

The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: AZLF3004
Title: An Open-label study to evaluate long-term (48 weeks) safety and efficacy of switch to <i>TRIZIVIR</i> after first line quadruple induction therapy: AZLF3004-Trisud
Rationale: Multisud (CNAF 3016), a pilot open-label trial, demonstrated that a protease inhibitor (PI) containing a quadruple (lamivudine + zidovudine + abacavir + nelfinavir [NFV]) therapy regimen led to a decline in levels of plasma HIV-1 RNA at 48 weeks in antiretroviral therapy (ART)-naïve adults. After this induction phase, this Trisud study was conducted as a follow up over 96 weeks with fixed combination of abacavir, lamivudine and zidovudine (TZV) alone. This study evaluated the efficacy and tolerance of switch to TZV following initial quadruple therapy with TZV plus NFV as first line therapy for 48 weeks. Maintenance therapy with TZV may be an option for long-term antiretroviral treatment.
Phase: IIIb
Study Period: 8 February 2001 to 31 August 2003
Study Design: Open-label study
Centres: 8 centres in France
Indication: Human Immunodeficiency Virus type I (HIV-1) infection in ART-naïve subjects
Treatment: Subjects were switched to TZV (abacavir 300 mg + epivir 150 mg + retrovir 300mg) 1 tablet twice a day for 48 weeks at the end of treatment of the Multisud study (fixed combination of abacavir, lamivudine and zidovudine + nelfinavir).
Objectives: Primary objective was to determine the proportion of patients with sustained plasma HIV-1 RNA concentration below 50 copies/mL at 24 and 48 weeks.
Primary Outcome/Efficacy Variable: Percentage of subjects with HIV-1 concentration <50 copies/mL at Week 48.
Secondary Outcome/Efficacy Variables: Changes in cholesterol level, in fasting cholesterol level, in triglycerides level, and in blood glucose level from baseline to Week 48 Number of subjects with ≥1 sign/symptom of lipodystrophy at Week 48 Median increase of CD4+ cell count from baseline to Week 48 Median change in CD4+ cell count from the start of quadruple therapy initiation to Week 48 Genotypic and phenotypic profiles presented for each virological escape case if viral load > 700 copies/mL
Statistical Methods: Undetectable viral load was defined as viral load <50 copies/mL. Virological escape was defined as viral load > 50 copies/mL, confirmed by an assessment 2-4 weeks later. Statistical analysis was scheduled as following : Percentage of subjects with undetectable viral load at Week 24 and Week 48 presented with 95% Confidence Interval Time to virological escape estimated by Kaplan-Meier time-to-event method Multivariable analysis using Cox's model performed, if subject number enough, in order to identify predictive factors of virological escape Median variation of viral load, CD4+ and CD8+ lymphocytes from CNAF 3016 baseline tested by a Wilcoxon non-parametric test Association between virological escape and phenotypic/genotypic resistance studied subject to sample size considerations Incidence of clinical event related to progression of HIV-1 infection Treatment impact on compliance tested by variance analysis for repeated measures with period effect However, due to a small sample size, statistical analyses were limited to descriptive statistics as enumerated below : - Quantitative data were described as median, minimum (min) and maximum (max). The Intent-to-Treat analysis population (ITT) included patients who received at least one dose of TZV and who had at least one efficacy criterion. Serious and non serious adverse event (AE) analysis was performed for all patients who received at least one dose of TZV (safety population).
Study Population: Adult subjects who had received TZV plus NFV over 48 weeks and who had a plasma HIV-1 RNA (pVL)< 50 copies/mL were eligible for study participation. Exclusion criteria comprised: current acute HIV infection; pregnant or breastfeeding women; malabsorption or other gastrointestinal condition; current treatment with radiotherapy, chemotherapy or immunosuppressant drugs; significant unexplained biological abnormality or disease, subjects who have stopped treatment with abacavir, and/or lamivudine, and/or zidovudine.
TZV

Number of Subjects:	
Entered, N	18
Completed, n (%)	15 (83)
Total Number Subjects Withdrawn, n (%)	3 (17)
Withdrawn Due to Adverse Events, n (%)	2 (11)
Withdrawn Due to Lack of Efficacy n (%)	0
Withdrawn For Other Reasons n (%)	1 (6)
Demographics	TZV
N (ITT)	18
Females: Males	3: 15
Median Age, years (Range)	43.5 (31-63)
Race	n/a
Centre for disease Control (CDC) Classification (n)	
A	7
B	5
C	6
Median HIV-1 RNA at Baseline Log ₁₀ copies/mL (Min, Max)	1.7 (1.7-2.4)
Primary Efficacy Results:	
	TZV N=18
Percentage of Subjects with HIV-1 Concentration <50 copies/mL at Week 48	61
Secondary Outcome Variables:	
	TZV
Median Change in Cholesterol Level from Baseline to Week 48 (mmol/mL)	-0.560
Range	(-1.78; 1.22)
Median Change in Fasting Cholesterol Level from Baseline to Week 48	not available (n/a)
Range	n/a
Median Change in Triglycerides Level from Baseline to Week 48 (mmol/mL)	+0.160
Range	(-0.76; +1.72)
Median Change in Blood Glucose from Baseline to Week 48 (mmol/mL)	+0.2
Range	(-0.7; +0.9)
Number of Subjects with ≥1 Sign/Symptom of Lipodystrophy at Week 48	9
Difference from baseline	-1
95% CI	n/a
Median Increase of CD4 Cell Count from Baseline to Week 48	+99
Range	(-6; +194)
Median Change in CD4 Cell Count from Baseline Quadruple Therapy Initiation to Week 48	290
Range	(42; 472)
Proportion of Subjects with a Virologic Rebound	n/a
95%CI	n/a
Genotype at Rebound	n/a
Safety Results: An on-therapy AE was defined as an AE with onset on or after the start date of study medication but not later than one day after the last date of study medication. An on-therapy serious adverse event (SAE) was defined as an SAE with onset on or after the start date of study medication and up to the last dose of medication.	
	TZV N=18
Most Frequent Adverse Events – On-Therapy	
Subjects with any AE(s)	14 (78)
Malaise and Fatigue	4 (22)
	TZV N=18
Serious Adverse Events - On-Therapy	
n (%) [n considered to be related to study medication by the investigator]	

Subjects with non-fatal SAEs, n (%)	3 (17)
	n (%) [related]
Fracture	1 (6) [0]
Angina pectoris	1 (6) [0]
Compressed nerve syndrome	1 (6) [0]
Subjects with fatal SAEs, n (%)	2 (11) [0]
Murder	1 (6) [0]
Stroke	1 (6) [0]

Conclusion:

See publication below.

Publications:

Ragnaud JM, Delmas B, Gallais H, Peyramond D et al. Efficacy and Safety of Trizivir Maintenance Treatment After First-line Therapy. 6th International Congress on Drug Therapy in HIV Infection. Glasgow, November 17-21, 2002.

Date Updated: 01-Dec-2005