Incorporation of Bedaquiline in the South African National TB Programme

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ABSTRACT

BACKGROUND:
In 2014, 844 extensively drug-resistant (XDR TB) cases were diagnosed in South Africa. Following a successful clinical access programme (December 2012 to February 2015) and drug registration with the national regulatory authority in October 2014, a national framework was compiled to support the introduction of bedaquiline into the South African National TB Programme (SA NTP).

METHODS:
SA NTP guideline indications for bedaquiline (updated June 2015) include at least rifampicin-resistant TB patients with resistance to a fluoroquinolone or/and a second-line injectable drug (pre/XDR TB), both inhA/katG mutations for isoniazid resistance, intolerance or toxicity to standardized second-line regimen (e.g. ototoxicity, renal dysfunction, or psychosis), or surgical intervention. In patients with pre/XDR TB, linezolid is started in combination with bedaquiline. Patients with HIV infection, including those on antiretroviral therapy (ART), are eligible. Guidelines advise ART initiation for all TB patients with HIV infection. Inpatient admission is recommended for first two weeks or until culture conversion if XDR TB. Surveillance for BDQ resistance is done on baseline, 8-week, and 24-week sputum specimens using minimum inhibitory concentration testing by the national TB reference laboratory. Standardized forms for all patients are completed with proposed background second-line regimen, submitted centrally to the NTP, and reviewed by provincial or national clinical committee.

RESULTS:
From March to end September 2015, 598 patients have been initiated on bedaquiline in 7 of 9 provinces. As of end July 2015, most bedaquiline patients had either preXDR (40%) or XDR TB (39%); 65% were HIV-infected. The most common reason for cases being declined for bedaquiline initiation was patients with insufficient potentially effective drugs in the proposed background regimen.
Provinces that were able to scale-up quickly were those that had access to stock of linezolid, genotypic second-line drug resistance results, and capacity to detect high-frequency hearing loss.

CONCLUSIONS:
Political commitment, national and provincial leadership, facilitation, and monitoring enabled rapid incorporation of clinical trial findings for DR-TB into the SA NTP.
Increased access to capacitated inpatient and outpatient DR-TB management, ECG monitoring, and enhanced pharmacovigilance are needed to continue this rapid expansion.

Results

Table 1. Baseline patient characteristics

Descriptive	Characteristic	Count	%
Sex	Male	422	57.9%
Age	0-14 years	6	0.8%
	15-29 years	219	30.0%
	30-44 years	327	44.9%
	45-59 years	140	19.2%
	60 years+	37	5.1%
Prior TB	New (no history)	266	36.5%
Baseline smear microscopy	Negative	257	35.3%
	Positive	259	35.5%
	Missing	213	29.2%
HIV and ART status	HIV-negative	198	27.2%
	HIV-positive, on ART	439	60.2%
	HIV-positive, no ART	27	3.7%
	HIV status unknown	65	8.9%
Drug resistance	Rifampicin	115	15.8%
	MDR TB	251	34.4%
	preXDR flq	75	10.2%
	preXDR slid	42	5.8%
	XDR TB	246	33.8%

Figure 1. Baseline patient resistance

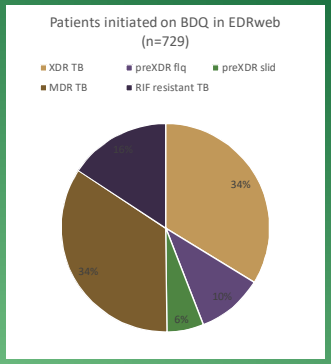
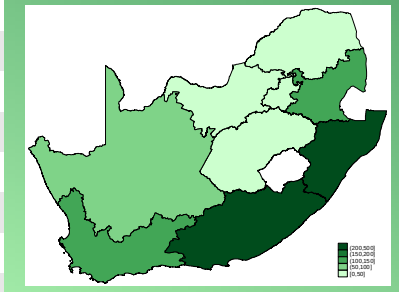


Figure 3. Counts by province, roll-out programme as of November 2015



Steps to implementation of bedaquiline roll-out

- Establishment of collaborative **public private working group**
- **Prepare regulatory documents** (protocol) for ethics and Regulatory approval
- **Communication and meetings** with regional TB Managers
- **Training** of medical, nursing and pharmaceutical staff including Good Clinical Practice (GCP)
- Bedaquiline Clinical **Access Programme**

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