19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE CENTRO CONGRESSI EUROPA
RESEARCH and CARE: FROM BENCH, TO BEDSIDE, TO COMMUNITY
16° CONGRESSO NAZIONALE ICAR Italian Conference on AIDS and Antiviral Research
P 30
POSTER 4 YOU ICAR 2024

Switch from ibalizumab to lenacapavir in a salvage therapy for a patient with multidrug-resistant HIV infection

S. Martini1, N. Cuomo2, A. Russo1, R. Palladino1, A. Raddi2, M. Pisaturo1, N. Coppola1

1UOC Malattie infettive Università degli studi della Campania Luigi Vanvitelli

2AORN dei COLLI, Unità di Malattie Infettive ospedale Cotugno, Napoli

Introduction

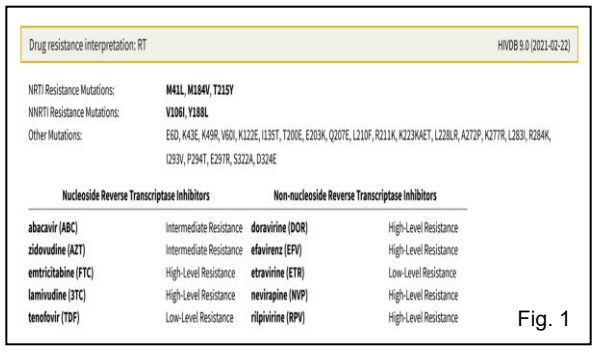
- Advances in antiretroviral therapy have improved efficacy, but some patients show multidrug resistances(MDR)[1].The guidelines in this case suggest using new generation drugs together to those with residual efficacy. Ibalizumab is a new monoclonal antibody that blocks the CD4 cell receptor. Lenacapavir is a new viral capsid inhibitor, which represents a new therapeutic target.

Study Design

- Our clinical case concerns a patient with MDR HIV infection. A salvage therapy was therefore set up combining drugs not completely effective (etravirine + tenofovir/emtricitabine + dolutegravir) with Ibalizumab.

Methods

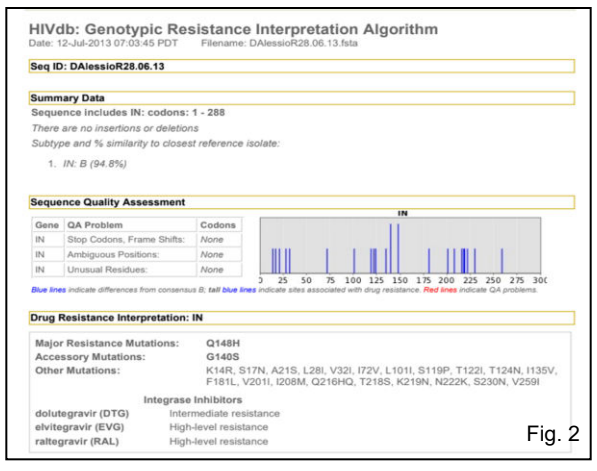
- At the time of introduction of this regimen, HIV-RNA resulted 37,800 copies/ml and CD4+ were 147 cells/μL (14%). Ibalizumab is administered intravenously and was started in April 2022, first as monotherapy with a loading dose of 2000 mg, then after 7 days an 800 mg dose associated with residual effective drugs. Subsequently, this dose was repeated every 15 days.


Drug resistance interpretation: RT — HIVDB 9.0 (2021-02-22)

NRTI Resistance Mutations: **M41L, M184V, T215Y**
NNRTI Resistance Mutations: **V106I, Y188L**
Other Mutations: E6D, K43E, K49R, V60I, K122E, I135T, T200E, E203K, Q207E, L210F, R211K, K223KAET, L228LR, A272P, K277R, L283I, R284K, I293V, P294T, E297R, S322A, D324E

Nucleoside Reverse Transcriptase Inhibitors		Non-nucleoside Reverse Transcriptase Inhibitors	
abacavir (ABC)	Intermediate Resistance	doravirine (DOR)	High-Level Resistance
zidovudine (AZT)	Intermediate Resistance	efavirenz (EFV)	High-Level Resistance
emtricitabine (FTC)	High-Level Resistance	etravirine (ETR)	Low-Level Resistance
lamivudine (3TC)	High-Level Resistance	nevirapine (NVP)	High-Level Resistance
tenofovir (TDF)	Low-Level Resistance	rilpivirine (RPV)	High-Level Resistance

Fig. 1


HIVdb: Genotypic Resistance Interpretation Algorithm
Date: 12-Jul-2013 07:03:45 PDT Filename: DAlessioR28.06.13.fsta

Seq ID: DAlessioR28.06.13

Summary Data
Sequence includes IN: codons: 1 - 288
There are no insertions or deletions
Subtype and % similarity to closest reference isolate:
1. IN: B (94.8%)

Sequence Quality Assessment

Gene	QA Problem	Codons
IN	Stop Codons, Frame Shifts:	None
IN	Ambiguous Positions:	None
IN	Unusual Residues:	None

Drug Resistance Interpretation: IN

Major Resistance Mutations: Q148H
Accessory Mutations: G140S
Other Mutations: K14R, S17N, A21S, L28I, V32I, I72V, L101I, S119P, T122I, T124N, I135V, F181L, V201I, I208M, Q216HQ, T218S, K219N, N222K, S230N, V259I

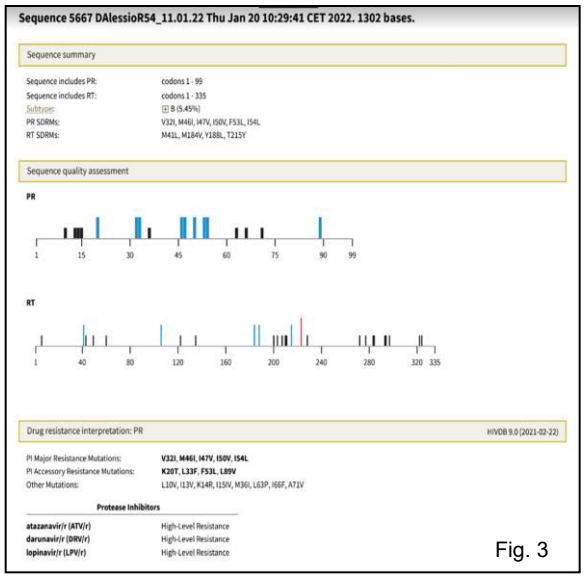
Integrase Inhibitors

dolutegravir (DTG)	Intermediate resistance
elvitegravir (EVG)	High-level resistance
raltegravir (RAL)	High-level resistance

Fig. 2

Results

- This salvage therapy showed viro-immunological efficacy. After 7 days, ibalizumab alone had already reduced the HIV viral load by 2 logs. Then, after association with other drugs that are still partially effective, viral suppression was achieved in only one month. The CD4 count improved from 147(14%)to 230 cells/μL(19.3%).There were no adverse events except hypertension after ibalizumab infusions. During the follow-up we also noticed a progressive reduction in the detectability of viral mutations in the reservoir. HIV-DNA genotyping test in fact no longer showed viral mutations that were evident before this salvage regimen. After 6 months of treatment, the patient voluntarily discontinued ibalizumab, without losing viro-immunological efficacy, however we modified the therapeutic regimen switching from ibalizumab to lenacapavir. This drug had a more favorable long-acting dosage, being administered subcutaneously every 6 months. The new drug showed good efficacy and tolerability. After 6 months of treatment, viro-immunological efficacy was maintained with CD4+ 259(20,2%),HIV-RNA undetectable and stable pressure on HIV-DNA in terms of reduced detectability of initial viral mutations pre-salvage therapy.


Sequence 5667 DAlessioR54_11.01.22 Thu Jan 20 10:29:41 CET 2022. 1302 bases.

Sequence summary
Sequence includes PR: codons 1 - 99
Sequence includes RT: codons 1 - 335
Subtype: B (5.45%)
PR SDRMs: V32I, M46I, I47V, I50V, F53L, I54L
RT SDRMs: M41L, M184V, Y188L, T215Y

Sequence quality assessment
PR
RT

Drug resistance interpretation: PR — HIVDB 9.0 (2021-02-22)

PI Major Resistance Mutations: **V32I, M46I, I47V, I50V, I54L**
PI Accessory Resistance Mutations: **K20T, L33F, F53L, L89V**
Other Mutations: L10V, I13V, K14R, I15V, M36I, L63P, I66F, A71V

Protease Inhibitors

atazanavir/r (ATV/r)	High-Level Resistance
darunavir/r (DRV/r)	High-Level Resistance
lopinavir/r (LPV/r)	High-Level Resistance

Fig. 3

Fig. 1, 2 and 3

HIV Drug Resistance Mutations

Results of 2

Fig. 4

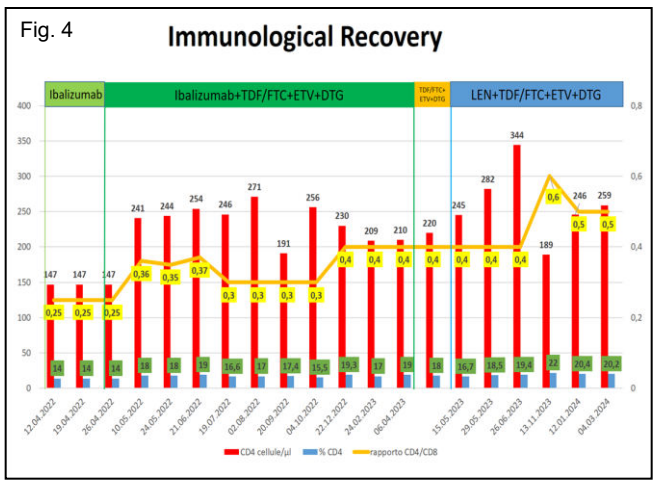


Fig. 5

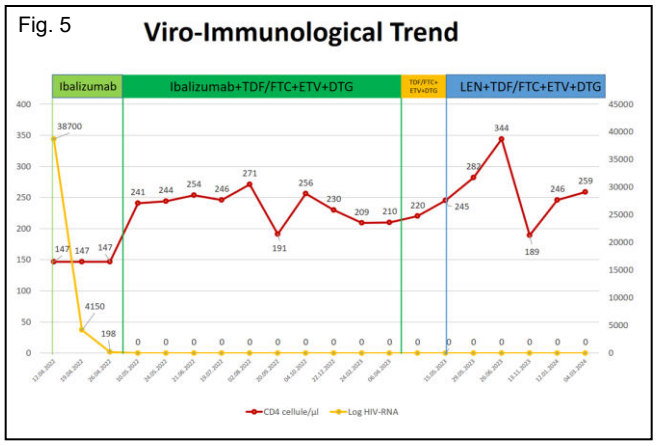


Fig. 4 and 5

Viro-immunological efficacy

Conclusion

- Our case report shows that ibalizumab was effective in a salvage regimen, obtaining virological suppression and an immunological recovery, never previously reached by the patient. The efficacy was also highlighted in the reservoir with a progressive reduction of HIV-DNA demonstrated by the impossibility of detecting initial previous mutations. The overall safety profile was good, despite hypertension following ibalizumab infusions. The subsequent switch to lenacapavir maintained the viro-immunological efficacy and stable pressure on HIV-DNA, showing good tolerability and better posology, being administered by subcutaneous injection, once every 6 months. This case report shows efficacy of lenacapavir in switch strategy in a salvage regimen, in a context in which there are no data in the literature.

Reference

1. Hannah A Blair. Ibalizumab: A Review in Multidrug-Resistant HIV-1 Infection. Drugs 2020 Feb;80(2):189-196. doi:10.1007/s40265-020-01258-3.