DR-TB STAT - August 2017 call

26 October 2017

Attendees: Vivian Cox (DR-TB STAT); Jennifer Furin (DR-TB STAT); Christophe Perrin (MSF), Fuad Mirzayev (WHO); Khairunisa Suleiman, Olga Pavlova (PATH), Sharonann Lynch (MSF); Ramon Crespo (GDF); Inoussa Zabsarone (USAID/Stop TB Partnership); Nataliya Morozova (PIH)

Agenda:

1. Discussion of third quarter global data (Jennifer Furin);

2. Feedback/discussion of main topics from the Union conference.

Minutes: Nataliya Morozova

1. General Update

- Discussion of third quarter global data (Jennifer Furin). Global data update includes the data from Quarter 3: July, August, September 2017. This information was not available for the Union meeting; data presented there was from the end of Q2 2017.
- DR-TB STAT reports on BDQ, DLM and the shorter regimen (SR). We collect the information from NTPs and our partners who support NTPs.
    - Main partners include - KNCV Challenge TB Project; Médecins Sans Frontières (MSF), Partners in Health (PIH), and Interactive Research & Development (IRD), who are the consortium partners in the Unitaid endTB project. STAT relies on partners and NTPs reporting to us. The country list is not comprehensive. STAT does not count patients who received drugs under compassionate use.
    - A number of the countries are early adopters of the new drugs, because they have high rates of resistance. Many of the countries have not started using the SR, because of high levels of resistance to FQ and injectable agents.
    - Some of the countries have started using the SR and we report those numbers on a per country basis in the STAT spreadsheet. We do not include a cumulative total of global SR uptake, since we are not confident we have collected accurate information from all countries that are rolling out the SR.
    - Francophone African countries are at the forefront of rolling out the shorter regimen, but these are countries where DR-TB STAT does not have strong ties with the NTP. We would appreciate to receive contact information if it is available from STAT members.
    - Cumulative number of patients on BDQ – 12,194. A large majority of them are being treated in South Africa, with almost 7500 patients started on BDQ.

- Other countries with large percentages of patients on BDQ – Belarus, Swaziland, Estonia and Latvia.
- There has been significant progress in many countries to make BDQ more widely available, but much more remains to be done; there are still countries (Ukraine, India) and regions (PAHO) where there has been extremely limited uptake of new drugs.
- DLM – access to this drug is extremely limited. As of end Q3 2017, there have been 976 patients treated with DLM under program conditions. Roughly 75% of patients treated with DLM have been through the endTB project.
- We report on the number of patients who receive drug, not the number of orders from GDF.
- Shorter Regimen –South Africa has started 2934 patients on SR.
- GDF orders:
  - BDQ orders from GDF: 13,825
  - DLM orders from GDF: 3,238
  - Notes: Russia and South Africa do not procure BDQ through GDF. Thus there is not complete overlap between orders and reported use.
- Graphs
  - Graph 1- Cumulative use of BDQ and DLM over time
    - The gap is wide between BDQ and DLM
  - Graph 2- Cumulative Delamanid and Bedaquiline Use Over Time Compared with Conservative Estimated Need
    - In 2016 we took the number pf patients started on MDR-TB treatment, according to the WHO 2015 data and we estimated 30% of patients started on treatment with benefits from the new drug. It is a very conservative estimate.
    - For this year, we took the number of the 2016 Global TB report.

- Comments:
  I. The difference between the dash (“-“) versus the zero (“0”) under the SR column – Vivian Cox
     - The dash means no reported information from the country, “0” means the country has not started any patients on SR.
  II. According to GDF orders, there are several countries that have put small orders for new drugs (e.g. 1 or 2 courses of BDQ). We are trying to get contacts from those countries to understand how many patients have been started and to include them into the DR-TB STAT report. Other countries, like Rwanda and Nepal, have ordered larger quantities of BDQ, but we have not been able to get reports from the NTP.
     - We are making a special push to reach out the countries in the PAHO region – we are aware of fewer than 200 patients in the PAHO region that have started new drugs. The major countries known using new drugs in the PAHO region are the Dominican Republic, Haiti, Peru, Colombia and Brazil. Brazil is only using BDQ under compassionate use.
     - If you know the contacts in the countries that are using BDQ, DLM or SR, please contact Jennifer Furin (jenniferfurin@gmail.com).
  - Khairunisa Suleiman –In Kenya we have tried to figure out why the NTP says it takes long time for the GDF to deliver BDQ courses to Kenya. It is difficult to get information at this point of time due to the presidential re-election. We are trying

to do more advocacy to increase uptake of BDQ and DLM. GDF says there is no delay, but the NTP says there is a delay from the GDF side.

- Jennifer Furin – the GDF has done a great job in terms of turnaround time for orders to get countries BDQ and even waive shipping costs for some countries. So it would be unusual if the delays in Kenya could be attributed to the GDF since they have not had delays with other countries. MSF has been supporting the roll out of new drugs in Kenya and compared with other MSF countries, the Kenya numbers are quite low. So there seem to be other barriers, thus important to keep up the conversation with the Kenya NTP about new TB drugs. We can continue this discussion about Kenya via email and follow up offline. The GDF has been very effective as a strong ally in the countries.
- Vivian Cox – there is a GLC mission scheduled for Kenya before the end of the year. Kenya is a priority country for USAID.

- Summary of the situation in Democratic Republic of Congo (DRC) – Inoussa Zabsarone (USAID/Stop TB Partnership MDR Clinical Consultant)
  - Currently, there are approximately 200 patients on SR, but this is not the most recent data. The country is implementing the guidelines that all rifampicin-resistant patients are eligible for SR. They are following the WHO recommendation for those patients who have been exposed to SL treatment.
  - There are 15 patients on BDQ in the country; and most of them are in Kinshasa
  - There are no patients on DLM. 3 treatment courses have been ordered. They ordered DLM thru GDF.
  - Laboratory – There is one LPA machine in the country. Some patient wait for 5-6 months before they get LPA results. It is challenging. There are two machines for doing cultures in the country, patients need to wait for several months before the result is returned. Clinicians rely more on microscopy for patients' follow –up. The NTP is supportive but they need support as well.

2. <u>Feedback/discussion of main topics from the Union conference.</u>

- The key findings from the Union conference included the results of STREAM I; the Otsuka 213 delamanid trial; the endTB programmatic data as well on the use of the newer drugs; and MSF's presentations on the use of BDQ in compassionate use, extension and combination with delamanid.
- We will focus on the results from the STREAM trial and DLM Phase III. There is a lot of discussion as to what to do with the results announced at the Conference.
- <u>STREAM 1 trial results</u>:
  - WHO and PIH have put out statements to follow up the STREAM results.
  - How to explain the results to the countries we are supporting and working with
    - Jennifer Furin – In terms of the STREAM results, there is a question from NTPs and care providers - given the result of the clinical trial, should we still be rolling out the shorter regimen (SR) in our country? There is confusion in the field and people are getting different opinions from different TA providers; some people say they should do it and some are advising more caution. Another opinion: with the SR not statistically proven to be equally effective to the longer regimen-should we exclude

certain groups from SR? Should we change/make modifications to the STREAM regimen now?

- Inoussa (USAID/Stop TB Partnership)– we cannot provide one answer, we should be careful and try to provide inputs according to each country's specific situation. I would recommend waiting for more data from the STREAM trial and the WHO. Some countries are quite confident in using SR.
- Fuad Mirzayev (WHO) – the results of the STREAM trial are not creating any confusion. The Union promised the results would come out early next year. When the results are finalized, they will be subjected to further review. Hopefully, the results will come out into the major review of the WHO guidance on MDR-TB treatment in the 2nd quarter next year. The results of the Otsuka Phase III trial are more worrisome. Something more urgent needs to be done. The WHO is asking Otsuka and all other implementers of DLM for the data to contribute to the review of the interim recommendations for DLM.
- Vivian Cox – To assist individual countries with what to do next, collaboration with external experts and their opinion are often needed. If countries have high level of resistance, can they pursue or modify SR under operational research?
- Fuad Mirzayev – countries are free to make modifications, but if new medications are used (other than modifications within the same therapeutic category), then the country should do it under controlled operational research conditions. The GDI previously developed a standardized protocol to help countries implement SR under operational research conditions. The GDI is considering developing a protocol that would cover this situation, a protocol for modified SR, so countries could use it as a foundation for an OR protocol. It will be helpful for countries to do it.
- Jennifer Furin – a number of countries are doing some modifications to SR through operational research conditions. South Africa has a significant number of patients under SR, they allow for drug substitution for patients with hearing loss. Up to 80% of patients have BDQ substitution. South Africa has a lot of infrastructure to follow up on these patients. It is a good example to look at.

- <u>Otsuka Phase III trial for DLM</u>
  - One of the larger concern - it will lead to worse uptake of DLM globally and it will potentially slow down access to DLM. Should we still be encouraging countries to order DLM, use it for BDQ failures, in children and adolescents?
  - Jennifer Furin – There is a number of questions from countries regarding DLM. One common question – "I have been using DLM, or thinking about using DLM but it's no better than placebo." The study was underpowered to be able to determine statistically significant findings. This trial raised more questions than it was able to answer. Now we need to look for further data.
  - Vivian Cox - DR-TB STAT is happy to provide inputs to countries if needed.
  - Sharonann Lynch – It will be good to have "frequently asked questions" to help address some of the questions to avoid confusion.

- Fuad Merzayev – A balanced messaging about both of the trials would be good. We should present the review of the final data as soon as possible to countries and partners helping them to have clear information.

Next DR-TB STAT call: **Thursday November 30th 2017,** at 11:00am EDT. The discussion will focus on off-label use of new TB drugs and will include a review of the recent WHO guidance document on off-label use; Dr. Cathy Hewison from MSF will share her perspective on off-label use in MSF projects.