NEW YORK CITY DEPARTMENT OF HEALTH AND MENTAL HYGIENE
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Dear Colleagues,

On January 11, 2019, the New York City (NYC) Bureau of Tuberculosis Control (BTBC) hosted a half-day conference with local experts to discuss innovative research, ongoing clinical trials, and updated guidelines for the treatment of multidrug-resistant TB (MDR-TB)*. With the availability of new and re-purposed drugs and the potential for novel MDR-TB treatment regimens, this is an innovative and exciting time for TB control efforts.

NYC has had tremendous success in treating patients with MDR-TB. From a peak of 441 cases in 1992, the incidence of MDR-TB now averages around 10 to 15 cases per year. Treatment completion rates are high, relapse rates are low, and very few patients require surgery. However, even with relatively successful patient outcomes, the burden of excessive medical visits for treatment monitoring and need for multiple medications is difficult for most patients. Length of therapy is 18 months and most of the commonly used medications have significant side effects and are poorly tolerated, particularly the injectable agents.

With these issues in mind, the January 11th meeting focused on new publications and guidance that could impact local MDR-TB treatment practices. Key publications discussed included the 2018 Lancet article from Ahmad, N., et al *"Treatment correlates of successful outcomes in pulmonary multidrug-resistant tuberculosis: an individual patient data meta-analysis"* and the World Health Organization's (WHO) December 2018 pre-final treatment guidelines. The 2018 WHO guidelines were based on findings in the Lancet article as well as other relevant clinical trial data. While the recommendation for length of therapy is still 18 months or longer, there was a significant re-categorization of the most effective drugs used for MDR-TB which will require a new approach to MDR-TB treatment (see Table 1).

Based on research, recommendations, and local experience, there was consensus among the group that while NYC has had great success in treating patients with MDR-TB and limiting the development of drug resistance, emerging data and recommendations may be helpful in continuing to ensure positive patient outcomes. Changes in practice discussed include:

- **Prioritizing bedaquiline, linezolid, and clofazimine as "first-line" MDR-TB drugs**
- **Crafting an all oral regimen, when possible**
- **Limiting use of injectable agents and prioritizing amikacin or streptomycin if an injectable agent is needed**
- **Ensuring susceptibility of medications prior to use**
- **Using at least 5 drugs in the initiation phase and at least 4 in the continuation phase**

ATS/CDC/IDSA/ERS is also in the process of developing guidelines for the treatment of MDR-TB. Until the statement is available, we must be aware of recommendations from other sources and incorporate updated guidance into our practice whenever it is of benefit to our patients. The BTBC will re-evaluate local treatment recommendations as additional information becomes available. The treatment of MDR-TB is never easy, but I am confident that new research and a continued dedication to the health of our patients will ensure positive patient outcomes.

Sincerely,

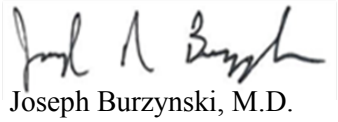

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Table 1: Grouping of Medicines Recommended for Use in Longer MDR-TB Regimens[1]

GROUPS & STEPS	MEDICINE	
Group A: Include all three medicines	Levofloxacin OR Moxifloxacin	Lfx Mfx
	Bedaquiline[2,3]	Bdq
	Linezolid[4]	Lzd
Group B: Add one or both medicines	Clofazimine	Cfz
	Cycloserine OR Terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E
	Delamanid[3,5]	Dlm
	Pyrazinamide[6]	Z
	Imipenem-cilastatin OR Meropenem[7]	Ipm-Cln Mpm
	Amikacin (OR Streptomycin)[8]	Am (S)
	Ethionamide OR Prothionamide[9]	Eto Pto
	p-aminosalicylic acid[9]	PAS

Adapted from: WHO treatment guidelines for multidrug- and rifampicin-resistant tuberculosis, 2018 update

1 This table is intended to guide the design of individualized, longer MDR-TB regimens (the composition of the recommended shorter MDR-TB regimen is largely standardized

2 Evidence on the safety and effectiveness of Bdq beyond 6 months and below the age of 6 years was insufficient for review. Use of Bdq beyond these limits should follow best practices in 'off-label' use

3 Evidence on the concurrent use of Bdq and Dlm was insufficient for review

4 Use of Lzd for at least 6 months was shown to increase effectiveness, although toxicity may limit use. The analysis suggested that using Lzd for the whole duration of treatment would optimize its effect. No patient predictors for early cessation of Lzd could be inferred from the IPD sub-analysis

5 Evidence on the safety and effectiveness of Dlm beyond 6 months and below the age of 3 years was insufficient for review. Use of Dlm beyond these limits should follow best practices in 'off-label' use

6 Z is only counted as an effective agent when DST results confirm susceptibility

7 Every dose of Imp-Cln and Mpm is administered with clavulanic acid, which is only available in formulations combined with amoxicillin (Amx-Clv). Amx-Clv is not counted as an additional effective TB agent and should not be used without Imp-Cln or Mpm.

8 Am and S are only to be considered if DST results confirm susceptibility and high-quality audiology monitoring for hearing loss can be ensured. S is to be considered only if Am cannot be used (unavailable or documented resistance) and if DST results confirm susceptibility (S resistance is not detectable with 2nd line molecular line probe assays and phenotypic DST is required). **Kanamycin (Km) and capreomycin (Cm) are no longer recommended for use in MDR-TB regimens**

9 These agents only showed effectiveness in regimens without Bdq, Lzd, Cfz or Dlm, and are thus only proposed when other options to compose a regimen are not possible

***Attendees of January 11, 2019 Conference:**

Shama Ahuja[1], PhD, MPH—NYC DOHMH
George Alonso, MD—Elmhurst Hospital
James Brust[1], MD—Montefiore Medical Center
Joseph Burzynski, MD, MPH—NYC DOHMH
Caralee Caplan-Shaw, MD—Bellevue Hospital
Rany Condos, MD—Bellevue Hospital
Demetre Daskalakis, MD, MPH—NYC DOHMH
Sneha Dedhia, MD—NYC DOHMH
Felicia Dworkin, MD—NYC DOHMH
Alfred Lardizabal[2], MD—Global TB Institute
Michelle Macaraig, DrPH—NYC DOHMH
Lindsay McKenna[2], MPH—Treatment Action Group
Herns Modestil, BS—NYC DOHMH
Diana Nilsen[2], MD—NYC DOHMH
Max O'Donnell[1], MD—Columbia University
Margaret Oxtoby, MD—NYS DOH
Farah Parvez[2], MD, MPH—NYC DOHMH
Shaila Rao, Ed.D—NYC DOHMH
Neil Schluger, MD—Columbia University
Jeanne Sullivan Meissner, MPH—NYC DOHMH
Lisa Trieu[1], MPH—NYC DOHMH

1. Attendees who contributed to the Ahmad, N., et al meta-analysis
2. Attendees who participated on ATS/CDC/IDSA/ERS MDR-TB guidelines workgroup