BRISTOL-MYERS SQUIBB COMPANY

ATAZANAVIR

Final Clinical Study Report for Study AI424128

SYNOPTIC REPORT

A Phase 4, Multi-center, Cross-sectional Study to Evaluate the I50L Substitution Among Subjects Experiencing Virologic Failure on a HAART Regimen Containing Atazanavir (ATV)

Indication:	HIV infection
Phase:	4
Study Initiation Date:	01-Oct-2004
Study Completion Date:	31-Mar-2009
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THIS STUDY WAS CONDUCTED IN ACCORDANCE WITH GOOD CLINICAL PRACTICE

Sponsor's Responsible Medical Officer:
[redacted]
Bristol-Myers Squibb
Plainsboro, New Jersey 08536
United States of America

SYNOPSIS

Final Clinical Study Report for Study AI424128

TITLE OF STUDY: A Phase 4, Multi-center, Cross-sectional Study to Evaluate the I50L Substitution among Subjects Experiencing Virologic Failure on a HAART Regimen Containing Atazanavir (ATV)

PURPOSE: The study AI424128 was initiated with the primary objective of comparing the prevalence of the I50L substitution in subjects failing atazanavir (ATV)-containing highly active antiretroviral treatment (HAART) regimens without ritonavir (RTV) with the I50L substitution prevalence in subjects failing HAART regimens containing ATV in combination with RTV. The last subject last visit for this study was on 31 March 2009.

NUMBER OF SUBJECTS: A total of 703 subjects were enrolled in this study, of these 611 subjects were evaluable.

All Studied subject population included all enrolled subjects with a successful drug resistance genotype result. All Evaluable subject population included subjects in the All Studied population, who did not directly switch from ATV to ATV/RTV or from ATV/RTV to ATV in the current regimens containing ATV.

DISPOSITION, DEMOGRAPHICS AND OTHER PERTINENT BASELINE CHARACTERISTICS:

Patient disposition and demographics are presented in the following table.

Table 1: Patient Disposition and Demographics

	With I50L		Without I50L		Overall Total
	ATV	ATV/RTV	ATV	ATV/RTV	
All Screened	15	48	163	753	979
All Enrolled	15	47	108	533	703
From US sites	14	39	92	454	599
From EU sites	1	8	16	79	104
All Studied	15	47	104	512	678
From US sites	14	39	88	435	576
From EU sites	1	8	16	77	102
All Evaluable	12	39	93	467	611
From US sites	11	32	78	396	517
From EU sites	1	7	15	71	94
Age (mean [SD]); years	42.3 (10.33)	44.2 (9.15)	46.3 (8.34)	44.9 (8.94)	45.0 (8.89)
Male, n (%)	11 (91.7)	30 (76.9)	79 (84.9)	376 (80.5)	496 (81.2)
Race, n (%)					
Caucasian/White	7 (58.3)	21 (53.8)	47 (50.5)	223 (47.8)	298 (48.8)
African American/Black	2 (16.7)	8 (20.5)	32 (34.4)	160 (34.3)	202 (33.1)
Hispanic/Spanish/ Latin American	3 (25.0)	8 (20.5)	12 (12.9)	73 (15.6)	96 (15.7)
Asian/Oriental	0	0	1 (1.1)	6 (1.3)	7 (1.1)
American Indian/Alaskan Native	0	0	0	3 (0.6)	3 (0.5)
Not Classified	0	2 (5.1)	1 (1.1)	2 (0.4)	5 (0.8)
Weight (mean [SD]); kg	77.9 (17.37)	75.6 (12.1)	76.4 (17.34)	76.8 (16.35)	76.7 (16.25)

ATV: atazanavir; EU: European Union; RTV: ritonavir; SD: standard deviation; US: United States

Note: Percentages were based on the number of evaluable subjects in each column.

SUMMARY OF RESULTS:

There was no treatment involved in this study. Complications of phlebotomy were to be recorded on a supplemental Case Report Form to include any incidences of hematoma, phlebitis, cellulitis, and vasovagal syncope. There were no such incidences during the conduct of this study.

The primary endpoint, prevalence of I50L substitution in subjects who received ATV without RTV as a component of their HAART therapy, versus I50L substitution in subjects who received ATV/RTV as a component of their HAART therapy, was not significantly different (p = 0.116).

Table 2: Primary Endpoint: Prevalence of I50L

	ATV N = 96[a]	**ATV/RTV N = 460[a]**
I50L Prevalence, n (%)	12 (12.5)	36 (7.83)
Crude Odds Ratio[b] (95% CI)	0.59 (0.30, 1.19)	
Adjusted Odds Ratio[c]	0.51 (0.22, 1.18)	
p-value[d]	0.116	

ATV: atazanavir; CI: confidence interval; RTV: ritonavir

[a] Subjects with unverified treatment gaps were excluded from analyses

[b] Crude odds ratios are estimated from simple logistic regression models

[c] Adjusted odds ratios are estimated from multiple logistic regression model

[d] P-values are from Wald Chi-square tests of the adjusted odds ratios

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