20th EUROPEAN AIDS CONFERENCE
15-18 October 2025 | Paris, France
eP162
EACS European AIDS Clinical Society

The role of doravirine in the treatment of multidrug-resistant HIV: data from the PRESTIGIO Registry

T. Clemente[1], N. Capra[1], V. Malagnino[2,3], R. Lolatto[1], S. Lo Caputo[4], L. Comi[5], A. Giacomelli[6,7], G. Cenderello[8], M. Colafigli[9], S. Rusconi[6,10], M. Zazzi[11], A. Castagna[1,12], on behalf of the PRESTIGIO Study Group

1 IRCCS San Raffaele Scientific Institute, Infectious Diseases, Milan, Italy; 2 Policlinic of Tor Vergata, Infectious Diseases Clinic, Rome, Italy; 3 University of Rome Tor Vergata, Department of Systems Medicine, Rome, Italy; 4 Università di Foggia, A.O.U. Policlinico Foggia, Foggia, Italy; 5 ASST Papa Giovanni XXIII Hospital, Infectious Diseases Unit, Bergamo, Italy; 6 Università degli Studi di Milano, Department of Biomedical and Clinical Sciences, Milan, Italy; 7 ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, III Infectious Diseases Unit, Milan, Italy; 8 Sanremo Hospital, Infectious Disease Unit, Sanremo, Italy; 9 Ospedale regionale "Umberto Parini" di Aosta, Struttura Complessa di Malattie Infettive, Aosta, Italy; 10 Ospedale Civile di Legnano ASST Ovest Milanese, University of Milan, Legnano, Italy; 11 University of Siena, Department of Medical Biotechnologies, Siena, Italy; 12 Vita-Salute San Raffaele University, Milan, Italy

CONTACT INFORMATION

clemente.tommaso@hsr.it

PURPOSE

- Doravirine (DOR) is a new NNRTI with improved antiviral activity against NNRTI-resistant viral strains compared to other drugs in the same class [1,2].
- A few small trials have investigated DOR-containing regimens in heavily treatment-experienced people with HIV (PWH) [3-5], but no real-life data are available in the population with 4-class drug-resistant (4DR) strains.
- Therefore, our aim was to explore outcomes of DOR-containing regimens in 4DR-PWH.

METHODS

- Cohort study on PWH with resistance to NRTIs, NNRTIs, PIs and INSTIs from the PRESTIGIO Registry (NCT04098315; https://registroprestigio.org) [6] on antiretroviral therapy (ART), who started a DOR-containing regimen.
- The primary outcome was DOR durability (by Kaplan-Meier curve).
- Secondary outcomes included:
  - ➢ virological suppression [(VS) ≥1 viral load (VL) <50 copies/mL] for viremic PWH (by cumulative incidence function);
  - ➢ virological failure [(VF) ≥2 consecutive VLs ≥50 copies/mL or ≥1 VL ≥1000 copies/mL] for non-viremic individuals (by cumulative incidence function)
  - ➢ CD4+ and CD4+/CD8+ changes (by Wilcoxon signed-rank test).
- Follow-up accrued from DOR initiation [baseline (BL)] to its discontinuation or the last available VL.
- Descriptions by median (interquartile range, IQR) or frequency (%); comparison by Mann-Whitney or Fisher's exact test.

CONCLUSIONS

- In our cohort of 4DR-PWH, DOR-containing regimens showed good durability and virological effectiveness.
- These findings support a role for DOR in heavily treatment-experienced individuals, particularly as a switch strategy in the context of suppressed viremia.

REFERENCES

1. **Asante-Appiah E et al.** *Antimicrob Agents Chemother* 2021; 65: e0121621.
2. **Saladini F et al.** *Int J Antimicrob Agents* 2023; 61: 106737.
3. **Sterman FL et al.** *AIDS* 2023; 37: 1057-64.
4. **Ballif M et al.** *BMJ Open* 2024; 14: e094912.
5. **Mngqibisa R et al.** Poster presented at EACS 2023 (eP.A.090).
6. **Clemente T et al.** *BMJ Open* 2024; 14: e080606.

RESULTS

- Overall, 29 viremic and 23 non-viremic 4DR-PWH initiated a DOR-containing regimen (Table 1).
- During a median follow-up of 2.4 [interquartile range (IQR)=0.9-3.2] years, 19 (36.5%) individuals discontinued DOR (Figure 1; Table 2).
- Among the 29 viremic 4DR-PWH, 17 (58.6%) achieved VS (Figure 2).
  - ➢ Three/17 (17.6%) had a new VF after undetectability: 2 of them (66.7%) regained VS on DOR (1 with and 1 without changes in accompanying drugs).
- Among the 23 non-viremic individuals, 4 (17.4%) experienced VF (Figure 3).
  - ➢ Three/4 (75%) regained undetectability on DOR (1 with and 2 without changes in accompanying drugs).
- Three PWH (all viremic at baseline) selected new resistance-associated mutations: all to DOR, 2 also to accompanying drugs.
- Regarding immunological outcomes, there was a trend towards improvement in the group viremic at baseline (Table 3).

Table 1. BL characteristics of 4DR-PWH who initiated a DOR-containing regimen

BL characteristics	4DR-PWH with BL VL ≥50 copies/mL (n=29)	4DR-PWH with BL VL <50 copies/mL (n=23)
Age (years)	57.4 (54.1-62.4)	57.7 (51.5-60.3)
Male sex assigned at birth	24 (82.8%)	16 (69.6%)
ART duration (years)	25.0 (22.6-28.7)	26.6 (23.9-28.8)
VL (copies/mL)	295 (123-17800)	19 (<1-29)
CD4+ T-cell count (cells/mm3)	360 (93-931)	630 (405-808)
CD4+ nadir (cells/mm3)	64 (8-171)	92 (27-201)
Number of drugs in the BL regimen	4 (4-6)	3 (2-5)
Drugs contained in the BL regimen		
≥1 NRTI	24 (82.8%)	10 (43.5%)
DOR	29 (100%)	23 (100%)
PI/b	16 (55.2%)	10 (43.5%)
2nd generation INSTI	18 (62.1%)	17 (73.9%)
MVC and/or T20	6 (20.7%)	4 (17.4%)
FTR and/or LEN and/or ISL	15 (51.7%)	7 (30.4%)
GSS of the BL regimen	2.5 (2-3)	2 (1.5-2.5)
DOR susceptibility	13 (44.8%)	14 (60.9%)

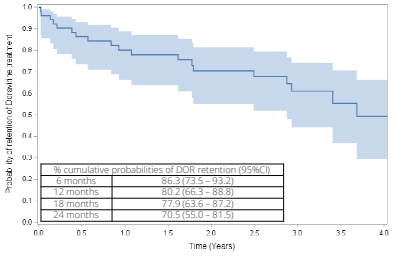
Table 2. Reasons for DOR discontinuation in 4DR-PWH

	4DR-PWH with BL VL ≥50 copies/mL (n=29)		4DR-PWH with BL VL <50 copies/mL (n=23)	
	VS (n=17)	no VS (n=12)	no VF (n=19)	VF (n=4)
DOR discontinuation	6 (35.3%)	7 (58.3%)	5 (26.3%)	1 (25%)
Upgrade	1 (16.7%)	4 (57.1%)	0 (0%)	1 (100%)
Pill burden reduction	2 (33.3%)	0 (0%)	3 (60%)	0 (0%)
Toxicity	1 (16.7%)	2 (28.6%)	1 (20%)	0 (0%)
Drug-drug interactions	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Loss to follow-up	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)
Death	1 (16.7%)	1 (14.3%)	1 (20%)	0 (0%)

Table 3. Immunological outcomes of DOR-containing regimens in 4DR-PWH

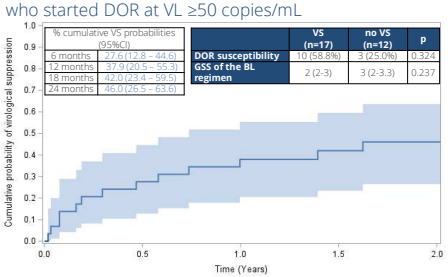
	BL CD4+ count (cell/mm3)	Last CD4+ count (cell/mm3)	p	BL CD4+/CD8+	Last CD4+/CD8+	p
Overall	494 (171-897)	558 (402-818)	0.372	0.56 (0.16-0.96)	0.45 (0.26-0.86)	0.372
4DR-PWH with BL VL ≥50 copies/mL	363 (93-931)	475 (120-888)	0.179	0.35 (0.11-1.38)	0.42 (0.15-1.68)	0.108
4DR-PWH with BL VL <50 copies/mL	652 (438-790)	614 (432-738)	0.708	0.6 (0.46-0.88)	0.57 (0.38-0.78)	0.782

Figure 1. Cumulative probabilities of DOR retention in 4DR-PWH



% cumulative probabilities of DOR retention (95%CI)
6 months	86.3 (73.5 – 93.2)
12 months	80.2 (66.3 – 88.8)
18 months	77.9 (63.6 – 87.2)
24 months	70.5 (55.0 – 81.5)

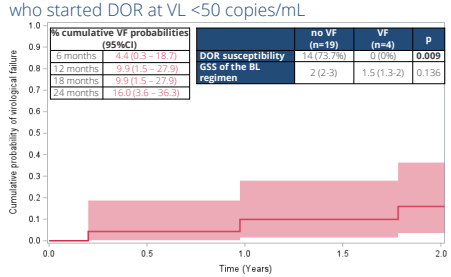
Figure 2. Cumulative probabilities of VS in 4DR-PWH who started DOR at VL ≥50 copies/mL



% cumulative VS probabilities (95%CI)
6 months	27.6 (12.8 – 44.6)
12 months	37.9 (20.5 – 55.3)
18 months	42.0 (23.4 – 59.5)
24 months	46.0 (26.5 – 63.6)

	VS (n=17)	no VS (n=12)	p
DOR susceptibility	10 (58.8%)	3 (25.0%)	0.324
GSS of the BL regimen	2 (2-3)	3 (2-3.3)	0.237

Figure 3. Cumulative probabilities of VF in 4DR-PWH who started DOR at VL <50 copies/mL



% cumulative VF probabilities (95%CI)
6 months	4.4 (0.3 – 18.7)
12 months	9.9 (1.5 – 27.9)
18 months	9.9 (1.5 – 27.9)
24 months	16.0 (3.6 – 36.3)

	no VF (n=19)	VF (n=4)	p
DOR susceptibility	14 (73.7%)	0 (0%)	**0.009**
GSS of the BL regimen	2 (2-3)	1.5 (1.3-2)	0.136

Prestigio Study Group

STEERING COMMITTEE: Antonella Castagna (Coordinatore), Vincenzo Spagnuolo (Coordinatore operativo), Daniele Armenia, Stefano Bonora, Leonardo Calza, Anna Maria Cattelan, Giovanni Cenderello, Adriana Cervo, Laura Comi, Antonio Di Biagio, Emanuele Focà, Roberta Gagliardini, Andrea Giacomelli, Filippo Lagi, Giulia Marchetti, Stefano Rusconi, Francesco Saladini, Maria Santoro, Maurizio Zazzi. **VIROLOGY TEAM AND BIOLOGICAL BANK**: Andrea Galli, Daniele Armenia, Francesco Saladini, Maria Santoro, Maurizio Zazzi, BioRep SRL. **STUDY COORDINATORS**: Elisabetta Carini, Sabrina Bagaglio, Girolamo Piromalli. **STATISTICAL AND MONITORING TEAM**: Riccardo Lolatto, Nicolò Capra. **ENROLLING CENTERS**: ANCONA: Marcello Tavio, Alessandra Mataloni Paggi; AOSTA: Silvia Maghrani; Manuela Colafigli AVANO: Ornella Schioppa, Stefania Zanussi, Valentina Da Ros, Silvia Rossetto; BARI: Annalisa Saracino, Flavia Balena; BERGAMO: Laura Comi, Daniela Valenti; BOLOGNA: Pierluigi Viale, Leonardo Calza; Federica Malerba, Silvia Cretella; Riccardo Riccardi; BRESCIA: Francesco Castelli, Emanuele Focà, Davide Minisci; BUSTO ARSIZIO: Barbara Menzaghi, Maddalena Farinazzo, Chiara Abeli; CATANIA: Bruno Cacopardo, Maurizio Celesia, Michele Salvatore Paternò Raddusa, Carmen Giarratana; CATANZARO: Paolo Fusco, Vincenzo Olivadese, Simona Mongiardi; CREMONA: Angelo Pan, Chiara Formabaio, Paola Brambilla; FIRENZE: Alessandro Bartoloni, Filippo Lagi, Paola Corsi, Trevisan Sasha, Gasparro Giuseppe, Cecilia Costa, Alessio Bellucci, Elisa Mariabelli; FOGGIA: Teresa Santantonio, Sergio Lo Caputo, Sergio Ferrara, Arianna Narducci; GENOVA: Emanuele Pontali, Marcello Feasi, Antonio Sarà, Matteo Bassetti, Antonio Di Biagio, Sabrina Bianchi; LECCO: Stefania Piconi, Martina Bottanelli, Silvia Pontiggia, Valsecchi Giada; LEGNANO: Stefano Rusconi, Cinzia Roberta Bassoli, Francesco Bassani, Liana Bevilacqua; MILANO: Antonella Castagna, Vincenzo Spagnuolo, Camilla Muccini; Elisabetta Carini, Sabrina Bagaglio, Riccardo Lolatto, Nicolò Capra, Andrea Galli, Rebecka Papaioannu Borjesson, Tommaso Clemente, Golnaz Torkjazi, Girolamo Piromalli, Spinello Antinori, Andrea Giacomelli, Tiziana Formenti, Giulia Marchetti, Lidia Gazzola, Fabiana Trionfo Fineo, Massimo Puoti, Cristina Mussini, Federico D'Amico, Simoncini Elena, Sassi Serena; MODENA: Cristina Mussini, Adriana Cervo, Giulia Nardini; NAPOLI: Elio Manzillo, Antonella Gallicchio; PADOVA: Anna Maria Cattelan, Maria Mazzitelli; PALERMO: Antonio Cascio, Marcello Trizzino; PARMA: Elisa Fronti, Diletta Laccabue, Federica Carli; PAVIA: Roberto Gulminetti, Layla Pagnucco, Mattia Demitri, Alessandra Ferrari; PERUGIA: Daniela Francisci, Giuseppe De Socio, Elisabetta Schiaroli; REGGIO EMILIA: Elisa Garlassi, Romina Corsini; ROMA: Roberta Gagliardini, Marisa Fusto, Loredana Sarmati, Vincenzo Malagnino, Tiziana Mulas, Mirko Compagno Carlo Torti, Simona Di Giambenedetto, Silvia Lamonica, Pierluigi Salvo; SANREMO: Giovanni Cenderello, Rachele Pincino, Davide Laurenda; SASSARI: Giordano Madeddu, Andrea De Vito; SIENA: Mario Tumbarello, Massimiliano Fabbiani, Francesca Panza, Ilaria Rancan; TORINO: Giovanni Di Perri, Stefano Bonora, Micol Ferrara, Andrea Calcagno, Silvia Fantino, Giancarlo Orofino, Guido Calleri, Guastavigna Marta; VERONA: Stefano Nardi, Marta Fiscon. **SUPPORTED BY**: ViiV Healthcare, Gilead Sciences, MSD, Janssen-Cilag.