

# EFFECT OF SIMPLIFICATION FROM PROTEASE INHIBITORS (PIs) TO BOOSTED ATAZANAVIR (ATV/R)-BASED REGIMENS IN REAL-LIFE CONDITIONS

## PRELIMINARY RESULTS OF GESIDA 44/04 SIMPATAZ STUDY

Poster  
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### Background

- HAART optimization strategies for virologically controlled patients are frequent in routine clinical practice.
- Some of the reasons considered for stable HAART switches are to:
  - Enhance adherence
  - Improve short-term tolerability
  - Avoid long-term toxicity
  - Improve quality of life
  - Manage other issues (drug-drug interactions, pregnancy, etc)
- Risk of treatment or virological failure should not be significantly increased.
- Switches from boosted or unboosted PI-containing regimens to NNRTI or abacavir-based ones have been demonstrated to be an option to mitigate some PI-related side effects while maintaining viral control and improving convenience.
- Ritonavir-boosted ATV is a potent, generally well-tolerated, once-daily PI with limited data available as a treatment simplification option for patients taking other PIs.

### Objective

To determine the effectiveness and safety of boosted atazanavir-containing regimens in patients who have simplified their antiretroviral treatment by physician's recommendation.

### Study Design

- Multicenter, prospective, non-interventional, post-authorization, 12 month study in patients under stable PI-based treatment who have simplified their antiretroviral therapy by physician's recommendation to boosted atazanavir-containing regimen and then were enrolled in the study.
- Patients were required to be on their current PI-based regimen unchanged and with HIV RNA below LOQ for at least 6 months and 4 months, respectively, before the simplification.
- Conducted at 27 sites in Spain.
- Inclusion period: Jul05-Oct06.
- Patients were followed up every 4 months for 1 year. HIV RNA, CD4, routine physical, analytical and lipid parameters, adherence and adverse reactions data were collected.
- For this interim analysis, data through the first 8 months of follow-up were evaluated.

### Endpoints

- Primary
  - Determine the effectiveness of boosted atazanavir-based simplification regimens by evaluating the proportion of patients maintaining undetectable viral loads (as per local lab. HIV-RNA LOQ) after one year of follow-up
- Secondary
  - Proportion of patients maintaining an undetectable viral load below 50 copies/ml (in centers with ultrasensitive techniques)
  - Time to virological failure\*
  - Changes in CD4 lymphocyte counts
  - Frequency and severity of clinical and laboratory adverse effects\* and withdrawals due to adverse events
  - Change versus baseline in fasting lipid values (total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides)
  - Change versus baseline in fasting glucose values\*
  - Degree of adherence reported by the patient and perceived quality of life\*

\*Not covered or only partially covered by this poster presentation; it will be completed in future communications

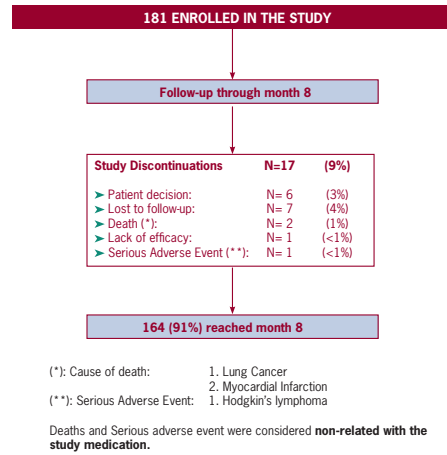
### Statistical Considerations

- The primary analysis of effectiveness and safety was performed in all patients included in the study who received at least one dose of atazanavir.
- Final events and study missing data were considered failures (intent-to-treat (ITT) analysis considering missing values as failures).
- A significance level of  $p=0.05$  was used in all cases.
- Baseline characteristics of all participants was analyzed on the baseline visit using descriptive statistics.

### Definition of Failure

- Effectiveness will be measured by the plasma viral load and CD4 lymphocyte count according to the following final events considered as treatment failures:
- Virological failure: Detectable viral load confirmed on at least two consecutive determinations separated by one month.
  - Immunological failure: Decrease in CD4 lymphocyte count >35% versus baseline values.
  - Discontinuations for any reason or deaths.

### GESIDA 44/04 SIMPATAZ Patient Disposition through month 8



### Baseline Characteristics

	N=181
Median age, years (Q1, Q3)	44 (40, 48)
Female: n (%)	36 (20%)
HIV-1 Risk Factors	
IDU	86 (47%)
Heterosexual	57 (31%)
Homosexual	35 (19%)
CDC Class C; n (%)	53 (29%)
Co-infected, Hep B or C Positive; n (%)	94 (52%)
Methadone consumption; n (%)	30 (17%)
CD4 count nadir, cells/ $\mu$ L; median (Q1, Q3)	164 (60, 261)
Median CD4 count, cells/ $\mu$ L (Q1, Q3)	511 (364, 748)
<200 cells/ $\mu$ L; n (%)	12 (7%)
HIV-1 RNA: Undetectable*; n (%)	181 (100%)
Patients at sites with HIV-1 RNA LOQ <20 or <50 cp/mL; n (%)	166 (92%)

\* As per local lab. HIV-RNA LOQ (20:50-200:400 cp/mL)

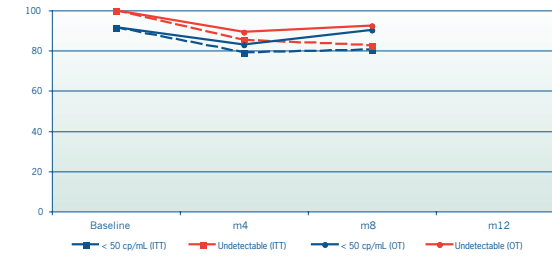
### Antiretroviral History and ARV Changes at Entry

	N=181
Median antiretroviral exposure, years (Q1, Q3)	7.9 (4.9, 10.3)
Previous exposure to at least 2 PIs; n (%)	143 (79%)
No previous ARV failures; n (%)	78 (46%)
Previous failures to:	
Any NNRTI; n (%)	57 (33%)
Any PI; n (%)	55 (32%)
NNRTI, NNRTI and PI classes; n (%)	28 (16%)
ARV treatment at entry	
Switched from Boosted PIs	122 (67%)
> LPV/r	112 (62%)
Switched from unboosted PIs	59 (33%)
Maintained NRTI backbone unchanged when switching	113 (62%)
Modified NRTI backbone when switching	68 (38%)

Top 7 PI-based regimens switched at study entry; n (%)	109 (60%)
> AZT+3TC+LPV/r	25 (14%)
> AZT+3TC+NFI	23 (13%)
> TDF+3TC/FTC+LPV/r	20 (11%)
> d4T+3TC+NFI	11 (6%)
> ddI+3TC+LPV/r	10 (5%)
> ddI+3TC/FTC+LPV/r	10 (5%)
> ddI+TDF+LPV/r	10 (5%)
Top 7 ATV/r regimens built at study entry; n (%)	164 (91%)
> TDF+3TC/FTC+ATV/r	52 (29%)
> ABC+3TC+ATV/r	35 (19%)
> AZT+3TC+ATV/r	28 (15%)
> DD+3TC+ATV/r	21 (12%)
> ddI+TDF+ATV/r	10 (5%)
> d4T+3TC+ATV/r	9 (5%)
> d4T+TDF+ATV/r	9 (5%)
Patients on once-daily regimens during the study; n (%)	129 (71%)

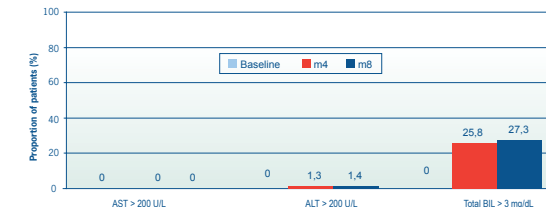
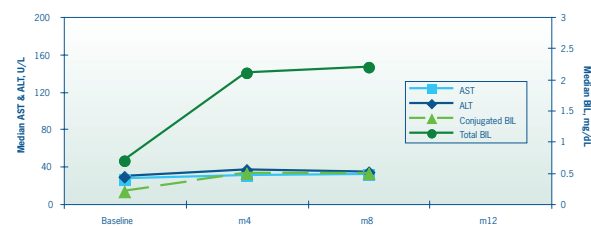
### Effectiveness

Proportions of patients with HIV-1 RNA < 50 copies per mL and undetectable as per local HIV testing LOQ (20-400 cp/mL):

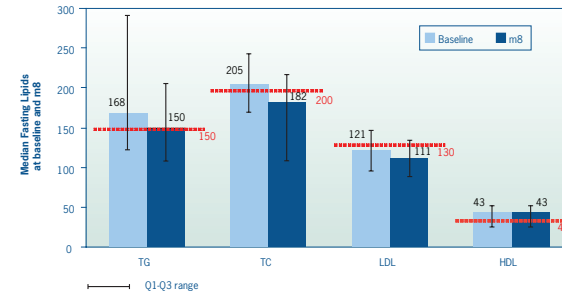


- The probability of maintaining HIV-1 RNA below the LOQ at m8 was significantly and inversely associated ( $p=0.042$ ) with a non-adherent classification in the Simplified Medication Adherence Questionnaire (SMAQ) assessment. While 96% of patients classified as adherent by the SMAQ remained undetectable at m8, only 85% did so when they were classified as non-adherent.
- The CD4 cell count median change (Q1, Q3) from baseline at m8 was +17 (-87, 137) and the median cell count at m8 was 567 (401, 730).

### Liver Function Tests



### Lipids



- Median values of fasting lipids at baseline and m8 are represented in the figure. For total cholesterol, LDL-cholesterol and triglycerides, the red horizontal bar is normal/desirable level +/- intervention level depending on other risk factors. For HDL-cholesterol, below the bar is the intervention level depending on other risk factors. The black vertical line represents the range between the first and the third quartile values.

Median changes from baseline in lipid values	M4 Mg/dL (%)	M8 Mg/dL (%)
TG	-32 (-21%)*	-27 (-17%)*
TC	-20 (-9%)*	-16 (-8%)*
LDL	-11 (-8%)*	-7 (-5%)*
HDL	0 (0)	+1 (+1%)

\*p<0.05

- The improvements in lipid profile was also confirmed with a significant reduction in Total Cholesterol/HDL-cholesterol ratio, from an average value of 5.1 at baseline to 4.6 at month 8 ( $p=0.003$ ) and a significant reduction in the proportion of patients receiving concomitant lipid-lowering agents, from 20% at baseline to 13% at m8 ( $p=0.013$ ).

### Conclusions

- In a real-life setting, switching from other stable PI-containing regimens to ATV/r based HAART seems to be effective in maintaining virological suppression.
- Additionally, this strategy provides a way to build convenient and generally well tolerated once-daily regimens.
- Switching to ATV/r-based HAART may also be an option to significantly improve the lipid profile.
- Final 12 months results will be analyzed to confirm these preliminary data and to complete the evaluations pending.

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