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1Competence Network for HIV/AIDS, Ruhr-Universität, Bochum, Germany; 2Karolinska Institute, Stockholm, Sweden; 3Nice University Hospital, Nice, France; 4Bristol-Myers Squibb Company (BMS), Wallingford, CT, USA; 5Hays Pharma, Paris, France; 6St. Josef-Klinik, Ruhr-Universität, Bochum, Germany; 7Clinical Trial Centre, Cologne, Germany; 8Clinical Centre Driesener Straße, Berlin, Germany; 9MVZ Karlsplatz-HIV Research and Clinical Care Centre, Munich, Germany; 10Ifi-Institut, Hamburg, Germany 11BMS, Paris, France.

Maria Jesús Jiménez-Expósito  
Bristol-Myers Squibb Company, Paris, France.  
E-mail: mariajesus.jimenezexpósito@bms.com

# Long-Term Efficacy and Safety of Atazanavir/Ritonavir Treatment in a Real-Life Cohort of Treatment-Experienced HIV patients

K Jansen<sup>1</sup>, A Sönnberg<sup>2</sup>, P Pugliese<sup>3</sup>, S Biguenet<sup>4</sup>, J-L Eychenne<sup>5</sup>, NH Brockmeyer<sup>1,6</sup>, C Michalik<sup>7</sup>, S Dupke<sup>8</sup>, H Jaeger<sup>9</sup>, A Plettenberg<sup>10</sup>, D Butcher<sup>11</sup>, MJ Jiménez-Expósito<sup>11</sup>, and Competence Network for HIV/AIDS<sup>1</sup>

## BACKGROUND

- Several studies have evaluated the duration of different first line antiretroviral (ARV) regimens<sup>1,2</sup>. Few data are available on long-term outcomes following switch
- ATV/r-based regimens have demonstrated efficacy, tolerability and safety in both ARV-naïve and -experienced patients<sup>3-6</sup>
- Time remaining on first line ATV-based regimens is higher compared with other PIs.<sup>1,2</sup> However, few reports have assessed ATV long-term effectiveness as non-first line regimen
- The aim of this study was to describe the long-term outcomes of ATV/r containing regimens in ARV-experienced patients in a real-life clinical setting

## OBJECTIVES

### Primary Endpoint

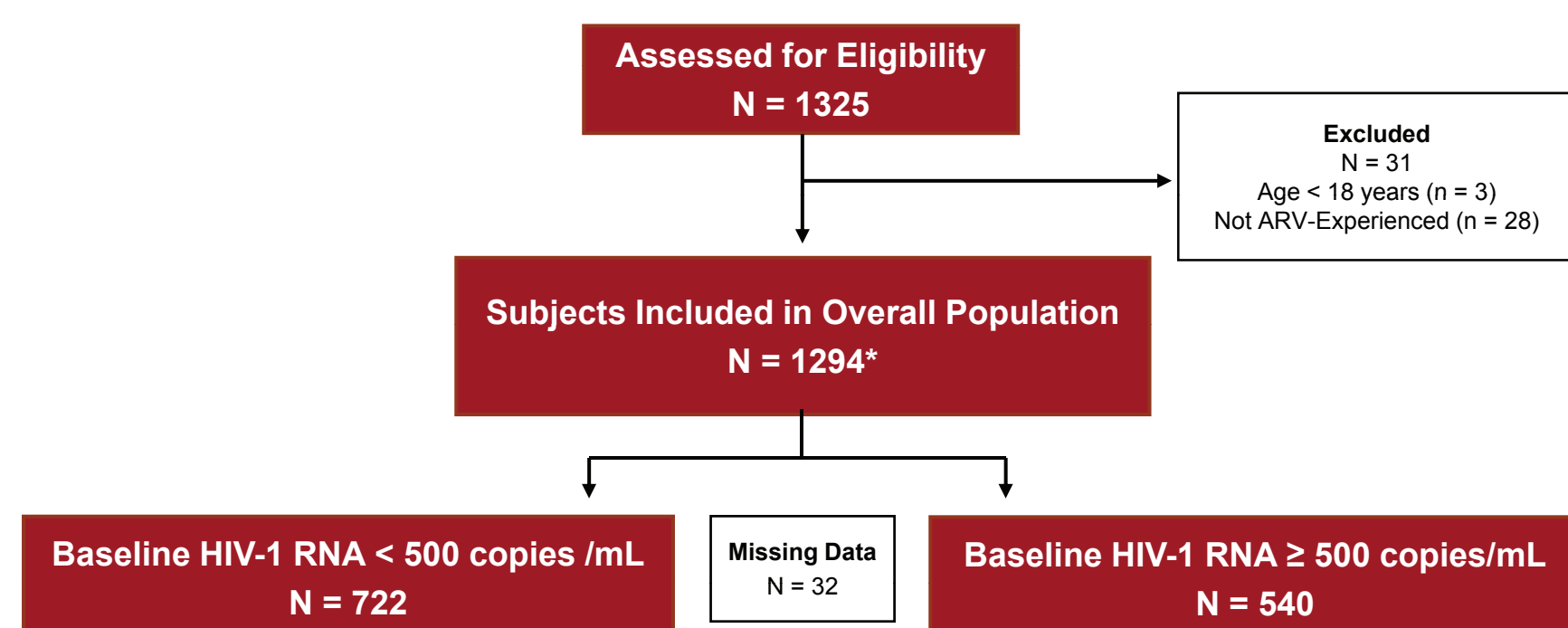
- Proportion of patients remaining on treatment over time by baseline HIV-1 RNA level (< 500 copies/mL and ≥ 500 copies/mL)
  - Estimated probability of remaining on treatment over time using the Kaplan-Meier method (lost to follow-up and missing data censored)

### Secondary Endpoints

- Reasons for discontinuation
- Time to virologic failure (defined as either two consecutive HIV-1 RNA ≥ 50 copies/mL or one HIV-1 RNA ≥ 50 copies/mL followed by discontinuation)
- Long-term safety profile

## STUDY DESIGN

- Non-comparative, retrospective, observational study which collected data from three European HIV databases (France – DatAids; Germany – KompNet; Sweden – InfCare)
- An integrated study database was generated and used for final analysis, and data were extracted at 6-monthly intervals
- ARV-experienced adult patients who started an ATV/r-based regimen between October 2004 and March 2007 were followed until October 2009 (follow-up period up to 5 years)



## RESULTS

### Baseline Characteristics

	Baseline HIV-1 RNA level <sup>a</sup>		Overall (n = 1294)
	< 500 copies/mL (n = 722)	≥ 500 copies/mL (n = 540)	
Age (years), median (min-max)	44 (18-85)	42 (20-77)	43 (18-85)
Female, n (%)	182 (25)	149 (28)	336 (26)
Intravenous drug users, n (%)	77 (11)	68 (13)	145 (11)
CDC Class C AIDS, <sup>b</sup> n (%)	152 (29)	119 (29)	272 (29)
TDF-containing NRTI backbone, <sup>c</sup> n (%)	403 (56)	335 (62)	761 (59)
Time of ARV exposure (years), mean (SD)	5.90 (3.97)	5.46 (3.97)	5.64 (3.97)
Prior exposure to PI, n (%)	586 (81)	362 (67)	964 (75)
LPV/r exposure <sup>d</sup>	256 (36)	145 (27)	412 (32)
Time of PI exposure (years), mean (SD)	3.11 (2.99)	2.10 (2.66)	2.64 (2.89)

<sup>a</sup>32 patients with a missing baseline HIV-1 RNA assessment using an assay precision of at least 500 copies/mL

<sup>b</sup>Available in 941 patients

<sup>c</sup>Available in 1287 patients

<sup>d</sup>Available in 1280 patients

### Proportion of patients remaining on treatment

- 56% [95%CI: 52%-60%] of patients with baseline viral suppression (< 500 copies/mL) and 53% [95%CI: 49%-58%] of those with detectable viraemia (≥ 500 copies/mL) remained on treatment after 3 years
- Median time to discontinuation 4 [95%CI: 3.3-4.3] versus 3.6 [95%CI: 3-4.2] years, respectively (Figure 1)

### Reasons for Discontinuation

	Baseline HIV-1 RNA level <sup>a</sup>		Overall (n = 1294)
	< 500 copies/mL (n = 722)	≥ 500 copies/mL (n = 540)	
Discontinued, n (%)	300 (42)	244 (45)	558 (43)
Lack of efficacy <sup>b</sup>	29 (4)	32 (6)	62 (5)
Adverse event	82 (11)	55 (10)	138 (11)
Death	8 (1)	12 (2)	20 (2)
Patient withdrew consent	26 (4)	44 (8)	72 (6)
Pregnancy	5 (<1)	3 (<1)	8 (<1)
Poor/non compliance	2 (<1)	3 (<1)	5 (<1)
Other <sup>c</sup>	43 (6)	28 (5)	75 (6)
Unknown <sup>d</sup>	105 (15)	67 (12)	178 (14)

<sup>a</sup>32 patients with a missing baseline HIV-1 RNA assessment using an assay precision of at least 500 copies/mL;

<sup>b</sup>Lack of efficacy includes "Treatment failure (clinical, virologic or immunologic), Resistance, Drug interaction, Other therapeutic reasons";

<sup>c</sup>Other includes "Other reason, End of treatment, Simplification, Start protocol, End protocol, Structured treatment interruption, Alternative therapy, Other reasons, Drug abuse, Other treatment, Impairment of quality of life, Dose adjustment"

<sup>d</sup>Discontinuation but reason unknown

### Time to Virologic Failure

- 75% [95%CI: 69%-80%] of patients with baseline HIV-1 RNA levels < 50 copies/mL remained suppressed after 3 years of treatment
- 51% [95%CI: 47%-55%] of patients with baseline HIV-1 RNA levels ≥ 50 copies/mL achieved virologic suppression and remained suppressed after 3 years of treatment (Figure 2)

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## RESULTS

Figure 1. Time to Discontinuation: Kaplan-Meier survival function

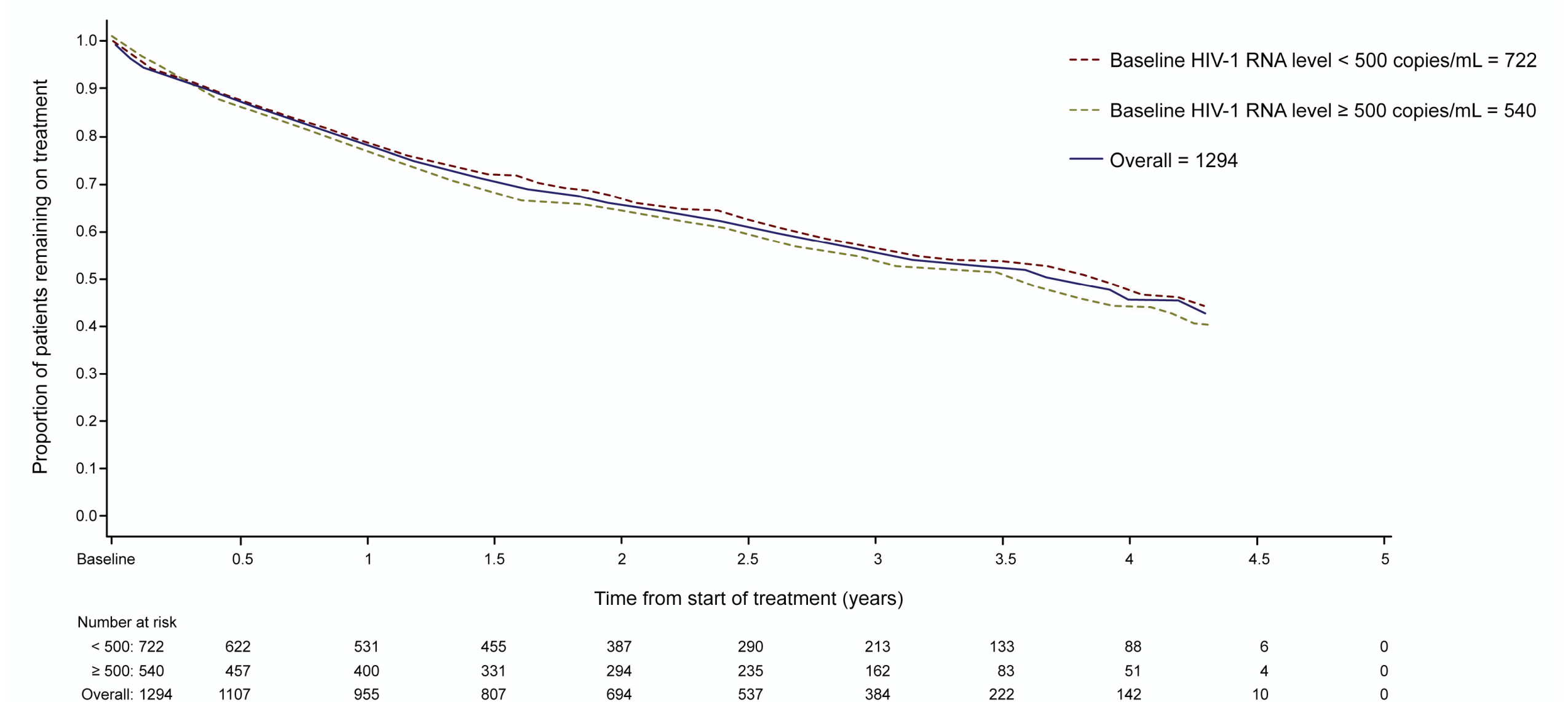
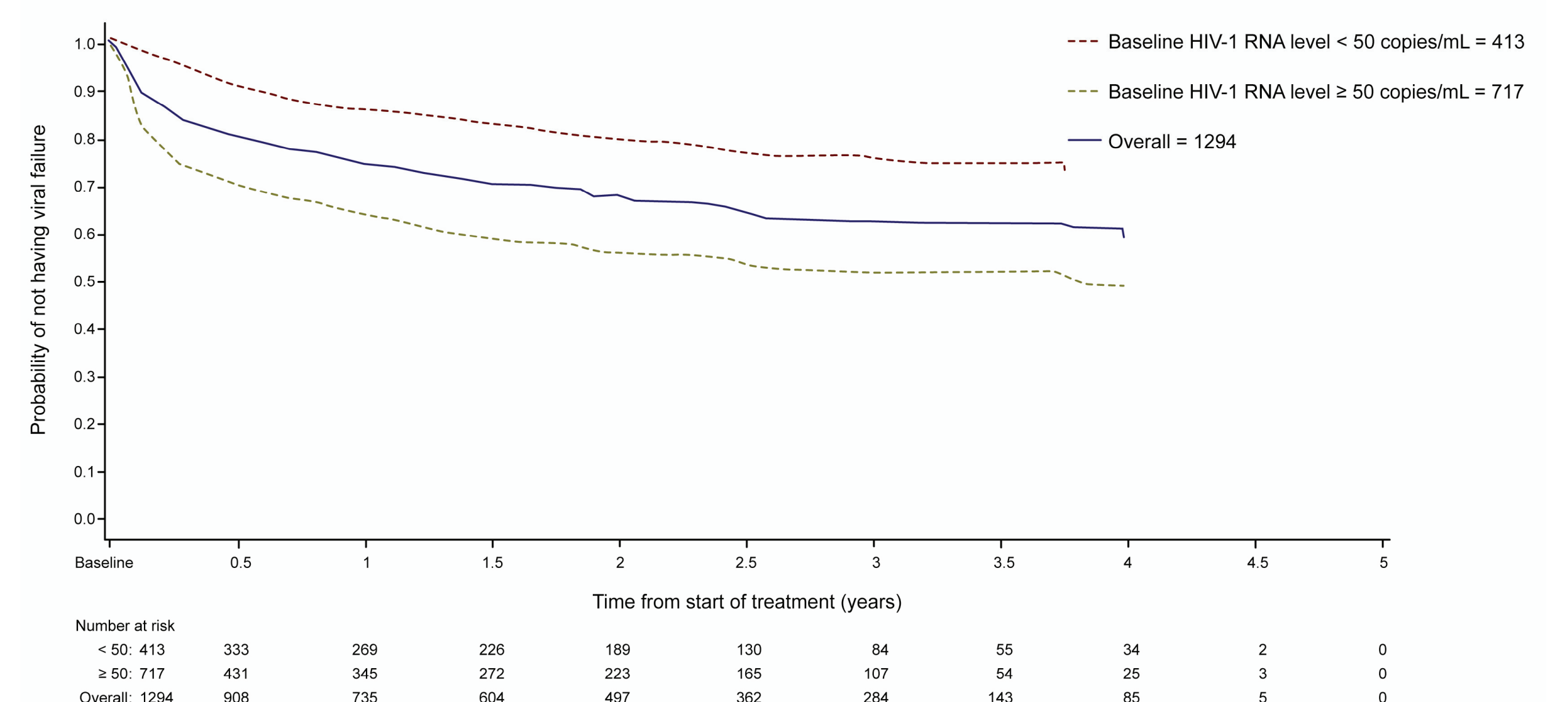


Figure 2. Time to Virologic Failure: Kaplan-Meier survival function



### Selected Adverse Events (Regardless of Causality)

	Baseline HIV-1 RNA level <sup>a</sup>		Overall
	< 500 copies/mL	≥ 500 copies/mL	
Clinical Adverse Events (Any grade), n (%)	N = 722	N = 540	N = 1294
Nausea	3 (<1)	4 (<1)	7 (<1)
Diarrhoea	30 (4)	20 (4)	52 (4)
Jaundice	3 (<1)	4 (<1)	7 (<1)
Renal & urinary disorders	22 (3)	15 (3)	37 (3)
Laboratory Adverse Events (Grade 3-4), n <sup>b</sup> /N <sup>c</sup> (%)			
Total cholesterol (≥ 300 mg/dL)	39/505 (8)	20/391 (5)	60/924 (7)
Triglycerides (≥ 751 mg/dL)	16/503 (3)	21/388 (5)	37/919 (4)
LDL-cholesterol (≥ 190 mg/dL)	38/386 (10)	17/258 (7)	57/669 (9)
Total bilirubin elevation (> 2.5 x ULN)	323/512 (63)	230/401 (57)	573/939 (61)
Creatinine (> 2 x ULN)	7/302 (2)	6/242 (3)	13/544 (2)

<sup>a</sup>32 patients with a missing baseline HIV-1 RNA assessment using an assay precision of at least 500 copies/mL

<sup>b</sup>Patients with at least one laboratory value above thresholds whilst on treatment; <sup>c</sup>Patients with laboratory parameter values while on treatment.

Toxicity grades were defined according to the Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events

### Adverse Events Leading to Discontinuation (Regardless of Causality)

Adverse events, n (%)	Baseline HIV-1 RNA level <sup>a</sup>		Overall (n = 1294)
	< 500 copies/mL (n = 722)	≥ 500 copies/mL (n = 540)	
Side effects – any of the below but unspecified	15 (2)	17 (3)	33 (3)
Cutaneous side effects	13 (2)	8 (1)	21 (2)
Gastrointestinal side effects	8 (1)	7 (1)	15 (1)
Liver/Pancreas toxicity	6 (<1)	2 (<1)	8 (<1)
Renal side effects	5 (<1)	2 (<1)	7 (<1)
Hyperbilirubinaemia	7 (<1)	5 (<1)	12 (<1)
Metabolic effects	6 (<1)	0 (0)	6 (<1)
Lipodystrophy	7 (<1)	4 (<1)	11 (<1)
Other <sup>b</sup>	15 (2)	10 (2)	25 (2)

<sup>a</sup>32 patients with a missing baseline HIV-1 RNA assessment using an assay precision of at least 500 copies/mL. <sup>b</sup>Other includes

"Other clinical side effects, Intolerance to treatment, Hypersensitivity syndrome, Neurologic side effects, Other Biological toxicity, Musculoskeletal, Co-morbidity"

### Study Limitations

- Due to the retrospective, cohort design of this study, bias from missing data or lost to follow-up cannot be excluded
- Adverse events could be under-reported. In addition, the limited available information makes difficult to establish whether there were causality relationships with ATV/r regimens
- Information on genotypic resistance was not available for this study
- Despite methodological challenges, real-life cohorts provide valuable clinical information on long-term efficacy and safety of ARV-treatment

## CONCLUSIONS

- In this real-life ARV-experienced cohort over a follow-up period up to 5 years, ATV/r-containing regimens:
  - Resulted in a low rate of discontinuation
  - Demonstrated sustained virologic suppression
  - Showed a long-term safety profile consistent with that previously observed in clinical trials:
    - Discontinuations due to hyperbilirubinaemia were infrequent
    - No new or unexpected AEs were observed