

## Phasing out the Use of Stavudine in Singapore: How Are We Doing in Compliance to World Health Organisation (WHO) Recommendations?

### Dear Editor,

In the 2010 revision of the Guidelines on Antiretroviral Therapy (ART) for human immunodeficiency virus (HIV) infection in adults and adolescents, the World Health Organization (WHO) gave recommendations of the need for countries to phase out stavudine-based regimens because of the drug's long-term irreversible side effects. The important toxicities associated with stavudine (d4T) included those associated with mitochondrial toxicity such as lactic acidosis, hepatic steatosis, peripheral neuropathy and lipodystrophy. WHO suggested using zidovudine (AZT) or tenofovir (TDF)-based first-line regimens instead of stavudine.<sup>1</sup>

We assessed our compliance with these WHO guidelines in our local setting. The Communicable Disease Centre (CDC) at Tan Tock Seng Hospital conducted a regular internal audit programme with standardised performance indicators to assess the standard of clinical care of HIV patients. The audit was a retrospective chart review of all cases seen at our HIV clinic during a one week period at the CDC. We aggregated data into 2 periods: the early period; before 2010 (2007 to 2009) and the late period; after 2010 (2010 to 2011) over 8 audits. Each period consisted of 4 audits. We used the chi-squared test to evaluate differences in categorical variables and Wilcoxon Rank-Sum test to compare median ages between the 2 groups.

A total of 691 patient records were included in the early period, and 736 records were from the late period. Patients from the early period were younger (median age, 44 years; interquartile range [IQR], 38 to 53 years) than those from the late period (median age, 46 years; IQR, 38 to 54 years), however it was statistically not significant ( $P = 0.064$ ). The proportions of HIV-positive patients among different age groups were statistically significant between the 2 periods: age group of 10 to 29 years were 8.5% and 5.6%, respectively, 30 to 49 years were 57.5% and 55.2% respectively, and those who aged 50 years or older were 34% and 39.2%, respectively ( $P = 0.024$ ). Distribution by gender was not significantly different over time (male, 83.9% vs 85.7%) ( $P = 0.344$ ).

Among those patients with first-line ART regimens, d4T usage was 33.7% in the early period and 18.7% in the late period respectively whereas TDF usage increased from 14.4% in the early period to 36.6% during the late period ( $P < 0.001$ ) (Fig. 1). The proportions of patients who had a viral load test done in the last 6 months were 22.4% and 45.4% respectively ( $P < 0.001$ ). This was due to better access to viral load monitoring with the availability of our in-house HIV viral load test which was considerably less costly than commercial HIV viral load assays used previously. Although 45% of the patients in the late period had viral load testing within the last 6 months, it was still unsatisfactory based

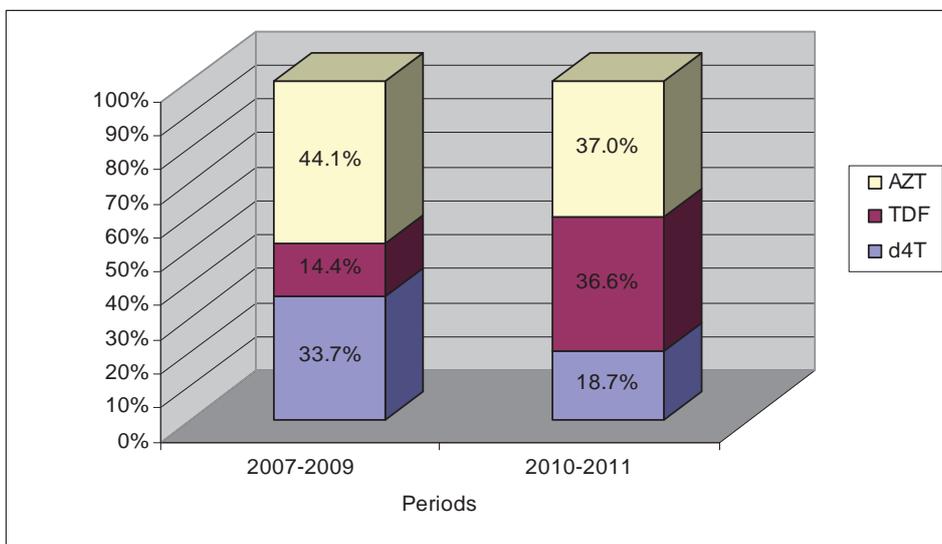


Fig. 1. ART usage over the periods. ART: antiretroviral therapy; AZT: zidovudine; TDF: tenofovir; d4T: stavudine. From 2007 to 2009: total patients (N = 549), stavudine (N = 185), tenofovir (N = 79), zidovudine (N = 242). From 2010 to 2011: total patients (N = 648), stavudine (N = 121), tenofovir (N = 237), zidovudine (N = 240).

on the DHHS (Department of Health and Human Services) guidelines on HIV monitoring as viral load was the most important indicator of response to ART.<sup>2</sup>

The limitations of our audit methodology include duplication of patients in the 4 audit periods as well as its representativeness of the total HIV patients seen at CDC. While not comprehensive, the audit data provided a snapshot of our compliance with WHO treatment guidelines. We have demonstrated that overall the number of patients receiving d4T-based ART has significantly decreased in view of the availability of TDF. However, we noted that there were still at least 18.7% of patients who continued to be on d4T. The most likely reason could be the generic version of d4T based regimen was relatively inexpensive compared to TDF. The other reason for using d4T over AZT was the presence of anaemia in patients with advanced HIV infection which precluded the use of AZT.

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1. World Health Organization. Antiretroviral therapy for HIV infection in adults and adolescents, 2010.
2. AIDSinfo Clinical Guidelines Portal. Available at: <http://www.aidsinfo.nih.gov/guidelines>. Accessed 10 October 2012.