CLINICAL APPLICATIONS OF RESCUE STRATEGIES IN EXTENSIVELY DRUG-RESISTANT HIV-1, A CASE REPORT

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Introduction

- There are limited therapeutic options for patients with multi-drug resistant HIV

Objectives: To describe the clinical management and potential rescue strategies for a patient with extensively drug-resistant HIV-1 infection. Virological failures were documented by serial genotyping analyses showing the evolution of mutations and resistances.

Materials & Methods

- The patient described in this report voluntarily agreed to participate through written informed consent.
- Genotyping analyses: Sanger sequencing followed by resistance prediction using Stanford HIV Drug Resistance Database.
- Phenotypic drug susceptibility: PhenoSense® (Monogram Biosciences Inc.).
- Tropism analyses: Trofile® (Monogram Biosciences Inc.).

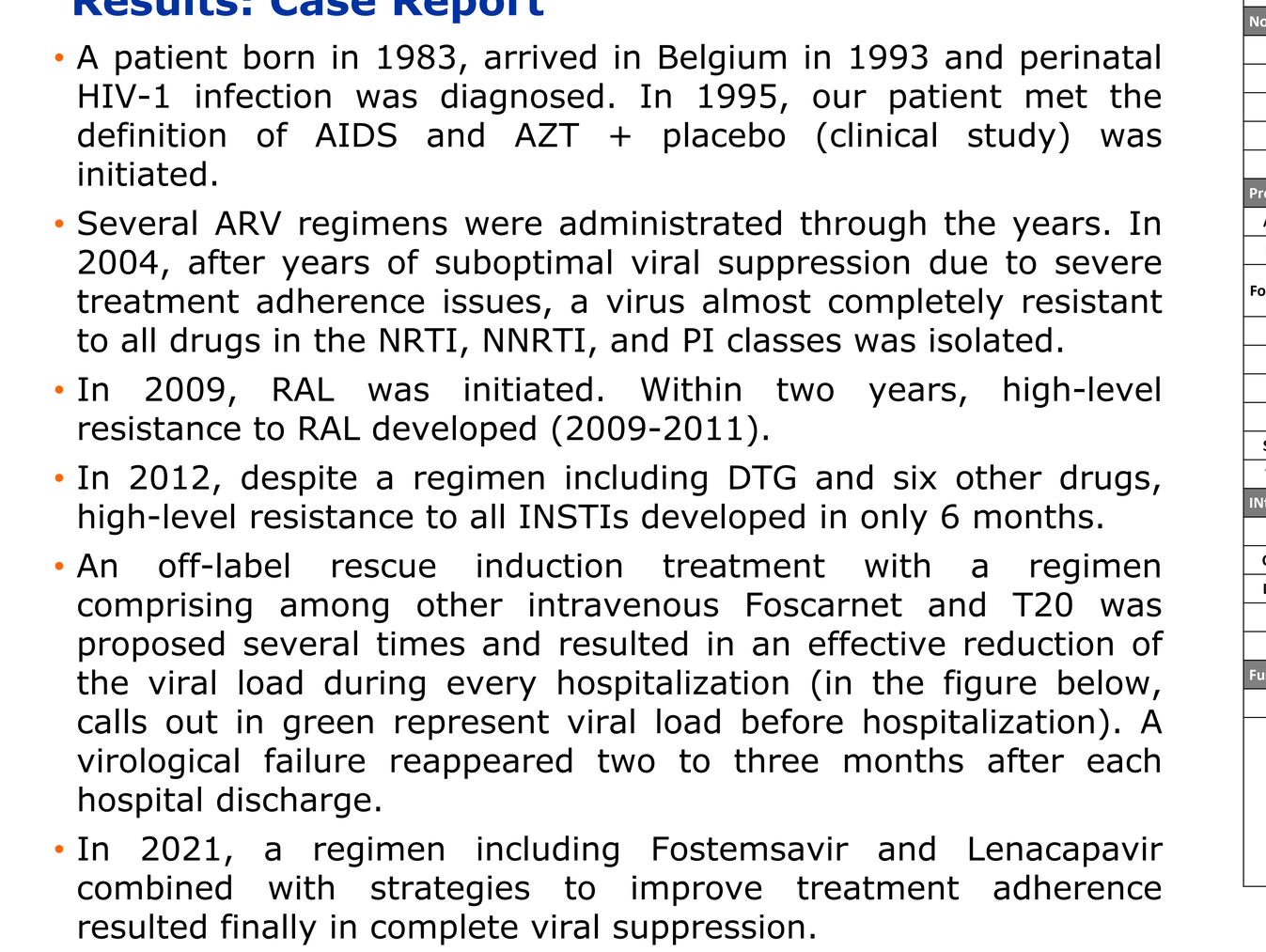
Results: Case Report

- A patient born in 1983, arrived in Belgium in 1993 and perinatal HIV-1 infection was diagnosed. In 1995, our patient met the definition of AIDS and AZT + placebo (clinical study) was initiated.
- Several ARV regimens were administrated through the years. In 2004, after years of suboptimal viral suppression due to severe treatment adherence issues, a virus almost completely resistant to all drugs in the NRTI, NNRTI, and PI classes was isolated.
- In 2009, RAL was initiated. Within two years, high-level resistance to RAL developed (2009-2011).
- In 2012, despite a regimen including DTG and six other drugs, high-level resistance to all INSTIs developed in only 6 months.
- An off-label rescue induction treatment with a regimen comprising among other intravenous Foscarnet and T20 was proposed several times and resulted in an effective reduction of the viral load during every hospitalization (in the figure below, calls out in green represent viral load before hospitalization). A virological failure reappeared two to three months after each hospital discharge.
- In 2021, a regimen including Fostemsavir and Lenacapavir combined with strategies to improve treatment adherence resulted finally in complete viral suppression.

Results: genotyping and phenotyping studies

- A 38-years old female, perinatally HIV-1 infected, has been treated with 14 different antiretroviral regimens over 27 years at our HIV reference clinic. Using the algorithms available at the time of sample collection, resistance to almost all the drugs of the four main antiviral classes was observed in 2011.
- The table below illustrates the evolution and cumulative result of HIV detected mutations interpreted by the Stanford algorithm available at sampling time or phenotypic result. ILL: low-level resistance, IR: intermediate resistance; SP: potential low-level resistance.

Sample date:	11 Oct 1999	10 Jul 2003	11 Oct 2004	23 Jan 2006	31 Jul 2006	10 May 2007	02 Nov 2009	10 Jun 2011	17 Nov 2011	19 Dec 2011	28 Aug 2012	20 Dec2012	07 Jan 2013	03 Oct 2013	31 Aug 2018	22 Nov 2021	Cumulative
Nucleoside Reverse Transcriptase Inhibitors (NRTI)																	
Lamivudine (3TC)	ILL	S	S	IR	IR	IR	R	R	R	R	R	R	ILL	R	R	S	R
Abacavir (ABC)	S	R	ILL	R	IR	ILL	R	R	R	R	R	R	R	R	R	R	R
Zidovudine (AZT)	R	R	ILL	ILL	ILL	ILL	R	R	R	R	R	R	R	R	R	R	R
Stavudine (D4T)	S	R	ILL	ILL	ILL	ILL	R	R	R	R	R	R	R	R	R	R	R
Didanosine (DDI)	S	R	R	ILL	ILL	IR	R	R	R	R	R	R	R	R	R	R	R
Emtricitabine (FTC)	-	-	-	R	R	R	R	R	R	R	R	R	ILL	R	R	S	R
Tenofovir (TDF)	-	R	R	IR	IR	ILL	ILL	ILL	ILL	S	R	R	R	R	R	IR	R
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)																	
Doravirine (DOR)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	IR	R
Efavirenz (EFV)	S	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
Etravirine (ETR)	-	-	-	-	-	-	R	R	R	S	R	SP	R	SP	R	R	R
Nevirapine (NVP)	S	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
Rilpivirine (RPV)	-	-	-	-	-	-	-	-	R	-	R	-	R	--	R	R	R
Protease Inhibitor (PI)																	
Atazanavir (ATV/r)	-	-	ILL	R	R	IR	R	R	R	R	R	R	R	R	R	R	R
Darunavir (DRV/r)	-	-	-	-	ILL	ILL	IR	IR	IR	SP	IR	SP	IR	SP	R	R	R
Fosamprenavir (FPV/r)	-	-	-	R	R	IR	R	R	R	R	R	R	R	R	R	R	R
Indinavir (IDV/r)	S	R	R	IR	S	ILL	R	R	R	S	R	R	R	S	R	R	R
Lopinavir (LPV/r)	-	R	R	IR	ILL	ILL	R	R	R	SP	R	SP	R	R	R	R	R
Nelfinavir (NFV)	R	R	R	IR	IR	IR	R	R	R	R	R	R	R	R	R	R	R
Ritonavir (/r)	R	R	R	R	-	-	-	-	-	-	-	-	-	-	-	-	-
Saquinavir (SQV/r)	ILL	R	R	IR	ILL	ILL	R	R	R	R	R	R	R	R	R	R	R
Tipranavir (TPV/r)	-	-	-	R	ILL	ILL	ILL	ILL	ILL	SP	IR	SP	IR	SP	R	R	R
INtegrase Strand Transfer Inhibitor (INSTI)																	
Bictegravir (BIC)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	S	R	R
Cabotegravir (CAB)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	R	R
Dolutegravir (DTG)	-	-	-	-	-	-	-	-	-	S	-	SP	R	R	S	R	R
Elvitegravir (EVG)	-	-	-	-	-	-	ILL	ILL	ILL	-	R	-	R	-	SP	R	R
Raltegravir (RAL)	-	-	-	-	-	-	ILL	ILL	R	R	R	SP	R	R	SP	R	R
Fusion and attachment inhibitors																	
Enfuvritide (T-20)	-	-	-	-	-	-	-	-	-	S	-	-	-	S	-	-	-
Maraviroc (MVC)	-	-	-	-	-	-	-	CXCR4 use	-	Dual/ Mixed CCR5 use predominant	-	Dual/ Mixed CCR5 use limited	-	Dual/ Mixed CCR5 use limited	-	-	-



CONCLUSION

Highly resistant HIV infections require a multidisciplinary approach with extensive expertise in viral infections, mental health problems and social issues, sometimes leading to unconventional but effective management under close supervision.

In heavily experienced patients with pan-resistant HIV, first-in-class newly available drugs may be a game-changer to achieve viral suppression.