The use of combination long-acting injectable antiretroviral agents indicated for heavily-treatment experienced patients with multi-drug resistant HIV-1 infection; a real-world case series on the use of ibalizumab and lenacapavir.

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Introduction

Multidrug resistance (MDR) may arise in people with human immunodeficiency virus (PWH), with extensive prior exposure to antiretrovirals (ARVs). For such heavily treatment-experienced (HTE) patients it can be challenging to establish and maintain virologic control, due to the dearth of active ARVs with which to construct a fully suppressive regimen. Ibalizumab and lenacapavir are two long-acting injectable (LAI) ARVs specifically indicated for this patient population, but their use in combination has not been formally studied. Here we present a case series (n=6) of the use of these two agents in real-world clinical practice.

Results

Figure 1: Summary of baseline characteristics

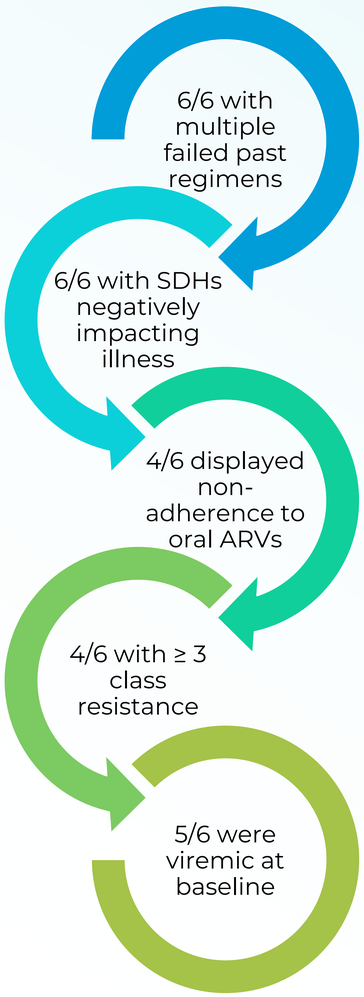

Table 1: Individual case summaries

Case n°	Previous adherence issues or barriers	Resistance profile				VL and CD4 before current regimen	Current regimen	VL and CD4 after current regimen	Time of follow up	Case comments
		NRTI	NNRTI	PI	INSTI					
1	Denial of diagnosis, work schedule, caregiver for other family members, complexity of regimen.					**2930 copies/mL** 298 cells/mm^3	IBA, FTR, LEN	**220 copies/mL** 222 cells/mm^3	24 weeks	69 yo AA male. Depression is in remission on current regimen; current treatment is life sustaining.
2	High pill burden, renal toxicity, DDI with chemotherapy. D/M virus, and prior failure on fusion inhibitor.					**50 copies/mL** 364 cells/mm^3	IBA, FTR, LEN, 3TC	**<20 copies/mL** CD4 not done	32 weeks	50 yo white male. Very happy with less pills and has no side effects from the new regimen.
3	Pill burden, side effects, insurance issues, transportation barriers, lack of family/social support, and later development of dementia and memory loss.					**258 copies/mL** 330 cells/mm^3	IBA, FTR, LEN	**60 copies/mL** 266 cells/mm^3	40 weeks	66 yo black Hispanic male. Goal is to optimize regimen as much as possible in setting of multiple barriers.
4	Self-discontinued due to side effects. Has unstable housing. Taking intermittently, "when she can." Patient was resentful of having to take daily, life-sustaining tablets after acquiring HIV at such a young age.					**11000 copies/mL** 232 cells/mm^3	IBA, LEN	**3120 copies/mL** 204 cells/mm^3	8 weeks	28 yo AA perinatally infected female. Certified nursing aide. Patient extremely pill averse. Provider estimated she was 40-50% adherent to her oral ARV regimens.
5	Access issues with medication.					**1200000 copies/mL** <32 cells/mm^3	IBA, LEN	**455 copies/mL** 113 cells/mm^3	56 weeks	54 yo AA female. Diagnosed during pregnancy then LTFU. Prefers IBA infusion to IV push.
6	Nonadherence due to constipation. TDF discontinued to preserve renal health. 40-50% adherent to his antivirals.					**343000 copies/mL** <32 cells/mm^3	IBA, LEN	**60 copies/mL** 143 cells/mm^3	36 weeks	42 yo AA male on disability and unable to work. Patient receives IBA through home health nurse.

Key virologic outcomes:

- 100% saw ≥ 0.5log$_{10}$ decrease in VL from baseline
- 100% of viremic patients saw ≥ 70% decrease in VL from baseline
- 50% achieved suppression (≤ 200 copies/mL) at follow up

Discussion

This series illustrates the diversity of HTE PWH in the United States, spanning multiple age ranges, sex, ethnicities/races, socioeconomic status, and geographic regions. It demonstrates many of the different factors that can lead to suboptimal adherence, subsequent drug resistance, and regimen failure. Every PWH in this series experienced a sharp decrease in viral load upon initiation IBA and LEN (+/- oral ARVs) with 6/6 showing at least a 0.5log$_{10}$ decrease in VL from baseline to EOS, and 3/6 achieving suppression (≤ 200 copies/mL). In each case, LAI was chosen due to the barriers it reduces, such as pill burden, psychosocial issues, occasional missed daily doses, DDIs and treatment complexity, as well as good tolerability. Notably, 3/6 patients in this series were only on LAI. This series is limited by the lack of long-term follow-up in most cases.

Conclusion

The combination of two LAI ARVs for this population with high unmet need allows patients and providers more flexibility and control and can even provide the option for a fully non-oral regimen in certain cases. Some of these patients still have low level viremia despite treatment with two new active agents but are now clinically stable in the challenging setting of MDR HIV-1 treatment. Suppression is the goal with most patients, but in some situations, the goal might be to control viremia as much as possible and minimize further resistance. The use of IBA and LEN in combination appears to be efficacious, safe, and well-tolerated in this treatment experienced patient population, although more long-term experience is needed.

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3TC, lamivudine; AA, African American; CD4, cluster of differentiation 4; EOS, end of study; DDI, drug-drug interaction; FTR, fostemsavir; HTE, heavily treatment experienced; IBA, ibalizumab; INI, integrase inhibitor; LEN, lenacapavir; MDR, multi-drug resistance; NNRTI, non-nucleoside reverse transcription inhibitor; NRTI, nucleoside reverse transcription inhibitor; PI, protease inhibitor; PWH, people with HIV; SDH, social determinants of health; VL, viral load; YO, year old.