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Real-World Use of Ibalizumab in Physician Office infusion Centers (POICs)

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Abstract

Background: Ibalizumab-uiyk (IBA) was recently approved for the treatment of multi-drug resistant HIV-1 infection in patients (pts) failing other antiretroviral regimens. Clinical trial data demonstrated a decrease in HIV-1 viral load in 83% and 43% of pts (n=40) receiving IBA for 2 and 25 weeks (wks), respectively. Real-world post marketing data are needed. This pilot study reports the experience of IBA utilization in POICs.

Methods: Medical records of pts receiving intravenous IBA from approval through 4/2019 were reviewed. Data collected include demographics, infection and treatment history, IBA regimen and adverse events. Plasma HIV-1 RNA viral load (log_{10} copies/mL) and CD4 count (cells/μL) were collected at baseline and as available during therapy. Based on available follow-up (FU) labs, response was assessed at 4 -10 wks (FU 1), 14-22 wks (FU 2), and 24-37 wks (FU 3).

Results: Nine pts (mean age: 48±11 years, 67% male) from 7 POICs received IBA for a median duration of 33 wks (range, 4-43). Median length of HIV-1 diagnosis was 22 yrs (range, 8-25). Resistance to ≥1 drug in at least 3 drug classes was reported in 56%. All pts received at least one concurrent anti-retroviral agent. IBA was initiated at 2000 mg followed by 800 mg every 2 wks. All pts received infusions as scheduled (151 total infusions) except for one requiring a second loading dose. Baseline mean CD4 count and viral load were 49 cells/μL and 4.9 log_{10} copies/mL, respectively. Labs obtained at FU 1 indicated a decrease in viral load of at least 0.5 log_{10} copies/mL in 6/8 pts (75%); a mean reduction of 2.1±1.8 log_{10} copies/mL (Table 1). Mean HIV-1 titers available for pts at FU 2 (n=6) and FU 3 (n=7) were 3.1±2.0 and 3.2±2.6 log_{10} copies/mL, respectively. Mean CD4 counts were 65±57 cells/μL at FU 1, 96±61 cells/μL at FU 2 and 88±82 cells/μL at FU 3. Adverse events were reported in 8 pts (89%), most common itching/rash, diarrhea and abdominal pain. None resulted in discontinuation of IBA.

Conclusion: This study confirms the antiviral activity of IBA in pts with advanced HIV-1 infection in the real-world setting. We observed well-tolerated therapy with an early reduction in HIV-1 viral load in 75% of pts, followed by a 43% reduction ≥24 wks, consistent with the clinical trial.

Background

Treatment options for pts infected with multidrug resistant HIV-1 are limited and medications exploiting new antiretroviral targets are needed [1].

Ibalizumab (IBA), the first humanized monoclonal antibody to CD4, was recently approved for the management of heavily treated HIV-1 pts as part of combination antiretroviral therapy [2]. IBA has demonstrated safety and efficacy in the treatment of HIV-1 in a phase 3 clinical trial [3]. However, real-world data are missing.

The aim of this study was to evaluate antiviral activity and safety of IBA administered in the outpatient setting.

Methods

Study design: observational, retrospective multicenter study

Study location: U.S. physician office infusion centers (n=7)

Study population: HIV-1 pts receiving IBA between May 2018 and August 2019

Data collection: demographics (age, sex), clinical characteristics (length of HIV-1 diagnosis, HIV-1 viral load, and CD4 cell count), baseline genotypic resistance pattern and IBA regimen including concurrent antiretroviral drugs

Safety: incidence and type of adverse events during IBA treatment

Antiviral activity: HIV-1 viral load and CD4 counts at week 10 (FU 1), week 22 (FU 2), week 37 (FU 3), and week 58 (FU 4), respectively

Analysis: continuous data are reported as mean ± SD or medians (range) and interquartile range (IQR), categorical data as counts and percentages.

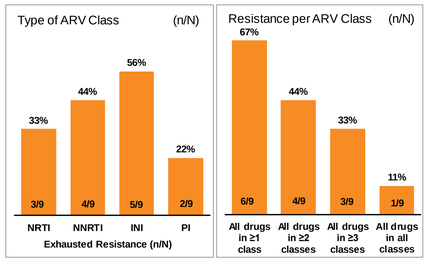
Results

Study Population

Demographics and Clinical Characteristics

Parameter	Results (N=9)
Demographics	
Age, years	
mean ± SD	48 ± 11
median (range)	49 (25-67)
Male, n (%)	6 (67)
Clinical Characteristics	
Length of HIV-1 diagnosis, years	
mean ± SD	18 ± 7
median (range)	22 (8-25)
HIV-1 viral load, log_{10} copies/mL	
mean ± SD	4.9 ± 0.8
median (range)	4.9 (3.1 - 6.0)
category, n (%)	
< 100,000 copies /mL	5 (56)
> 100,000 copies /mL	4 (44)
CD4 count, cells/μL	
mean ± SD	49 ± 64
median (range)	47 (0 - 205)
category, n (%)	
> 200 cells/μL	1 (11)
< 100 cells/μL	8 (89)
< 10 cells/μL	3 (33)

Baseline Resistance to Antiretroviral (ARV) Therapy



Abbreviations. ARV: antiretroviral; NRTI: nucleoside/nucleotide reverse transcriptase inhibitor; NNRT: non-nucleoside transcriptase inhibitor; INI: integrase inhibitor; PI: protease inhibitor.

- Exhausted resistances were most frequently observed for INI (56%) and NNRTI (44%) drug classes
- 67% of pts had resistance to all drugs in at least 1 ARV class, 44% to all drugs in ≥2 classes, 33% to all drugs in ≥3 classes, and 11% to all approved drugs in all classes

Therapy & Safety

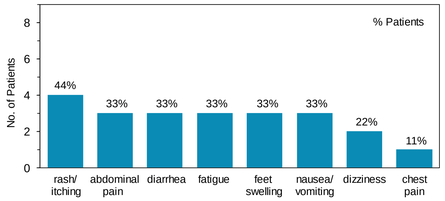
IBA Therapy Characteristics

Patient ID	Length of IBA Therapy (weeks)*	No. of Office Visits*	Concurrent ARV Therapy to IBA	Resistance by AVR Drug Class
#1	45	24	darunavir/cobicistat	NRTI: resistant to all NNRTI: resistant to all INI: resistant to all PI: resistant to all but 1
#2	44	22	efavirenz lopinavir/ritonavir maraviroc	NRTI: resistant to all NNRTI: sensitive to all INI: resistant to all PI: sensitive to all
#3	53	30	abacavir/lamivudine doravirine	NRTI: resistant to all NNRTI: resistant to all INI: resistant to all PI: resistant to all
#4	58	31	tenofovir alafenamide maraviroc	NRTI: resistant to 3 NNRTI: resistant to 1 INI: resistant to 2 PI: sensitive to all
#5[1]	40	22	emtricitabine/rilpivirine/ tenofovir alafenamide	NRTI: sensitive to all NNRTI: sensitive to all INI: sensitive to all PI: sensitive to all
#6	40	21	darunavir/cobicistat dolutegravir doravirine	NRTI: resistant to 5 NNRTI: resistant to all INI: sensitive to all PI: sensitive to all
#7	26	14	tenofovir alafenamide dolutegravir	NRTI: resistant to all but 2 NNRTI: sensitive to all INI: resistant to all PI: resistant to all but 1
#8	17	9	atazanavir tenofovir alafenamide darunavir ritonavir	NRTI: resistant to all but 1 NNRTI: resistant to all INI: resistant to all PI: resistant to all
#9	4	3	emtricitabine/rilpivirine/ tenofovir alafenamide	NRTI: sensitive to all NNRTI: resistant to 2 INI: resistant to 2 PI: sensitive to all

*; calculated per patient from date of first IBA infusion to last with available labs.
1; pt #5 experienced unsatisfactory response to all ARV drug classes despite the above results of genotypic assessment.

- All pts received an initial IBA dose (2000 mg/kg IV) followed by maintenance doses (800 mg/kg IV) every 2 weeks
- IBA infusions were received as scheduled by all except for one pt, who received a 2nd loading dose

Safety of IBA Therapy



- 8 pts experienced a total of 23 adverse events
- No infusion site reactions or discontinuation of IBA due to adverse events were reported

Antiviral Activity

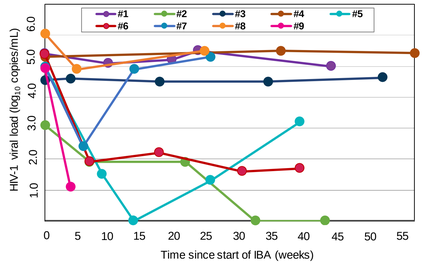
HIV-1 Viral Load and CD4 Count During IBA Therapy

Parameter	Baseline (n=9)	FU 1 4-10 wks (n=8)	FU 2 14-22 wks (n=6)	FU 3* 24-37 wks (n=8)	FU 4* 40-58 wks (n=6)
HIV-1 viral load, log_{10} copies/mL					
mean ± SD	4.9 ± 0.8	2.8 ± 1.8	3.1 ± 2.0	3.5 ± 2.5	2.9 ± 2.1
median (IQR)	4.9 (0.5)	2.2 (2.8)	3.3 (2.8)	4.9 (4.3)	3.9 (2.8)
median reduction from baseline		-2.7	-1.6	-0.07	-1.6
no. pts with decrease of ≥0.5 log_{10} copies/mL		6/8 (75%)	3/6 (50%)	4/8 (50%)	3/6 (50%)
CD4 count, cells/μL					
mean ± SD	49 ± 64	65 ± 57	96 ± 61	77 ± 82	111 ± 95
median (IQR)	47 (50)	58 (78)	102 (91)	60 (114)	80 (126)

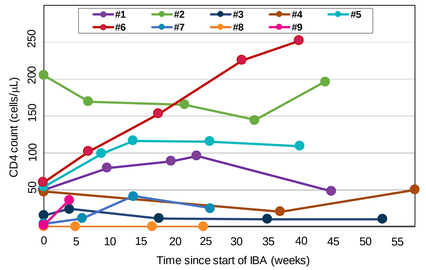
*; additional data not included in submitted abstract.

- HIV-1 viral load reduction was highest at FU 1, with 75% of pts experiencing a decrease of at least 0.5 log_{10} copies/mL
- Mean CD4 count increased from 49 cells/μL at baseline to 111 cells/μL at week 58, largely due to one responder
- 2 pts discontinued IBA at weeks 6 and 30 due to death and non-response to IBA, respectively

Changes in HIV-1 Viral Load by Patient



Changes in CD4 Count by Patient



Discussion

To our knowledge, this study presents the first real-world data on the antiviral activity and safety of IBA administered to heavily pre-treated HIV-1 patients in POICs.

- 9 patients (mean age: 48 years, 67% male) received IBA in conjunction with ARV drugs for a median duration of 40 weeks (range, 4 to 53)
- At baseline, 67% of patients reported resistance to all drugs in at least one ARV class, including one patient with resistance to all approved ARV drugs. Resistance was most frequently reported for INIs (56%) and NNRTIs (44%).
- IBA was well tolerated and no patient discontinued therapy due to adverse events. The most common adverse event was rash/itching (44%) and 2 pts discontinued IBA at weeks 6 and 30.
- Antiviral activity of IBA indicated the greatest reduction in viral load between 4 and 10 weeks with 75% of patients experiencing a decrease of at least 0.5 log_{10} HIV-1 copies/mL. Continued IBA therapy indicated a decrease in viral load of 50% each at week 22, week 37, and week 58.
- Increase in CD4 counts occurred in 55% of pts, however, overall remained relatively unchanged over time. One patient attained a CD4 count >200 cell/μL while on IBA therapy.
- Limitations of the study include the small sample size and retrospective study design.

Conclusion

This pilot study provides the first real-world experience of efficacy and safety of IBA in patients with advanced HIV-1 disease:

- **Reduction of HIV-1 viral load was highest between weeks 4 and 10 following the start of IBA. Lower response rates were observed over time.**
- **IBA was safe and well tolerated.**
- **Additional studies are needed to investigate long-term efficacy of IBA in HIV-1 patients.**

References

1. Bettiker RL, Koren DW, Jacobson JM. Ibalizumab. Curr Opin HIV AIDS 13 (4): 354-8, 2018.
2. Theratechnologies Inc., Montreal, Canada. TROGARZO (ibalizumab-uiyk) injection, intravenous use. Prescribing information 03/2018.
3. Emu B, Fessel J, Schrader S et al. Phase 3 study of ibalizumab for multidrug-resistant HIV-1. N Engl J Med 379 (7): 645-54, 2018.