

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.

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------|
| <b>Study No.:</b> AZLF 3006                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |            |
| <b>Title:</b> An open label study to evaluate long term (96 weeks) safety and efficacy of switch to <i>TRIZIVIR</i> after first line quadruple induction therapy: AZLF 3006 – Suburbs 2                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |            |
| <b>Rationale:</b> Initial study CNAF 3008 (La Francilienne) demonstrated that a protease inhibitor sparing quadruple therapy regimen abacavir plus Zidovudine/lamivudine (TZV) 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-naive HIV-1-infected adults. Following this induction therapy, a continuation study was performed to evaluate a simplified regimen with TZV for 48) weeks (AZLF3002 – Suburbs study), for those subjects with plasma HIV-1 RNA levels maintained below 50 copies/mL at the end of a 48-week treatment. The aim of AZLF 3006 study was to evaluate long term efficacy and safety of TZV, for at least 96 weeks throughout AZLF 3002 (Suburbs study), and AZLF 3006 (Suburbs 2 study), in HIV-1 infected adults previously receiving TZV plus EFZ for 48 weeks (CNAF 3008 – La Francilienne study). |            |
| <b>Phase:</b> IIIb                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |            |
| <b>Study Period:</b> 18 July 2001 – 11 Sept 2002                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |            |
| <b>Study Design:</b> Multicentre, open-label study                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |            |
| <b>Centres:</b> 10 French centres.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |            |
| <b>Indication:</b> HIV                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |            |
| <b>Treatment:</b> Fixed combination of zidovudine 300mg + lamivudine 150mg+ abacavir 300mg (TZV), one tablet morning and evening, for 48 weeks.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |            |
| <b>Objectives:</b> The primary objective was to assess the efficacy of long term TZV as a simplification treatment based on the proportion of subjects maintaining plasma HIV-1 RNA concentration below 50 copies/mL after at least 2 years.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |            |
| <b>Primary Outcome/Efficacy Variable:</b> Proportion of subjects maintaining plasma HIV-1 RNA concentration <50 copies/mL after at least 96 weeks (48 weeks of AZLF 3002 study included).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |            |
| <b>Secondary Outcome/Efficacy Variable(s):</b><br>Change in viral load from day 0 to Week 48 (La Francilienne) and to 96 weeks of maintenance treatment (Suburbs plus Suburbs 2); variation of lymphocytes CD4 cell count from day 0 to Week 48 (La Francilienne) and to 96 weeks of maintenance treatment (Suburbs plus Suburbs 2); Clinical evolution: B and C events (classification CDC), cholesterol evolution.<br>Compliance : physician questionnaire,<br>Profile of phenotypic and genotypic HIV-1 resistance in case of viral escape (Viral load >1000 copies/mL).                                                                                                                                                                                                                                                                                                                                                                      |            |
| <b>Statistical Methods:</b> Results are presented from day 0 to Week 48 (La Francilienne) and to 96 weeks of maintenance treatment (Suburbs plus Suburbs 2). Quantitative data were described as median and 95% exact Confidence Interval (95%CI) and qualitative data as frequency.<br>Intent-to-treat (ITT) population included all subjects of Suburbs study who had received at least one dose of TZV after EFZ withdrawal and with at least one efficacy measure available.<br>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. Median variations of CD4 cell count from baseline of Suburbs study were calculated and tested with Wilcoxon signed rank test.<br>All subjects who had received at least one dose of TZV were included in the safety population.                                                       |            |
| <b>Study Population:</b> Included subjects involved in AZLF 3002 study and with a viral load <50 copies/mL at inclusion and at least one time within 3 months before inclusion; subjects 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.<br>Excluded were subjects who had definitively stopped TZV, 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | n/a        |
| Entered, N                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 17         |
| Completed, n (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 17 (100)   |
| Total Number Subjects Withdrawn, N (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 0          |

|                                                                                                                                                                                                                                                                                                                                                                                                                        |                             |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Withdrawn due to Adverse Events n (%)                                                                                                                                                                                                                                                                                                                                                                                  | 0                           |
| Withdrawn due to Lack of Efficacy n (%)                                                                                                                                                                                                                                                                                                                                                                                | 0                           |
| Withdrawn for other reasons n (%)                                                                                                                                                                                                                                                                                                                                                                                      | 0                           |
| <b>Demographics</b>                                                                                                                                                                                                                                                                                                                                                                                                    |                             |
| N (ITT)                                                                                                                                                                                                                                                                                                                                                                                                                | 17                          |
| Females: Males                                                                                                                                                                                                                                                                                                                                                                                                         | 1: 16                       |
| Median Age, years (Min; Max)                                                                                                                                                                                                                                                                                                                                                                                           | 38 (24; 59)                 |
| Race, n (%)                                                                                                                                                                                                                                                                                                                                                                                                            | n/a                         |
| <b>Primary Efficacy Results:</b>                                                                                                                                                                                                                                                                                                                                                                                       |                             |
| Proportion of subjects maintaining plasma HIV-1 RNA concentration below 50 copies/mL (log <sub>10</sub> copies/mL)                                                                                                                                                                                                                                                                                                     | <b>TZV</b>                  |
| Median Baseline (Day 0 of Suburbs 2), % [95%CI]                                                                                                                                                                                                                                                                                                                                                                        | 100 [80; 100]               |
| From baseline (Day 0 of Suburbs study) to Week 96, % [95%CI]                                                                                                                                                                                                                                                                                                                                                           | 100 [80; 100]               |
| p-value                                                                                                                                                                                                                                                                                                                                                                                                                | n/a                         |
| <b>Secondary Efficacy Results:</b>                                                                                                                                                                                                                                                                                                                                                                                     |                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                        | <b>TZV</b>                  |
| Change in viral load from baseline (Day 0 of La Francilienne Study) to 48 weeks                                                                                                                                                                                                                                                                                                                                        | n/a                         |
| Change in viral load from baseline (Day 0 of Suburbs study) to 96 weeks (log <sub>10</sub> copies/mL) (Week 48 of Suburbs 2 study) [95% CI]                                                                                                                                                                                                                                                                            | -3.00 [-4.23; -1.90]        |
| Variation of CD4 cell count from baseline (Day 0 of La Francilienne Study) to 48 weeks) [95% CI]                                                                                                                                                                                                                                                                                                                       | n/a                         |
| Variation of CD4 cell count from baseline (Day 0 of Suburbs study) to 96 weeks ; cells/mm <sup>3</sup> (Week 48 of Suburbs 2 study) [95% CI]                                                                                                                                                                                                                                                                           | +56 [-206; +270]            |
| Clinical evolution: B and C events (classification CDC)                                                                                                                                                                                                                                                                                                                                                                | n/a                         |
| Compliance at 48 weeks of Suburbs 2 study                                                                                                                                                                                                                                                                                                                                                                              |                             |
| Bad %                                                                                                                                                                                                                                                                                                                                                                                                                  | 53                          |
| Good %                                                                                                                                                                                                                                                                                                                                                                                                                 | 47                          |
| <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. (adverse events reported below are for the continuation study - AZLF 3006 (Suburbs 2) – please see AZLF3002 (Suburbs) for adverse events reported in these subjects for the intial trial] |                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                        | <b>TZV</b><br><b>N = 17</b> |
| <b>Most Frequent Adverse Events – On-Therapy (Suburbs 2)</b>                                                                                                                                                                                                                                                                                                                                                           | <b>n (%)</b>                |
| Subjects with any AE, n(%)                                                                                                                                                                                                                                                                                                                                                                                             | 12 (71)                     |
| Bronchitis                                                                                                                                                                                                                                                                                                                                                                                                             | 4 (24)                      |
| Seborrheic dermatitis                                                                                                                                                                                                                                                                                                                                                                                                  | 2 (12)                      |
| Viral respiratory infections                                                                                                                                                                                                                                                                                                                                                                                           | 2 (12)                      |
| <b>Serious Adverse Events - On-Therapy (Suburbs 2)</b><br><b>n (%) [n considered by the investigator to be related to study medication :</b>                                                                                                                                                                                                                                                                           |                             |
|                                                                                                                                                                                                                                                                                                                                                                                                                        | <b>TZV</b><br><b>N = 17</b> |
|                                                                                                                                                                                                                                                                                                                                                                                                                        | <b>n (%) [related]</b>      |
| Subjects with non-fatal SAEs                                                                                                                                                                                                                                                                                                                                                                                           | 0                           |
| Subjects with fatal SAEs                                                                                                                                                                                                                                                                                                                                                                                               | 0                           |
|                                                                                                                                                                                                                                                                                                                                                                                                                        |                             |

**Conclusion:**

Plasma viral load was maintained below 50 copies/mL over 96 weeks maintenance in all subjects. Immune system response was maintained with a continuous CD4 count increase. Adverse events were reported in 12 (71%) subjects, with bronchitis, seborrheic dermatitis, and viral respiratory infections being the most frequently reported. No fatal or non-fatal serious adverse events were reported.

**Publications:**

AN OPEN-LABEL STUDY TO EVALUATE LONG TERM (96 WEEKS) SAFETY AND EFFICACY OF SWITCH TO TRIZIVIR AFTER FIRST LINE QUADRUPLE INDUCTION THERAPY: AZLFL3006 SUBURBS de Truchis, P.; Rouveix, E.; Zucman, D.; Chemlal, K.; Mathez, D.; Devidas, A.; Welker, Y.; Leibowitch, J.; Khuong, A.; Force, G., and Praindhui, D. 9th European AIDS Conference (EACS) 1st EACS Resistance and Pharmacology Workshop; Warsaw; Poland. 2003 Oct 25

Date Updated: 14-Dec-2005