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AIDS 2020, **34**:159–163

HIV viral load algorithm: what are the needs in the field?

We have read with interest the study published by Shoufri *et al*. [1] and share the idea that the current application of the WHO viral load algorithm does not allow for effective management of patients with virological failure, whereas the emergence of HIV drug resistance, so-called the fourth HIV epidemic, is obvious [2].

We would like to provide some comments based on our experience in implementing viral load in the framework of the OPP-ERA project, which implements an open viral load platform technique in West and Central Africa (WCA).

First, we regret that data from WCA have not been included, as too often in research, when this region represents a quarter of people living with HIV in sub-Saharan Africa, which makes these conclusions less generalizable at the sub-Saharan African level. In WCA, primary non-nucleoside reverse transcriptase inhibitors resistance data are currently lower than in East and Southern Africa [3]. In the framework of the OPP-ERA project, adherence strengthening targeting more than 9000 patients with viral load at least 1000 copies/ml in Guinea and Burundi made it possible to obtain a viral load less than 1000 copies/ml in 50% of cases, avoiding unjustified use of second line (personal data).

Second, even if a simplified algorithm could be applied for efavirenz-based treatment, this strategy is unlikely to be adapted to the higher genetic barrier of the dolutegravir, used as first-line regimen, for which adherence strengthening is more likely to be effective, as shown with boosted protease inhibitors-based second-line strategies [4]. As suggested, drug regimen-specific failure algorithm may be an option; however, it seems complex to implement, as evidenced by the difficulties faced in using the current algorithm, despite its apparent simplicity.

Indeed, the use of the current viral load algorithm in case of failure is very low: in the OPP-ERA project, less than 15% of patients with viral load at least 1000 copies/ml benefited from a viral load control within 3–6 (or 9) months and second-line switch is anecdotal (personal data), as shown in previous study [5]. These problems should be explored before any new recommendations.

We have conducted qualitative surveys, which allows formulation of hypotheses.

From HIV programmes' point of view, the decrease in international funding pushes programmes to make difficult choices: should we favour the purchase of first-line drugs to treat all new patients in a test and treat perspective or rather second-line drugs, knowing that second-line drugs cost about two to five times more than first-line drugs?

A minimal use of the second-line seems thus to have been promoted by adapting the WHO algorithm: in case of viral load at least 1000 copies/ml, 'evaluate for adherence concern' has been changed into 'adherence strengthening'.

From the prescribers' point of view, ensuring that adherence has been sufficiently strengthened seems a major concern in the absence of an objective measure of adherence and this especially since patients in virological failure suffer from negative representation such as 'liars' or 'delinquent'. Viral load seems often considered as a measure of nonadherence, which should therefore be sufficiently strengthened before proposing second line. Moreover, even if the viral load algorithm is well known, its interpretation is difficult: the 1000 copies/ml threshold is poorly respected in practice. Even a modest decrease in viral load after adherence strengthening is considered as a success, which often leads to further adherence interventions to 'give a chance to the first line' to reach a viral load less than 1000 copies/ml, leading to repeated adherence interventions and viral load control with very low and delayed switch to second line, with deleterious effects to the patients and to the epidemic.

In addition, prescribers and patients are not prepared for failure, the announcement is most often dramatic and guilt-ridden, the mechanisms of failure are poorly analysed and patients are not prepared for second line, generating the subsequent risk of failure, even more dramatic because of the very low availability of the third line [6]. To overcome this issue, we have set up the 'let's talk about failure' working group, which is currently working on a practical guideline.

It is therefore necessary to keep in mind the need to accompany the current algorithm and any potential modifications with a practical translation corresponding to the realities in the field. Above all, future algorithms should be designed as to be integrated into the reality of the countries' health system and its various components,

DOI:10.1097/QAD.0000000000002382

particularly in terms of finance, procurement, health information system, lab and clinical human resources capacity building, so that efforts to increase access to viral load can lead to improving patient care and not just informing the third 90%.

Acknowledgements

Conflicts of interest

Response to Shoufri A, *et al.* AIDS 2019;33:1635–44.

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Received: 5 August 2019; accepted: 30 August 2019.

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DOI:10.1097/QAD.0000000000002382

HIV viral load algorithm: what are the needs in the field?: authors' response

Thank you for the opportunity to respond to the letter of Breton *et al.* [1]. We welcome the authors' engagement on the challenge of underuse of second-line antiretroviral treatment, expressing, as they do, the notion that the application of the algorithm can hinder effective patient management.

We do not, however, disassociate the viral load algorithm itself from the results of its application in the real world, recalling the axiom that 'systems are perfectly designed to achieve the results they get', this system being an interplay between the prescribed approach and real world factors, giving rise to widespread second-line underuse and significant global morbidity and mortality.

In a similar way to Breton *et al.* [1], we have observed in practice the situation whereby a modest decline in viral load – after an adherence intervention – results in procrastination and delayed switch, often with disastrous patient consequences. The current approach may potentiate conservatism and inertia.

Considering the generalizability of our results, pretreatment resistance to NNRTIs in South Africa is estimated to be around 10% [2] with similar findings published for Guinea Bissau [3] and a range of West African countries [4]. Indeed, given that in these settings, advanced disease is seen more frequently than in many Southern African countries [5], there is likely a greater need to ensure prompt switch to second-line. In MSF-supported sites in Kinshasa, Democratic Republic of Congo, a simplified switch algorithm is already in practice for patients admitted with advanced HIV [6]; a response to the appallingly high mortality and HIV drug resistance levels observed in patients entering hospital with advanced HIV having failed therapy [7].

Breton *et al.* [1] provide personal data showing that 50% of patients with viral load at least 1000 copies/ml