P061

Durability of doravirine containing regimens in people with HIV in real-life settings in the ANRS CO3 - AQUIVIH-NA cohort

O. Leleux[1], A. Peyrouny-Mazeau[1], A. Perrier[1], M. Hessamfar[1,2], G. Le Moal[3], D. Neau[4], L. Alleman[5], C. Cazanave[4], E. Lazaro[6], P. Duffau[2], A. Riché[7], Y. Gérard[8], M-A Vandenhende[9], F. Bonnet[1,2]

[1]Bordeaux Population Health Research Center, INSERM U1219, CIC-EC 1401, Univ. Bordeaux - ISPED, 33076, Bordeaux, France; [2]Centre Hospitalier Universitaire (CHU) de Bordeaux, Service de Médecine Interne et Maladies Infectieuses, Hôpital Saint-André, Bordeaux, France; [3]Centre Hospitalier Universitaire (CHU) de Poitiers, Service de Maladies Infectieuses et Tropicales, Poitiers, France; [4]Centre Hospitalier Universitaire (CHU) de Bordeaux, Service de Maladies Infectieuses et Tropicales, Hôpital Pellegrin, Bordeaux, France; [5]Centre Hospitalier de la Côte Basque, Service de Maladies Infectieuses, Bayonne, France; [6]Centre Hospitalier Universitaire (CHU) de Bordeaux, Service de Médecine Interne et Maladies Infectieuses, Hôpital Haut-Lévèque, Pessac, France; [7]Centre Hospitalier d'Angoulême, Service de Medecine Interne, Angoulême, France; [8]Centre Hospitalier de Dax, Service de Maladies Infectieuses, Dax, France; [9]Centre Hospitalier Universitaire (CHU) de Bordeaux, Service de Médecine Interne, Hôpital Pellegrin, Bordeaux, France;

BACKGROUND

- Since 2019, people living with HIV (PWH) in France have had access to doravirine (DOR), a once-daily non-nucleoside reverse transcriptase inhibitor (NNRTI). DOR is commonly used in combination with other antiretroviral drugs to maintain viral suppression.
- Although clinical trials have shown promising results, real-life data on DOR containing regimen in PWH with suppressed (sRNA) and unsuppressed (usRNA) HIV RNA at the time of treatment switch remain limited, particularly with regard to long-term efficacy, tolerability and persistence.

METHODS

- The **ANRS-CO3 - AquiVIH-NA cohort** is an open, prospective hospital-based cohort of adults (≥18 years), followed in 15 hospitals in the Nouvelle Aquitaine region of south-west France. Since 1987, it has been collecting epidemiological, clinical, biological and therapeutic data from the medical records of consenting**.**
- We conducted a retrospective analysis to evaluate in PWH included in the cohort the persistence of the switch to DORcr between 2019/04/01 and 2022/12/31 with the following criteria:
  - First DOR initiation
  - Documented HIV-1 viral load (VL) for at least 12 months prior switching.
  - Documented CD4 count for at least 24 months prior switching.
- Virological failure (VF) was defined by one HIV-1 RNA >1000 cp/ml VL or two consecutive HIV RNA >50 cp/ml VL and <1000 cp/ml VL during the follow-up period.

RESULTS

- At switch time, **541** PWH had received at least one time DOR (Table 1) :
  - ✓ 466 with suppressed HIVRNA (sRNA),
    - median age was 52.8 years, 34.5% were women, 23% at AIDS stage, median BMI was 25.8 and median CD4 count was 720/mm3 [IQR: 530-949].
  - ✓ 75 unsuppressed HIVRNA (usRNA), including 6 naive;
    - median age was 53.1 years, 30.7% were women, 16% were at AIDS stage, median BMI was 24.8 and median CD4 count was 525/mm3 [IQR: 277-947], median HIV viral load was 205 cp/mL [IQR: 84-5774].

Table 1. Baseline characteristics of patients switching to DOR

Characteristics	usRNA N=75		sRNA N=466		Total N=541	
Age (in years), Median (IQR)	53.1	(45.2;60.3)	52.8	(44.2;59.4)	52.9	(44.3;59.5)
Sex, Female (%)	23	(30.7)	161	(34.5)	184	(34.0)
Contamination group, n (%)						
Homo/bisexual	30	(40.0)	189	(40.6)	219	(40.5)
Heterosexuals	32	(42.7)	200	(42.9)	232	(42.9)
IV drug users	8	(10.7)	43	(9.2)	51	(9.4)
Other	5	(6.7)	34	(7.3)	39	(7.2)
Time from first positive serology (in years), Median (IQR)	19.2	(8.6;26.5)	18.6	(9.8;28.7)	18.8	(9.7;28.4)
AIDS stage of infection, n (%)	12	(16.0)	107	(23.0)	119	(22.0)
BMI (kg.m^{-2}), Median (IQR)	24.8	(21.2;27.9)	25.8	(23.2;29.3)	25.6	(22.9;29.3)
Origin of birth, n (%)						
France	51	(68.0)	331	(71.0)	382	(70.6)
Sub-Saharan Africa	16	(21.3)	98	(21.0)	114	(21.1)
CD4 count (cells/mm^3), Median (IQR)	525	(277;947)	720	(530;949)	705	(485;947)
HIV VL (copies/mL), Median (IQR)	205	(84;5774)	0	(0;20)	20	(0;36)
Nb of previous treatment lines, Median (IQR)	6.0	(2.0;10.0)	5.0	(3.0;9.0)	5.0	(3.0;9.0)
Previous VF , n (%)						
0	16	(21.3)	267	(57.3)	283	(52.3)
1	17	(22.7)	70	(15.0)	87	(16.1)
≥ 2	42	(56.0)	129	(27.7)	171	(31.6)
HCV co-infection* (anti-HCV+ or RNA+), n (%)	14	(20.0)	75	(17.0)	89	(17.4)
HBV co-infection* (HbsAg+ or DNA+), n (%)	6	(8.8)	27	(6.4)	33	(6.7)
Co-prescription of statins, n (%)	10	(13.3)	92	(19.7)	102	(18.9)
Co-prescription of anti-DM treatments, n (%)	2	(2.7)	42	(9.0)	44	(8.1)
Co-prescription of antihypertensive treatments, n (%)	26	(34.7)	125	(26.8)	151	(27.9)
Cardiovascular event** (CV), n (%)	13	(17.3)	67	(14.4)	80	(14.8)
Myocardial infarction** (CV-MI), n (%)	5	(6.7)	39	(8.4)	44	(8.1)
CNS vascular event** (CV-CNS), n (%)	4	(5.3)	18	(3.9)	22	(4.1)
Peripheral vascular event** (CV-PV), n(%)	7	(9.3)	32	(6.9)	39	(7.2)
Chronic renal failure** (CKD), n	5	(8.8)	54	(14.3)	59	(13.6)
Diabetes mellitus** (DM), n (%)	7	(9.3)	69	(14.8)	76	(14.0)
Hypertension** (HTA), n (%)	40	(71.4)	211	(58.4)	251	(60.2)
Osteoporosis** (OS), n (%)	1	(1.3)	34	(7.3)	35	(6.5)
Cancer** (Ca), n (%)	10	(13.3)	74	(15.9)	84	(15.5)
Number of comorbidities, n (%)	54		356		410	
0	12	(22.2)	109	(30.6)	121	(29.5)
1	23	(42.6)	114	(32.0)	137	(33.4)
2	12	(22.2)	73	(20.5)	85	(20.7)
≥ 3	7	(13.0)	60	(16.9)	67	(16.4)

*The HBV and HCV and also the comorbitities CKD and HTA have some missing data so the % isn't on the 541(466/75) patients.
**The comorbidities are obtain by diagnosis or for somme of them : CV-MI : treatment by bypass surgery or angioplasty; CV-PV : treatment by endarterectomy; CKD : 2 consecutive eGFR<60 measurement; DM : 2 consecutive blood glucose ≥7mmol/L or 1 ≥11mmol/L or antidiabetic treatment; HTA : 2 consecutive SBP≥140mmHg and/or DBP ≥90mmHG or antihypertensive therapy; OS : Bone T-score ≤ -2,5

ACKNOWLEDGMENTS

Scientific committe : P. Bellecave, P. Blanco, F. Bonnet (Chair), S. Bouchet, D. Breilh, C. Cazanave, S. Desjardin, V. Gaborieau, A. Gimbert, M. Hessamfar, L. Lacaze-Buzy, ME. Lafon, E. Lazaro, O. Leleux., G. Le Moal, D. Malvy, P. Mercié, D. Neau, I. Pellegrin, A. Perrier, V. Petrov-Sanchez, A. Peyrouny-Mazeau, C. Tumiotto, M.O. Vareil, L. Wittkop (Methodologist); *Participating centers :* Hôpital Saint André, CHU de Bordeaux, Médecine Interne et Maladies Infectieuses, (N. Bernard, F. Bonnet, D. Bronnimann H. Chaussade, D. Dondia, P. Duffau, I. Faure, V. Hémar, M. Hessamfar, W. Jourde, C. Martell, P Mercié, A. Monier, P. Morlat, E. Mériglier, F. Paccalin, R. Paz, E. Ribeiro, C. Rivoisy, MA Vandenhende); Hôpital Pellegrin, CHU de Bordeaux, Maladies Infectieuses et Tropicales, (L. Barthod, C. Cazanave, FA. Dauchy, A. Desclaux, H. Dutronc, A. Duvignaud, J. Leitao, D. Neau, D. Nguyen, D. Malvy, T. Pistone, M. Puges, C. Tinevez, C. Vignal, G. Wirth); Hôpital Haut-Lévêque, CHU de Bordeaux, Médecine Interne et Maladies Infectieuses, (C. Courtault, F. Camou, C. Greib, E. Lazaro, JL. Pellegrin, C. Prot-Laurent, E. Rivière, JF. Viallard); Hôpital d'Agen, Médecine Interne (E. Klément-Fructos, A. Nonis, P. Rispal); Hôpital de Libourne, Médecine Interne (O. Caubet, S. De Faucal, M. Favarel-garrigues, H. Ferrand, S. Tchamgoué); Hôpital de Bayonne, Maladies Infectieuses (M. Acquier, L. Alleman, S. Farbos, MO. Vareil, H. Wille); Hôpital de Dax, Médecine Interne et Maladies Infectieuses, (K. André, L. Caunegre, Y. Gérard, M. Lauda-Maillen); Hôpital Saint-Cyr/Villeneuve-sur-Lot, Maladies Infectieuses, (I. Chossat); Hôpital de Mont de Marsan, Médecine Interne et Maladies Infectieuses, (Y. Gerard, F. Lacassin, C. Lasbasses-Depis); Hôpital d'Arcachon, Médecine Interne, (A. Barret, M. Bouet, C. Courtault, M. Roucoules, M. Videcoq); Hôpital de Périgueux, Médecine Interne et Maladies Infectieuses, (C. Belzunce, B. Castan, J. Koffi, N. Rouanes, A. Saunier, J.B. Zabbe); Hôpital de Pau, Médecine Interne et Maladies Infectieuses, (G. Dumondin, V. Gaborieau); Hôpital d'Orthez, Médecine Interne, (Y. Gerard) ; CHU de Poitiers, Médecine Interne et Maladies Infectieuses, (G. Beraud, G. Le Moal, M. Catroux, M. Garcia, V. Giraud, JP. Martellosio, F. Roblot, JM. Turmel) ; Hôpital de Saintes, Médecine Interne, (T. Pasdeloup) ; Hôpital d'Angoulême, Médecine Interne, (A. Riché, M. Grosset, S. Males, C. Ngo Bell) ; Hôpital de Jonzac, Maladies Infectieuses, (T. Pasdeloup), Hôpital de Saint Jean d'Angely, Maladies Infectieuses, (T. Pasdeloup) ; Hôpital de Royan, Médecine Interne, (P. Mottaz, T. Pasdeloup) ; Hôpital de Châtellerault, Médecine Interne (A. Elsendoorn); *Other departements :* *Immunology:* P. Blanco, I. Pellegrin ; CRB-BBS: C. Carpentier, I. Pellegrin ; *Virology:* P. Bellecave, C. Tumiotto ; *Pharmacology:* S. Bouchet, D. Breilh, G. Miremeont-Salamé ; *Data collection :* G. Arnou, A. Barhoumi, P. Camps, S. Delveaux, S. Lawson-Ayayi, E. Lenaud, D. Plainchamps, A. Pougetoux, I. Stragier, B. Uwamaliya, K. Zara; *IT department:* V. Conte, M. Gapillout ; *Project Team :* O. Leleux (Project Leader), A. Perrier (Data Manager), A. Peyrouny-Mazeau (Statistitien) ; Participants of the Cohort ANRS CO3-AQUIVIH-NA,

Sponsor:CHUdeBordeaux,
Funding: ANRS | MIE, CHU de Bordeaux and MSD

- The most frequent treatment prior switch were regimens containing 42.1% TAF and 19.8% DTG with the most frequent reasons for switching to DORcr were simplification or drug reducing 31.8% (22.8% in usRNA and 33.3% in sRNA); Non optimal treatment 27.8% (21.5% in usRNA and 28.9% in sRNA) and avoid side effects 27.1% (10.1% in usRNA and 30.0% in sRNA). - *data not show.*

Table 2. Main reason of DOR discontinuation

Characteristics	usRNA N=75		sRNA N=466		Total N=541	
Reason of discontinuation at 12 months , n (%)*	21		97		118	
Any side-effects	2	(9.5)	34	(35.1)	36	(30.5)
Physician choice / drug reducing	7	(33.3)	17	(17.5)	24	(20.3)
Patient choice	5	(23.8)	17	(17.5)	22	(18.6)
Non-optimal treatment	2	(9.5)	13	(13.4)	15	(12.7)
Virological failure	4	(19.0)	3	(3.1)	7	(5.9)
Pregnancy or desire	0	(0.0)	6	(6.2)	6	(5.1)
Death	1	(4.8)	4	(4.1)	5	(4.2)
Others	0	(0.0)	3	(3.1)	3	(2.5)

* Over the 541 (466sRNA / 75usRNA) patients 116 have discontinu DOR at 12M but 2 of them (1 sRNE and 1 usRNA) have 2 reasons of discontinuation. That's why there is 118 (97sRNA / 21usRNA) reasons of discontinuation.

- At 12 months, 118 PWH discontinued DOR including 97 sRNA and 21 usRNA:
  - Any side-effects: 30.5% (sRNA: 35.1% / usRNA 9.5%), including:
    - neurological toxicity: 7,6% (sRNA: 9.3% / usRNA 0.0%);
    - general sign: 5.9% (sRNA: 7.2% / usRNA 0.0%);
    - digestive toxicity: 5.9% (sRNA: 7.2% / usRNA 0.0%);
  - Physician's choice / drug reducing: 20.3% (sRNA: 17.5% / usRNA 33.3%);
  - Patient's choice: 18.6% (sRNA: 17.5% / usRNA 23.8%);

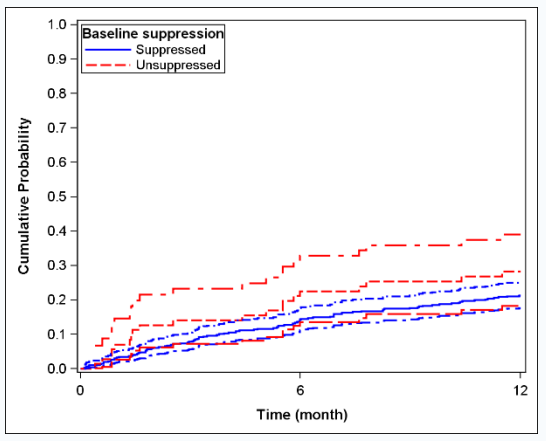

Figure 1. Risk curve of DOR discontinuation

- The cumulative probability of DOR discontinuation at 12 month (Fig 1) was:
  - 22,3% [CI : 18.8-25.9%] at M12;
    - 21.3% [CI : 17.7-25.2%] in sRNA
    - 28.2% [CI : 18.3-39.0%] in usRNA (included 2 of 6 naïve)

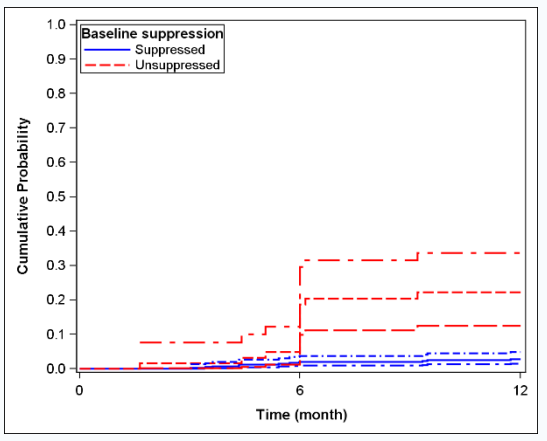

Figure 2. Risk curve of VF in PWH switching to DOR

- The cumulative probability of DOR VF at 12 months (Fig 2) was:
  - 5.3% [CI : 3.5-7.7%] at M12;
    - 2.8% [CI : 1.5-4.8%] in sRNA
    - 22.3%[CI : 12.6-33.7%] in usRNA

Table 3. Incidence under DOR of comorbidities 12 months after switching to DOR

Comorbidities*	usRNA Incidence density per 1000 PY	CI 95%	sRNA Incidence density per 1000 PY	CI 95%	Total Incidence density per 1000 PY	CI 95%
Chronic kidney disease	25.7	[3.6 ; 182.2]	11.2	[3.6 ; 34.8]	13.0	[4.9 ; 34.8]
Diabetes mellitus	.	.	18.4	[8.2 ; 40.9]	15.9	[7.1 ; 35.4]
Cardiovascular event	21.4	[3.0 ; 152.1]	6.0	[1.5 ; 24.1]	7.9	[2.6 ; 24.6]
Myocardial infarction	18.8	[2.6 ; 133.4]	2.8	[0.4 ; 19.9]	4.9	[1.2 ; 19.5]
CNS vascular event	.	.	2.7	[0.4 ; 19.0]	2.3	[0.3 ; 16.6]
Peripheral vascular event	.	.	5.5	[1.4 ; 22.2]	4.8	[1.2 ; 19.4]
Hypertension	82.1	[11.6 ; 582.9]	100.7	[57.2 ; 177.3]	99.0	[57.5 ; 170.4]
Osteoporosis	18.1	[2.5 ; 128.2]	2.8	[0.4 ; 19.6]	4.8	[1.2 ; 19.2]
Cancer	.	.	15.3	[6.4 ; 36.7]	13.2	[5.5 ; 31.8]

* The description of comorbidities is under table 1 and if no new comorbidities appear in the 12 months following the switch, the incidence is not calculated.

- The incidence of commorbidities during the 12 months following switch to DOR did not appear to differ between the PWH usRNA and sRNA populations.
- The highest incidence was for the development of arterial hypertension 99.0 [CI : 57.5-170.4] with 100.7 [CI : 57.2.1-177.3] and 82.1 [11.6-582.9] respectively for sRNA and usRNA.

CONCLUSION

- **The risk of discontinuation of DOR at 12 months was substantially the same for PWH sRNA and usRNA at the time of switch with: 21.3% [CI: 17.7-25.2%] for sRNA and 28.2% [CI: 18.3-39.0] for usRNA.**
- **The most frequent reason of discontinuation was side-effects followed by physician's choice/drug reducing.**
- **The risk of VF under DOR at 12M was different between sRNA: 2.8% [CI: 1.5-4.8%] and usRNA: 22.3% [CI: 12.6-33.7%].**
- **We observe no difference between comorbidities incidence under DOR in sRNA and usRNA during the 12 month following switch to DOR.**