

# Efficacy, Safety and Tolerability of Etravirine as Salvage Therapy in HIV-1-Infected Paediatric Patients in Clinical Practice

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## INTRODUCTION

The assessment of etravirine (ETR) efficacy in HIV-infected children and adolescents is still under evaluation in ongoing clinical trials.

## PURPOSE

To evaluate the efficiency of ETR in HIV-vertically infected pediatric patients.

## PATIENTS & METHODS

- Multicenter retrospective study of 23 ARV-experienced vertically HIV-1 infected paediatric patients, 5 children and 18 adolescents, with documented genotypic evidence of NNRTI resistance but one NRTI-naïve adolescent.
- Analysis of CD4<sup>+</sup> T-cells, viral load (VL) and clinical status at baseline and during follow-up every 3 months were performed.
- Backbone regimen included NRTIs and a boosted PI, with or without other newer agents: RAL, MVC and/or ENF.

## RESULTS

• At baseline, median VL was 4.5 and 4.3log<sub>10</sub> in children and adolescents. Median CD4<sup>+</sup> T-cell was 11% and 20%, respectively. 7/23 (30%) had received NVP, 10/23 (43%) EFV and 5/23 (22%) both drugs. 16/23 (70%) harbored RAMs according to DUET trials: G190A/S (7/23), Y181C/I (6/23), K101E/P (5/23), A98G (4/23), V106I (2/23), V90I (1/23), L100I (1/23). 20/23 showed at least 3 PI resistance mutations. BR included DRV/r in 19/23 and/or RAL in 7/23. MVC or ENF were administrated in 3/23 patients.

• After ETR treatment, 20/23 (87%) patients achieved VL <400copies/mL and 18/20 <50copies/mL: 3/18 (17%) the first month, including the NNRTI-naïve adolescent, 11/18 (61%) within the first 4 months and the rest within the first 8 months. 78% patients (3 children and 15 adolescents) maintained undetectable VL during follow-up. Immunological recovery was observed in 19/23 (83%) patients: Δ240 and Δ204 cells/μL in children and adolescents, respectively, and no patient presented severe immunologic suppression. Median follow-up was 60.6 weeks (35.0-94.1) and 47.8 weeks (34.6-66.4) in children and adolescents, with 8/23 (35%) exposed >60 weeks of whom 4 had >120 weeks. No death or AIDS-defining illness were noticed. No patient experienced complete resistance to ETR although 4/20 (20%) presented poor adherence. ETR therapy was replaced in 3 patients by emtricitabine/tenofovir, ENF/RAL and MVC respectively, because of insufficient virological and immunological response.

**Table 1 : Baseline characteristics and outcome of ETR-based HAART**

Baseline characteristics	Children N=5	Adolescents N=18
Age in years; median (IQR)	11 (7-11)	15 (13-16)
Gender, girls; n (%)	1 (20)	8 (44)
Geographic origin; n (%)		
Western Europe (Spain, France)	3 (60)	16 (89)
Central America (Guatemala)	1 (20)	--
North Africa (Morocco)	--	2 (11)
Sub-Sahara Africa (Mozambique)	1 (20)	--
HIV-1 RNA log <sub>10</sub> copies/mL; median (IQR)	4.5 (3.9-5.3)	4.3 (3.6-4.8)
CD4 <sup>+</sup> T-cell count, cells/μL; median (IQR)	221 (71-883)	449 (251-678)
Immune category; n (%)		
≥500 cells/μL	2 (40)	8 (44)
200-499 cells/μL	1 (20)	7 (39)
<200 cells/μL	2 (40)	3 (17)
Clinical category; n (%)		
A	--	4 (22)
B	--	4 (22)
C	5 (100)	10 (56)
Years of HAART prior ETR; median (IQR)	9.2 (6.5-10.1)	10.6 (10.3-11.4)
HIV-1 tropism; n (%)		
R5	2 (40)	7 (39)
DM	1 (20)	2 (11)
X4	--	3 (17)
Unknown	2 (40)	6 (33)
HIV subtype		
B	3 (60)	13 (72)
C	1 (20)	--
Unknown	1 (20)	5 (28)
<b>Outcome</b>		
Weeks of ETR regimen; median (IQR)	60.6 (35.0-94.1)	47.8 (34.6-66.4)
Responder (HIV-1 RNA <50 copies/mL)	3 (60)	15 (83)
CD4 <sup>+</sup> T-cell count, cells/μL; median (IQR)	571 (332-911)	586 (505-796)
Immune category		
≥500 cells/μL	3 (60)	14 (78)
200-499 cells/μL	2 (40)	4 (22)
<200 cells/μL	--	--
Regimen of HAART with ETR; n (%)		
NRTI + PI	3 (60)	9 (50)
NRTI + PI + New ARV	1 (20)	--
NRTI + New ARV	--	1 (6)
PI + New ARV	1 (20)	8 (44)
Adherence; n (%)		
Complete	1 (20)	6 (33)
Good	3 (60)	5 (28)
Moderate	--	4 (22)
Poor	1 (20)	3 (17)
Laboratory data		
Hypercholesterolemia	3 (60)	8 (44)
Hypertriglyceridemia	3 (60)	5 (28)
HDL reduction	3 (60)	7 (39)
ARV-related adverse event		
Mild/short-term skin rash	--	3 (17)
Moderate skin rash	--	2 (11)
Cause of FPV interruption		
Virological failure	1 (20)	2 (11)
Comorbidity (oral candidiasis)		

**CONCLUSION:** ETR-based therapy showed sustained antiviral response and immunologic improvement in the HIV-1-vertically infected paediatric patients of our cohort.

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