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Long-Term Safety and Efficacy of Atazanavir-Based Therapy in HIV-Infected Infants, Children and Adolescents: The Pediatric AIDS Clinical Trials Group Protocol 1020A

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Abstract

Background—Atazanavir is an attractive option for the treatment of Pediatric HIV infection, based on once daily dosing and the availability of a formulation appropriate for younger children. PACTG 1020A was a phase I/II open label study of atazanavir (ATV) (with/without ritonavir [RTV] boosting)-based treatment of HIV-infected children; here we report the long-term safety and virologic and immunologic responses.

Methods—Antiretroviral-naïve and experienced children, ages 91 days to 21 years, with baseline plasma HIV RNA >5000 copies/ml (cpm) were enrolled at sites in the United States and South Africa.

Results—Of 195 children enrolled 142 (73%) subjects received ATV-based regimens at the final protocol recommended dose. 58% were treatment naïve. Overall, at week 24, 84/139 subjects (60.4%) and at week 48, 83/142 (58.5%), had HIV RNA <400 cpm. At week 48, 69.5% of naïve

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and 43.3% of experienced subjects had HIV RNA < 400 cpm; median CD4 increase was 196.5 cells/mm³. The primary adverse event was increased serum bilirubin; 9% of subjects had levels > 5.1 times upper limit of normal and 1.4% noted jaundice. 3% of subjects experienced Grade 2 or 3 prolongation in PR or QTc intervals. At week 48, there was a 15% increase in total cholesterol (TC), with TC >199 mg/dL increasing from 1% at baseline to 5.7%.

Conclusions—Use of once-daily ATV, with/without RTV, was safe and well tolerated in children, with acceptable levels of viral suppression and CD4 count increase. The primary adverse event, as expected, was an increase in bilirubin levels.

Keywords

atazanavir; pediatric HIV; antiretroviral treatment

Combination antiretroviral therapy (CART) has led to remarkable improvements in immune status, suppression of viral replication, and reduced morbidity and mortality in HIV-infected adults and children.^{1–4} Nevertheless, many children have not achieved complete virologic suppression and in addition, there is a large population of aging perinatally infected children and adolescents with extensive antiretroviral (ARV) experience and therefore resistance to many existing agents.⁵

Atazanavir (ATV) is an attractive option for inclusion in CART regimens, given its low pill burden, convenient once daily dosing, acceptable safety profile, and less marked effect on serum lipids when compared to other available protease inhibitor (PI) agents^{6–13}.

Unboosted ATV and ATV/ritonavir (RTV) have been shown to be comparable to efavirenz in ARV-naïve adults, and lopinavir/RTV based regimens in ARV-naïve and ARV-experienced adults.^{7–9, 14} Once daily dosing of ATV, with and without RTV, was approved for use in HIV- infected adults in June, 2003. The recommended adult dose is 400 mg daily, unboosted, for ARV-naïve adults, and 300 mg, with 100 mg of RTV for ARV-experienced and ARV-naïve adults.

Pediatric AIDS Clinical Trials Group 1020A (clinical trial NCT 00006604) was a phase I/II open-label, individual dose adjusted, pharmacokinetic and safety study of ATV designed to determine the optimal dosage of ATV powder & capsules in treatment naïve and experienced HIV-infected children and adolescents. As previously described¹⁵, we were able to develop dosing guidelines (designed to achieve protocol specified pharmacokinetic [PK] targets) for subjects 6 months to 21 years of age. In 2008, based on data from this study, ATV was approved for children ≥ 6 years. Here, we report on the long-term safety and efficacy of ATV-based regimens in infants, children and adolescents.

METHODS

HIV-infected, ARV- naïve and ARV-experienced patients, between the ages of 3 months (91 days) and 21 years, with plasma HIV RNA viral levels < 5000 cpm, were eligible for enrollment. Patients with prior ARV experience with two or more PIs underwent phenotypic resistance testing at screening and allowed to enroll if the sensitivity to ATV was <10 fold less than the reference virus. Patients with NRTI treatment experience had genotypic

resistance testing performed at screening, and allowed to enroll if they were found to be sensitive to at least two NRTIs (with tenofovir and abacavir excluded). The study was initially open to U.S. based PACTG sites, but subsequently was opened for enrollment to South African subjects.

Dose Finding

Patients were stratified by age and formulation (capsule [c] or powder [p]) and by the use of RTV as a pharmacologic boosting agent into nine dosing cohorts. The initial starting dose for each cohort was 310mg/m² once daily, based on studies in HIV-infected adults. All patients underwent intensive PK evaluation after one week of therapy and again at study week 56, as described previously.¹⁵ Individual patient dosing of ATV was adjusted (increased or decreased) if concentrations were outside the area under the concentration-time curve (AUC) target range of 30–90 mcg*hr/mL. AUC targets were established based on exposures in adults in early studies of unboosted ATV. A repeat intensive PK evaluation was performed two weeks after any PK-based or toxicity-related dose adjustment.¹⁵ The starting dose for each age and formulation cohort was adjusted based on the safety and PK evaluations of the initial five subjects, and PK evaluations of the initial ten subjects for the group. Table 1 shows the final dosing cohorts. The unboosted ATV/p cohorts (groups 1 and 2) were closed based on the inability to achieve target exposures. Six of the nine dosing cohorts had at least one dose modification, as previously described, based on failure to meet protocol defined AUC targets.¹⁵ No cohort dose modification was required for safety issues.

Laboratory Methods

Over the duration of the protocol, the assay used to determine Plasma HIV RNA levels was transitioned from the Amplicor HIV-1 Assay to the Amplicor HIV-1 Monitor 1.5 UltraSensitive Assay (Roche Molecular Systems, Branchburg, NJ) to finally the Abbott Realtime HIV-1 RNA assay. The assays were performed according to the manufacturer's instructions in a laboratory accredited by the College of American Pathologists and certified by the NIH Virology Quality Assurance (VQA) in the United States, and VQA certified in South Africa. Genotypic analysis was performed using the Applied Biosciences ViroSeq HIV-1 Genotyping System according to the manufacturer's instructions. Interpretation of genotypic resistance was performed using HIV RT and Protease Sequence Database (<http://hivdb.stanford.edu>). Phenotypic ARV susceptibility was determined using the ViroLogic PhenoSense™ HIV Assay, ViroLogic Inc. (South San Francisco, California, USA). In this assay, drug susceptibility is expressed as the fold change of the drug concentration required to inhibit viral replication by 50% (IC50) compared with control (wild-type virus), i.e., IC50 Fold Change = IC50 patient/IC50 control.

Safety and Efficacy Evaluations

Standard laboratory tests (complete blood counts, comprehensive chemistry panels, and non-fasting lipid panels) were obtained at protocol specified intervals (every 8 weeks for first 96 weeks of study). EKGs were performed at time of screening and during intensive PK studies (pre-dose, then 2 and 4–6 hours post-dose) at week 1 and 56 and 2 weeks after any dose modification (other than dose increases for weight gain). EKGs were reviewed by the site at the time of the study, and sent to a central site for official reading, which used for study

safety analysis. All subjects who received ATV at the final accepted dose (n=142) were included in the safety analysis. Adverse events (AE) were coded as per DAIDS toxicity tables. Total serum bilirubin levels were reviewed and graded based on their relation to the upper limit of normal (ULN) range at the reporting laboratory. Toxicity management dictated a dose reduction for subjects with total serum bilirubin $\geq 5.1 \times$ ULN and discontinuation for a total serum bilirubin $\geq 10 \times$ ULN.

Virologic failure (VF) was defined as failure to achieve, or maintain VL ≤ 400 cpm. Subjects with VF were allowed to remain on study drug if the local clinical treatment team felt it was in the subject's best interest to continue the study drug and regimen. AEs are reported through week 96; all patients on study drug, with AEs, are reported here, even if they had previous VF.

Statistical Methods

The safety and efficacy analyses focused on patients enrolled at the final ATV (+/-RTV) group doses through week 96 of treatment, presented in aggregate, and some analyses stratified whether ATV was boosted or not with RTV. Descriptive statistics were used to summarize baseline demographic data. Proportion of patients having certain types of adverse events that were deemed treatment-related were bounded by 95% Exact Confidence Intervals. Median total bilirubin changes, and lipid (triglyceride [TG]/total cholesterol [TC]) percent changes from baseline, as well as the proportion of patients falling within abnormal TG/TC levels were calculated in an 'as-treated analysis' which only included a subgroup of patients who were still on-treatment and had available data at the time point of interest. Virologic response, defined as achieving HIV-RNA < 400 cpm and remaining on treatment, was analyzed at weeks 24, 48, 96 using an 'intent-to-treat' (ITT) approach, in which children who discontinued study treatment for any reason were considered failures. Rates of virologic response and the corresponding 95% Exact Confidence intervals are presented. Median $\log_{10}$ HIV RNA and CD4 changes from baseline were calculated in an 'as-treated' analysis. For analysis of virologic and immunologic responses, two analyses were performed; one included all subjects who were enrolled at the final recommended dose (n=142); and the second included a subset of those subjects, including only those subjects who did not require a dose adjustment (n=100). P-values less than 0.05 were considered significant. SAS version 9 (Cary, NC) was used for data analyses.

RESULTS

Demographics

195 patients were enrolled onto P1020A. Baseline demographics and lab values, and dosing for patients (N=142) enrolled at the final group doses are shown in Table 1. 49.3% of subjects were enrolled at South African (SA) sites with the majority (78%) of ARV-naïve patients enrolled at the SA sites.

Virologic and Immunologic Response

At week 24, for all patients who started ATV at the final dose, 60.4% (95% CI [52%,69%], n=139, 3 subjects with missing data) had a VL < 400 cpm; 58.5% (95% CI [50%,65%],

n=142), and 49.6% (95% CI [41%,58%], n=135) of patients remained undetectable at weeks 48 and 96, respectively. For ARV-naïve patients, at week 48, the VL suppression rate was 69.5%; for ARV-experienced patients, 43.3% ($p < 0.01$). At week 96, the respective rates of VL suppression were 57.0% and 39.3%, $p=0.043$ (Table 2). There was no difference in response rate between boosted and unboosted ATV when comparing patients 6–21 years of age on capsule formulation (week 48, undetectable rate for ATV/RTV 50%, and for unboosted ATV, 45.65%, $p=0.69$; at week 96, 44.7% for ATV/RTV and 32.6% for unboosted ATV, $p=0.25$). For the patients starting at the final dose, and not needing any protocol-defined dose adjustment (other than for weight gain), at week 48, 53% (95% CI: 43%, 63%, $n=100$) had VL < 400 cpm. At week 96 the rate of continued suppression overall was 41.3% (95% CI [30%, 53%], $n=80$), (Table 2), with 51.1% of treatment naïve and 27.3% of treatment experienced subjects suppressed ($p=0.03$).

For all patients remaining on study treatment, the median increase in CD4 counts from baseline was +196.5 (range –1388 to +2306) cells/mm³ at 20 weeks ($N=114$) and +282 (–938 to +1693) cells/mm³ at week 96 ($N=83$).

Treatment discontinuations

Of the 142 patients enrolled at the final dose, 52 remained on study, at a median of 257 weeks (4.9 years), range 62–373 weeks. There were two deaths, (one from pneumonia, the other due to bacterial meningitis) neither judged related to study drug. One subject discontinued study treatment secondary to worsening of baseline cardiomyopathy, unrelated to study drug.

Of those 90 patients no longer on study, the median time on study was 76.5 weeks, range 1–383 weeks. 19 patients came off study at study completion. See Supplemental Digital Table 1 for reasons for treatment discontinuation other than study completion.

Hyperbilirubinemia

As expected, the primary adverse event (AE) reported was an increase in total serum bilirubin levels. For patients enrolled at the final group doses, 9.2% had at least one total bilirubin level $\geq 5.1 \times \text{ULN}$, and 1.4% experienced jaundice. The median increase in total bilirubin from baseline to week 24 was +0.85mg/dL (–0.5 to +8.2). Bilirubin levels tended to rise quickly, within the first 2 weeks of treatment, without evidence of ongoing liver damage (no change in ALT/AST levels) and then stayed level through 48 and 96 weeks on treatment. No patient on ATVp/RTV ($n=58$) had a total bilirubin $\geq 5.1 \times \text{ULN}$, while 5/46 (10.9%) on unboosted ATVc, and 8/38 (21.1%) on boosted ATVc had total bilirubin $\geq 5.1 \times \text{ULN}$ (Treatment Related Toxicities, Supplemental Digital Table 2).

Electrocardiographic Changes

Three patients (2.1%) had a grade 3 increase in QTcB interval on electrocardiogram. Two patients came off study for an increased QTc interval, without associated clinical symptoms. A grade 1 increase in the PR interval was seen in 20% of patients, and 2 patients (1.4%) experienced grade 2 increases (both of whom discontinued treatment; one also had a grade 2

bradycardia). No patient had a second degree heart block noted. Two patients (1%) had grade 3 bradycardia. (Supplemental Digital Table 2)

Effect on Lipids

Median baseline TC and TG levels were 127 mg/dL (42 to 306) and 105mg/dL (24 to 593), respectively. In an as-treated analysis, at week 48, there was a median 15% increase in TC from baseline ($p < 0.001$), while there was no significant change in TG values. In evaluating the effect of ATVc compared to ATVc/RTV, there was no significant difference in week 24 and 48 levels for TC or TG between treatment arms. Overall, at baseline 3% of patients had TC between 170–199 mg/dL, and 1% of patients had TC >199 mg/dL; at week 48, 24.76% had TC between 170–199 mg/dL and 5.7% had TC >199 mg/dL (Table 3).

Other Adverse Events

There were few grade 2 or higher AEs except those mentioned above. The AEs that occurred in >1% of patients were: elevation of serum levels of alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) (2.8% and 4.2%, respectively), alkaline phosphatase (2.8%), and direct bilirubin (14.8%), and alteration of serum sodium (7%) and potassium (4.9%). Among elevations in direct bilirubin, 20/21 were judged related, or possibly related to study drug; for elevations in ALT and/or AST, half were judged possibly related to study drug, while all alterations in serum sodium and potassium were judged not related.

CONCLUSION

In P1020A, using dosing that met protocol defined PK targets, ATV-based CART, with and without RTV boosting, was safe and well tolerated, and was associated with long-term immunologic and virologic responses.

The VL suppression rate (< 400 cpm) at 48 weeks, for ARV-naïve children was 69.5% at week 48 (ITT). This is similar to studies in ARV-naïve adults treated with ATV, with/without RTV, where VL suppression rates at week 48 ranged from 64–85%^{7, 8, 16}. Reported rates of VL suppression (<400cpm) for ARV-naïve children and adolescents on PI-based HAART were 72% at 24 weeks for fosamprenavir/RTV-based¹⁷, and 80–85% at 48 weeks for lopinavir/RTV-based regimens¹⁸.

Among ARV-experienced children who started ATV at the final dose (including those that needed a dose adjustment) the VL suppression rate at week 48 was 43.3%, and 39.3% at week 96 (ITT). In the BMS Study 045, among ARV-experienced adults, at 48 weeks, 56%, and at 96 weeks, 44%, of patients on ATV/RTV had a VL <400cpm.^{9, 11, 19} Cohen reported 48% of PI-experienced subjects on unboosted ATV had VL <400 cpm at 48 weeks¹¹.

Direct comparison between this study and others of ARV-experienced pediatric patients is difficult, as the extent of previous ARV experience with PIs, presence of pre-existing NRTI and PI mutations, and age range of subjects vary considerably among these studies. Darunavir/RTV-based CART regimens, given to ARV-experienced patients 6–17 years of age (n=80) resulted in virologic suppression (VL <400cpm) in 59% of patients at 48

weeks.²⁰ For fosamprenavir, the 24 week VL <400cpm rate among 40 PI-experienced subjects 2–18 years of age was 55%.²¹ For lopinavir/RTV, 75% of ARV-experienced patients aged 8 months–12 years (32 of 56 were PI-naïve) had VL <400cpm at 48 weeks.¹⁸ Among 115 ARV-experienced patients 2–18 years receiving one of two doses of tipranavir/RTV based CART, 39.7–45.6% had VL < 400cpm at 48 weeks.²²

The lower rate of suppression among ARV-experienced children in this study, compared to adult studies of ATV, may be partly related to the enrollment of patients with significant loss of viral sensitivity to ATV, as we used a screening phenotypic resistance fold cutoff level of 10, whereas now the suggested cutoff in clinical practice is a 3–5 fold loss of sensitivity to ATV. In addition, archived, but not detected, resistance mutations to NRTIs could have contributed to the lower rate of virologic suppression among our HIV-experienced patients as we allowed patients to re-cycle NRTIs if there was genotypic evidence of viral susceptibility at the screening visit.

It should be noted that when comparing patients of the same age group, who were on ATVc with or without RTV boosting in this study, the immunologic and virologic response was the same, regardless of prior treatment history. In contrast, in a study of ARV-experienced adults on ATV or ATV/RTV, 51.1% and 68.6%, respectively, had VL < 500 cpm at week 48.¹⁰ Of note, in that study, 50% of patients on unboosted ATV used tenofovir as part of the CART regimen, which may reduce ATV plasma concentrations.²³

The improved response for ARV-experienced children treated with unboosted ATVc may reflect that P1020A required individual dose adjustment, if needed, to achieve protocol-determined AUC and Cmin targets, so that both ARV-naïve and ARV-experienced subjects, with or without boosting, had near equivalent drug exposures. The recommended approved adult dose for unboosted ATV, 400 mg, may not be sufficient to maintain adequate plasma concentrations in all subjects, particularly adolescents; among adults on unboosted ATV, 62.9% had trough ATV concentrations less than the suggested minimum of 0.15 mg/L, while none of those on ATV/RTV had levels below the cutoff.²⁴ In the P1020A cohort of subjects aged 13 and older, the median average daily dose of unboosted ATV required to achieve protocol PK targets was 900 mg; for those 6–13 years of age, a median daily dose of 475 mg was required¹⁵.

As expected, the main side effect reported in this study was an increase in serum unconjugated and total bilirubin levels, and risk of jaundice, without evidence of liver inflammation. ATV competitively inhibits a key enzyme (uridine-glucuronosyl transferase (UGT) 1A1) responsible for bilirubin conjugation. Elevations of serum indirect and total bilirubin, without evidence of ongoing liver inflammation, are common during treatment with ATV, and related to ATV serum levels as well as certain genotypes involved in the expression of UGT 1A1 activity.^{25–27} In P1020A, 9% of patients had bilirubin levels > 5.1 times the upper limit of normal, and the incidence of jaundice was 1.4%. Despite the higher mg/kg doses required in these patients, given to achieve specified target concentrations, the rate of hyperbilirubinemia and jaundice was comparable to that reported for adults on ATV-containing regimens. In studies of ARV-naïve and experienced adults, on ATV/RTV or unboosted ATV, the rate of combined grade 3 (2.6–5.0×ULN) and grade 4 (>5.0×ULN)

elevations of total bilirubin ranged from 30 to 53% with 4.2–9 % having levels $>5.0 \times \text{ULN}$. Jaundice was reported in 3%–7%. The incidence of hyperbilirubinemia and jaundice was increased in those on ATV/RTV compared to unboosted RTV.^{9, 27}

There was a low incidence of gastrointestinal complaints in P1020A; only one (1%) of the 142 subjects reported here discontinued study drug for persistent gastrointestinal upset. In the BMS 045 and CASTLE studies, 3% of adults on ATV/RTV developed grade 2–4 diarrhea and 3–5% nausea, compared to 10–13% and 3–7%, respectively, of those on lopinavir/RTV.^{9, 16} Although there was a significant incidence of prolonged PR intervals on electrocardiogram monitoring, the prolongations were not believed to be clinically significant. Mild prolongation ($>98\%$ of normal range for age) of PR intervals were noted in 20% of subjects, and 1.4% had more prolonged PR intervals (first-degree atrio-ventricular (AV) block). No subject had a second-degree AV block. Two subjects had grade 3 bradycardia. Among HIV-infected adults treated with ATV, 5–5.9% of subjects were noted to have asymptomatic first-degree AV block, and in one study the rate was the same for adults on ATV/RTV or lopinavir/RTV.^{28, 29}

In the present study, TG levels did not increase from baseline through 48 weeks of treatment. Median TC did increase from baseline through 48 weeks, but even at 48 weeks, only 5.7% of subjects had TC levels above 199 mg/dL. In contrast, in a multisite observational study of 2000 HIV-infected children on CART, 13% developed a TC >220 mg/dL over a median follow up of 50 months.³⁰ In a single site study of 178 children on CART, 72.8% had TC >180 mg/dL and 53.4% had TC >199 mg/dL.³¹ In both pediatric studies, use of a PI was associated with elevated TC.

ATV use in adults has been associated with less hyperlipidemia than reported with many other PI-containing CART regimens.^{12, 13} In a meta-analysis, ATV and ATV/RTV were associated with less impact on lipids than other boosted PIs; however, ATV/RTV did result in increased lipid values compared to unboosted ATV.¹²

Limitations of this study include that it was a safety and dose-finding study, not powered to assess virologic or immunologic efficacy. Patients underwent individual dose adjustments, if needed, to meet protocol defined PK parameters; therefore, virologic and immunologic results may not be generalizable to clinical settings.

Protocol 1020A has demonstrated that protocol-defined PK parameters could be met with once daily ATV, with acceptable tolerability, a low level of serious adverse events, and acceptable long-term rates of virologic and immunologic response in children 6 months to 21 years of age. In children less than six years of age receiving the powder formulation of ATV, we were unable to achieve acceptable PK parameters without RTV boosting; use of this formulation should always be administered with RTV boosting. For the youngest cohort, three to six months of age, wide inter-patient variability in PK results prevented us from recommending an optimal dose. Further research is underway in this age group.

ATV with/without RTV boosting, represents an important once daily option for pediatric and adolescent patients initiating a PI-based CART regimen. For children and adolescents

initiating unboosted ATV/c, higher doses than presently recommended may be required, if the goal is to replicate drug exposures consistent with this study.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline Demographics and Immune Status

Group Dose mg/m2/day Formulation	Group 3 520 Capsule	Group 4 620 Capsule	Group 5 310 Powder +RTV ¹	Group 6 310 Powder +RTV	Group 7 205 Capsule +RTV	Group 8 205 Capsule +RTV	Group 5A 310 Powder +RTV	Total
Total Number of patients	21	25	21	26	24	14	11	142
Number with no dose adjustments through week 48	14	19	11	15	20	13	8	100
Gender: Female	11 (52%)	18 (72%)	8 (38%)	12 (46%)	11 (46%)	9 (64%)	6 (55%)	75 (53%)
Race/Ethnicity*: White	4 (19%)			1 (4%)				5 (4%)
Black	14 (67%)	17 (71%)	18 (86%)	18 (69%)	17 (74%)	8 (57%)	10 (91%)	102 (73%)
Hispanic	3 (14%)	7 (29%)	2 (10%)	7 (27%)	5 (22%)	5 (36%)	1 (9%)	30 (21%)
Other			1 (5%)		1 (4%)	1 (7%)		3 (2%)
Age(yrs) Median Range	8.6 6.3–12.5	14.3 13.1–20.2	1.2 0.3–2	4.4 2–12	9 5.6–12.7	17 13.9–21	0.4 0.3–0.5	7 0.3–21
CD4 Count (cells/mm ³) Median Range	374 105–963	286 11–476	1306 392–4875	466 62–1537	540 24–1800	334 1–548	2125 583–2715	457 1–4875
CD4 Percent Median Range	18 7–36	14 1–39	19 7–53	16 2–34	21 1–43	19 0–40	35 10–46	18 0–53
Log ₍₁₀₎ RNA Median Range	4.4 3.5–5	4.7 3.6–6.5	5 4.4–5.6	4.8 4.1–5.1	4.5 3.4–5	4.3 3.5–5	5 5–6.5	4.8 3.4–6.5
ARV ² -Experienced	11 (52%)	10 (40%)	5 (24%)	10 (38%)	11 (46%)	7 (50%)	6 (55%)	60 (42%)

¹ RTV- ritonavir² ARV-antiretroviral therapy

* -2 subjects' race unknown

Table 2Rate of Virologic Response (VL¹ < 400cpm) to ATV²-Based Regimens^{3,4}

	<u>Week 24</u>	<u>Week 48</u>	<u>Week 96</u>
All subjects	60.4%	58.5%	49.6%
(N=142)	52%, 69%	50%, 65%	41%, 58%
95% CI	N=139	N=142	N=135
ARV-Naïve	73.4%	69.5%	57.0%
ARV-Experienced	43.3%	43.3%	39.3%
No dose Adjustment ^{**}	56.6%	53.0%	41.3%
(N=100)	46%, 66%	43%, 63%	30%, 53%
95% CI ⁵	N=99	N=100	N=80
ARV-Naïve	70.4%	63.6%	51.1%
ARV-Experienced	40.0%	40.0%	27.3%

¹ VL-Viral load, plasma HIV RNA levels² ATV-Atazanavir³ Combines all age cohorts, formulations, and with/without RTV boosting⁴ ARV- Antiretroviral therapy⁵ CI- Confidence Intervals^{**} Patients who did not have pharmacokinetic-driven dose adjustments at week 1 and/or week 56 per protocol.

Table 3
Effect of Atazanavir Based Therapy on Total Cholesterol (TC) and Triglycerides (TG)

Week	Total N	TC < 170 mg/dL N (%)	TC: 170–199 mg/dL N (%)	TC > 199 mg/dL N (%)	TG < 150 mg/dL N (%)	TG 150 mg/dL N (%)
0	142	136 (96%)	4 (3%)	2 (1%)	105 (74%)	37 (26%)
24	117	94 (80%)	16 (14%)	7 (6%)	82 (70%)	35 (30%)
48	105	73 (69.5%)	26 (24.8%)	6 (5.7%)	90 (86%)	15 (14%)