Case Report

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Maintenance of Viral Suppression after Optimization Therapy from Etravirine Plus Raltegravir to Rilpivirine Plus Dolutegravir in HIV-1-Infected Patients

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Abstract

Non-nucleoside reverse-transcriptase inhibitor plus integrase strand transfer inhibitor–based dual therapies are an attractive simplification, nucleoside reverse transcriptase inhibitor-sparing strategy for experienced human immunodeficiency virus-infected patients. Thus, we performed a 24-week real-life observational study to assess efficacy and safety of switching from raltegravir plus etravirine to dolutegravir plus rilpivirine in 7 previously heavily treated patients. This simplification strategy reduced pill burden and preserved viral suppression in treatment-experienced patients with no major mutations to rilpivirine at historical genotyping.

Keywords

dolutegravir, rilpivirine, dual-therapy, optimization

What Do We Already Know about This Topic?

Nucleoside reverse transcriptase inhibitor (NRTI) sparing regimens are effective in patients with VL <50 copies/mL to avoid NRTI-related side effects.

How Does Your Research Contribute to the Field?

Switching from etravirine/raltegravir to rilpivirine (RPV)/dolutegravir (DTG) is an attractive strategy both to reduce pill burden and to preserve viral suppression in patients with no major mutations to RPV at historical genotypic resistance test.

What Are Your Research's Implications toward Theory, Practice, or Policy?

In the near future, all patients eligible to RPV/DTG dual therapy will be able to receive a STR regimen.

Manuscript

The introduction of a new single-tablet regimen based on dolutegravir (DTG)/rilpivirine (RPV) has expanded the range of nucleoside reverse transcriptase inhibitor (NRTI) sparing options for the management of human immunodeficiency virus (HIV)-experienced patients.[1,2] For some patients, NRTI sparing therapy has different advantages: avoiding NRTI-related toxic effects and/or poor virological responses due to the progressive accumulation of resistance mutations.[3]

Currently, DTG/RPV is indicated as an attractive simplification option in patients with HIV-1 RNA <50 copies/mL and on a stable antiretroviral regimen for at least 6 months, with no history of treatment failure and without substitutions associated with resistance to DTG or RPV.[4]

In the past, etravirine (ETR) plus raltegravir (RAL) were an alternative NRTI sparing option, even if burdened by a daily 4 pills regimen.[5,6]

Rilpivirine has an improved safety and a better lipid tolerability, but with a lower genetic barrier compared to ETR.[7-9] On the contrary, DTG has a higher genetic barrier but a lower neuropsychiatric tolerability compared to RAL.[10,11]

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Table 1. Pattern of Patients' Mutations at Historical Genotyping.

Patient	K101E/P	E138K/A/G/Q/R/S	L100I	M230I/L	Y188L	Other Mutations	RPV Resistance
Patient 1	No	No	No	No	No	K103N, 108I, 184V	No
Patient 2	NA	NA	NA	NA	NA	NA	NA
Patient 3	No	No	No	No	No	41L 69D 103Nw 118I 184Iw 208Y 210W 215D 215Y 219R 228R 238Tw	No
Patient 4	No	No	No	No	No	K103N	No
Patient 5	No	No	No	No	No	M41L, K65R, M184V	No
Patient 6	No	No	No	No	No	K103N	No
Patient 7	No	No	No	No	No	A98G, P225H, K103N, D67N, T69N, K70R, M184V, K219Q	No

Abbreviations: NA, not available; RPV, rilpivirine.

Intraclass de-escalation from ETR to RPV may successfully reduce pill burden and preserve future options.[9,11,12]

In this retrospective analysis, we present a case series of 7 patients switching from ETR/RAL to RPV/DTG. We evaluated tolerability, virological, and immunological profile and discuss the reasons that brought to non-nucleoside reverse transcriptase inhibitor (NNRTI)—Integrase Strand Transfer Inhibitor (INSTI)–based regimens. All patients were in treatment with ETR/RAL and switched to RPV/DTG; all of them were HIV-RNA <50 copies/mL since at least 6 months, no history of RPV or RAL failure.

The HIV-RNA, CD4 count, adherence, and any side effects were evaluated at baseline, 4 and 24 weeks after the switch. All data have been retrieved from electronic medical records and no supplementary patients' data were asked. All patients signed informed consent at admission to our Institution for the use of clinical data in case of retrospective observational study, and all data were stored in the "The Ligurian HIV Clinical network," which has been approved by the Regione Liguria ethical committee.[13,14]

Five of 7 patients were males. The mean (standard deviation) patient age was 52.2 (13.6) years. Median year since the diagnosis of HIV-infection was 23.4 years (range: 18-31 years). Genotypic resistance test (GRT) of protease and transcriptase was available in 6 of 7 patients, NNRTI mutations are shown in Table 1.[15]

Patients 1, 4, 5, and 6

These 4 patients were 50, 52, 57, and 75 years old, respectively, who had a long history of HIV-1 infection and multiple treatments with several regimens. Due to long-term treatment, few major mutations and many thymidine analogues mutations were accumulated over the years (Table 1), forcing to spare NRTI and leading to the use of a NNRTI/INSTI-based regimen. Optimization to RPV/DTG was aimed to reduce pill burden.

Patient 2

A 55-year-old male, with 20 years history of HIV-1 treatment, did not experience any virological failures; therefore, no GRT was performed. High cardiovascular risk and renal failure narrowed the treatment options leading to the use of a NNRTI/INSTI regimen in order to minimize side effects. Optimization to RPV/DTG was aimed at reducing pill burden, maintaining the advantage of a kidney-friendly regimen, thus not needing renal adjustment in case of glomerular filtration rate decline below 50 mL/min.

Patient 3

A 48-year-old male, with 16 years of infection, acquired HIV-1 virus with associated resistance mutations to NRTI, efavirenz, and nevirapine with complete susceptibility to ETR. Due to its high genetic barrier, ETR was chosen to overcome NNRTI resistance and then replaced with RPV. Optimization to RPV/DTG was aimed to reduce pill burden.

Patient 7

A 29-year-old female with mother-to-child transmission of HIV-1 has a peculiar pattern of resistance, with A98G substitution, that has a debated role in conferring a low-level resistance to RPV, thus not relevant according to IAS-USA Drug Resistance Mutations Group.[16] Treatment with ETV was started in order to avoid ritonavir-related toxicity and then successfully simplified to RPV/DTG.

Discussion

At the time of switch, the median CD4 count was 662 cells/mm^3 (range: 173-989 cells/mm^3). At week 4 and 24, HIV-RNA was <50 copies/mL in all patients. After 4 weeks, the median CD4+ T-cell count was 665 cells/mm^3 (range: 173-1057 cells/mm^3). At week 24, there were no significant variations in CD4 count (median: 602 cells/mm^3, range: 230-917 cells/mm^3).

The pill burden has been decreased and all patients in the study regularly withdrew the antiretroviral therapy from our outpatients' service. No side effects were reported and there were no cases of hospitalization or discontinuation in the first 24 weeks. Patient 7 confirmed virological suppression at week 96.

In conclusion, switching from ETR/RAL to RPV/DTG is an attractive strategy, both to reduce pill burden and preserve viral suppression in treatment-experienced patients with no major mutations to RPV at historical GRT. In the near future, all patients included will be able to receive the new DTG/RPV-based Single Tablet Regimen (STR).

Declaration of Conflicting Interests

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