Commentary
A push for 90-90-90: Initial treatment with INSTI-based regimens against HIV-1 infection

Stefano Rusconi*, Andrea Giacomelli

Department of Biomedical and Clinical Science DIBIC “Luigi Sacco”, University of Milan, Milan, Italy

ARTICLE INFO

Article history:
Received 9 July 2019
Accepted 16 July 2019
Available online 20 July 2019

In recent years, the global scenario of HIV infection has dramatically changed with the widespread implementation of antiretroviral treatment (ART) and the aim to reach the goals of the UNAIDS initiative “90-90-90: Treatment for all” ([www.unaids.org/en/resources/909090]) by 2030. Furthermore, ground-breaking scientific evidence has revolutionized the life of people living with HIV/AIDS (PLWH). Undetectable equals untransmittable (U = U) is one of the most important messages that there are no changes in the behaviours of a newly infected PLWH. However, it could not be excluded that changes in the sexual behaviours after the diagnosis – due to extensive counselling and a novel risk perception – could impact on the risk of HIV transmission [7].

The authors focus their attention on a high-risk gbMSM population who show the highest number of previous condomless sexual intercourse. In this population, the use of INSTIs is advisable not only to reduce the risk of HIV transmission when compared to non INSTI-based regimens in their cohort. In particular, a HIV transmission risk reduction of 25%, according to the model by Fraser C et al, has been estimated for gay, bisexual and other men who have sex with men (gbMSM) starting an INSTI-based regimen with a viral load ≥5log10 copies/mL irrespectively of HIV stage [5]. Authors concluded that INSTI-based regimens have the potential to avert onward HIV transmission by achieving a fast virologic suppression, in particular among gbMSM with pretreatment high viral load.

Although these data are sound, some potential pitfalls should be acknowledged to correctly interpret the findings reported by Zhu J et al. Firstly, the time span covered by the study is between 2011 and 2016 and only 376/1459 (25.8%) of the patients in the cohort started the treatment with and INSTI-based regimen. These findings are partially overcome by the widespread use of INSTIs in recent years due to the high efficacy, improved safety profile and, more recently, dolutegravir-based antiretroviral drug regimens implementation strategies in resource limited setting. Secondly, 46% of the patients started antiretroviral treatment with <350 CD4 cells/mm², reflecting the prescription recommendations followed until 2015, when the INSIGHT START trial demonstrated the incontrovertible beneficial effects of starting ART irrespectively of the CD4 cells count [6]. In other words, the findings of the authors should be considered as confirmatory and add a strong scientific evidence to a change in the prescribing behaviour occurring in everyday clinical practice. Moreover, the study relies on the assumption that there are no changes in the behaviours of a newly infected PLWH.

*Corresponding author at: Infectious Diseases Unit, DIBIC “Luigi Sacco”, University of Milan, Via G.B. Grassi, 74, 20157 Milan, Italy.
E-mail address: stefano.rusconi@unimi.it (S. Rusconi).
universal ART coverage with highly effective, well tolerated new drugs, such as INSTIs in resource limited setting, would be able to close the gap within 2030, making 90-90-90 not just a dream but a matter of fact.

Declaration of Competing Interest

SR received research grants to his Institution from ViiV Healthcare, Gilead Sciences and Janssen, outside the submitted work; he was also a paid consultant for ViiV Healthcare, Gilead Sciences, Merck Sharp and Dohme, Bristol-Myers Squibb, Janssen and Mylan. AG was a paid consultant for Mylan.

Acknowledgements

This manuscript is dedicated to the memory of Professor Andrea De Luca: a great friend, physician, mentor, and scientist.

References

[1] Eisinger RW, Dieffenbach CW, Fauci AS. HIV viral load and transmissibility of HIV infection: undetectable equals Untransmittable. JAMA 2019;321(5):451–2.
[2] Rodger AJ, Cambiano V, Bruun T, et al, PARTNER Study Group. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive PARTNER taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet 2019;393(10189):2428–38.
[3] Zhu J, Roxada I, David J, et al. The potential impact of initiating antiretroviral therapy with integrase inhibitors on HIV transmission risk in British Columbia, Canada. EClinicalMedicine 2019;13:101–11.
[4] Wilson DP, Law MG, Grulich AE, Cooper DA, Kaldor JM. Relation between HIV viral load and infectiousness: a model-based analysis. Lancet 2008;372(9635):314–20.
[5] Fraser C, Hollingsworth TD, Chapman R, de Wolf F, Hanage WP. Variation in HIV-1 set-point viral load: epidemiological analysis and an evolutionary hypothesis. Proc Natl Acad Sci U S A 2007;104(44):17441–6.
[6] INSIGHT START Study Group. Lundgren JD, Babiker AG, Gordin F, et al. Initiation of antiretroviral therapy in early asymptomatic HIV infection. N Engl J Med 2015;373(9):795–807.
[7] Steward WT, Remien RH, Higgins JA, et al. Behavior change following diagnosis with acute/early HIV infection a move to serosorting with other HIV-infected individuals. The NIMH multisite acute HIV infection study: III. AIDS Behav 2009;13(6):1054–60.
[8] Bracchi M, Stuart D, Castles R, Khoo S, Back D, Boffito M. Increasing use of ‘party drugs’ in people living with HIV on antiretrovirals: a concern for patient safety. AIDS 2015;29(13):1585–92.
[9] Demarest J, Underwood M, St Clair M, Dorey D, Brown D, Zolopa A. Dolutegravir-based regimens are active in integrase strand transfer inhibitor-naive patients with nucleoside reverse transcriptase inhibitor resistance. AIDS Res Hum Retroviruses 2018;34(4):343–6.
[10] Pilcher CD, Osprina-Norvell C, Dasgupta A, et al. The effect of same-day observed initiation of antiretroviral therapy on HIV viral load and treatment outcomes in a US public health setting. J Acquir Immune Defic Syndr 2017;74(1):44–51.