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<b>Study No.:</b> AZLF 3002	
<b>Title:</b> Multicentre, open-label, pilot study to evaluate the efficacy and safety of a triple therapy combining AZT/3TC/ABC as a combined tablet of <i>Trizivir</i> ®, in HIV-infected patients with an undetectable viral load after quadruple therapy (COM, ABC, EFV) during CNAF 3008 study (La Francilienne).	
<b>Rationale:</b> Initial study CNAF 3008 (La Francilienne) demonstrated that a protease inhibitor sparing quadruple therapy regimen abacavir plus lamivudine plus zidovudine plus efavirenz (EFZ) led to a sustained decline in levels of plasma human immunodeficiency virus type 1, ribonucleic acid (HIV-1 RNA) in antiretroviral therapy-naïve HIV-1-infected adults. Following this induction therapy, a continuation study was performed to evaluate a simplified regimen with fixed combination (zidovudine 300mg + lamivudine 150mg+ abacavir 300mg)(TZV) for 48 weeks, for those subjects with plasma HIV-1 RNA levels maintained below 50 copies/mL at the end of CNAF 3008 study.	
<b>Phase:</b> IIIb	
<b>Study Period:</b> From 18 January 2000 to 20 March 2001	
<b>Study Design:</b> Open-label, multicentre, non comparative study	
<b>Centres:</b> 12 active French centres	
<b>Indication:</b> HIV	
<b>Treatment:</b> Fixed combination TZV (zidovudine 300mg + lamivudine 150mg+ abacavir 300mg), one tablet morning and evening, for 48 weeks	
<b>Objectives:</b> The primary objective was to determine if, in subjects with undetectable viral load after a powerful quadruple therapy, a simplified regimen with triple therapy combined in one tablet maintains a low viral load.	
<b>Primary Efficacy Variable:</b> Proportion of subjects with a plasma viral load (HIV-1 RNA) below detectable threshold (50 copies/mL) after 24 and 48 weeks of treatment.	
<b>Secondary Efficacy Variables:</b> Change in viral load from baseline (Day 0 of Suburbs Study) to 24 and 48 weeks; Variation of lymphocytes CD4 cell count from baseline (Day 0 of Suburbs Study) to 24 and 48 weeks, Number of subjects with a virological escape (viral load > 50 copies/mL); Incidence of adverse events and description of serious adverse events, Clinical evolution: B and C events (classification Centre for Disease Control, CDC), Specific morphological and metabolic evaluations of lipodystrophic syndrome, Incidence of clinical cases due to HIV-1, Compliance : drug return, physician questionnaire, patient questionnaire, Profile of phenotypic and genotypic HIV-1 resistance in case of virological escape (Viral load >500 copies/mL).	
<b>Statistical Methods:</b> Results are presented from day 0 to Week 48 (La Francilienne) and to 48 weeks of maintenance treatment (Suburbs). Quantitative data were described as median and 95% exact Confidence Interval (95%CI) and qualitative data as frequency. Percentage of subjects with a viral load <50 copies/mL were calculated, considering missing data and treatment switch as failure. They are presented with 95% exact CI. Mean variation of CD4 cell count, cholesterol, triglycerides and glucose from baseline of Suburbs study were calculated and tested with Wilcoxon signed rank test. Intent-to-treat (ITT) population included all subjects of Suburbs study who had received at least one dose of TZV after efavirenz withdrawal and with at least one efficacy measure available. All subjects who had received at least one dose of TZV were included in the safety population.	
<b>Study Population:</b> Subjects involved in La Francilienne study, and with a viral load below detectability threshold for at least 6 months before inclusion, with CD4 cell count >200 cells/mm <sup>3</sup> . Subjects aged 18 years or more; females of childbearing potential should have had a negative pregnancy test and used mechanical contraception. <i>Excluded</i> were subjects who had definitively stopped abacavir and/or retrovir and/or lamivudine and/or EFZ, subjects with acute infectious disease, related or not to HIV; malabsorption, gastrointestinal disorders, or other factors which might, upon investigator's opinion, interfere with drug absorption; ongoing radiotherapy (except locally for Kaposi's syndrome), chemotherapy or immune modulators (interferon, corticosteroids through general route, on long term and high doses), or possible use of these medications during the study.	
<b>Number of Subjects:</b>	<b>TZV</b>
Planned, N	Not Available (n/a)
Entered, N	20
Completed, n (%)	17 (85)

Total Number Subjects Withdrawn, N (%)	3 (5)
Withdrawn due to Adverse Events n (%)	1 (5)
Withdrawn due to Lack of Efficacy n (%)	0
Withdrawn for other reasons n (%)	2 (10)
<b>Demographics</b>	
N (ITT)	20
Females: Males	2: 18
Median Age, years (range)	37 (22; 58)
Race, n (%)	n/a
<b>Primary Efficacy Results:</b>	
Proportion of subjects with a plasma viral load (HIV-1 RNA) below detectable threshold (50 copies /mL)	<b>TZV</b>
Median Baseline, log <sub>10</sub> copies/mL	<1.7
After 24 weeks of treatment [95%CI]	n/a
After 48 weeks of treatment [95% CI]	85 [62; 97]
p-value	n/a
<b>Secondary Efficacy Results:</b>	
	<b>TZV</b>
Change in viral load from baseline (Day 0 of Suburbs Study) to 24 weeks < 400 copies/mL, % [95% CI] < 50 copies/mL, % [95% CI] < 5 copies/mL, % [95% CI]	95 [75; 100] 95 [75 ; 100] 65 [41 ; 85]
Change in viral load from baseline (Day 0 of Suburbs Study) to 48 weeks < 400 copies/mL, % [95% CI] < 50 copies/mL, % [95% CI] < 5 copies/mL, % [95% CI]	90 [68; 99] 85 [62%; 97] 50 [27%; 73]
Mean variation of CD4 cell count (cells/mm <sup>3</sup> ) from baseline (Day 0 of Suburbs Study) to 24 weeks (SD)	34.5 (164.8)
95% CI	n/a
Mean variation of CD4 cell count (cells/mm <sup>3</sup> ) from baseline (Day 0 of Suburbs Study) to 48 weeks (SD)	42.9 (156.3)
95% CI	n/a
Number of subjects with a viral escape (viral load > 50 copies/mL)	3
95% CI	n/a
Clinical evolution: B and C events (classification CDC)	n/a
Specific morphological and metabolic evaluations of lipodystrophic syndrome:	
Presence of at least one sign at Week 48 when no sign at baseline	4/8
Presence of at least one moderate or severe sign at Week 48 when slight at baseline	0/4
Presence of severe sign at Week 48 when moderate sign at baseline	1/5
Absence of signs at Week 48 when moderate sign at baseline	3/5
Mean cholesterol change from baseline to Week 48, mmol/L (SD)	-0.81 (0.75)
Mean triglycerides change from baseline to Week 48, mmol/L (SD)	-0.07 (0.80)
Mean glucose change from baseline to Week 48, mmol/L (SD)	-0.10 (1.42)
Incidence of clinical cases due to HIV-1	n/a
Compliance : drug return, physician questionnaire, patient questionnaire	n/a
Profile of phenotypic HIV-1 resistance in case of viral escape (Viral load >500 copies/mL)	0/2
Profile of genotypic HIV-1 resistance in case of viral escape (Viral load >500 copies/mL)	1/2 (211K mutation)
<b>Safety Results:</b> An on-therapy adverse event/serious adverse event (AE/SAE) was defined as an AE/SAE with onset on or after the start date of study medication and up to 4 weeks after the last evaluation of week 48.	
	<b>TZV</b>
<b>Most Frequent Adverse Events – On-Therapy</b>	<b>n (%)</b>

Subjects with any AE(s), n (%)	16 (80)
Bronchitis	4 (20)
Gastrointestinal hernia	3 (15)
Malaise & fatigue	3 (15)
Nausea & vomiting	2 (10)
Muscle pain	2 (10)
Disorder of lipid metabolism	2 (10)
Gastrointestinal infection	2 (10)
Tooth decay	2 (10)
Dyspeptic syndrome	2 (10)
Viral respiratory infections	2 (10)
Neuralgia	2 (10)
Compressed nerve syndromes	2 (10)
<b>Serious Adverse Events - On-Therapy</b>	
<b>n (%) [n considered by the investigator to be related to study medication]</b>	
	<b>TZV</b>
	<b>n (%) [related]</b>
Subjects with non-fatal SAEs	2 (10)
Gastrointestinal hernia	1 (5) [0]
Insulin-dependent diabetes	1 (5) [1]
Subjects with fatal SAEs	0

**Conclusion:**

After 48 weeks of a potent quadruple therapy, simplified treatment with TZV maintained viral load below 50 copies/mL and a good immune response. Hypercholesterolaemia during the induction phase improved after efavirenz withdrawal. Adverse events were reported in 16 (80%) subjects, with the most frequently reported being Bronchitis, gastrointestinal hernia, and malaise and fatigue. Two subjects reported serious adverse events. No fatal serious adverse events were reported.

**Publications:**

No publication

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