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Fostemsavir plus doravirine for the treatment of heavily treatment-experienced (HTE) people with HIV (PWH) with multi-drug resistant (MDR) HIV-1 infection: 48 weeks results in a real-life setting

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BACKGROUND

- **HTE** individuals, albeit a minority, represent a crucial demographic facing unique challenges in the context of HIV management.
- **Fostemsavir** is approved for the treatment of HIV-1 infection in HTE PWH with **MDR** HIV-1 infection.
- **Doravirine**, a new-generation NNRTI, stands out as a noteworthy addition to the ARV armamentarium. Its effectiveness even in presence of the K103N mutation, makes it a robust therapeutic option even for individuals contending with **resistances**.
- The aim of this study was to evaluate viroimmunological efficacy and clinical tolerability of this molecules over **48 weeks** in a real-life setting.

METHODS

- We selected **HTE-PWH** with MDR HIV-1 infection and **detectable viremia**.
- Participants switched to fostemsavir in combination with an **optimized background therapy** (OBT) with at least 2 active ARV molecules, one of them being doravirine.
- We collected clinical and viroimmunological data at baseline (BL, time of switch), 4W, 10W, 24W and 48W of follow-up.

	N tot = 10 (100.0)
Age, years (Median, IQR)	62.5 (61.0 – 64.5)
Gender, n (%)	
• Male	8 (80.0)
• Female	2 (20.0)
Risk factor for HIV acquisition, n (%)	
• MSM	3 (30.0)
• Heterosexual	3 (30.0)
• PWID	4 (40.0)
CDC stage C, n (%)	7 (70.0)
Time since HIV diagnosis, years (Median, IQR)	31.5 (29.5 – 34.3)
Time of exposure to ART, years (Median, IQR)	28.0 (26.8 – 32.3)
Zenith HIV-RNA, log10 copies/mL (Median, IQR)	5.6 (5.3 – 5.7)
Nadir CD4 cells, cells/mmc (Median, IQR)	38.5 (6.5 – 182.0)

Table 1. Characteristics of the study population.

RESULTS

- We enrolled **10** HTE-PWH. Characteristics of the population at BL are summarized in **Table1**.
- For 4 participants a previous **genotypic resistance testing** (GRT) was available, documenting resistance to at least 3 ARV classes; for the other 6 the GRT was not available at BL, but resistances were deducible from previous documented virological failures with antiretroviral agents belonging to at least 3 different classes.
- At **4W** a viroimmunological determination was available for 8/10 participants: one participant achieved virological suppression with target non detectable (TND), two participants achieved HIV-RNA levels < 50 cps/mL. One participant had HIV-RNA levels > 200 cps/mL.
- At **10W** a viroimmunological determination was available for 8/10 participants: none of the enrolled participants had TND; 3 participants had HIV-RNA levels < 50 cps/mL. One participant had HIV-RNA levels > 200 cps/mL.
- At **24W** a viroimmunological determination was available for 7/10 participants: no one had a TND; 4 participants had HIV-RNA levels < 50 cps/mL. One participant had HIV-RNA levels > 200 cps/mL.
- Out of the enrolled population, 5 participants reached **48 weeks** of follow-up: none of the participants had TND, 4 had HIV-RNA levels < 50 cps/mL. One participant had HIV-RNA > 200 cps/mL.
- During the study period we observed **5** treatment discontinuations, due to treatment-related gastrointestinal side effects in 2 cases, headache and insomnia in 1 case and persistent low-level viremia in the other 2 cases.
- Median **CD4 cells count** at BL was 741 cells (IQR 386 – 1315) with a median CD4/CD8 ratio of 0.81 (0.23 – 1.27). At 24W median CD4 cells count was 653 (265 – 1076) with a median CD4/CD8 ratio of 0.81 (0.24 – 1.45). At 48W median CD4 cells count was 526 (291 – 1398) with a median CD4/CD8 ratio of 0.78 (0.27 – 1.46).

CONCLUSIONS

- **Fostemsavir** in association with **doravirine** seemed to show good antiviral potency against MDR HIV-1.
- However, observations from our experience raise concern due to the apparently unfavourable immunological profile and tolerability, prompting the need for further evaluations.