20th EUROPEAN AIDS CONFERENCE
15-18 October 2025 | Paris, France
Abs eP156
EACS European AIDS Clinical Society

# Potential for replacing the boosted-PI with doravirine in ART-experienced subjects successfully treated with darunavir-cobicistat plus dolutegravir dual regimen

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DoDaco Cohort

## PURPOSE

Doravirine (DOR) retains full activity against many single resistance-associated mutations (RAMs) selected by older NNRTIs (1,2) and DOR may increase dolutegravir (DTG) exposure (3). Although not formally recommended as dual therapy in in people with HIV (PWH), real-life data support such a dual combination as switch option (4-6). We aimed to explore the potential for replacing darunavir-cobicistat DRV-c) with DOR in PWH receiving the dual combination of DTG + DRV/c in the DoDaco Cohort, based on the presence of RAMs in their historical genotypes.

## METHODS

The DoDaco Cohort includes antiretroviral-experienced PWH on DTG+DRV/c dual regimen from 7 HIV centers. In Italy. Cumulative plasma genotypic resistance testing (GRT) of all participants were evaluated for the presence of **NNRTI**-associated RAMs (namely: V106A/M, V108I, Y188L, G190S, F227C/L/V, M230I/L, L234I, K103N/P225H, K103N/L100I and K103N/Y181C) and their combinations conferring low, intermediate or high resistance, according to Stanford algorithms.

DRV/c was deemed replaceable by DOR if no major DTG RAMs were concomitantly

present, although, in selected cases with low-level DTG resistance, the double DTG dose (i.e. bid) was allowed for the option of DRV/c removal.

## CONCLUSIONS

According to historical genotypes, two thirds of PWH included in the DoDaco cohort are eligible for replacing DRV-c with DOR in the combination to DTG, with potential benefits in lipid profile, cardiovascular risk, drug-drug interactions and overall costs.

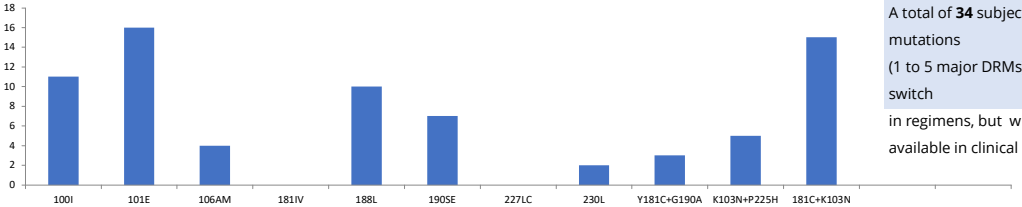
## RESULTS

A total of **327** individuals (66% males; median age 60 [IQR 55-63] years; median CD4+ count 618 (IQR 386–925] cells/ml, 118 (36%) had AIDS, median (IQR) duration of HIV therapy was 24 (19–28) years, 128 (39%) received more than 8 treatment lines) were included in our cohort. For those with available historical genotypes, RAMs were present in 240 (88%), **191** (70%), 67 (24%), and 18 (6.6%) cases for NRTI, **NNRTI**, PI and INSTI, respectively. DTG resistance (low to intermediate) was found in 18 (6,6 %) individuals. Figure 1 shows the distribution of NNRTI-associated mutations.

Among **219** (67% of the cohort) with documented NNRTI RAMS, 78/219 (35%) had **low, intermediate or high** DOR-associated resistance (Table 2).

DTG was not fully active in 2 individuals, so DRV/c may be replaceable by DOR in up to 247/327 (75%) PWH based on the historical genotypes if no specific contraindications. In 31/219 (14%) individuals, DTG bid may be desirable (based on the past INSTI genotype) if DRV/c removal is requested or considered.

Figure 1: Most frequent major NNRTI-resistance mutations (alone or in combination) for DOR




A total of **34** subjects had NNRTI-associated mutations
(1 to 5 major DRMs) in the past history, causing switch
in regimens, but without detailed list of mutations available in clinical notes.

Table 2: distribution of susceptibility to doravirine according to the past genotypic resistance in the DoDaco Cohort

| HIV Centre | PWH | PWH with NNRTI RAMs | Grade of susceptibility to doravirine by genotypic resistance (in 113 PWH) | | | |
|---|---|---|---|---|---|---|
| | | | Potentially Low | **Low** | **Intermediate** | **High** |
| **Bergamo** | 124 | 90 | 16 | 15 | 10 | 10 |
| **Milano** (L. Sacco) | 59 | 26 | 1 | 1 | 4 | 4 |
| **Monza** | 44 | 28 | 2 | 4 | 1 | 1 |
| **Pavia** | 50 | 40 | 8 | 3 | 7 | 3 |
| **Padova** | 27 | 19 | 5 | 6 | 3 | - |
| **Milano** (Santi Paolo e Carlo) | 6 | 4 | - | - | - | - |
| **Siena** | 17 | 12 | 3 | 2 | - | 4 |
| **Total** | 327 | 219 | 35 | **31** | **25** | **22** |

* according to the Stanford Algorithm interpretation

## ACKNOWLEDGEMENTS

All participants and investigators involved into the current study and their families.

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