ACTHIV15

Demographic and Clinical Characteristics of Patients Living With HIV Treated With Darunavir- and Atazanavir-based Regimens in the Real-world Setting

Xiaolong Jiao,[1,*] Keith J. Dunn,[1] Jianbin Mao,[2] Michael P. Johnson,[2] Kimberly Woodruff,[1] Neeta Tandon[1]

[1]Janssen Scientific Affairs, LLC, Titusville, NJ; [2]Optum, Eden Prairie, MN.

*Presenting author.

Introduction

- Multiple protease inhibitors (PIs) have been approved by the US Food and Drug Administration for the treatment of human immunodeficiency virus (HIV)-1 infection in the United States (US), and darunavir (DRV) is the latest approval (2006) in this class[1]
- According to current guidelines (2016) from the US Department of Health and Human Services (DHHS), a DRV/ritonavir (r)-based regimen is the only PI-based Recommended regimen for treatment-naive HIV-1–infected patients[2]
  - DRV/cobicistat (c), as well as atazanavir (ATV)/r and ATV/c, are each considered part of an Alternative regimen
  - Lopinavir (LPV)/r was removed from the list of Other regimens because regimens containing this PI combination have a larger pill burden and greater toxicity than other currently available options
- In comparing DRV to ATV, a phase 3, randomized clinical trial conducted by the AIDS Clinical Trials Group (ACTG 5257) demonstrated superior combined virologic efficacy and tolerability with DRV/r versus ATV/r, and the development of treatment-emergent antiretroviral (ARV) agent resistance was more common with ATV/r than DRV/r[3]
- It is important to understand the demographic and clinical characteristics of the patients who receive DRV- and ATV-based regimens beyond the clinical trial setting

Objective

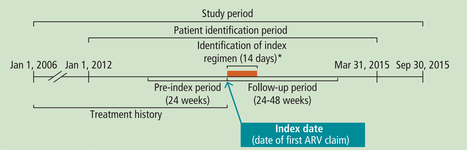
- To describe demographic and clinical characteristics of HIV-1–infected patients treated with DRV- or ATV-based ARV regimens using data from a large US population with commercial or Medicare insurance

Methods

Study Design

- Retrospective cohort study using administrative claims data from the Optum Research Database (ORD) and the Impact National Benchmark Database (IMPACT). Patients were identified using data from January 1, 2012 to March 31, 2015 (**Figure 1**)
  - The date of the first pharmacy fill for an ARV agent was designated as the index date

Figure 1. Study design.



*The index regimen included any ARV agent filled within 14 days of the index date.

- Inclusion criteria:
  - Adults (aged ≥18 years as of the year of the index date)
  - Evidence of HIV-1 diagnosis (defined as International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] codes: 042, 795.71, V08)
  - Continuous enrollment with medical and pharmacy benefit coverage for 24 weeks prior to the index date (pre-index period) and ≥24 weeks beginning on the index date (follow-up period)
  - ≥1 pharmacy claim for either DRV/r 800 mg once daily (QD), DRV/c 800 mg QD, ATV/r, ATV/c, or LPV/r (plus ≥2 nucleos[t]ide reverse transcriptase inhibitors [NRTIs] in addition to the PI)
- Exclusion criteria:
  - Evidence of HIV-2 diagnosis at any time during the study period
  - Presence of >1 anchor agent (i.e., DRV, ATV, LPV)
  - Lack of a boosting agent and/or lack of ≥2 NRTIs in the regimen
  - For patients in the DRV group, a dose other than DRV 800 mg QD at the first fill

Data Sources

- ORD is a proprietary research database that contains administrative, medical, and pharmacy claims data (1993 to present) for both commercial and Medicare Advantage enrollees. Data are geographically diverse and fairly representative of the privately insured US population. For 2015, data for ~15 million individuals with both medical and pharmacy benefit coverage were available
- IMPACT is a comprehensive, de-identified, US healthcare claims database that is representative of the commercially insured and Medicare population in the US. It contains inpatient, outpatient, and pharmacy claims; lab results; and enrollment information on ~29.2 million lives (2004 to present)

Measures

- Patient demographic characteristics were assessed and included age, gender, race/ethnicity, geographic region, insurance type, and data source (i.e., ORD or IMPACT)
- Clinical characteristics were assessed during the 24-week pre-index period and included the following:
  - Modified Quan-Charlson comorbidity score and conditions (excluding HIV/acquired immunodeficiency syndrome [AIDS])[4]
  - Presence of an AIDS-defining condition and/or opportunistic infection diagnosis (based on ICD-9-CM diagnosis codes)
  - Presence of potential opportunistic infections (based on medication claims; see **Figure 4** footnote for a list of medications)
  - Among patients with available HIV RNA viral load or CD4+ count results, a viral load >1,000 copies/mL and/or a low CD4+ count (defined as <200 cells/mm³)
  - Hyperlipidemia (defined as ≥1 of the following: a triglycerides result ≥150 mg/dL, a total cholesterol result ≥200 mg/dL, or a low-density lipoprotein cholesterol result ≥130 mg/dL)
  - Diabetes (defined as ≥2 medical claims [≥30 days apart] with a diagnosis code for diabetes [ICD-9-CM: 250.xx])

Statistical Analyses

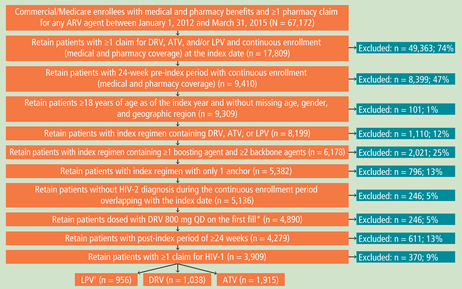
- Descriptive statistics were conducted; numbers and percentages are reported for categorical variables, and mean ± standard deviation (SD) is reported for continuous variables
- *P* values were calculated using univariate statistics (Pearson chi-square test for categorical variables and *t* test for continuous variables)

Results

Study Population Identification

- Among 67,172 enrollees with medical and pharmacy benefits and ≥1 pharmacy claim for any ARV agent during the patient identification period, 3,909 individuals met all inclusion criteria (**Figure 2**)
  - 1,038 patients who used DRV and 1,915 patients who used ATV were included in the analysis. The 956 patients who used LPV were not evaluated further due to removal of LPV from US DHHS guidelines

Figure 2. Identification of study population.



*For patients who had a claim for DRV.
†The LPV group was included in the initial analysis, but not evaluated further due to removal of LPV from US DHHS guidelines.

Baseline Demographic Characteristics

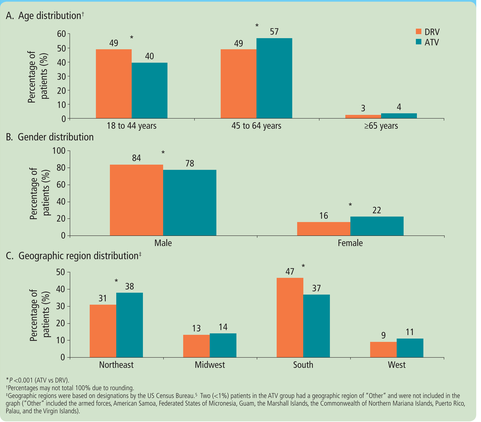
- The majority of patients in both the DRV and ATV groups were identified in the ORD (69% and 63%, respectively), and the remaining patients were from IMPACT (31% and 37%, respectively; **Table 1**)
- On average, patients in the DRV group were significantly younger than patients in the ATV group (mean [SD] ages: 44 [11] and 47 [10] years; *P* <0.001; **Table 1**)
  - Correspondingly, the percentage of patients aged 18 to 44 years was greater in the DRV versus ATV group (49% vs 40%; *P* <0.001); the percentage of patients aged 45 to 64 years was lower in the DRV versus ATV group (49% vs 57%; *P* <0.001; **Figure 3A**)
- A higher percentage of patients in the DRV versus ATV group was male (84% vs 78%; *P* <0.001; **Figure 3B**)
- Similar percentages of patients in the DRV and ATV groups were white (36% vs 33%) and African American/black (20% vs 19%; **Table 1**)
- A higher percentage of patients in the DRV versus ATV group was from the South (47% vs 37%; *P* <0.001), and a lower percentage was from the Northeast (31% vs 38%; *P* <0.001; **Figure 3C**)

Table 1. Baseline Demographic Characteristics*

Characteristic	DRV (n = 1,038)	ATV (n = 1,915)	*P* value (ATV vs DRV)
Age, y, mean (SD) [median]	44 (11) [45.0]	47 (10) [47.0]	<0.001
Race/ethnicity, n (%)†			
White	373 (36)	640 (33)	NS
African American/black	203 (20)	360 (19)	NS
Asian	11 (1)	15 (1)	NS
Hispanic	108 (10)	143 (7)	0.006
Other	3 (<1)	7 (<1)	NS
Unknown‡	19 (2)	42 (2)	NS
Not available§	321 (31)	708 (37)	<0.001
Data source, n (%)			
ORD	719 (69)	1,212 (63)	0.001
IMPACT	319 (31)	703 (37)	0.001

NS, not significant.
*One patient in the DRV group received DRV/c; all others received DRV/r. No patients in the ATV group received ATV/c; all received ATV/r.
†Percentages may not total 100% due to rounding.
‡Patients had missing data on race/ethnicity, but other socioeconomic status data were available.
§Patients without any socioeconomic status data available.

Figure 3. Baseline demographic characteristics.

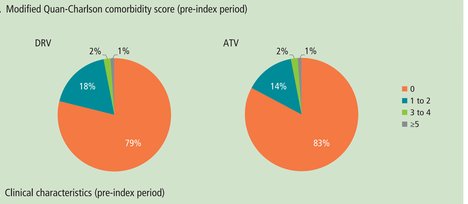


*P <0.001 (ATV vs DRV).
†Percentages may not total 100% due to rounding.
‡Geographic regions were based on designations by the US Census Bureau.[5] Two (<1%) patients in the ATV group had a geographic region of "Other" and were not included in the graph ("Other" included the armed forces, American Samoa, Federated States of Micronesia, Guam, the Marshall Islands, the Commonwealth of Northern Mariana Islands, Puerto Rico, Palau, and the Virgin Islands).

Pre-index Period Clinical Characteristics

- A higher percentage of patients in the DRV versus ATV group had a modified Quan-Charlson comorbidity score ≥1 (21% vs 17%; *P* <0.01; **Figure 4A**)
  - More patients in the DRV versus ATV group had a comorbidity of malignancy (5% vs 3%; *P* = 0.014); all other modified Quan-Charlson comorbidities were not statistically different between treatment groups (**Table 2**)
- A higher percentage of patients in the DRV versus ATV group had an AIDS-defining condition and/or opportunistic infection diagnosis (15% vs 7%; *P* <0.001), potentially used opportunistic infection medications (34% vs 25%; *P* <0.001), and had HIV RNA >1,000 copies/mL and/or a low CD4+ count (21% vs 14%; *P* <0.001; **Figure 4B**)
- The percentages of patients with hyperlipidemia (33% vs 34%) and diabetes (4% vs 4%) were not significantly different between the DRV and ATV groups

Figure 4. Pre-index period comorbidities and clinical characteristics.



OI, opportunistic infection.
*P <0.001 (ATV vs DRV).
†Potential OI medications included various formulations of acetaminophen, amphotericin B, atovaquone, atovaquone/proguanil, azithromycin, cidofovir, clarithromycin, clindamycin, dapsone, fluconazole, foscarnet, ganciclovir, isoniazid, itraconazole, leucovorin, pentamidine, primaquine, pyrimethamine, rifabutin, rifamp/isoniazid/pyrazinamide, rifampin, rifampin/INH/pyrazinamide, rifampin/isoniazid, rifampin/isoniazid/pyrazinamide, sulfamethoxazole/trimethoprim, valganciclovir, and voriconazole.

Table 2. Modified Quan-Charlson Comorbid Conditions*

Parameter	DRV (n = 1,038)	ATV (n = 1,915)	*P* value (ATV vs DRV)
Modified Quan-Charlson comorbidity score, mean (SD)	0.40 (0.92)	0.32 (0.82)	0.013
Comorbidity, n (%)			
Chronic pulmonary disease	77 (7)	120 (6)	NS
Mild liver disease	58 (6)	104 (5)	NS
Any malignancy, including leukemia and lymphoma	52 (5)	61 (3)	0.014
Renal disease	38 (4)	52 (3)	NS
Heart failure	15 (1)	17 (1)	NS
Diabetes with chronic complication	14 (1)	21 (1)	NS
Rheumatologic disease	6 (1)	5 (<1)	NS
Metastatic solid tumor	3 (<1)	3 (<1)	NS
Hemiplegia or paraplegia	2 (<1)	9 (<1)	NS
Moderate or severe liver disease	2 (<1)	1 (<1)	NS
Dementia	0	1 (<1)	NS

*Excluding HIV/AIDS.

Discussion

- In clinical studies of DRV versus ATV, patients are randomized to control for baseline characteristics, which leads to similar patient populations in each treatment group. In this study using real-world data, we found that patients who received DRV-based regimens were younger, had more advanced HIV infection, and had more comorbidities than patients who received ATV-based regimens
- Other real-world studies of DRV/r and ATV/r have also demonstrated that patients receiving DRV-based regimens are generally less healthy than those receiving ATV-based regimens[6,7]
- Such differences in baseline characteristics for patients receiving DRV versus ATV may reflect the individualized approach taken by healthcare providers when making clinical decisions (e.g., to maximize the benefits of different ARV regimens in different patients)
  - With regard to the potential metabolic effects of ARV agents, clinical studies have not demonstrated substantial differences between DRV and ATV[8-10]
- This current study had several limitations
  - This study utilized administrative claims data from a US commercially insured and Medicare Advantage–insured population and, thus, the results may not be generalizable to other populations that are limited by the sample criteria (e.g., noninsured populations, untreated HIV/AIDS patients)
  - As a claims-based analysis, this study may be subject to inherent limitations of the source data (e.g., selection bias, coding errors, misclassifications, prescription fill and refill information that represents medication receipt but not necessarily that the medication was taken as prescribed)
  - The analysis focused on claims data obtained from 2012 to 2015, which may not reflect current practice patterns based on US DHHS guidelines (e.g., only 1 patient used cobicistat as a boosting agent)

Conclusion

- **In the real-world setting, patients treated with DRV-based regimens were younger, had more advanced HIV-1 infection, and had more comorbidities at baseline compared with patients treated with ATV-based regimens. Such differences should be considered when comparing outcomes between DRV and ATV treatment regimens**

References

1. AIDSinfo. https://aidsinfo.nih.gov/education-materials/fact-sheets/21/58/fda-approved-hiv-medicines#. Accessed March 28, 2017.
2. US DHHS Panel on Antiretroviral Guidelines for Adults and Adolescents. https://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf. Accessed January 26, 2017.
3. Lennox JL, et al. *Ann Intern Med.* 2014;161(7):461-471.
4. Quan H, et al. *Am J Epidemiol.* 2011;173(6):676-682.
5. US Census Bureau. http://www.census.gov/econ/census/help/geography/regions_and_divisions. html. Accessed October 4, 2016.
6. Farr AM, et al. *J Med Econ.* 2016;19(4):386-396.
7. Charpentier C, et al. *J Antimicrob Chemother.* 2014;69(10):2819-2825.
8. Skiest D, et al. Presented at: Conference on Retroviruses and Opportunistic Infections (CROI); February 27-March 2, 2011; Boston, MA.
9. Aberg JA, et al. *AIDS Res Hum Retroviruses.* 2012;28(10):1184-1195.
10. Overton ET, et al. *HIV Clin Trials.* 2016;17(2):72-77.

Acknowledgments

- This study was funded by Janssen Scientific Affairs, LLC. X. Jiao, K.J. Dunn, K. Woodruff, and N. Tandon contributed to the design of the study and interpretation of the data; J. Mao contributed to the design of the study, statistical analysis, and interpretation of the data; M.P. Johnson contributed to the statistical analysis and interpretation of the data. All authors contributed to drafting the poster and approved the final version.
- The authors would like to thank Shiqiang Li and Yiyu Fang, both employees of Optum, for programming the study dataset and variables. Medical writing support was provided by Courtney St. Amour, PhD, of MedErgy, and was funded by Janssen Scientific Affairs, LLC.
- If you have any additional questions or would like to request a copy of this poster, call +1-800-JANSSEN (+1-800-526-7736) or go to www.janssenMD.com.
- For more information about darunavir at this conference, please see Poster ACTHIV18 entitled "Evaluation of Cardiovascular Disease (CVD) Risk in HIV-1–infected Patients Treated With Darunavir/Ritonavir (DRV/r)."

An electronic version of the poster can be viewed by scanning the QR code.
The QR code is intended to provide scientific information for individual reference.
The PDF should not be altered or reproduced in any way.

Poster presented at the 11th Annual American Conference for the Treatment of HIV (ACTHIV); April 20-22, 2017; Dallas, Texas.