**Appendices**

## **Appendix 1: Standardised regimens**

Table A.1: Standardised regimens used by participants through different treatment eras of this study.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
|  | **Short regimen****(9-11 months)** | **Long regimen****(³18 months)** |  |  |
|  |  |  |  |  |
| **Old regimen era**1st January 2015 – 3rd April 2017 |  |  |  |
|  |  |  |  |  |
|  | - | Moxifloxacin/Levofloxacin1 |  |  |
|  |  | Terizidone |  |  |
|  |  | Isoniazid2, 3 |  |  |
|  |  | Ethionamide4 |  |  |
|  |  | Ethambutol |  |  |
|  |  | Pyrazinamide |  |  |
| *Discontinued in continuation phase* |  | Amikacin/Kanamycin5 |  |  |
|  | (Bedaquiline)6 |  |  |
|  |  |  |  |  |
| **Short regimen era**3rd April 2017 – 1st July 2018 |  |  |  |
|  |  |  |  |  |
|  | Moxifloxacin/Levofloxacin1 | Moxifloxacin/Levofloxacin1 |  |  |
|  | Clofazimine | Clofazimine |  |  |
|  | Ethambutol | Ethambutol |  |  |
|  | Pyrazinamide | Pyrazinamide |  |  |
| *Discontinued in continuation phase* | Isoniazid2 | Isoniazid2 |  |  |
| Amikacin/Kanamycin5 | Amikacin/Kanamycin5 |  |  |
|  | Ethionamide | Ethionamide |  |  |
|  | (Bedaquiline)6 | (Bedaquiline)6 |  |  |
|  |  |  |  |  |
| **All-oral regimen era**1st July 2018 – 31st March 2019 |  |  |  |
|  |  |  |  |  |
|  | Linezolid | Linezolid |  |  |
|  | Bedaquiline | Bedaquiline |  |  |
|  | Levofloxacin | Levofloxacin |  |  |
|  | Clofazimine | Clofazimine |  |  |
| *Discontinued in continuation phase* | - | Terizidone |  |  |
| Isoniazid2 |  |  |  |
|  | Ethambutol |  |  |  |
|  | Pyrazinamide |  |  |  |
|  |  |  |  |  |

Notes: 1. Moxifloxacin preferred, but replaced with levofloxacin if bedaquiline incorporated into the regimen.

2. Isoniazid used at a high dose of 15mg/kg daily, or according to weight bands for adults (600mg daily for 33-70kg, 900mg daily for >70kg).

3. Isoniazid would be stopped if *katG* mutation detected.

4. Ethionamide would be stopped if *inhA* mutation detected.

5. Madwaleni site used kanamycin for adults and amikacin for children, while Zithulele site only used amikacin.

6. Bedaquiline would only be incorporated if needed as a substitute, for instance where aminoglycosides could not be used due to ototoxicity or nephrotoxicity.

## **Appendix 2: Table of adverse drug reactions**

Table A.2: Adverse drug reactions diagnosed.1

|  |  |  |  |
| --- | --- | --- | --- |
|  | All | Regimen |  |
|  | Short Course | Long Course | *p* value |
|  | n = 282 | n = 105 | n = 177 |  |
|  |  |  |  |  |
| **Any ADR** | 106 (37.59) | 40 (38.10) | 66 (37.29) | 0.446 |
|  |  |  |  |  |
| **Hearing loss**2 | 66/158 (41.77) | 21/45 (46.67) | 45/113 (39.82) | 0.255 |
|  Drug stopped3 | 62/66 (93.94) | 21/21 (100) | 41/45 (91.11) |  |
|  Patient died2 | 0/158 (0) | 0/21 (0) | 0/45 (0) |  |
|  |  |  |  |  |
| **Prolonged QTcF**4 | 22/117 (18.80) | 18/72 (25.00) | 4/45 (8.89) | 0.059 |
|  QTcF: 450 – 500msec5 | 20/22 (90.91) | 17/18 (94.44) | 3/4 (75.00) |  |
|  QTcF: >500msec5 | 2/22 (9.09) | 1/18 (5.56) | 1/4 (25.00) |  |
|  Bedaquiline stopped5 | 1/22 (4.55) | 0/18 (0) | 1/4 (25.00) |  |
|  Patient died5 | 0/22 (0) | 0/18 (0) | 0/4 (0) |  |
|  |  |  |  |  |
| **Other ADRs** |   |   |  |  |
|  Drug induced liver injury | 1 (0.35) | 1 (0.95) | 0 (0) | 0.097 |
|  Nephrotoxicity | 6 (2.13) | 2 (1.90) | 4 (2.26) | 0.421 |
|  Peripheral neuropathy | 3 (1.06) | 1 (0.95) | 2 (1.13) | 0.444 |
|  Psychiatric | 8 (2.84) | 0 (0) | 8 (4.52) | 0.014 |
|  Ophthalmological | 1 (0.35) | 0 (0) | 1 (0.56) | 0.221 |
|  Other | 28 (9.93) | 5 (4.76) | 23 (12.99) | 0.013 |
|  |  |  |  |  |

Notes: 1. All data are n (%) unless specified otherwise.

2. n/Total exposed to injectables (%).

3. n/Total diagnosed with hearing loss (%).

 4. QTcF: QT corrected using Fridericia formula, n/Total exposed to Bedaquiline (%).

 5. n/Total diagnosed with prolonged QTcF (%).