Data on drug-resistant tuberculosis in Tanzania

1 E-learning objectives

This module provides a general overview of the current status of TB management in Tanzania. The objectives of this module are:

- Increase student's knowledge on the anti-TB drugs commonly used in the Tanzania, including both first line and second line drugs;
- Increase student's knowledge on how the local Active Drug Safety Monitoring and management (aDSM) Programme in force at present works and how the local network of DR-TB treatment facilities is structured;
- Increase student's knowledge pharmacovigilance reporting tools that are currently available in Tanzania.

2 Tuberculosis drugs in Tanzania

- **First line**: Isoniazid (300mg and 100mg), Pyrazinamide 400mg, Rifampin 150mg, Ethambutol (400mg and 100mg)
- **Second Line Drugs** Pyrazinamide, Capreomycin inj, Kanamycin inj, Amoxicillin/Clavulanic acid, Bedaquiline, Clofazimine, Ethambutol, Ethionamide, Levofloxacin, Linezolide, Moxifloxacin, Para-AminoSalicylate Sodium, Prothionamide, Cycloserine, Pyridoxine (Vitamin B6), delamanid

3 Treatment of drug-resistant tuberculosis and a DSM in Tanzania

Currently, there are 75 DR-TB treatment facilities (initiation sites) in the country, of which 45 are covered with all diagnostic resources for treatment monitoring; scale-up to include all 75 facilities was planned to conclude by the end of 2018, but due to funding issues, this deadline was not achieved (information of February 2019). Once treatment with DR-TB drugs is successfully initiated, patients are transferred to in- or outpatient facilities closer to their homes.

- The recording and reporting of aDSM primarily target serious adverse events (SAEs) and ADR as a core requirement. Tanzania has chosen to implement the intermediate aDSM package (includes serious adverse events as well as adverse events (AE) of special interest) for all patients receiving DR-TB treatment. An adverse event of special interest is an AE documented to have occurred during clinical trials and for which the monitoring programme is specifically sensitized to report regardless of its seriousness, severity or causal relationship to the TB treatment.
- There is a TB program website (www.ntlp.go.tz) where pharmacovigilance data will be published once generated.

- January 2018: Bedaquiline and delamanid were introduced in November 2017. Tanzania started to roll out the shorter DR-TB treatment regimen. In the first half year of 2018, 104 patients have been enrolled on the shorter treatment regimen (STR). Till end June 2018, five patients were initiated on these new drugs from the start (4 on bedaquiline-containing regimens and 1 on a regimen containing delamanid) and 20 DR-TB patients were shifted from other regimens to bedaquiline-containing regimens, mainly because of ototoxicity. Thus, in total, **till the end of June 2018, there were 25 patients on regimens containing new drugs.**
- July 2017: A pilot study was done for active drug safety management (aDSM) in 9 DR-TB facilities. The pilot was gradually expanded through appointing regional aDSM focal persons. The regions covered so far are Kilimanjaro, Arusha, Tanga, Mbeya, Dar es salaam, Zanzibar, and Mwanza. In about 90% of these facilities, the shorter treatment regimen is prescribed.

The flow of information on adverse events is shown in Figure 1. National tuberculosis and leprosy programme (NTLP) has its own aDSM reporting form for MDR-TB treatment (see attachment_1).

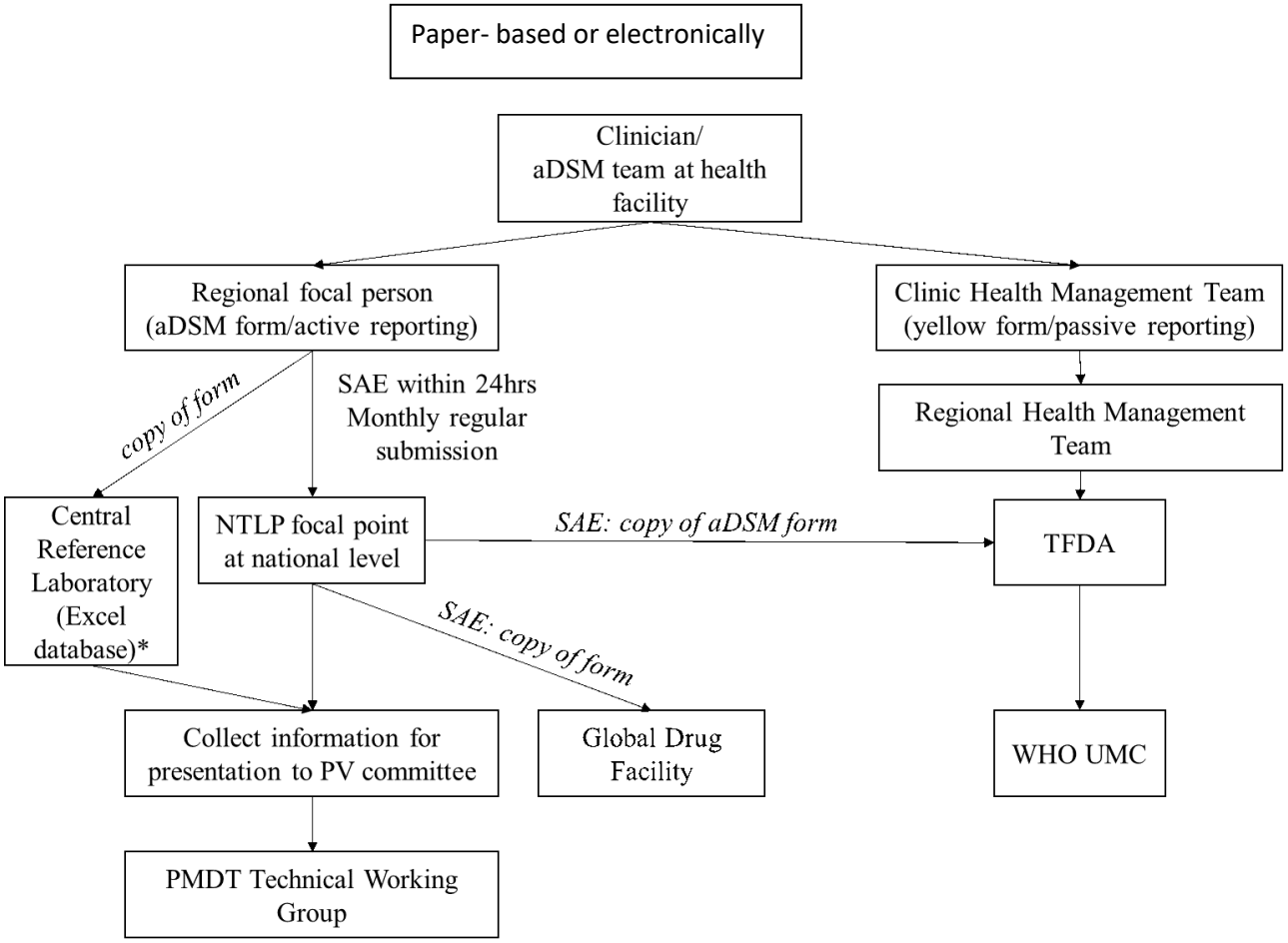

*Figure 1. Flow of information on adverse events from health care providers to the national PV centre (TFDA) and the Uppsala Monitoring Centre.**

* abbreviations used in this figure: aDSM: active drug safety management; SAE: serious adverse event; NTLP: National tuberculosis and leprosy programme; PMDT: programmatic management of drug-resistant TB; TFDA: Tanzanian Food and Drug Authority; UMC: Uppsala Monitoring Centre.

4 Reporting tools

Currently, there is potential double reporting done by health care facilities; health care professionals are supposed to fill in:

- The aDSM form for NTLP in case any adverse event arises that is reportable under aDSM
- The yellow form for TFDA for any adverse drug reaction
- To reduce double reporting, TFDA and NTLP are discussing if the aDSM form could be used as the only reporting tool for adverse events from DR-TB facilities collecting such information. If possible, only electronic forms will be used in future. All health care providers interviewed during the baseline assessment (BLA) of PAVIA Project agreed that aDSM contributes to improved patient care and thought it is time saving if the form is integrated to TFDA system of reporting so that they don't have to report twice.

5 Reporting of adverse events on DR-TB treatment

The flow of data on adverse events has been explained in paragraph in Figure 1. From July 2017 – June 2018, NTLP received 114 reports of suspected adverse events on DR-TB treatment, including 14 SAEs. These reports have been compiled in the KNCV/CTB report and the raw data have been entered in the national aDSM database. For MDR-TB treatment, a web-based adverse event reporting form (aDSM form) has been developed, which is coupled to a central database.

However, the database is not yet functional (currently the regional PV focal persons enter data in an Excel database and send it to a data manager dedicated to the aDSM database) and there is no connectivity with the TFDA database. Possibilities for an improved database and automatic connectivity with the TFDA database will be explored in the future.

6 Key-points

- Bedaquiline and delamanid, two of the most recent anti-TB drugs, are currently available in Tanzania;

- the local aDSM programme is part of an ongoing effort to keep anti-TB drugs safety monitored by reporting ADRs and serious adverse events, including the ones occurring in clinical trials;

- the two main reporting tools used to report adverse events and ADRs potentially linked to anti-TB treatments, the aDSM form for NTLP and the yellow form for TFDA, are collected into different databases.

7 Intermediate Questionnaire

A) Tanzania network of DR-TB treatment facilities currently counts 75 structures

B) Bedaquiline and delamanid are yet to be approved in Tanzania

a. A false, B false

b. A false, B true

c. A true, B false

d. A true, B true

Teaching:

"Currently, there are 75 DR-TB treatment facilities (initiation sites) in the country. Bedaquiline and delamanid were introduced in November 2017.".

In Tanzania, yellow form is used to report:

a. only adverse drug reactions occurred in clinical trials

b. any adverse drug reaction

c. only serious adverse events

d. none of the above

Teaching:

"The yellow form for TFDA for any adverse drug reaction.".