

## Letter to the Editor

### Is the Treatment Response Different in Treatment Naive HIV Infected Patients with Very High Viral Load (>1 Million Copies)? Three Year Data

Özlem Kandemir, Elif Şahin Horosan, Serhat Şahinoğlu  
Department of Infectious Diseases and Clinical Microbiology Mersin University School of Medicine, Mersin, Turkey

**Address of Correspondence:** Özlem Kandemir, Department of Infectious Diseases and Clinical Microbiology Mersin University School of Medicine, Mersin, Turkey  
+90 532 738 44 38  
[kandemir68@gmail.com](mailto:kandemir68@gmail.com)

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#### To the Editor,

The main objectives of antiretroviral therapy (ART) are to suppress virus replication, to preserve and improve immunological functions, to reduce HIV-related morbidity and mortality. In phase 3 ART related studies, results of patients with baseline viral load >100,000 c/mL were reported (1,2,3), whereas data with  $\geq 1$  million c/mL in real life study are limited. Here, we represented virological and immunological responses in patients with HIV-1 infection who had virological load more than a million copies and receiving ART with an integrase inhibitor (INI) combination.

We evaluated a single center, retrospective study of HIV infected adult patients who had virological load of more than a million copies followed in our Clinic of Infectious Diseases, between 2015 and 2018. HIV-RNA value <50c/mL at week 24 was defined as virological success. The increase in the number of CD + T lymphocyte count 50-100 cells / mm<sup>3</sup> in the first year is considered as an immunological success. 16 patients were enrolled. The mean age of patients was 40 (range of 18- 73) years, 93.8% of the patients were male. Eleven patients were on a single tablet regimen; 5 patients were on elvitegravir, cobicistat, emtricitabine, tenofovir alafenamide (EVG/c/ FTC/TAF), 3 patients were on EVG/c/TFC/ tenofovir disoproxil fumarate (EVG/c/ FTC/ TDF) and 3 patients were on dolutegravir, abacavir, lamivudine (DTG/ABC/3TC) and 5 patients were using multi-tablet therapy. Mean viral load of the patients was found to be 4.467.618 (1.025032- 10.000.000) c/mL. The virological response of the patients to the treatment at 4<sup>th</sup>, 24<sup>th</sup> and 48<sup>th</sup> weeks are shown in **Figure 1**.

Immunological response was detected in 87.5% (14 patients) at 24<sup>th</sup> and 94% (15 patients) at 48<sup>th</sup> week.

None of the seven responders at 24<sup>th</sup> week used additional medication. Three of the nine patients who did not respond at 24<sup>th</sup> week, were receiving other medical treatments for their co-morbidities. Of the 7 responders at 24<sup>th</sup> week, only 1 received a multi-tablet regimen, whereas 4 out of 9 unresponsive patients at 24<sup>th</sup> week were receiving multi-tablet therapy. Age, the number of co-morbidities and the use of multi-tablet regimens were higher in those who didn't receive virological response at 24<sup>th</sup> week.

In a study of Santoro et al., 1430 treatment naïve cases were divided into 3 groups according to viremia levels ( $\leq 30,000$ , 30.001-500.000 and > 500,000 c / mL) and evaluated for virologic response to treatment (4). The lowest virological success rate at 48 weeks was observed in the group with viral load > 500.000 c / mL. They stated that the revision of the frequently used 100.000 threshold value can be considered.

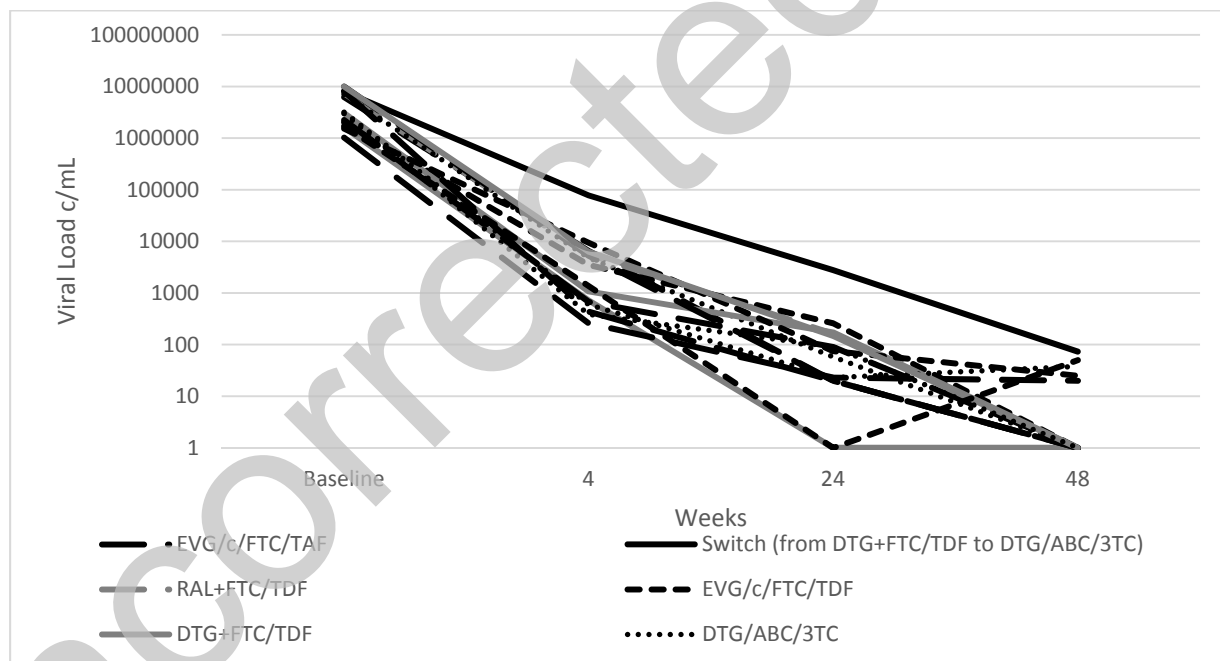
Sax et al. wrote a letter on 41 treatment naïve cases with pre-treatment virological load  $\geq 1.000.000$  c / mL in phase 3 clinical trials. (5). They found that the rate of virological success (HIVRNA <50 c/ mL) was 33% at 12<sup>th</sup> week, 67% at 24<sup>th</sup> week and 97% at 48<sup>th</sup> week. Similar to this study, our cases had lower virological response rates at 24<sup>th</sup> weeks compared to 48<sup>th</sup> weeks.

Although the low number of patients in our study is the most important limitation, INI combination regimens were found to be very successful in patients with viral load > 1,000,000 c / mL. However, reasons such as the presence of some co-medication or taking the drug in the form of a single tablet or multiple tablets may cause some disruptions in compliance and delays in virological response. In this context, we believe that the 24 week period for virological failure in the guidelines can be kept more flexible for these cases.

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**FIG. 1.** Virological response at 4<sup>th</sup>, 24<sup>th</sup> and 48<sup>th</sup> week.