

TB-PRACTECAL: Imibuzo Evame Ukubuzwa

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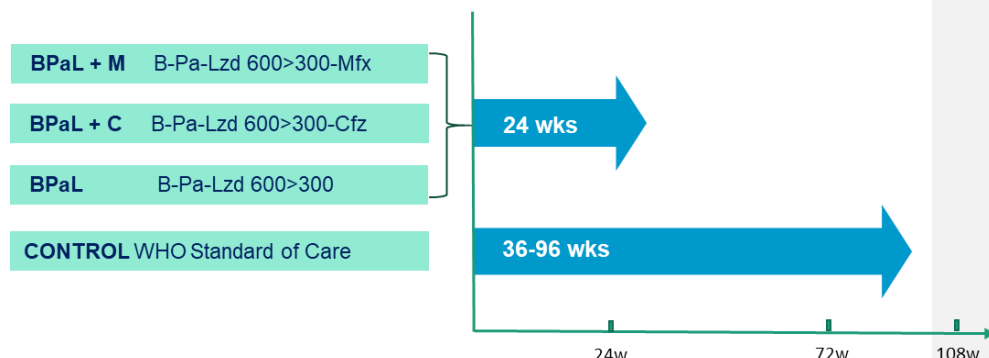
1. Umklamo Nokuqhutshwa Kocwaningo

1.1 Yini i-TB-PRACTECAL?

I-TB-PRACTECAL iwucwaningo olungafihlekile lwesigaba II/III olwenziwa ezikhungweni eziningi olungakhethi, olulawulwayo, oluhlola ukusebenza ngokufana kwemithi oluhlaziya ukuphepha nokusebenza kwemithi engu-3 yonke ethathwa ngomlomo amaviki angu-24 ene-bedaquiline, i-pretomanid ne-linezolid ekwelapheni isifo sofuba esingazweli kwi-rifampicin. Ucwaningo lunezigaba ezimbili, ezinokudlulela kolunye okushelelayo.

Iziguli zafakwa ngokungakhethi emikhakheni engu-3 ephenywayo nasemkhakheni wokulawula esitejini 1, okuhambisana nocwaningo lwesigaba IIB. Imithi yemikhakha ephenywayo ihlaziyelwa ukufaneleka eSitejini 2 (Isigaba III). Iziguli zesiteji 1 ezibhaliswe kunoma yimuphi umkhakha (noma imikhakha) eziqhubekela esitejini 2 zifakwa kusayizi wesampula lesiteji 2. Ekuphelani kweSiteji 1 (kwabhaliswa iziguli ezingu-240, ngo-Agasti 2019) kwahlaziywa yonke imikhakha engu-3 ngokwezimfuneko zokuphepha nokuphumelela ezibekwe kusengaphambili. Yonke imithi esaphenywa engu-3 yayifaneleka ukuba ihlaziywe eSitejini 2. Ngemva kokucabangela idatha yeSiteji 1 (efihlekile ngokomkhakha), iKomiti Eleluleka Ngezesayensi (i-Scientific Advisory Committee (SAC)) yancoma ukuba umkhakha 1 we-Practecal nomkhakha 2 we-Practecal idluliselwe kuSiteji 2. IKomiti Eqondisa Ucwaningo ngemva kokucabangela ukulibaziseka kokubhalisa futhi isibonisane ne-SAC kanye neBhodi Eqapha Idatha Nokuphepha (Data Safety and Monitoring Board (DSMB)) yaphetha ngokuthi umkhakha owordwa – umkhakha 1 we-Practecal kufanele udluliselwe kuSiteji 2. ISiteji 2 saqala ngoNovemba 2020.

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1.2 Yimaphi amaqembu abantu afakwa nangafakwanga ocwaningweni?

- Iziguli ezazineminyaka engu-15 nangaphezulu, kungakhathaliseki isimo sazo se-HIV noma isibalo se-CD4, ezivela e-Belarus, e-Uzbekistan, naseNingizimu Afrika ezinesifo sofuba eziqinisekisiwe ngokuthi azizweli kwi-rifampicin (**kungakhathaliseki** ukuthi azizweli kwi-fluoroquinolone) futhi ezanikeza imvume esekelwe olwazini yokuba zifakwe.
- Iziguli ezingafakwanga ocwaningweni kwakuyilezi: iziguli ezikhulelwe nezincelisayo, iziguli ekuqaleni ezatholakala zine-QTcF >450 noma zinesici esisodwa noma ezengeziwe ze-prolongation ye-QTcF, isifo sohlaka lwenhliziyo, i-ALT/AST > yesigaba 3, kanye neziguli ezake zasebenzisa i-BDQ, LZD, i-Delamanid noma i-pretomanid isikhathi esingaphezu kwenyanga e-1. Ezinye ezingafakwanga kwakuyiziguli ezine-TB meningo-encephalitis, amathumba ebuchosheni, i-osteomyelitis, nesifo samathambo.
- Ucwaningo lwabhalisa iziguli ezingu-552 sezizonke. Kulokhu kuhlaziya kokuqala, kwafakwa iziguli ezingu-301 kule miphumela.

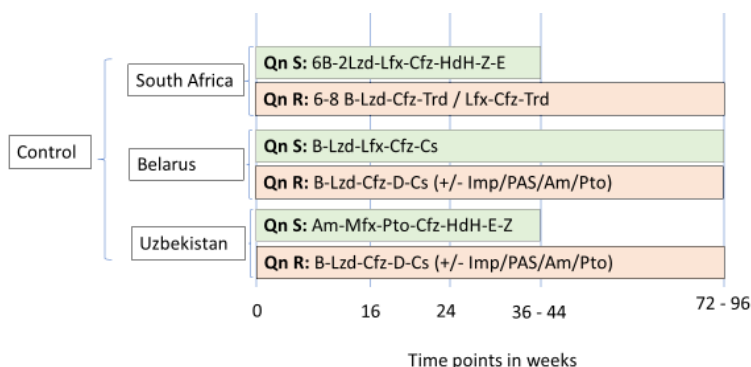
1.3 Yimiphi imithi eyasetshenziswa kwi-PRACTECAL?

- I-Pretomanid:** I-nitroimidazole ethathwa ngomlomo eyakhiwa yi-Global Alliance for TB Drug Development. I-FDA yayigunyaza ukuba isetshenziswe ekwelapheni ngo-2019, ihambisane ne-bedaquiline ne-linezolid. I-Pretomanid kwathiwa mayithathwe ngomthamo ongu-200mg nsuku zonke. Imithelela engemihle elindelekile ibandakanya ukulimala kwesibindi, ukuqubuka okunjengamaqhubu, kanye nokwenyuka kwamanani e-creatinine okungeyona ingozi. I-Pretomanid ingase ibe nokusebenzalana kwemithi okuningana – ikakhulukazi nezimbangeli ze-CYP 3A4. Akunconywa ukuba isetshenziswe ne-Efavirenz noma ne-Rifampicin.
- I-Bedaquiline:** I-Bedaquiline iyi-diarylquinoline antimycobacterial, njengamanje ewumuthi we-WHO oseqenjini A wesifo sofuba esingazweli kwi-rifampicin. I-Bedaquiline yayinikezwa njengomthamo okuqalwa ngawo ongu-400mg nsuku zonke amaviki angu-2 bese kuba ngu-200mg izikhathi ezintathu ngeviki emavikini angu-24 asele. Imithelela engemihle eyinhloko

ekhathazayo iwukungasebenzi kahle kwesibindi, i-prolongation ye-QT nokuhlobana ne-amylase eningi kolunye ucwaningo. Ukuchayeka kwi-Bedaquiline kuphazanyiswa yizimbangela ezinamandla ze-CYP3A4. Ukusetshenziswa ndawonye ne-Efavirenz akunconywanga ocwaningweni, phakathi nocwaningo izivimbi ze-integrase zancanywa njengendlela yokuqala yokwelapha i-HIV okwenza lokhu kwangaba yinkinga ezigulini ezazinyayo. Izivimbi ze-protease ziyayinyusa i-AUC ye-bedaquiline futhi kudingeka isetshenziswe ngokuqapha.

- **I-Linezolid** iyi-antibhayothiki ye-oxazolidinone ebuye yalungiselwa ukusetshenziselwa ukutheleleka ngama-mycobacteria. Ngo-2019, yaqashelwa njengomuthi weQembu A ngemva kokwanda kolwazi locwaningo lwezokwelapha, lwamaqembu nolwezinhlelo olusekela ukuphumelela kwayo. I-Linezolid yanikezwa nsuku zonke ngo-600mg amaviki angu-16 yabe seyhleiswa yaba ngu-300mg nsuku zonke amaviki angu-8. I-Linezolid inemithelela engemihle eyaziwayo ye-myelotoxicity ne-neurotoxicity kanye nezehlakalo eziyimvelakancane kodwa ezimbi kakhulu ze-lactic acidosis nesifo samanyikwe.
- **I-Moxifloxacin** iyi-8-methoxyquinolone esebenza kakhulu ekulweni nebhakteriya e-Gram-positive ne-Gram-negative nama-anaerobe. Lo muthi uwabulala ngokushesha amabhakteriya futhi ufinyelela amazinga aphakeme ezicutshini kubandakanya nephaphu. I-Moxifloxacin yanikezwa njengomthamo ongu-400mg othathwa ngomlomo nsuku zonke. Imithelela emibi eyayilindelekile emuthini eyayivame kakhulu kwakuyisicanucanu, uhudo, ubuhlungu bekhandu nesiyezi. Ukuvuvukala kwezicubu ezihlanganisa imisipha namathambo nokudabuka kwazo, ne-prolongation ye-QT kungeminye yemithelela emibi kakhulu yomuthi engase yenzeke nge-moxifloxacin.
- **I-Clofazimine**, i-iminophenazine ewudayi obomvu ngokugqamile, isalokhu iwumuthi we-WHO oseqenjini B futhi uthathwa ngomlomo. Wawunikezwa njengomthamo wansuku zonke oxhomeke esisindweni somzimba; iziguli ezazinesisindo esingu >33kg zazithola umthamo wansuku zonke ongu-100mg kanti lezo ezinesingu <33kg zazithola umthamo wansuku zonke ongu-50mg. Izingcwaningo eziningana zokwelapha zasikisela ukuthi kunenzuzo eyengeziwe emithini yokwelapha nasekunciphiseni imithi ibe yizinyanga ezingu-9-12. Imithelela engemihle elindelekile kwakuyi-prolongation ye-QT, ikakhulukazi lapho isetshenziswa kanye ne-BDQ ne-Pretomanid. Ibanga futhi ukushintsha kwesikhumba sibe mnyama ngokubomvu.

1.4 Yimiphi imithi Yokunakekela okuvamile iziguli ezayithola emikhakheni yokulawula:



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Iphrothokholi evunyelwe yemithi Yokunakekela Okuvamile izobuyekwezwa ngokweziqondiso ezibuyekwezwe yi-WHO phakathi nalo lonke ucwaningo. Lokhu kwakusho ukuthi isikhathi sokuthatha imithi sasizohlukahluke sisuka emavikini angu-36 siya kwangu-96. Imithi ejowwayo enikezwa isikhathi esifushane yayitholakala kuzo zonke izikhungo kusukela ekuqaleni. I-Bedaquiline ne-Linezoid yomibili yayitholakala kuzo zonke izikhungo kusukela ekuqaleni. Umklamo wokusebenza ngokufana kwemithi usho ukuthi uma umuthi omusha ufana nomuthi ongcono kakhulu otholakalayo, kusamele uhlangabezane nokusebenza ngokufana. Kuhlelwa izihlaziyo zokuzwela.

1.5 Yaba yini imiphumela yokuqala neyesibili?

Imiphumela yokuqala eyafakwa:

- Isiteji 1:
 - ☐ Ukuphumelela: Amaphesenti eziguli emkhakheni ngamunye ophenywayo ayengasenaso isifo sofuba kwi-MGIT liquid media emavikini angu-8 ngemva kokufakwa ngokungakhethi
 - ☐ Ukuphepha: Umphumela oyinhloko wokuphepha wawuyisibalo seziguli ezafa noma ezayeka ukwelashwa nganoma yisiphi isizathu ngeviki 8.
- Isiteji 2:
 - ☐ Amaphesenti eziguli ezaba nemiphumela engemihle (ukwehluleka kokwelashwa, ukufa, ukuyeka ukwelashwa, ukubuya kwesifo, ukungalandelelwa) emavikini angu-72 ngemva kokufakwa ngokungakhethi.

Imiphumela Yesibili:

- Isiteji 1
 - ☐ Amaphesenti eziguli ezine-prolongation yesigaba 3 noma ngaphezulu ye-QT, isigaba 3 noma ngaphezulu Zesehlakalo Esimbi, nokubhekana okungenani neSehlakalo esisodwa Esibi Kakhulu phakathi namaviki angu-8 ngemva kokufakwa ngokungakhethi
- Isiteji 2
 - ☐ Ukuphumelela: imiphumela kwakuwukuphela kwesifo emavikini angu-12, isikhathi esiya ekupheleni kwesifo, imithelela engemihle exubile emavikini angu-24 nasemavikini angu-108 ngemva kokufakwa ngokungakhethi, nokuqubuka kabusha

kwesifo ngeviki 48 ngemva kokufakwa ngokungakhethi (imikhakha ephenywayo kuphela).

- 2 Ukuphepha: imiphumela yesigaba 2 yayingamaphesenti eziguli ezazinesehlakalo esibi okungenani esisodwa noma isigaba 3 noma ngaphezulu sesehlakalo esibi ngamaviki 72 namaviki 108 ngemva kokufakwa ngokungakhethi, ekupheleni kokwelashwa, nokunwebeka okuyizikhawu kwe-QT ngeviki 24. Ukufa nesehlakalo esimbi sentshisekelo ekhethekile nako kwabikwa.

1.6 Zaziyni izimfuneko ezazinqunywe kusengaphambili zokuphepha nokuphumelela ezazinquma ukudlulela esigabeni 2?

Izimfuneko zokuphumelela ezazinqunywe kusengaphambili zeSiteji 1 zaziwukuphela kwesifo okungu >40% ngeviki 8. Izimfuneko ezazinqunywe kusengaphambili zokuphepha zeSiteji 1 ziwumphumela ongemuhele oxubile ongu <45%.

1.7 Kwanqunywa kanjani ukuthi umkhakha we-BPaLM kuphela owawuzodlulela esigabeni 1 uye ku-2 (isigaba II kuya ku-III)?

Ekupheleni kwesiteji 1 ngo-Agasti ka-2019, kwaqedwa ukuqoqwa kwedatha yemiphumela yokuphepha nokuphumelela emavikini angu-8. Yanikezwa i-DSMB ukuba iyibuyekeze, futhi kwaqinisekiswa ukuthi yonke imikhakha emithathu ephenywayo yayihlangabezana nezimfuneko ezazishiwo kusengaphambili futhi yayikufanelekela ukusetshenziswa esitejini 2. Idatha engafakiwe amagama yethulwa eKomitini Eleluleka Ngezesayensi eyabe seyincoma Umkhakha 1 (BPALM) Nomkhakha 2 (BPALC). Ikomiti Eqondisa Ucwangingo icabangela lesi sincomo nezinsalela zokubhalisa nobhubhane lwe-COVID-19 yakhethe ukudlulela kuSiteji 2 **nomkhakha owodwa**. Ngenxa yezingcwangingo ezedlule ezibonisa ukusebenza okusezingeni eliphakeme lokubulala ibhaktheriya kwe-Moxifloxacin, kanye nokukhathazeka okukhulayo ngokungazweli kwe-clofazimine ne-bedaquiline, Umkhakha 1 wakhethwa ukuba ungene eSitejini 2 owaqala ngoNovemba 2020.

1.8 Kungani kwathatha isikhathi eside kangaka ukugunyaza ukudlula kusuka Esigabeni 1 kuya Esigabeni 2?

Ukubhalisa kwaphela ngoJulayi 2019, kodwa-ke ababambiqhaza kwakusadingeka baqede amaviki angu-8 okwelashwa, nama-culture e-MGIT adingekayo ukuba acutshungulwe (okuthatha amaviki afika ku-6). Idatha yabe isihlanzwa ukuze ihlaziye. Ngemva kwale nqubo isinqumo asithathanga isikhathi eside kodwa saqondana nezinkinga zokubhalisa, kanye nokuqala kobhubhane lwe-COVID-19 okwenza zaphuza ukutholakala izimvume zeSiteji 2.

1.9 I-TB-PRACTECAL ihluke kanjani kwi-NIX ne-Ze-NIX?

Okuvamile: Lezi zingcwangingo zokwelapha ezintathu ziye zacwaninga imithi eyisishiyagalombili esekelwe kwi-BPaL ezinokwahluka okuncane esikhathini ezisithathayo, imithamo yocwaningo noma ukwengezwa kwe-Mfx noma kwe-Clofazimine. Alukho kulezi

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zingcwaningo olwaluklanyelwe ukuqhathanisa le mithi komunye nomunye. Ukuqhathanisa i-Ze-NiX ne-PRACTECAL akulinganiselwe nje kuphela emiphakathini yocwaningo ehluahlukene kodwa futhi nasemahlukweni kumaphrothokholi, ikakhulukazi, imikhawulo yokuyeka kusengaphambi kwesikhathi.

1. Ucwangingo lwe-Nix:

- a. Luwucwaningo olungafihlekile, lweqembu elilodwa olubandakanya iziguli ezine-MDR ne-XDR engasabeli ekwelashweni noma okwayekwa kulo ukwelashwa kwesibili ngenxa yemithelela engemihle.
- b. Zonke iziguli zathola amaviki angu-26 omuthi othathwa nsuku zonke ngomlomo, kanti zazingakhetha ukwelula ukwelashwa kube amaviki angu-39 uma zazisenesifo evikini 16.
- c. Umklamo wokwelashwa wawumi kanje:
 - i. I-Bedaquiline ngomthamo ongu-400 mg othathwa kanye ngosuku amaviki angu-2 kulandelwe u-200 mg othathwa kathathu ngeviki amaviki angu-24
 - ii. I-Pretomanid ngomthamo ongu-200 mg nsuku zonke amaviki angu-26
 - iii. I-Linezolid ngomthamo ongu-1200 mg nsuku zonke kuze kufike emavikini angu-26
- d. Imiphumela:
 - i. Ezinyangeni ezingu-6 ngemva kokuphela kokwelashwa iziguli ezingu-11 (10%) zaba nomphumela ongemuhle futhi iziguli ezingu-98 (90%; i-confidence interval engu-95%, 83 kuya ku- 95) zaba nomphumela omuhle. Imithelela yobuthi eyayilindelekile obabangwa yi-linezolid ye-peripheral neuropathy yenzeka ezigulini ezingu-81% futhi i-myeleosuppression yenzeka kwezingu-48%.

2. Ucwangingo lwe-Ze-NiX:

- a. I-Ze-Nix iwucwaningo lwezokwelapha olwalandela i-Nix lwesigaba 3, oluqhutshwa ezikhungweni eziningi, olufihleke nganxanye oluhlola ukuthi ukuphumelela kwemithi ye-BPaL kungaqhubeka yini, kuyilapho lunciphisa ubuthi, ngomthamo omncanyana nesikhathi sokwelashwa esifushane se-linezolid.
- b. Iziguli zathola amaviki angu-26 okwelashwa nokukhetha ukukwelulela emavikini angu-39 uma iziguli zisenaso isifo ngobufakazi bezokwelashwa kwe-TB phakathi kweviki 16 no-26.
- c. Umklamo wokwelashwa wawumi kanje: Zonke iziguli zathola i-Pretomanid 200mg ethathwa nsuku zonke + i-Bedaquiline 200mg ethathwa nsuku zonke amaviki angu-8 bese kuba engu-100mg ethathwa nsuku zonke amaviki angu-18 futhi zafakwa ngokungakhethi emikhakheni elandelayo ye-Linezolid:
 - i. 1200mg nsuku zonke amaviki angu-26 NOMA
 - ii. 1200mg nsuku zonke amaviki angu-9 NOMA
 - iii. 600mg nsuku zonke amaviki angu-26
 - iv. 600mg nsuku zonke amaviki angu-9
- d. Imiphumela ayikakashicilelwa

1.10 Lapho umbambiqhaza eyeka umkhakha we-SOC, yikuphi ukwelashwa anikezwa kona?

Njengoba kuchazwe kwiphrothokholi, iziguli zocwaningo zanikezwa imithi yokuzihlangula, ngemva kokuthola imihlahlandlela yezwe ye-TB nangokusekela komqaphi wezokwelapha. Ucwangingo lwaqinisekisa ukuthi iyaphumelela noma yimiphi imithi eyayidingeka ukwakha ukwelashwa okuhle kakhulu okuqondene nomuntu. Iziguli zanikezwa futhi ukukhetha ukuba

zilandelelwe ngocwaningo noma ngohlelo oluvamile lwe-TB. Uma zaqhubekela ekunikezeni imvume, zalandelelwa ukuphepha kwaze kwaba semavikini angu-108 kusukela ekufakweni ngokungakhethi.

1.11 Ukuthi 'yelaphekile' kwachazwa kanjani kulolu cwaningo?

Phakathi nocwaningo, njalo ngezikhathi ezithile kuthathwa amasampula esikhwehlela. Ngemva kokuthathwa kwezikhwehlela ezimbili ezingenaso isifo, iziguli zifakwa esigabeni 'sezilaphekile' uma zingasabonisi izimpawu ze-TB. Ngemva kwamaviki angu-72, uma izikhwehlela zeziguli zihlala zingenaso isifo futhi zingasenazo izimpawu ze-TB zibe sezibhekwa ngokuthi 'sezilaphekile' ngaleso sikhathi. Emiphumeleni ye-TB-PRACTECAL, iziguli ezingu-89% ezaqeda ukwelashwa nokulandelelwa azibonisanga izimpawu ze-TB futhi zabhekwa njengezilaphekile ngeviki 72. Amaviki angu-72 ayisikhathi esivamile sokukala ezingcwaningweni zokwelapha i-TB.

1.12 Ukuyeka kwachazwa kanjani ocwaningweni?

Ngokwephrothokholi iziguli zazizoyekiswa nganoma yiziphi izizathu ezilandelayo:

- I-prolongation yesigaba 3 noma ngaphezulu ye-QT nokunye ukuphazamiseka kokushaya kwenhliziyo
- Ukuvaleka kwezindlebe kwesigaba 3 noma ngaphezulu
- Iziguli Umphenyi aba nomuzwa wokuthi zazinganamatheli njengoba kwafakazelwa ukuphuthelwa amaviki angaphezu kwangu-2 alandelayo okwelashwa noma ezinye izimfuneko eziqondene nesikhungo.
- Isiguli sahxoxisa imvume
- Ukuyeka unomphela noma ukwenezela okungenani umuthi owodwa emkhakheni ophenywayo noma imithi emibili kwi-SOC. Ukunciphisa umthamo noma amaholide amafushane amaviki angaphansi kwangu-2 ngeke kubhekwe njengoshintsho olukhulu.
- Ngokuzibonela koMphenyi, isiguli singase siyeke ukwelashwa kunoma yisiphi isimo sesehlakalo esibi, okungavamile okutholakale elebhorethri, noma ukuqala kwesinye isifo, ngokubona koMphenyi, esiyingozi kakhulu ngokwezokwelapha kumbambiqhaza oqhubekayo esebenzisa imithi yocwaningo.

1.13 Ziyini izingcwaningo ezincane ze-TB PRACTECAL?

- Ucwangingo oluncane lwe-PRACTECAL PKPD – Umgomo oyinhloko wocwaningo lokusebenza komuthi emzimbeni nolwemithelela yawo ukukala ukugcwala kwe-plasma ye-bedaquiline, i-linezolid, i-pretomanid, i-moxifloxacin noma i-clofazimine ezigulini ezimbalwa ezisocwaningweni lwe-TB-PRACTECAL
- Ucwangingo oluncane lwe-PRACTECAL PRO – Isiguli sabika umphumela ohlaziya ukushintsha kwezimpawu kubandakanya nezehlakalo ezimbi, ukusebenza kanye nezinye izikali zezinga lokuphila.
- Ucwangingo oluncane lwe-PRACTECAL EE – Ucwangingo lokuhlola umthwalo wezomnotho we-MDR-TB. Idatha yezindleko okwabhekwana nazo ekunamatheleni ekwelashweni nasekuphathweni kwemithelela engemihle kanye neminingwane

yokuthola isimo sezomnotho nezenhlalo seziguli kuzoqoqwa ekuqaleni kocwaningo nangezikhawu ezinqunyiwe.

2. Ukuyekiswa kusengaphambi kwesikhathi

2.1 Sasiyini izizathu sokuyekiswa ucwaningo kusengaphambi kwesikhathi?

I-DSMB yayinikezwa idatha yokuphepha njalo ezinyangeni ezintathu nedatha yokuphumelela kabili ngonyaka ngokwemigomo ye-DSMB. Umgomo we-DSMB wabalula ukuthi i-DSMB kufanele icabangele ukuncoma ukuyekiswa ucwaningo uma isihlaziyo sihlalabezana nemithetho yokuyeka enqunye kusengaphambili (bheka u-7.2). I-DSMB yacela isihlaziyo saphakathi nendawo ngoNovemba 2020 kubandakanya Nomkhakha 1 nomkhakha Wokulawula kusukela ekuqaleni kocwaningo. Kwahlangatshezwana nomehluko omkhulu ngokwezimali onqunye kusengaphambili emphumeleni wokuqala phakathi kwemikhakha yokufakwa ngokungakhethi kuSiteji 2, owavuna Umkhakha Ophenywayo 1 (BPALM) uma kuqhathaniswa nomkhakha wokulawula. NgoFebhuwari 2021, i-DSMB yancoma ukuba ukufakwa ngokungakhethi ocwaningweni kuyekwe. UMxhasi, ngokuvumelana nesinqumo seKomiti Eqondisa Ucwaningo nangeseluleko se-SAC Yocwaningo wamukela lesi sincomo futhi isiguli sokugcina safakwa ngokungakhethi mhla ka-18 Mashi 2021 lapho kwase kubhaliswe iziguli ezingu-552. Ngaleso sikhathi kwase kufakwe iziguli ezingu-75% kasayizi wesampula elalihleliwe lesiteji 2 lezingu-201 ngomkhakha ngamunye.

Ngesikhathi sokubhala, ukulandelela kwakuqhubeka. Isiguli sokugcina, ukuvakasha kokugcina kulindeleke ngo-Agasti 2022 lapho isiguli sokugcina esasifakwe ngokungakhethi sifika emavikini angu-72 ngemva kokufakwa ngokungakhethi. Ngaleso sikhathi, zonke iziguli ezisasele zizokhishwa, idathabheyisi ikhiywe, futhi uMxhasi uzokhipha umbiko wokuphela kocwaningo.

3. Abantu nokwenziwa kusebenze kabanzi

3.1 Usho ukuthini u-ITT/ mITT no-PP?

- **Inhloso Yokwelapha:** lokhu kwakubandakanya bonke ababambiqhaza abanikezwa umuthi wocwaningo okungenani kanye
- **Inhloso Eshintshiwe Yokwelapha:** yayakhiwa abantu ababekwiNhloso Yokwelapha kodwa bengekho labo ababengenako ukungazweli kwi-Rifampicin okufakazelwe ngokuhlolwa ngezibonakhulu.
- **Ngokwephrothokholi:** Abantu bephrothokholi bakhiwa abantu ababekwiNhloso Eshintshiwe Yokwelapha kodwa zingekho 1) iziguli ezingakuqedanga ukwelashwa okunamathela kwiphrothokholi (>80% wemithamo phakathi no-120% wesikhathi esinqunyiwe), ngaphandle kokwehluleka kokwelashwa noma ukufa, futhi 2) iziguli ezayeka ukwelashwa kusengaphambi kwesikhathi ngenxa yokungahlangabezani nezimfuneko zokufakwa/zokukhishwa

3.2 Zingaki sezisonke iziguli ezabhaliswa uma zihlukaniswa ngokwemikhakha?

	ukulawula			Umkhakha-1 we-Practecal			Umkhakha-2 we-Practecal			Umkhakha-3 we-Practecal		
	ITT	mITT	PP	ITT	mITT	PP	ITT	mITT	PP	ITT	mITT	PP
Konke ukufakwa ngokungakhethi	150	141	42	151	138	98	126	116	93	122	111	92

3.3 Zazithini izici zokuqalisa?

Izici zokuqalisa zeziguli ezikubantu abakwiNhloso Yokwelapha

	ukulawula	Umkhakha-1 we-Practecal	Umkhakha-2 we-Practecal	Umkhakha-3 we-Practecal
Isibalo sisonke	150	151	126	122
Ubudala (iminyaka), median (i-range)	37 (18 to 71)	35 (17 to 71)	32 (15 to 67)	36 (15 to 72)
Abesifazane, n (%)	55 (36.7)	66 (43.7)	42 (33.3)	58 (47.5)
Isikhombo sesisindo somzimba (MBI) (kg/m ²), i-median (i-interquartile range, IQR)	19.9 (17.5 to 22.8) Abangekho = 1	19.8 (17.7 to 22.7) Abangekho = 0	19.5 (17.7 to 22.2) Abangekho = 0	20.2 (18.1 to 22.4) Abangekho = 0
Abaphozithivu nge-HIV, n (%)	40 (26.7)	38 (25.2)	33 (26.2)	41 (33.6)
Isibalo se-CD4 (amaseli/μL), i-median (IQR)	260 (132 to 460) Missing = 2	330 (209 to 547) Missing = 2	297 (114 to 481) Missing = 1	326 (153 to 550) Missing = 2
Abaphozithivu nge-smear, n (%)	97 (64.7)	91 (60.3)	84 (66.7)	77 (63.1)
Abane-cavity present, n (%)	94 (62.7)	80 (53.0)	79 (62.7)	73 (59.8)
Abangazweli kwi-Fluoroquinolone, n (%)	32 (24.8) Abangekho = 21	32 (23.9) Abangekho = 17	22 (18.6) Abangekho = 8	25 (24.3) Abangekho = 19
QTcF (ms), i-mean (SD)	401 (19)	398 (19)	395 (19) Abangekho = 0	398 (19) Abangekho = 0
ALT (IU/l), i-median (IQR)	20 (15 to 28)	19 (14 to 28)	17 (14 to 26)	20 (14 to 29)

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	Abangekho = 1	Abangekho = 1	Abangekho = 1	Abangekho = 0
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3.4 Ngokuvamile abantu abasemhlabeni wonke abaphethwe yi-TB bahlukahlukeni kakhulu kunabantu abafakwa ezingcwaningweni zokwelapha ze-TB. Ingabe ikhona idatha etholakalayo yala maqembu asengozini?

I-TB Practecal yayiklanyelwe ukuba ibandakanye imiphakathi eminingi ehlukahlukene ngokuphepha kangangokunokwenzeka ngokwalokho okuvunyelwa yizindikimba ezishaya imithetho namakomiti enkambiso elungile. Iziguli ezazigula kakhulu ukuba zibambe iqhaza ezingcwaningweni (njenge-slit lamp nama-audiogram) kwakumele zicatshangelwe, kanye nalezo okwakungenzeka zalinyazwa ngokuqondile yimithi esaphenywa I.e. : izinkinga zenhliziyo nokungasebenzi kahle kwesibindi. Lapho sikhuluma ngemiphakathi ethile ekhethekile kumele sinezele okulandelayo:

- I-PLHIV: Bonke abantu abakuleli qembu, kungakhathaliseki isibalo se-CD4 bafakwa ocwaningweni okwenza abangaphansana nje kwengxenywe eyodwa kwezine zababambiqhaza bocwaningo kwaba abaphozithivu nge-HIV. Izikhungo zocwaningo zakhethwa kucatshangwa ngalokhu.
- Intsha esukela eminyakeni engu-15 yafakwa kodwa kunesikhala kulolu cwano olungazuza ocwaningweni lokusebenza olungase lwenziwe.
- Ababambiqhaza abakhulelwa, noma ababambiqhaza abakhulelisa ophathina bakwazi ukuqhubeka besocwaningweni ngokokubona komphenyi inqobo nje uma kuhlalabazana nezimvume zendawo zenkambiso elungile. Konke ukukhulelwa kwabikwa esikhungweni esiqapha imithi futhi kwalandelelwa lapho kwakungenzeka khona ukuze kutholwe imiphumela yokukhulelwa kanye nemiphumela yokubeletha neyezinsana. Le miphumela izoshicilelwa kwi-MSF Science Portal maduzane
- Iziguli zahlolwa i-Hepatitis B no-C futhi zagcinwa ocwaningweni.
- Isifo sofuba esiba kwezinye izindawo ngaphandle kwasemaphashini sasingeyona imfuneko yokukhishwa ngaphandle kwalapho yayengekho indawo eyaziwayo – bheka umbuzo ongenhla ngababambiqhaza abafakwa nabangafakwanga.

4. Ukuphumelela

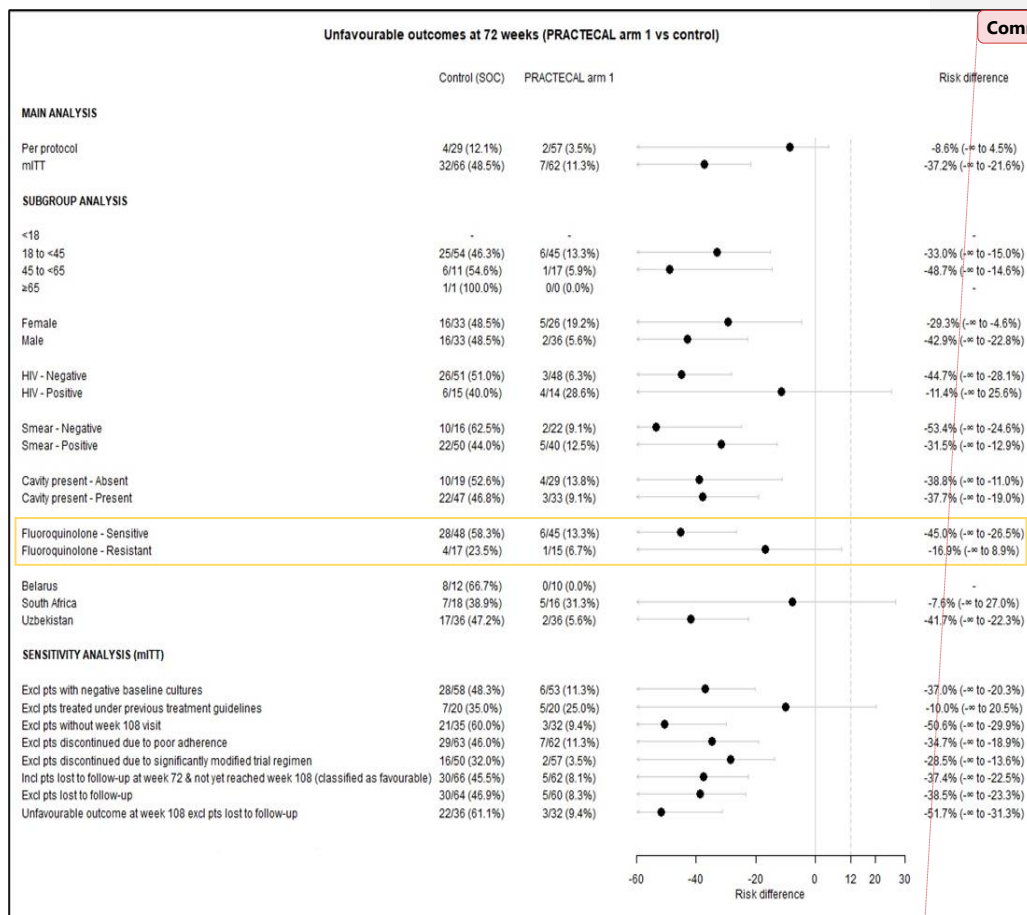
- 4.1 Bangaki abantu ababeseMkhakheni 1 (imithi ye-BPaLM) abase befinyelele iqophelo lokucina lesiteji 2 socwaningo emavikini angu-72 ngemva kokufakwa ngokungakhethi?

Ngosuku ukubhaliswa okwayekwa ngalo, abangu-145 (abokulawula abangu-73, abomkhakha-1 we-Practecal abangu-72), abangu-128 (abokulawula abangu-66 abomkhakha-1 we-Practecal abangu-62) nabangu-90 (abokulawula abangu-33, abomkhakha-1 we-Practecal abangu-57) babekubantu benhloso yokwelapha, inhloso eshintshiwe yokwelapha neyephrothokholi, ngokulandelana, futhi baba nethuba lokulandelelwa amaviki angu-72. Ngamaviki angu-72 okulandelela, kubantu benhloso eshintshiwe yokwelapha, iziguli ezingu-48.5% (32/66) nezingu-11.3% (7/62) bawugculisa umphumela oxubile ongemuhle ekulawuleni nasemkhakheni-1 we-Practecal, ngokulandelana.

- 4.2 Waba yini umphumela oyinhloko wocwaningo?

Kulolu cwaningo lwesigaba II/III, emphumeleni wokuqala oxubile, umkhakha-1 we-Practecal wawuyikho kokubili ukusebenza ngokufana nokusebenza kangcono emkhakheni wokulawula kubantu abanenhloso eshintshiwe yokwelapha, njengoba iziguli ezingu-88.7% zazinomphumela omubi uma kuqhathaniswa nezingu-51.5% bokulawula.

- 4.3 Kukhona yini ongabelana ngako nathi mayelana nokuphumelela eqenjini elincane leziguli nokungazweli kwi-fluoroquinolone?



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4.4 Ukuyeka ukwelashwa yiko ikakhulukazi okwenza umehluko emiphumeleni engemihle phakathi kwamaqembu amabili, ikhona imininingwane onayo ngaloku?

Izifuneko zokuyeka kusengaphambi kwesikhathi ocwaningweni zazifana kuyo yonke imikhakha. Abaphenyi babekwazi kwiphrothokholi ukuyeka umuthi owodwa emithini ye-SoC noma ukufaka omunye esikhundleni sawo ukuze basingathe izehlakalo ezimbi. Esihlaziyweni sephrothokholi, esasingakufaki ukuyeka kusengaphambi kwesikhathi, umehluko phakathi komkhakha wokulawula nemikhakha ephenywayo wawungacacile. Lokhu kusikisela ukuthi ngokuqhathaniswa umkhakha olawulwayo wawusebenza uma uzwana nemizimba yababamqibazela.

Izihlaziyo eziyinhloko zokuphumelela emiphakathini yamaviki angu-72 yenhloso eshintshiwe yokwelapha neyephrothokholi

	Umphakathi wenhloso eshintshiwe yokwelapha		Umphakathi wephrothokholi	
	ukulawula (n = 66)	umkhakha-1 we-Practecal (n = 62)	ukulawula (n = 33)	umkhakha-1 we-Practecal (n = 57)
Awukho umphumela omubi	34 (51.5)	55 (88.7)	29 (87.9)	55 (96.5)
Umpumela omubi	32 (48.5)	7 (11.3)	4 (12.1)	2 (3.5)
Ukufa	2 (3.0)	0 (0.0)	2 (6.1)	0 (0.0)
Ukuyeka kusengaphambi kwesikhathi	28 (42.4)	5 (8.1)	-	-
Izinkinga zokunamathela	3	0	-	-
Isehlakalo esimbi	17	5	-	-
Abangahlangabezana ngemva nezimfuneko zokufakwa/zokungafakwa (batholakala ngemva komthamo woku-1)	0	0	-	-
Abahoxisa imvume beselashwa	6	0	-	-
Okunye*	2	0	-	-
Ukwehluleka kokwelashwa	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abalahleka ekulandelelweni ngamaviki 72	2 (3.0)	2 (3.2)	2 (6.1)	2 (3.5)
Ukuqubuka kabusha kwesifo	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Umehluko wobungozi (ngohlangathi olulodwa 98.3% CI)	-	-37.2% (- to - 21.6%)	-	-8.6% (- to 4.5%)
I-p-value** yokusebenza ngokufana kwemithi	-	p<0.001	-	p<0.001
I-p-value yokubenza kangcono komuthi	-	p<0.001	-	p=0.13

4.5 I-TB-PRACTECAL inezelani kulokho esesikwazi nge-Pretomanid?

- Ukuphepha: I-TB PRACTECAL yathola ukuthi i-pretomanid iyezwana nomzimba, kulula ukuyisebenzisa, ngokuvamile iphephile, kanti nobuthi besibindi buyasingatheka. Manje sesinezingcwano eziningi ezitholakalayo ezinikeza idatha enhle ngokuphepha kwe-Pretomanid, kubandakanya ne-Ze-NIX okukhulunywe ngayo ngaphambilini (<https://www.tballiance.org/portfolio/trial/11883>), ne-NIX (<https://www.nejm.org/doi/full/10.1056/NEJMoa1901814>)

- Ukuphumelela: I-TB-PACTECAL ayikuvezi ukuphumelela kwe-pretomanid iyodwa, futhi azikho izingcwaningo ezilawulwa ngesithipha kodwa iye yabonisa ukuba nemithelela ebulala ama-bhaktheriya ezingcwaningweni ezedlule zesigaba II (<https://aac.asm.org/content/56/6/3027.short>)

4.6 Uma ucabanga ngokuyekwa kusengaphambi kwesikhathi kokufakwa ngokungakhethi, ingabe i-TB PRACTECAL izoba nedatha yocwaningo eyanele ukuba iphawule ngokuqubuka kabusha kwesifo phakathi kwemikhakha?

Iziguli ezingaba ngu-390, ezingu-97 emkhakheni ngamunye, ezaba nethuba lokufinyelela iviki 48 i.e. izinyanga ezingu-6 ngemva kokuqedwa ukwelashwa ngemithi esaphenywa. Lesi yisikhathi okwenzeka ngaso kaningi ukuqubuka kabusha kwesifo okubonakala njengomphumela owusizo noqhathanisekayo oye wakalwa ezingcwaningweni zamuva ze-TB. Lesi sikhathi kufanele sithambeleke ekutheni awukho umehluko.

5. Ukuphepha

5.1 Ingabe ukhona umehluko kwi-prolongation ye-QTcF phakathi kwe-SOC Nomkhakha 1

Izehlakalo ezimbi noma Zebanga ≥ 3 ezenzeka ngeviki 72, abantu benhloso yokwelapha, ngethemu ekhethiwe

	Ukulawula (n=73)		Umkhakha-1 we-Practecal (n=72)		Umkhakha-2 we-Practecal (n=72)		Umkhakha-3 we-Practecal (n=69)	
	izehlakalo	iziguli	izehlakalo	iziguli	izehlakalo	iziguli	izehlakalo	iziguli
I-prolongation ye-QT**	12	10	1	1	3	3	0	0
Isibalo esihlobene kanye ne-%	11	91.7%	0	0%	2	66.67%	-	-

** I-Electrocardiogram QT prolonged (ukulawula 9 nomkhakha-2 we-Practecal); I-Syncope (ukulawula 3, umkhakha-1 we-Practecal 1 nomkhakha-2 we-Practecal 1).

5.2 Yayiyini imbangela yokufa okwabikwa?

Isikhun go socwani ngo	Imbangela yokufa	Isikhathi	Kwakhulobene nokwelashwa?	Kwakhulobene ne-TB?	Umkhakha We-TB-PRACTECAL
UZ-01	Ukuvuvukala komgudu	Ngemva kokuyeka kusengaphambi kwesikhathi	Cha	Cha	ukulawula

	wokugaya ukudla				
UZ-01	Ukudlikiza	Phakathi nokulandelela	Cha	Cha	Umkhakha 3 we-PRACTECAL
UZ-01**	Ukuzibulala okuphumelelile	Beselashwa	Yebo	Cha	ukulawula
SA-03	Ukuthelaleka kwamanyikwe okubi	Ngemva kokuyeka kusengaphambi kwesikhathi	Yebo	Cha	ukulawula
BY-02	Ukufa okungazelelwe	Beselashwa	Yebo	Cha	ukulawula
UZ-04**	Inyuniya ye-Covid-19	Beselashwa	Cha	Cha	ukulawula
UZ-01	Inyuniya	Ngemva kokuyeka kusengaphambi kwesikhathi	Cha	Cha	Umkhakha 2 we-PRACTECAL
BY-02	Ukumelwa yinhliyo ngokungazelelwe	Beselashwa	Yebo	Cha	ukulawula
SA-03**	I-COPD	Phakathi nokulandelelwa	Cha	Cha	Umkhakha 2 we-PRACTECAL
SA-03	Ukugwazwa	Phakathi nokulandelelwa	No	Cha	ukulawula

*Bonke ababebhaliswe kwaze kwaba mhla ka-18 Mashi 2021 ababenikezwe imithi.

**Ukufa okwakufakiwe emphumeleni oyinhloko oxubile ngeviki 72, kuhlanguke nezihlaziyo ezengeziwe

5.3 Ukuqapha ama-cataract kuzoba nzima ngaphansi kwezimo ezinezinhlelo? Ingabe imiphumela ye-TB PRACTECAL isikisela ukuthi lesi akusona isinyathelo sokuphepha esidingekayo ?

Ukukhathazeka ngama-cataract kwavela kwidatha yangaphambi kokwelashwa. Ngenxa yalokho, i-PRACTECAL nezinye izingcwaningo ze-pretomanid zaqapha ababambiqhaza be-cataract. Ubufakazi obanqwabelana kuze kube manje abukahlonzi ulwazi olungalandelekile lwe-cataract futhi asikuncomi ukuba baqashwe ngokuqhubekayo.

5.4 Ingabe ikhona idatha ebonisa ukuthi i-Pretomanid ibanga izinkinga zokuzala?

Njengamanje kunocwaningo oluhlola umthelela we-Pretomanid esidodeni sowesilisa. Ukubhalisa kusaqhubeka (Meyi 2022) <https://clinicaltrials.gov/ct2/show/NCT04179500>

5.5 Yayivame kangakanani i-Peripheral Neuropathy emikhakheni ephenywayo?

	Ukulawula (n=150)		Umkhakha-1 we- Practecal (n=151)		Umkhakha-2 we-Practecal (n=126)		Umkhakha-3 we- Practecal (n=122)	
	izehlakalo	pts	izehlakalo	pts	izehlakalo	pts	izehlakalo	pts
I-Neuropathy peripheral	14	14	3	3	4	4	4	4

6. Ukubandakanyeka komphakathi

6.1 Chaza amazinga okubandakanyeka komphakathi phakathi nalo lonke ucwaningo kusukela ekuluklameni kuya ekwenziweni kwalo?

I-TB-Practecal yaklanywa kucatshangwa ngokuyinhloko ngeziguli futhi yaqala ngokulalela ngokucophelela iziguli emhlabeni wonke lapho i-MSF iye yasebenza khona, ngokwesibonelo: <https://blogs.msf.org/blogs/topics/tb-me>

Ekubandakanyekeni komphakathi wocwaningo kunokuhlukana okungale ndlela:

- Ukubandakanyeka kweziguli kwakuhlanganisa:
 - a. Ukubonisana nemiphakathi ngezinhloso zokuqala zephrojekthi
 - i. 'Izimiso zokuklama ukwelashwa kwe-MDR-TB kwesikhathi esizayo'
 - 1. Ukufakwa ekuthuthukisweni kwephrothokholi
 - 2. Ukuthuthukiswa kokuqala kwezinto zeziguli nama-ICF
 - b. Amaqembu aqondile Eziguli ze-TB esayithini yase-UZB
 - i. Inqubo yokuhlunga
 - ii. Inqubo yemvume esekelwe olwazini
 - iii. Ukuvakashela esibhedlela
 - iv. Ukusekela ngokwelulekwa
 - c. Ukubandakanyeka ngokungaqondile ngokufakwa yiBhodi Eleluleka Imiphakathi eNingizimu Afrika – iqembu elimelela iziguli
- Ukubandakanyeka kweziguli okuhlobene ne-Covid
 - Amathesti / impendulo ye-VOT
 - Ukulethwa kwemithi, ukuqoqwa kwamasampula ekhaya / izinkinga zobumfihlo

7. Izindaba zezibalo

7.1 I-TB PRACTECAL yaklanywa njengocwaningo olwaluhlola ukusebenza ngokufana kwemithi, kodwa kuye kwaba nokuphawula komphakathi ngokuphathelene nokusebenza kangcono kwemithi Yomkhakha 1 emkhakheni olawulwayo. Ingabe ukuhlola ukusebenza kangcono kwenziwa njengoba kwahlangatshezwana nokusebenza ngokufana?

Uhlelo lokuhlaziya kwezibalo luzotholakala nombhalo. Uma iqophelo lokugcina lafinyelela ukusebenza ngokufana kwemithi, kwenziwa ithesti ehlola ukusebenza kangcono.

Ingxoxo mayelana nokusebenza kangcono ihlobene kakhulu nokuyeka kusengaphambi kwesikhathi kuyilapho empeleni lokhu kufanele kwenziwe ngaphambi kokuba ucwaningo lokusebenza ngokufana komuthi luyekwe ngenxa yokungasebenzi kangcono kwawo.

7.2 Zaziyni izimfuneko zezibalo ezazinqunywe kusengaphambili ezazidingeka zokuyeka kusengaphambi kwesikhathi, futhi izihlaziyo zenziwa nini?

Sinye kuphela isihlaziyo saphakathi nendawo, ngokwephrothokholi, sokushintsha ukusuka kusiteji 1 kuya kusiteji 2. Isihlaziyo sesibili sahlalwa ngemva kokuba iziguli ezingu-90 sezifakwe kusiteji 2 kodwa asizange sifike kulelo qophelo. Umgomo we-DSMB wathi i-DSMB kufanele icabangele ukuncoma ukuyekwa kocwaningo uma kwafinyelelwa umehluko okungenani wokuchezuka okuthathu okuvamile esihlaziyweni saphakathi nendawo seqophelo lokugcina elikhulu, ngokufanayo nomthetho we-Haybittle-Peto. I-DSMB yacela isihlaziyo saphakathi nendawo ngoNovemba 2020 esibandakanya Umkhakha 1 nomkhakha Wokulawula kusukela ekuqaleni kocwaningo. Ngokuqonda kwethu, i-DSMB yazenza izihlaziyo ezezeziwe lapho sezazi ukuthi yagculiswa imithetho yokuyeka.

8. Ukufinyelela

8.1 I-Pretomanid iwumuthi omusha futhi manje onconywayo ezigulini eziningi. Ungachaza yini ukuthi imigoqo yokuwufinyelela ixazululwa kanjani?

I-TB Alliance manje inezinkontileka nabakhi abangu-4 ukuba basihlinzeke nge-pretomanid (i-Viatrix, i-Macleods, i-Lupin ne-Hongqi). Siye saqinisekiswa yi-Alliance ukuthi ukuhlinzeke nge-pretomanid ngeke kube yisici esivimbayo ekuhlangabezaneni nesidingo. Leli yiphuzu i-MSF ezoliquapha ngokuqhubekayo ezinyangeni ezizayo.

8.2 Ucabanga ukuthi i-Pretomanid izobiza malini?

Ikhathalogi yamava yomuthi we-STOP TB GDF:

https://www.stoptb.org/sites/default/files/gdfmedicinescatalog_1.pdf

newebhusayithi: <https://www.stoptb.org/global-drug-facility-gdf/gdf-product-catalog>

Meyi 2022: I-Pretomanid yayibiza u-\$52 USD ngephakethe lamaphilisi angu-26 = \$ 2 USD ngephilisi. Lokhu kulingana no-\$336 USD ngesiguli ngemithi yezinyanga ezingu-6 nge-pretomanid iyodwa.

9. Umongo wezokwelapha

9.1 Isaziso se-WHO esiphuthumayo sangomhla ka-3 Meyi 2022, siyaqhubeka nokuncoma ukuba yonke imithi ithathwe ngomlomo izinyanga ezingu-9. Kungaba usizo ukuyisebenzisa kuphi i-BPaLM?

- I-BPaLM yayisetshenziswa ezigulini kungakhathaliseki ukuthi ayizweli kwi-fluoroquinolone kwi-TB PRACTECAL futhi iwukhetho oluphephile, oluphumelelayo ezigulini ezingazweli kwi-rifampicin – i.e. ezahlonzwa kusetshenziswa i-GeneXpert

noma amathesti afanayo okuhlonza ngokusheshayo. Lokhu kusho ukuthi iziguli akudingeki zilinde ithesti yokungazweli kwi-fluoroquinolone noma zikhathazeke ngokuthi ukwelashwa kwazo kungase kungasebenzi uma amathesti e-FQ abuya ethi ayizweli.

- Ukuphumelela kwe-BPaLM akwaziwa lapho kuye kwatholakala khona ukungazweli kwi-fluoroquinolone ngoba lena bekumane kuyingxenye eyodwa kwezine yeziguli ezikwi-PRACTECAL. Kunconywa i-BPaL ngaleli qembu. Izindaba ezinhle ukuthi kwi-TB-PRACTECAL, i-BPaLM yayinamazinga afanayo emithelela emibi nemibi kakhulu njenge-BPaL ngakho kuba nobungozi esigulini ngasinye uma i-BPaLM iqalwa futhi kamuva, kubonakala ukungazweli kwi-FQ.
- Imithi yezinyanga ezingu-9 ayifanelekile ezigulini ezinesifo samaphaphu esibi kakhulu, kodwa-ke i-BPaLM yabonakala iphumelela kungakhathaliseki isimo se-smear noma se-cavity.
- Imithi yamanje ethathwa ngomlomo yezinyanga ezingu-9 inomthwalo omkhulu wamaphilisi lapho iqhathaniswa ne-BPaLM.

9.2 Ingabe kukhona ukukhathazeka okuvela kwi-TB PRACTECAL ngokuthi ukuba khona kwe-Moxifloxacin emithini kushayisana nemvume elindelwe ye-4HPMZ mayelana nokungazweli?

Okungenani okwesikhathi esifushane, silindele ukuthi le mithi izoba nezigaba ezimbalwa zabantu lapho kunethemba lokuthi kuzoba nesibalo esincane sabantu engeke izwele kwi-fluoroquinolone noma lokuthi izifunda zizokwazi ukwenza ama-DST e-fluoroquinolone DST asheshayo.

9.3 Ziyini izikhala zolwazi mayelana nale mithi?

Kudingeka idatha emaqenjini athile i.e: Ukukhulelwa, intsha nezingane, i-osteomyelitis, i-meningo-encephalitis. Ngokungazweli kwi-fluoroquinolone, kunconywa ukuba kusetshenziswe imithi ye-BPaL. Indima ye-BPaL ayiqinisekile futhi ayizange inconywa yi-WHO okwamanje kodwa izoqhubeka icwaningwa nge-MSF. Izingcwaningo zokuthola imithamo ezinganeni kulindeleke ukuba ziqale ekupheleni kuka-2022. Kuzodingeka ukuqashelwa eduze kweziguli ezinenkinga embi kakhulu yesibindi noma ukungasebenzi kahle kwenhliziyo.

9.4 Ungathi yimiphi imiyalezo oyitholile kulolu cwaningo, phakathi kokunye?

Lezi zingcwaningo zokwelapha ziye zabanisa ngokucacile ukuthi izici zemithi yokwelapha engcono kakhulu ye-RR, MDR ne-TB yangaphambi kwe-XDR namuhla yilena:

- I-Bedaquiline, i-Pretomanid nezine-Linezolid
- Yonke ethathwa ngomlomo
- Isikhathi esingadluli ezinyangeni ezingu-6
- Amaphilisi angadluli kwangu-5 ngosuku
- Umthamo owodwa nsuku zonke

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- Izinga lokuphumelela lifana nelokwelashwa kwe-DS-TB ezigulini ezingu-8-9 kuzo zonke ezingu-10

Izingcwaningo futhi ziye zanikeza isiphetho esilandelayo mayelana nokusetshenziswa kwemithi esekelwe kwi-B-Pa-Lzd:

- Ngokuvamile i-Pretomanid iphephile njengoba ingenazo izimpawu ezintsha

9.5 Yimuphi umehluko oyinhloko phakathi kwesaziso se-WHO esiphuthumayo nemithi ekwi-TB PRACTECAL?

- Isincomo esisheshayo se-WHO siqokomisa ukusetshenziswa komthamo we-Ze-NIX's ongu-600mg LZD amaviki angu-26. I-TB PRACTECAL yasebenzisa imithi yemithamo ye-Linezolid eyehliselwa ku-300mg ngosuku ngemva kwamaviki angu-16. Kungenzeka kwaziswe ngokwehliswa komthamo uma kuba nobuthi.

9.6 Yimiphi imithelela engemihle eyayiyinselele/ eyayivame kakhulu abezokwelapha abasebenzisa le mithi okufanele bakwazi ukuyilawula kahle?

- **I-Peripheral neuropathy** – I-PN ehlobene ne-Linezolid yayingesinye sezehlakalo ezimbi eziyinkelele kakhulu ukubhekana nazo ngenxa yokungapheli kwaso, ububi baso nokufinyelela izidambisa-zinhlungu ezanele kwezinye izikhungo.
- **Ama-enzyme esibindi anhlathayo** – Ngenxa yemiphakathi ehluhlukene ocwaningweni, abaphenyi kwadingeka bazi izimbangela eziwumehluko wezinkinga zama-enzyme esibindi. Imithi ethathwa ngesikhathi esifanayo, kuhlenganisa nemishanguzo yengculazi, nokusebenzisa kabi utshwala kwakuvamile kwabanye ababambiqhaza.
- **I-Myelosuppression** – Yayibonakala ngokuvamile ezigulini ezazithatha i-Linezolid. Nakuba iziguli eziningi zaziphelelwa yigazi ekuqaleni, okungenzeka kwakubangwa ukuhlonzwa kwe-TB, kubalulekile ukwazi ukuthi kunini lapho kumele ucabangele ubuthi be-Linezolid nalokho ozokwenza ngabo. Kwi-TB- Practecal sasebenzisa ukwehlisa i-Linezolid ukuze sisingathe lobo buthi.
- **I-QTcF eyeluliwe** – Ngenxa yokuthi ukwelashwa kunemithi eminingi engase yelule izikhawu ze-QTcF, kuyatuseka ukuba abezokwelapha bazi indlela yokuhlonza, ukuqapha nokubheka izimbangela ze-QTcF eyeluliwe. Lokhu kwakuvamile ocwaningweni kokubili kwi-SoC nasemikhakheni ephenywayo.