The potential for six-monthly mass administration of moxidectin to accelerate onchocerciasis elimination

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Introduction

African onchocerciasis control and elimination programmes rely predominantly on annual community-directed treatment with ivermectin (aCDTI). However, modelling results indicate that aCDTI may not be sufficient to reach the current goals of eliminating onchocerciasis in 80% of endemic African countries by 2025.

Phase II and III clinical trials have shown that moxidectin, a veterinary anthelmintic, is a more efficacious treatment, suppressing skin microfilarial loads for longer. This study assessed the potential impact of community-directed treatment with moxidectin given annually (aCDTM) or biannually (bCDTM) compared to increasing CDTI to biannual (bCDTI).

Methods

Using clinical trial data [1] and our individual-based, stochastic transmission model EPIONCHO-IBM, we capture skin microfilarial (mf) dynamics in response to treatment with ivermectin and moxidectin [2].

Skin mf dynamics for ivermectin (red) and moxidectin (blue) matching clinical trial:
- *Baseline endemicity*
- *Inclusion/exclusion criteria*
- *Pregnancy status*
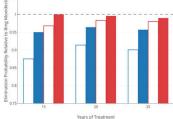
Results

Moxidectin Dose

Phase II trial data [1] showed that lower moxidectin doses (2mg, 4mg) have shorter microfilarial suppression than 8mg moxidectin.

In line with the reduced trial efficacy, **the probability of eliminating the parasite was greatest for 8mg moxidectin**, regardless of:
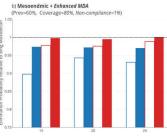- *Programme duration (15, 20, 25y)*
- *Endemicity (40-60% prevalence)*
- *Treatment coverage (65% or 80%)*

Elimination probability when using 2mg (blue) or 4mg (red) moxidectin administered annually (no fill) or biannually (filled).

Rates are relative to the equivalent scenarios using an 8mg dose (horizontal dashed line). (Values <1 indicate a lower ability to eliminate.)
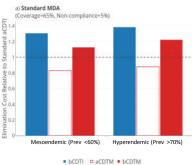

Health Economics

Biannual distribution of ivermectin in Ghana was shown to have an approximate 50–60% increase in cost compared to aCDTI [3]. Thus, despite faster times to elimination, bCDTI and bCDTM incur increased costs of elimination compared to aCDTI.

Annual moxidectin does not have the added costs of biannual distribution and is thus more cost-effective for achieving elimination (assuming donation of moxidectin).

The economic costs required to achieve elimination relative to aCDTI with ivermectin (blue) or moxidectin (red) given annually (no fill, aCDTM) or biannually (filled, bCDTM). (Values <1 indicate that the cost of elimination is less than aCDTI.)

Elimination is defined as having 95% of runs showing no infection (in humans and vectors) 50 years after treatment cessation.

Annual = 0.45 USD/person/year
Biannual = 0.71 USD/person/year

Times to Elimination

We modelled CDTI (150 μg/Kg) and CDTM (8mg), comparing the probability of achieving local onchocerciasis elimination (95% of simulations with no infection 50 years after treatment cessation).

Annual CDTM is as effective as biannual CDTI (bCDTI). However, bCDTM always eliminates onchocerciasis fastest, with the reductions in times to elimination dependent on baseline endemicity and therapeutic coverage. Therefore, elimination times follow:

(*slowest*) aCDTI > bCDTI ≈ aCDTM > bCDTM (*fastest*)

Years to Elimination (% Reduction Relative to aCDTI)				
MDA Scenario	aCDTI	bCDTI	aCDTM	bCDTM
Mesoendemic Focus (CMFL = 9.1 mf/ss, Prevalence < 60%)				
Standard [*1]	22	19 (14%)	19 (14%)	17 (23%)
Enhanced [*2]	18	14 (22%)	14 (22%)	11 (39%)
Hyperendemic Focus (CMFL = 31.3 mf/ss, Prevalence > 70%)				
Standard [*1]	30	26 (13%)	26 (13%)	23 (23%)
Enhanced [*2]	17	15 (12%)	15 (12%)	13 (24%)

1 – Standard MDA: 65% therapeutic coverage, 5% systematic non-compliance
2 – Enhanced MDA: 80% therapeutic coverage, 1% systematic non-compliance
CMFL = Community microfilarial load; ss = skin snip

Conclusions

- **Moxidectin would be superior to ivermectin for the treatment and elimination of onchocerciasis via MDA**, achieving faster times to elimination for a given treatment frequency and coverage.
- The increased cost incurred with biannual distribution indicates **that annual moxidectin would be more economically viable than the currently proposed alternative treatment strategy of switching from aCDTI to bCDTI** (assuming that moxidectin would be donated).
- To achieve the fastest possible elimination or **for areas of very high pre-treatment endemicity, bCDTM could be used** and remains more economical than bCDTI.

References

[1] Awadzi et al. PLoS Negl Trop Dis 2014, 7(6): e2953
[2] Turner et al. Parasites & Vectors 2014, 7:241
[3] Turner et al. PLoS Negl Trop Dis 2013 7(9): e2452