily versus thrice weekly
  - Intermittent dosing introduced:
    - 1) from treatment start
    - 2) after initial period of daily dosing
  - Some possible antagonism so strain to strain difference investigated
- Daily dosing of linezolid for 1 – 2 months had greatest efficacy but after that results similar if intermittent dosing or drug stopped



# Negative Outcomes

- 2 Deaths attributable to TB
  - Neither due to treatment failure
- 1 patient with CNS TB clinically improved at week # 3 and then worsened clinically. Evaluation showed fungal sepsis (Candida) in blood and urine. Patient was poorly controlled diabetic, advanced age and on high dose steroids along with BPaLM and cycloserine
- 1 patient with pulmonary and CNS TB and newly diagnosed HIV with high viral load cleared sputum and improved then developed multiple complications. He received 9 months of BPaLM plus cycloserine



# Key Considerations for Selecting a Regimen

- DST: Fluoroquinolone resistant? - BPaL preferred
- **For other patients BPaLM may be more active based on preliminary information from TB Practecal study and early WHO guidance**
- BPaLM and BPaL-not recommended/contraindicated:
  - CNS disease (lacking good data on CNS penetration)
  - Pregnancy
  - Age < 15
  - Extensive disease or Extrapulmonary disease
    - may need RX extended or drugs added





# What is Next?

- New resistance to current agents
  - Some parts of the world are seeing resistance rates of 3% or more to Bedaquiline and Linezolid
- A few cases of relapse in U.S. on BPaL regimens
  - Importance of following up patients after treatment completion – please share with us your assessments
- Many new drugs and regimen are out there being studied
  - It is about to get more complicated again
- However major benefit to our patients to have these **shorter, more effective and less toxic regimens**

