DR-TB STAT - April 2017 call

20 April 2017

Attendees: Vivian Cox (DR-TB STAT); Jennifer Furin (SWIFT); Erica Lessem (TAG); Khairunisa Suleiman (South Africa); Michael Rich (PIH); Dr. Gunar Gunther (Namibia); Nununrai Ruswa (Namibia); Phuong Nguyen (Vietnam); Ramon Crespo (GDF); Heather Stone (FDA); Lice Gonzales (WHO); Edmund Rutta (USAID); Brian Kaiser (GDF); Jane Coyne (UCSF); Nataliya Morozova (PIH); Dennis Falzon (WHO); Fuad Mirzayev (GDI); Mamel Quelapio (KNCV)

Agenda:

1. General update and global numbers for new drugs (10 minutes)
2. Country presentation on access to new drugs: Namibia (20 minutes)
3. Country presentation on access to shorter regimen and access to new drugs: Vietnam (20 minutes)
4. Wrap up and date for May call (10 minutes)

Minutes: Nataliya Morozova

General Update

- Global data summary from April 2017 has been sent to the larger group; the data was summarized as of end March 2017
- Adjusted data as of 20 April 2017:
    - Philippines: BDQ – 97; DLM -1; shorter regimen – 503 total, 328 under operational research and 175 under program conditions; SL-LPA – since July 2015.
    - Swaziland: BDQ – 132; DLM -10; shorter regimen – 190 through MSF-OCA; SL-LPA – plans to start using in May 2017. 7 patients on both new TB drugs in combination.
- Adjusted totals for programmatic use as of 20 April 2017: BDQ - 8,874, DLM – 564, and shorter regimen – 3,199.
- GDF orders:
    - BDQ orders from GDF: 8,599
    - DLM orders from GDF: 2,223
- Notes:
    - We will be moving to quarterly reporting but will keep monthly calls going
        - Some countries collect data on quarterly basis only
        - We're unable to get monthly updates from every country on our list

    - Multiple groups are collecting additional data from countries on the use of shorter regimens and second line LPA (SL LPA) in countries they support: KNCV/Challenge TB, the Triage Task Force of GDI, the Union (through the DR-TB working group and a questionnaire sent to Francophone African countries), WHO, GDF
    - STAT will start a collaboration with all partners to assimilate country level data on new drugs, shorter regimen, and SL LPA, create denominators/targets for countries, and summarize in a report on an annual/semi-annual basis
    - South Africa accounts for 61% of patients on BDQ; 81 patients are receiving DLM through the DLM clinical access programme, and 350 patients are now on a shorter regimen
    - Most global DLM use still within MSF projects
    - DR-TB STAT website will be updated to make it more interactive and accessible for information and two-way communication
- Questions
    - Erica Lessem (TAG) - Disconnect between some of the data that could be collected at the program level to help inform the use of new TB drugs moving forward and what gets put into the guidelines development group process when guidelines on BDQ/DLM are being updated. It took a lot of effort to have South Africa cohort data be included in the BDQ review in the WHO meeting report that was recently released. Is it possible to work with countries and WHO to set up a tool for communication of data that is available and have a dialogue between countries how to make that data more useful for informing guidelines and make sure WHO can incorporate the data into reviews? We now have more patients on BDQ than the shorter regimen and the guidelines do not reflect that.
        - Answer, Vivian Cox (STAT) – An excellent suggestion to try and improve communication between groups collecting data and the entities making recommendations/guideline updates. DR-TB STAT doesn't collect data on what is needed to inform change in guidelines – like treatment outcomes – but the global data on new drug access and challenges in the field that STAT does collect is useful to inform strategies to improve uptake. The team from WHO involved in the recent comprehensive survey will be a part of the collaboration on data collection that STAT is leading, which will hopefully lead to improved communications and sharing of data.
- Comments
    - Michael Rich (PIH) – endTB, the UNITAID sponsored project, has a clinical study and a large observational study going on in 15 countries hoping to enroll 2600 patients on BDQ, DLM, or both (www.endTB.org). This is the project run by PIH, RID and MSF; it is done across several countries and in a high-quality manner; and it has an independent PV Unit that reviews all SAEs and assigns outcomes. It will include extensive data from those countries, which will contribute substantially to the experience of using new drugs. We have started getting

results and we will be able to provide more evidence to influence the WHO guidelines with new TB drugs.
    - Fuad Mirzayev (GDI) - A global aDSM database has been set up and countries can submit active PV data, which can be a great help for future WHO guidelines. Several countries like Belarus, Philippines and possibly in the future the endTB project countries will be adding some data into the aDSM database. The link to aDSM database is http://www.who.int/tdr/research/tb_hiv/adsm/en/ or contact aDSM-database@who.int.

Country presentations on access to new drugs, shortened regimen, diagnostics capabilities

1.Namibia (Dr. Gunar Gunther and Nunurai Ruswa)

- A new algorithm implemented March 2017 that allows GeneXpert as initial test among resistant TB cases followed by SL-LPA
- BDQ is provided exclusively through the USAID donation project; DLM – 1 patient, through the compassionate use program
- Shorter regimen not started yet; at the stage of finalizing guidelines which incorporate shorter regimen
- Last year (2016): ~10,000 cases notified in the country with population of about 2.5 million
- Total – 380 MDR-TB cases, basically RR cases, detected by GeneXpert
- Data from 2014, 2015 and 2016 was analyzed:
    - 3.9% - new MDR-TB cases
    - 8.7% re-treatment cases
- Treatment
    - One big center in the capital city with TB hospital - 50 MDR-TB patients can be treated, mostly during the intensive phase; try to push ambulatory treatment but many logistical issues
- New TB drugs
    - Available for 12 months; prior to this the XDR-TB regimen was not adequate as it was mostly based on changing moxifloxacin to levofloxacin and adding clofazamine
    - All patients treated on new TB drug regimen have converted
    - Patients with advanced lung destruction and those who are hospitalized late have a lot of comorbidities
    - Many MDR and XDR-TB patients come to Namibia from Angola because of lack of DR-TB care in Angola
    - A model of mixed ambulatory and hospitalization approach. Most patients are hospitalized at the beginning of the treatment for the intensive phase, and provide ambulatory treatment at the continuation phase
- Challenges
    - There are issues with DST and diagnostics of MDR-TB

Comments:

- Jennifer Furin - How can you roll out shortened regimens in Namibia? Specific challenges for treatment of patients with HIV?
    - Answer: We have 50-60% pyrazinamide resistance, ~40% of HIV co-infection. There are more questions than the answers now, although we follow WHO recommendations.
- Vivian Cox – What is the plan for the country to access delamanid?
    - Answer: There is no specific plan, we have few patients for whom it would be available. We have one case, 11 year old boy, who has a history of DLM/BDQ combination treatment for 6 months, he has converted and is doing well.

2. Vietnam (Dr. Phuong Nguyen).

- DRTB in Vietnam - estimated 4% among new TB cases; 25% - among re-treatment DR-TB cases; MDR-TB rate – 25.6%; 16% - FQ resistance
- PMDT coverage: 63 provinces
- Enrollment until December 2016:
    - Cumulative number – 8,500 cases
    - Vietnam needs more effective treatment regimen
    - Estimated number of XDR-TB – 900 cases
- Shorter treatment regimen and BDQ cohort study – only 3 cities chosen, 100 patients per study
    - Inclusion criteria – BDQ regimen: pre-XDR and XDR-TB; intolerance to existing regimen; STR – Resistance to R, not to SLD
- SL LPS started in 2015 in 2 labs, 3 pilot sites for all RR detected
    - In 2016 – 524 cases tested with SL LPA
    - Encountered some difficulties at the start of shortened regimen, some patients refused to be enrolled into 9-month regimen because it is a study
- The enrollment into shorter regimen has been temporarily stopped. We need to receive approval from the MoH for the study cohort to enroll more patients in the next few months.
- Initial results of the 2 cohorts:
    - 6^{th} month culture – 68% negative; 28% - not evaluated
    - AEs – around 15%, the most common AE is decreased potassium, AST elevation and urea
- BDQ cohort (December 2015- March 2017)
    - 99 patients enrolled in BDQ regimen; 1/3 of them are XDR-TB cases; more than 40% are pre-XDR who are FQ resistant
    - Culture conversion - by the time of reporting, 39 patients had culture conversion
    - More than 40% had adverse events; QT prolongation in ~17% of patients. Most AEs are Grade 1 and 2
    - In 11.4% of patients treatment regimen was changed due to AEs (treatment interruption/ dose adjustment/ stop treatment)
    - The updated results will be provided

  The link to Vietnam presentation is http://drtb-stat.org/wp-content/uploads/2017/05/Vietnam_DRTB-STAT_Apr17.pdf

Questions:

- Jennifer Furin - Do you have a plan how treat patients who are not successful on shorter regimen?
    - Answer: We have discussed options for these patients. DLM is one of the options, or combo DLM+BDQ. Vietnam is open for using many options and opportunities to help our patients.
- Erica Lessem – You are waiting for permission to extend the observational study. When will you transition to routine programmatic use? Why does it have to keep being in an observational study? What would the MoH see to be able to move it to the normal programmatic use, either of the new drugs or of the shorter regimen?
    - Answer: The difference of our shorter regimen compared to the most recent WHO recommendation is that we use levofloxacin instead of moxifloxacin or gatifloxacin in the regimen. Now when we have some results from the observational study, we have to report to MoH on the rationale of the use of the regimen based on the results of this cohort. Now we are trying to convince MoH that we can use shorter regimen as routine, but since we may be delayed for programmatic implementation of the shorter regimen, we proposed to extend the study cohort.

Next DR-TB STAT call: **Thursday 18 May 2017 at 11:00am EDT, agenda to follow**