# Supplementary Material

**Striking differences in weight gain after cART initiation depending on early or advanced presentation**: **Results from the ANRS CO4 FHDH cohort**

Sophie GRABAR\*1, Valérie POTARD2, Lionel PIROTH3, Sophie ABGRALL4, Louis BERNARD5, Clotilde ALLAVENA6, Fabienne CABY7, Pierre de TRUCHIS8, Claudine DUVIVIER9, Patricia ENEL10, Christine KATLAMA11, Marie-Aude KHUONG12, Odile LAUNAY13, Sophie MATHERON14, Giovanna MELICA15, Hugues MELLIEZ16, Jean-Luc MEYNARD17, Juliette PAVIE18, Laurence SLAMA19, Sylvie BREGIGEON20, Pierre TATTEVIN21, Jacqueline CAPEAU22, and Dominique COSTAGLIOLA2

1 Sorbonne Université, INSERM, Institut Pierre Louis d’Epidémiologie et de Santé Publique, AP-HP, Hôpital St Antoine, F75012, Paris, France

2 Sorbonne Université, INSERM, Institut Pierre Louis d’Epidémiologie et de Santé Publique, F75013, Paris, France

3 Infectious Diseases Department, CHU Dijon, and Inserm CIC 1432 Université de Bourgogne, France

4 AP-HP, Hôpital Béclère, Service de Médecine Interne, Clamart and Université Paris-Saclay, CESP INSERM U1018, Le Kremlin-Bicêtre, France

5 Université de Tours, Tours, France

6 Infectious Diseases Department, INSERM EA1413, CHU de Nantes, France

7 Unité VIH-IST, Service d’Immuno-Hematologie, Hopital Victor Dupouy, Argenteuil and Sorbonne Université, INSERM, Institut Pierre Louis d’Epidémiologie et de Sante Publique, F-75013 Paris, France

8 AP-HP Hôpital Raymond Poincaré, Université Paris-Saclay, Garches, France

9 AP-HP, Hôpital Necker-Enfants Malades, Service de Maladies Infectieuses et Tropicales, Centre d’Infectiologie Necker-Pasteur, Paris, France, IHU Imagine, Paris, France. Institut Cochin - CNRS 8104 - INSERM U1016, Université Paris Cité, Paris, France. Institut Pasteur, Centre Médical de l’Institut Pasteur, Paris France

10 Assistance Publique-Hôpitaux de Marseille, Public Health Department, Marseille and Aix-Marseille University, CEReSS, Health Service Research and Quality of Life Center, Marseille, France.

11 AP-HP, Sorbonne Université, INSERM, Institut Pierre Louis d’Epidémiologie et de Santé Publique, AP-HP, Hôpital Pitié-Salpêtrière, Paris, France  
12 Hôpital Delafontaine, Saint-Denis, France

13 Université Paris-Cité; AP-HP, Hôpital Cochin; Inserm, CIC 1417; Paris, France

14 Service de Maladies infectieuses et tropicales, Hospital Bichat-Claude Bernard, GHU Paris Nord, AP-HP, France

15 Clinical Immunology and Infectious Diseases Department, Henri Mondor Hospital, Creteil, France

16 Médecine Interne, Hôpital Riaumont, 62 800, Liévin, France

17 AP-HP, Department of Infectious Diseases, Saint-Antoine Hospital, Paris, France

18 Department of Immunology and Infectious Diseases, AP-HP Hôtel-Dieu, Paris, France

19 Infectious diseases Unit, Hôtel Dieu Hospital, APHP, Paris, France

20 Aix-Marseille Université, APHM, Hôpital Sainte-Marguerite, Marseille, France

21 Maladies Infectieuses et Réanimation Médicale, Hôpital Pontchaillou, Centre Hospitalo-Universitaire, Rennes, France

22 Sorbonne Université, INSERM UMR\_S 938, Centre de Recherche Saint-Antoine (CRSA), Institute of Cardiometabolism and Nutrition (ICAN), F75012 Paris, France

**Table S1. Description of initiated cART**

|  |  |
| --- | --- |
|  | **n** |
| **Initiated cART** | 12773 |
|  |  |
| **combined with INSTI :** |  |
| TDF/FTC/RAL | 469 |
| ABC/3TC/DTG | 1171 |
| TDF/FTC/DTG | 751 |
| TDF/FTC/EVG/cobi | 1214 |
| TAF/FTC/EVG/cobi | 652 |
| **combined with PI :** |  |
| TDF/FTC/DRV/rtv | 3815 |
| ABC/3TC/DRV/rtv | 633 |
| TDF/FTC/ATV/rtv | 694 |
| ABC/3TC/ATV/rtv | 185 |
| **combined with NNRTI :** |  |
| TDF/FTC/EFV | 854 |
| TDF/FTC/RPV | 2187 |
| TAF/FTC/RPV | 148 |

**Abbreviations:** cART, combined antiretroviral treatment; INSTI integrase strand transfer inhibitor; PI, Protease Inhibitor; NNRTI, Non-nucleoside reverse transcriptase inhibitor; RAL, raltegravir; DTG, dolutegravir; EVG, elvitegravir; DRV, darunavir; ATV, atazanavir; EFV, efavirenz; RPV, rilpivirine; COBI, cobicistat; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil; FTC, emtricitabine; 3TC, lamivudine; ABC, abacavir

**Table S2. Comparison over time between drugs for a weight gain of at least 10% (Table a)  
 and weight gain (Table b) for all PWH (n=12773)**

**a- All PWH – Multivariable Cox model for a weight gain of at least 10%**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **KM estimates at 30 months [95% CI]** | **HR [95% CI]** | **P** |  |  |  |  |  |
| **Total** | 12773 | 34.5 [33.5-35.6] |  | **vs** | **vs** | **vs** | **vs** | **vs** | **vs** |
| **3rd agent** |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 469 | 44.3 [38.9-50.1] | 1.44 [1.18-1.76] |  | 0.78 | 0.02 | 0.64 | 0.22 | <0.0001 |
| DTG | 1922 | 36.9 [34.2-39.7] | 1.48 [1.26-1.74] | 0.78 |  | 0.0009 | 0.25 | 0.06 | <0.0001 |
| EVG/COBI | 1866 | 34.0 [31.3-36.9] | 1.12 [0.96-1.30] | 0.02 | 0.0009 |  | 0.002 | 0.20 | 0.03 |
| DRV/RTV | 4448 | 44.0 [42.0-46.1] | 1.38 [1.22-1.56] | 0.64 | 0.25 | 0.002 |  | 0.21 | <0.0001 |
| ATV/RTV | 879 | 38.1 [33.8-42.7] | 1.26 [1.06-1.50] | 0.22 | 0.06 | 0.20 | 0.21 |  | 0.002 |
| EFV | 854 | 24.9 [21.6-28.6] | 0.90 [0.74-1.08] | <0.0001 | <0.0001 | 0.03 | <0.0001 | 0.002 |  |
| RPV | 2335 | 20.9 [19.1-22.8] | 1 | 0.0003 | <0.0001 | 0.16 | <0.0001 | 0.01 | 0.25 |
| **Backbone** |  |  |  | **vs TDF** | **vs TAF** |  |  |  |  |
| TDF/FTC | 9984 | 33.6 [32.4-34.8] | 1 |  | <0.0001 |  |  |  |  |
| TAF/FTC | 800 | 41.1 [36.9-45.6] | 1.52 [1.29-1.79] | <0.0001 |  |  |  |  |  |
| ABC/3TC | 1989 | 36.1 [33.6-38.7] | 0.95 [0.84-1.06] | 0.36 | <0.0001 |  |  |  |  |

1. **All PWH – Multivariable mixed model for weight gain**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **Weight change at 12 months (kg)** | **Weight change at 24 months (kg)** | **Weight change at 30 months (kg)** | **P** |  |  |  |  |  |
| **Total** | 12773 | 5.45 (5.04-5.87) | 7.84 (7.27-8.41) | 7.85 (7.13-8.57) | **vs** | **vs** | **vs** | **vs** | **vs** | **vs** |
| **3rd agent** |  |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 469 | 6.04 (5.33-6.74) | 8.69 (7.77-9.61) | 8.51 (7.33-9.69) |  | 0.75 | 0.40 | 0.21 | 0.08 | 0.0008 |
| DTG | 1922 | 5.97 (5.43-6.50) | 8.82 (8.10-9.55) | 8.71 (7.81-9.61) | 0.75 |  | 0.13 | 0.02 | 0.005 | <0.0001 |
| EVG/COBI | 1866 | 5.52 (5.04-6.01) | 7.74 (7.07-8.40) | 8.03 (7.20-8.86) | 0.40 | 0.13 |  | 0.57 | 0.18 | 0.0003 |
| DRV/RTV | 4448 | 5.50 (5.04-5.95) | 7.71 (7.08-8.33) | 7.84 (7.05-8.63) | 0.21 | 0.02 | 0.57 |  | 0.29 | 0.0004 |
| ATV/RTV | 879 | 5.23 (4.64-5.81) | 7.33 (6.54-8.12) | 7.44 (6.46-8.42) | 0.08 | 0.005 | 0.18 | 0.29 |  | 0.05 |
| EFV | 854 | 4.28 (3.69-4.86) | 6.88 (6.10-7.66) | 6.51 (5.56-7.47) | 0.0008 | <0.0001 | 0.0003 | 0.0004 | 0.05 |  |
| RPV | 2335 | 5.65 (5.17-6.14) | 7.73 (7.08-8.37) | 7.93 (7.11-8.74) | 0.27 | 0.05 | 0.74 | 0.75 | 0.20 | <0.0001 |
| **Backbone** |  |  |  |  | vs TDF | vs TAF |  |  |  |  |
| TDF/FTC | 9984 | 4.78 (4.39-5.17) | 7.02 (6.47-7.57) | 7.04 (6.36-7.71) |  | <0.0001 |  |  |  |  |
| TAF/FTC | 800 | 7.21 (6.53-7.88) | 9.00 (8.20-9.81) | 8.80 (7.79-9.82) | <0.0001 |  |  |  |  |  |
| ABC/3TC | 1989 | 6.57 (5.96-7.18) | 7.50 (6.80-8.20) | 7.72 (6.84-8.60) | 0.04 | 0.05 |  |  |  |  |

Note : 95% confidence intervals are in parentheses

**Abbreviations:** 95% CI, 95% confidence interval; RAL, raltegravir; DTG, dolutegravir; EVG, elvitegravir; DRV, darunavir; ATV, atazanavir; EFV, efavirenz; RPV, rilpivirine; COBI, cobicistat; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil; FTC, emtricitabine; 3TC, lamivudine; ABC, abacavir

**Table S3. Mean weight change at 12, 24, and 30 months for PWH presenting early (n = 5794)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Multivariable mixed model** | | | |
|  | **N** | **Weight change at 12 months (kg)** | **Weight change at 24 months (kg)** | **Weight change at 30 months (kg)** | **P** |
| **Total** | 5794 | 2.53 (1.94-3.11) | 2.84 (2.10-3.57) | 2.82 (1.97-3.68) |  |
| **3rd agent** |  |  |  |  |  |
| RAL | 155 | 2.69 (1.70-3.68) | 3.24 (2.07-4.41) | 3.45 (2.00-4.90) | <0.0001 |
| DTG | 877 | 3.16 (2.47-3.85) | 3.83 (2.95-4.70) | 3.51 (2.43-4.59) |  |
| EVG/COBI | 931 | 2.50 (1.84-3.16) | 3.22 (2.39-4.06) | 3.14 (2.16-4.12) |  |
| DRV/RTV | 1401 | 2.46 (1.82-3.09) | 2.67 (1.87-3.47) | 3.00 (2.03-3.98) |  |
| ATV/RTV | 364 | 2.53 (1.70-3.36) | 2.35 (1.27-3.44) | 2.06 (0.75-3.38) |  |
| EFV | 363 | 1.63 (0.84-2.43) | 1.71 (0.71-2.70) | 1.78 (0.62-2.94) |  |
| RPV | 1703 | 2.71 (2.05-3.36) | 2.85 (2.02-3.67) | 2.82 (1.86-3.79) |  |
| **Backbone** |  |  |  |  |  |
| TDF/FTC | 4417 | 1.95 (1.39-2.51) | 2.27 (1.58-2.97) | 2.27 (1.47-3.90) | <0.0001 |
| TAF/FTC | 419 | 3.66 (2.88-4.43) | 3.81 (2.80-4.82) | 3.73 (2.54-4.91) |  |
| ABC/3TC | 958 | 1.97 (1.23-2.70) | 2.43 (1.49-3.38) | 2.48 (1.33-3.62) |  |
| **Age and gender** |  |  |  |  |  |
| Women ≤ 50 years | 1043 | 2.58 (1.92-3.24) | 3.30 (2.48-4.12) | 3.92 (2.98-4.87) | 0.05 |
| Women > 50 years | 270 | 2.53 (1.68-3.37) | 2.84 (1.77-3.92) | 2.75 (1.48-4.02) |  |
| Men ≤ 50 years | 3831 | 2.35 (1.76-2.94) | 2.52 (1.78-3.26) | 2.08 (1.23-2.94) |  |
| Men > 50 years | 650 | 2.64 (1.95-3.33) | 2.53 (1.50-3.56) | 2.54 (1.50-3.57) |  |
| **Transmission Group** |  |  |  |  |  |
| MSM | 3309 | 2.30 (1.65-2.94) | 2.76 (1.96-3.57) | 2.89 (1.95-3.83) | 0.0006 |
| Other | 2485 | 2.75 (2.17-3.34) | 2.92 (2.18-3.65) | 2.76 (1.96-3.57) |  |
| **Geographic origin** |  |  |  |  |  |
| Sub-Saharan Africa | 1175 | 2.78 (2.13-3.43) | 3.24 (2.43-4.06) | 3.17 (2.21-4.14) | <0.0001 |
| Other | 4619 | 2.27 (1.69-2.86) | 2.43 (1.70-3.17) | 2.47 (1.63-3.32) |  |
| **BMI (kg/m2)** |  |  |  |  |  |
| Underweight (< 18.5) | 287 | 3.72 (2.88-4.57) | 4.10 (3.06-5.15) | 3.71 (2.49-4.92) | <0.0001 |
| Normal [18.5-25[ | 3589 | 2.60 (2.01-3.18) | 3.07 (2.34-3.80) | 3.08 (2.21-3.95) |  |
| Overweight [25-30[ | 1368 | 2.48 (1.86-3.09) | 2.56 (1.79-3.33) | 2.53 (1.62-3.44) |  |
| Obese (≥ 30) | 550 | 1.31 (0.60-2.01) | 1.63 (0.73-2.52) | 1.98 (0.93-3.02) |  |
| **CD4 (cells/mm3)** |  |  |  |  |  |
| < 200\* | 43 | 2.59 (0.95-4.22) | 2.23 (0.35-4.11) | 1.56 (-0.61-3.73) | 0.006 |
| 200-350\* | 216 | 2.56 (1.73-3.38) | 3.08 (2.00-4.16) | 3.01 (1.62-4.41) |  |
| 350-500 | 2390 | 2.70 (2.18-3.22) | 3.21 (2.52-3.91) | 3.72 (2.88-4.55) |  |
| ≥ 500 | 3145 | 2.26 (1.75-2.78) | 2.83 (2.13-3.52) | 3.01 (2.16-3.85) |  |
| **Viral load (copies/ml)** |  |  |  |  |  |
| ]50-30 000] | 3658 | 1.57 (0.97-2.17) | 1.91 (1.18-2.63) | 1.77 (0.90-2.65) | <0.0001 |
| ]30 000-100 000] | 1708 | 1.71 (2.42-4.02) | 2.22 (1.48-2.97) | 2.28 (1.38-3.18) |  |
| ]100 000-500 000]\* | 269 | 3.22 (2.42-4.02) | 3.29 (2.29-4.28) | 3.41 (2.13-4.69) |  |
| > 500 000\* | 159 | 3.61 (2.44-4.78) | 3.94 (2.25-5.62) | 3.84 (1.93-5.74) |  |

Note: 95% confidence intervals are in parentheses

\* Diagnosed at primary infection

**Abbreviations:** RAL, raltegravir; DTG, dolutegravir; EVG, elvitegravir; DRV, darunavir; ATV, atazanavir; EFV, efavirenz; RPV, rilpivirine; COBI, cobicistat; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil; FTC, emtricitabine; 3TC, lamivudine; ABC, abacavir; MSM, male who have sex with male; BMI, body-mass index

**Table S4. Mean weight change at 12, 24, and 30 months for PWH presenting with advanced HIV disease (n = 3106)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **Multivariable mixed model** | | | |
|  | **N** | **Weight change at 12 months (kg)** | **Weight change at 24 months (kg)** | **Weight change at 30 months (kg)** | **P** |
| **Total** | 3106 | 6.65 (5.94-7.36) | 9.05 (8.04-10.07) | 9.70 (8.35-11.06) |  |
| **3rd agent** |  |  |  |  |  |
| RAL | 186 | 7.66 (6.26-9.07) | 10.97 (8.80-13.14) | 10.59 (7.97-13.20) | <0.0001 |
| DTG | 460 | 7.45 (6.38-8.53) | 10.85 (9.38-12.33) | 10.88 (8.98-12.78) |  |
| EVG/COBI | 354 | 6.27 (5.30-7.24) | 7.46 (6.03-8.90) | 8.37 (6.62-10.12) |  |
| DRV/RTV | 1522 | 6.77 (5.96-7.59) | 8.70 (7.54-9.87) | 8.80 (7.25-10.34) |  |
| ATV/RTV | 223 | 6.44 (5.30-7.59) | 8.17 (6.48-9.87) | 10.19 (8.09-12.28) |  |
| EFV | 188 | 6.44 (5.06-7.82) | 9.36 (7.56-11.15) | 9.55 (7.32-11.79) |  |
| RPV | 173 | 5.50 (4.34-6.66) | 7.85 (6.34-9.36) | 9.55 (7.54-11.56) |  |
| **Backbone** |  |  |  |  |  |
| TDF/FTC | 2495 | 5.86 (5.26-6.46) | 7.87 (6.99-8.75) | 8.40 (7.34-9.47) | <0.0001 |
| TAF/FTC | 153 | 7.34 (5.91-8.78) | 10.86 (8.75-12.98) | 11.04 (8.10-13.97) |  |
| ABC/3TC | 458 | 6.74 (5.81-7.67) | 8.42 (7.17-9.67) | 9.67 (8.11-11.22) |  |
| **Age and gender** |  |  |  |  |  |
| Women ≤ 50 years | 723 | 6.53 (5.67-7.39) | 9.33 (8.13-10.53) | 9.71 (8.14-11.29) | 0.0001 |
| Women > 50 years | 217 | 7.34 (6.12-8.55) | 9.84 (8.09-11.59) | 10.41 (8.21-12.60) |  |
| Men ≤ 50 years | 1544 | 5.86 (5.13-6.59) | 7.81 (6.76-8.85) | 8.81 (7.40-10.23) |  |
| Men > 50 years | 622 | 6.87 (6.00-7.74) | 9.23 (7.99-10.46) | 9.88 (8.28-11.48) |  |
| **Transmission Group** |  |  |  |  |  |
| MSM | 900 | 6.22 (5.34-7.10) | 8.37 (7.11-9.63) | 8.93 (7.28-10.59) | <0.0001 |
| Other | 2206 | 7.08 (6.40-7.76) | 9.73 (8.76-10.70) | 10.47 (9.17-11.77) |  |
| **Geographic origin** |  |  |  |  |  |
| Sub-Saharan Africa | 1127 | 6.60 (5.78-7.42) | 9.25 (8.07-10.43) | 9.97 (8.41-11.53) | 0.54 |
| Other | 1979 | 6.70 (5.97-7.43) | 8.86 (7.81-9.90) | 9.44 (8.05-10.83) |  |
| **BMI (kg/m2)** |  |  |  |  |  |
| Underweight (< 18.5) | 391 | 8.31 (7.32-9.31) | 9.62 (8.20-11.03) | 10.59 (8.64-12.54) | <0.0001 |
| Normal [18.5-25[ | 1925 | 6.80 (6.08-7.53) | 9.00 (7.98-10.02) | 9.34 (8.02-10.66) |  |
| Overweight [25-30[ | 591 | 5.58 (4.69-6.46) | 9.02 (7.83-10.22) | 10.04 (8.47-11.61) |  |
| Obese (≥ 30) | 199 | 5.91 (4.77-7.04) | 8.57 (6.90-10.23) | 8.84 (6.68-11.01) |  |
| **Viral load (copies/ml)** |  |  |  |  |  |
| ]50-30 000] | 391 | 4.84 (3.92-5.76) | 6.16 (4.87-7.46) | 6.88 (5.21-8.55) | <0.0001 |
| ]30 000-100 000] | 1925 | 6.24 (5.35-7.12) | 8.11 (6.84-9.37) | 8.18 (6.58-9.79) |  |
| ]100 000-500 000] | 591 | 7.40 (6.60-8.20) | 10.17 (9.03-11.32) | 11.07 (9.53-12.61) |  |
| > 500 000 | 199 | 8.13 (7.28-8.98) | 11.77 (10.56-12.97) | 12.68 (11.08-14.27) |  |
| **Prior AIDS defining event** |  |  |  |  |  |
| No | 2009 | 5.57 (4.87-6.27) | 6.69 (5.70-7.69) | 7.46 (6.14-8.77) | <0.0001 |
| Tuberculosis | 261 | 7.75 (6.59-8.91) | 9.26 (7.67-10.85) | 11.01 (8.64-13.38) |  |
| AIDS cancer | 173 | 4.77 (3.47-6.06) | 9.14 (7.27-11.01) | 9.17 (7.00-11.35) |  |
| Other AIDS defining event | 663 | 8.51 (7.65-9.37) | 11.11 (9.87-12.36) | 11.17 (9.54-12.81) |  |

Note: 95% confidence intervals are in parentheses

**Abbreviations:** RAL, raltegravir; DTG, dolutegravir; EVG, elvitegravir; DRV, darunavir; ATV, atazanavir; EFV, efavirenz; RPV, rilpivirine; COBI, cobicistat; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil; FTC, emtricitabine; 3TC, lamivudine; ABC, abacavir; MSM, male who have sex with male; BMI, body-mass index

**Table S5. Comparison overtime between drugs for weight gain of at least 10% (Tables a, b) and weight gain (Tables c, d) according to the clinical presentation**

**a- PWH presenting early – Multivariable Cox model for a weight gain of at least 10%**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **KM estimates at 30 months [95% CI]** | **HR [95% CI]** | **P** |  |  |  |  |  |
| **Total** | 5794 | 20.9 [19.6-22.2] |  | **vs** | **vs** | **vs** | **vs** | **vs** | **vs** |
| **3rd agent** |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 155 | 19.6 [13.1-28.8] | 1.07 [0.68-1.67] |  | 0.28 | 0.64 | 0.32 | 0.14 | 0.06 |
| DTG | 877 | 21.2 [18.0-24.9] | 1.41 [1.04-1.90] | 0.28 |  | 0.33 | 0.74 | 0.58 | 0.0003 |
| EVG/COBI | 931 | 25.3 [21.9-29.1] | 1.19 [0.95-1.49] | 0.64 | 0.33 |  | 0.35 | 0.11 | 0.002 |
| DRV/RTV | 1401 | 24.8 [21.6-28.4] | 1.34 [1.10-1.64] | 0.32 | 0.74 | 0.35 |  | 0.33 | <0.0001 |
| ATV/RTV | 364 | 26.8 [21.1-33.7] | 1.55 [1.16-2.07] | 0.14 | 0.58 | 0.11 | 0.33 |  | <0.0001 |
| EFV | 363 | 11.4 [8.0-16.1] | 0.62 [0.43-0.90] | 0.06 | 0.0003 | 0.002 | <0.0001 | <0.0001 |  |
| RPV | 1703 | 17.7 [15.8-19.9] | 1 | 0.78 | 0.03 | 0.12 | 0.005 | 0.003 | 0.01 |
| **Backbone** |  |  |  | **TDF** | **TAF** |  |  |  |  |
| TDF/FTC | 4417 | 19.8 [18.4-21.4] | 1 |  | 0.0004 |  |  |  |  |
| TAF/FTC | 419 | 32.0 [26.5-38.3] | 1.59 [1.23-2.06] | 0.0004 |  |  |  |  |  |
| ABC/3TC | 958 | 20.7 [17.7-24.1] | 0.79 [0.61-1.03] | 0.08 | 0.0002 |  |  |  |  |

**b- PWH presenting with advanced HIV disease – Multivariable Cox model for a weight gain of at least 10%**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **KM estimates at 30 months [95% CI]** | **HR [95% CI]** | **P** |  |  |  |  |  |
| **Total** | 3106 | 63.1 [60.9-65.3] |  | **vs** | **vs** | **vs** | **vs** | **vs** | **vs** |
| **3rd agent** |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 186 | 74.1 [65.5-81.9] | 2.19 [1.53-3.14] |  | 0.86 | 0.003 | 0.33 | 0.11 | 0.20 |
| DTG | 460 | 68.8 [63.2-74.2] | 2.24 [1.60-3.14] | 0.86 |  | 0.0005 | 0.11 | 0.04 | 0.13 |
| EVG/COBI | 354 | 55.6 [49.1-62.3] | 1.39 [0.98-1.97] | 0.003 | 0.0005 |  | 0.003 | 0.16 | 0.10 |
| DRV/RTV | 1522 | 65.6 [62.4-68.8] | 1.96 [1.44-2.66] | 0.33 | 0.11 | 0.003 |  | 0.24 | 0.51 |
| ATV/RTV | 223 | 63.5 [54.7-72.3] | 1.72 [1.20-2.47] | 0.11 | 0.04 | 0.16 | 0.24 |  | 0.75 |
| EFV | 188 | 62.7 [54.1-71.3] | 1.80 [1.25-2.61] | 0.20 | 0.13 | 0.10 | 0.51 | 0.75 |  |
| RPV | 173 | 36.6 [28.7-45.8] | 1 | <0.0001 | <0.0001 | 0.07 | <0.0001 | 0.003 | 0.002 |
| **Backbone** |  |  |  | **TDF** | **TAF** |  |  |  |  |
| TDF/FTC | 2495 | 62.5 [59.9-65.0] | 1 |  | 0.007 |  |  |  |  |
| TAF/FTC | 153 | 65.1 [55.1-75.0] | 1.52 [1.12-2.05] | 0.007 |  |  |  |  |  |
| ABC/3TC | 458 | 65.6 [60.4-70.7] | 0.98 [0.83-1.15] | 0.77 | 0.01 |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |

**c-PWH presenting early – Multivariable mixed model for weight change**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **Weight gain at 12 months (kg)** | **Weight gain at 24 months (kg)** | **Weight gain at 30 months (kg)** | **P** |  |  |  |  |  |
| **Total** | 5794 | 2.53 (1.94-3.11) | 2.84 (2.10-3.57) | 2.82 (1.97-3.68) | **vs** | **vs** | **vs** | **vs** | **vs** | **vs** |
| **3rd agent** |  |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 155 | 2.69 (1.70-3.68) | 3.24 (2.07-4.41) | 3.45 (2.00-4.90) |  | 0.94 | 0.65 | 0.51 | 0.08 | 0.02 |
| DTG | 877 | 3.16 (2.47-3.85) | 3.83 (2.95-4.70) | 3.51 (2.43-4.59) | 0.94 |  | 0.53 | 0.32 | 0.04 | 0.006 |
| EVG/COBI | 931 | 2.50 (1.84-3.16) | 3.22 (2.39-4.06) | 3.14 (2.16-4.12) | 0.65 | 0.53 |  | 0.77 | 0.08 | 0.006 |
| DRV/RTV | 1401 | 2.46 (1.82-3.09) | 2.67 (1.87-3.47) | 3.00 (2.03-3.98) | 0.51 | 0.32 | 0.77 |  | 0.12 | 0.01 |
| ATV/RTV | 364 | 2.53 (1.70-3.36) | 2.35 (1.27-3.44) | 2.06 (0.75-3.38) | 0.08 | 0.04 | 0.08 | 0.12 |  | 0.67 |
| EFV | 363 | 1.63 (0.84-2.43) | 1.71 (0.71-2.70) | 1.78 (0.62-2.94) | 0.02 | 0.006 | 0.006 | 0.01 | 0.67 |  |
| RPV | 1703 | 2.71 (2.05-3.36) | 2.85 (2.02-3.67) | 2.82 (1.86-3.79) | 0.32 | 0.19 | 0.37 | 0.62 | 0.17 | 0.01 |
| **Backbone** |  |  |  |  | **vs TDF** | **vs TAF** |  |  |  |  |
| TDF/FTC | 4417 | 1.95 (1.39-2.51) | 2.27 (1.58-2.97) | 2.27 (1.47-3.90) |  | 0.002 |  |  |  |  |
| TAF/FTC | 419 | 3.66 (2.88-4.43) | 3.81 (2.80-4.82) | 3.73 (2.54-4.91) | 0.002 |  |  |  |  |  |
| ABC/3TC | 958 | 1.97 (1.23-2.70) | 2.43 (1.49-3.38) | 2.48 (1.33-3.62) | 0.67 | 0.07 |  |  |  |  |

**d- PWH presenting with advanced HIV disease – Multivariable mixed model for weight change**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **Weight change at 12 months (kg)** | **Weight change at 24 months (kg)** | **Weight change at 30 months (kg)** | **P** |  |  |  |  |  |
| **Total** | 3106 | 6.65 (5.94-7.36) | 9.05 (8.04-10.07) | 9.70 (8.35-11.06) | vs | vs | vs | vs | vs | vs |
| **3rd agent** |  |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 186 | 7.66 (6.26-9.07) | 10.97 (8.80-13.14) | 10.59 (7.97-13.20) |  | 0.84 | 0.12 | 0.14 | 0.78 | 0.48 |
| DTG | 460 | 7.45 (6.38-8.53) | 10.85 (9.38-12.33) | 10.88 (8.98-12.78) | 0.84 |  | 0.03 | 0.01 | 0.52 | 0.29 |
| EVG/COBI | 354 | 6.27 (5.30-7.24) | 7.46 (6.03-8.90) | 8.37 (6.62-10.12) | 0.12 | 0.03 |  | 0.64 | 0.13 | 0.35 |
| DRV/RTV | 1522 | 6.77 (5.96-7.59) | 8.70 (7.54-9.87) | 8.80 (7.25-10.34) | 0.14 | 0.01 | 0.64 |  | 0.11 | 0.46 |
| ATV/RTV | 223 | 6.44 (5.30-7.59) | 8.17 (6.48-9.87) | 10.19 (8.09-12.28) | 0.78 | 0.52 | 0.13 | 0.11 |  | 0.62 |
| EFV | 188 | 6.44 (5.06-7.82) | 9.36 (7.56-11.15) | 9.55 (7.32-11.79) | 0.48 | 0.29 | 0.35 | 0.46 | 0.62 |  |
| RPV | 173 | 5.50 (4.34-6.66) | 7.85 (6.34-9.36) | 9.55 (7.54-11.56) | 0.45 | 0.24 | 0.30 | 0.39 | 0.57 | 1.00 |
| **Backbone** |  |  |  |  | **vs TDF** | **vs TAF** |  |  |  |  |
| TDF/FTC | 2495 | 5.86 (5.26-6.46) | 7.87 (6.99-8.75) | 8.40 (7.34-9.47) |  | 0.07 |  |  |  |  |
| TAF/FTC | 153 | 7.34 (5.91-8.78) | 10.86 (8.75-12.98) | 11.04 (8.10-13.97) | 0.07 |  |  |  |  |  |
| ABC/3TC | 458 | 6.74 (5.81-7.67) | 8.42 (7.17-9.67) | 9.67 (8.11-11.22) | 0.08 | 0.40 |  |  |  |  |

**Table S6. Increase in BMI of at least 5 kg/m2**

**a – Factors associated with an increase in BMI of at least 5 kg/m2: univariable and multivariable Cox regression analyses for all PWH**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristics** | **N** | **∆ BMI ≥ 5 kg/m2** | **Univariable Cox** |  |  | **Multivariable Cox** |  |
|  |  | **Kaplan-Meier estimates at 30 months [95% CI]** | **HR [95% CI]** | **P** |  | **HR [95% CI]** | **P** |
| **Total** | 12773 | 9.1 [8.5-9.8] |  |  |  |  |  |
| **3rd agent** |  |  |  |  |  |  |  |
| RAL | 469 | 17.6 [13.5-22.7] | 4.54 [3.20-6.44] | <0.0001 |  | 1.60 [1.10-2.34] | 0.02 |
| DTG | 1922 | 10.6 [8.9-12.6] | 2.55 [1.93-3.36] |  |  | 1.12 [0.79-1.58] |  |
| EVG/COBI | 1866 | 8.4 [6.9-10.3] | 2.02 [1.51-2.70] |  |  | 1.02 [0.73-1.42] |  |
| DRV/RTV | 4448 | 12.7 [11.3-14.3] | 3.09 [2.42-3.94] |  |  | 1.06 [0.80-1.40] |  |
| ATV/RTV | 879 | 8.3 [6.0-11.4] | 1.89 [1.29-2.75] |  |  | 0.80 [0.54-1.19] |  |
| EFV | 854 | 6.2 [4.5-8.6] | 1.56 [1.06-2.28] |  |  | 0.79 [0.53-1.18] |  |
| RPV | 2335 | 4.4 [3.5-5.4] | 1 |  |  | 1 |  |
| **Backbone** |  |  |  |  |  |  |  |
| TDF/FTC | 9984 | 8.5 [7.9-9.2] | 1 | 0.01 |  | 1 | 0.001 |
| TAF/FTC | 800 | 11.4 [8.7-14.8] | 1.27 [0.97-1.67] |  |  | 1.68 [1.19-2.38] |  |
| ABC/3TC | 1989 | 11.1 [9.5-13.0] | 1.28 [1.07-1.53] |  |  | 1.28 [1.02-1.61] |  |
| **Age and gender** |  |  |  |  |  |  |  |
| Women ≤ 50 years | 2440 | 16.6 [14.7-18.6] | 2.98 [2.52-3.52] | <0.0001 |  | 1.91 [1.57-2.33] | <0.0001 |
| Women > 50 years | 680 | 18.1 [14.7-22.3] | 3.41 [2.66-4.38] |  |  | 1.95 [1.49-2.55] |  |
| Men ≤ 50 years | 7831 | 5.6 [5.0-6.4] | 1 |  |  | 1 |  |
| Men > 50 years | 1822 | 10.1 [8.4-12.1] | 1.87 [1.51-2.31] |  |  | 1.20 [0.97-1.50] |  |
| **Transmission Group** |  |  |  |  |  |  |  |
| MSM | 6147 | 4.0 [3.4-4.7] | 1 | <0.0001 |  | 1 | <0.0001 |
| Other | 6626 | 13.8 [12.8-14.9] | 3.65 [3.05-4.35] |  |  | 1.82 [1.47-2.27] |  |
| **Geographic origin** |  |  |  |  |  |  |  |
| Sub-Saharan Africa | 3288 | 14.6 [13.1-16.2] | 2.00 [1.73-2.31] | <0.0001 |  | 1.14 [0.96-1.36] | 0.14 |
| Other | 9485 | 7.1 [6.5-7.9] | 1 |  |  | 1 |  |
| **BMI (kg/m2)** |  |  |  |  |  |  |  |
| Underweight (<18.5) | 917 | 17.0 [14.1-20.5] | 2.39 [1.92-2.96] | <0.0001 |  | 1.33 [1.07-1.67] | 0.001 |
| Normal [18.5-25[ | 7974 | 8.5 [7.7-9.4] | 1 |  |  | 1 |  |
| Overweight [25-30[ | 2838 | 7.2 [6.1-8.6] | 0.83 [0.68-1.00] |  |  | 0.83 [0.68-1.01] |  |
| Obese (≥30) | 1044 | 12.4 [10.0-15.3] | 1.39 [1.10-1.76] |  |  | 1.26 [0.98-1.61] |  |
| **CD4 (cells/mm3)** |  |  |  |  |  |  |  |
| <200 | 2861 | 24.0 [21.9-26.2] | 8.28 [6.56-10.44] | <0.0001 |  | 2.98 [2.27-3.92] | <0.0001 |
| 200-350 | 2911 | 8.0 [6.7-9.4] | 2.29 [1.75-3.00] |  |  | 1.69 [1.28-2.23] |  |
| 350-500 | 3178 | 5.2 [4.3-6.4] | 1.52 [1.14-2.02] |  |  | 1.36 [1.02-1.80] |  |
| ≥ 500 | 3823 | 3.5 [2.8-4.4] | 1 |  |  | 1 |  |
| **Viral load (copies/ml)** |  |  |  |  |  |  |  |
| ]50-30000] | 5058 | 5.0 [4.3-5.8] | 1 | <0.0001 |  | 1 | <0.0001 |
| ]30000-100000] | 3110 | 5.7 [4.7-6.8] | 1.18 [0.93-1.49] |  |  | 1.01 [0.79-1.28] |  |
| ]100000-500000] | 3018 | 14.8 [13.1-16.7] | 3.06 [2.52-3.71] |  |  | 1.89 [1.51-2.36] |  |
| > 500000 | 1587 | 23.2 [20.4-26.5] | 5.49 [4.47-6.73] |  |  | 2.64 [2.07-3.37] |  |
| **Prior AIDS defining event** |  |  |  |  |  |  |  |
| No | 11665 | 7.0 [6.4-7.6] | 1 | <0.0001 |  | 1 | <0.0001 |
| Tuberculosis | 262 | 37.1 [29.7-45.8] | 6.84 [5.21-8.98] |  |  | 2.69 [1.98-3.65] |  |
| AIDS cancer | 175 | 20.0 [12.8-30.6] | 2.98 [1.87-4.78] |  |  | 1.77 [1.09-2.86] |  |
| Other AIDS pathology | 671 | 39.0 [34.1-44.4] | 8.08 [6.77-9.66] |  |  | 3.01 [2.45-3.70] |  |

**b – Comparison between drugs for an increase in BMI of at least 5 kg/m2 for all PWH**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **n** | **KM estimates at 30 months [95% CI]** | **HR [95% CI]** | **P** |  |  |  |  |  |
| **Total** | 12773 | 9.1 [8.5-9.8] |  | **vs** | **vs** | **vs** | **vs** | **vs** | **vs** |
| **3rd agent** |  |  |  | **RAL** | **DTG** | **EVG** | **DRV** | **ATV** | **EFV** |
| RAL | 469 | 17.6 [13.5-22.7] | 1.60 [1.10-2.34] |  | 0.06 | 0.02 | 0.01 | 0.002 | 0.001 |
| DTG | 1922 | 10.6 [8.9-12.6] | 1.12 [0.79-1.58] | 0.06 |  | 0.60 | 0.67 | 0.08 | 0.09 |
| EVG/COBI | 1866 | 8.4 [6.9-10.3] | 1.02 [0.73-1.42] | 0.02 | 0.60 |  | 0.78 | 0.25 | 0.23 |
| DRV/RTV | 4448 | 12.7 [11.3-14.3] | 1.06 [0.80-1.40] | 0.01 | 0.67 | 0.78 |  | 0.10 | 0.10 |
| ATV/RTV | 879 | 8.3 [6.0-11.4] | 0.80 [0.54-1.19] | 0.002 | 0.08 | 0.25 | 0.10 |  | 0.96 |
| EFV | 854 | 6.2 [4.5-8.6] | 0.79 [0.53-1.18] | 0.001 | 0.09 | 0.23 | 0.10 | 0.96 |  |
| RPV | 2335 | 4.4 [3.5-5.4] | 1 | 0.02 | 0.53 | 0.92 | 0.68 | 0.27 | 0.25 |
| **Backbone** |  |  |  | **vs TDF** | **vs TAF** |  |  |  |  |
| TDF/FTC | 9984 | 8.5 [7.9-9.2] | 1 |  | 0.003 |  |  |  |  |
| TAF/FTC | 800 | 11.4 [8.7-14.8] | 1.68 [1.19-2.38] | 0.003 |  |  |  |  |  |
| ABC/3TC | 1989 | 11.1 [9.5-13.0] | 1.28 [1.02-1.61] | 0.03 | 0.19 |  |  |  |  |

**Table S7:  Factors associated with a weight gain of at least 10%: univariable and multivariable Cox regression models for PWH without prior AIDS defining event**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Characteristics** | **N** | **∆ weight > 10%** | **Univariable Cox** |  |  | **Multivariable Cox** |  |
|  |  | Kaplan-Meier estimates at 30 months [95% CI] | HR [95% CI] | P |  | HR [95% CI] | P |
| **Total** | 11665 | 30.9 [29.8-31.9] |  |  |  |  |  |
| **3rd agent** |  |  |  |  |  |  |  |
| RAL | 340 | 33.2 [27.5-39.8] | 1.89 [1.49-2.40] | <0.0001 |  | 1.49 [1.17-1.90] | <0.0001 |
| DTG | 1751 | 32.8 [30.1-35.7] | 1.76 [1.53-2.03] |  |  | 1.43 [1.20-1.70] |  |
| EVG/COBI | 1768 | 32.1 [29.4-35.0] | 1.70 [1.48-1.95] |  |  | 1.12 [0.95-1.31] |  |
| DRV/RTV | 3949 | 39.2 [37.0-41.4] | 2.24 [1.99-2.52] |  |  | 1.32 [1.16-1.51] |  |
| ATV/RTV | 821 | 35.7 [31.4-40.4] | 1.87 [1.57-2.23] |  |  | 1.26 [1.05-1.52] |  |
| EFV | 748 | 19.3 [16.1-23.0] | 0.93 [0.75-1.15] |  |  | 0.76 [0.61-0.95] |  |
| RPV | 2288 | 20.7 [18.9-22.7] | 1 |  |  | 1 |  |
| **Backbone** |  |  |  |  |  |  |  |
| TDF/FTC | 9077 | 29.8 [28.6-31.0] | 1 | 0.0002 |  | 1 | <0.0001 |
| TAF/FTC | 755 | 39.1 [34.7-43.8] | 1.34 [1.16-1.54] |  |  | 1.48 [1.24-1.76] |  |
| ABC/3TC | 1833 | 32.4 [29.9-35.1] | 1.07 [0.97-1.19] |  |  | 0.94 [0.83-1.08] |  |
| **Age and gender** |  |  |  |  |  |  |  |
| Women ≤ 50 years | 2210 | 42.9 [40.4-45.6] | 1.78 [1.62-1.95] | <0.0001 |  | 1.44 [1.29-1.62] | <0.0001 |
| Women > 50 years | 596 | 44.0 [39.2-49.1] | 1.93 [1.66-2.25] |  |  | 1.54 [1.30-1.82] |  |
| Men ≤ 50 years | 7286 | 26.1 [24.8-27.4] | 1 |  |  | 1 |  |
| Men > 50 years | 1573 | 29.8 [27.1-32.8] | 1.25 [1.11-1.41] |  |  | 1.07 [0.95-1.21] |  |
| **Transmission Group** |  |  |  |  |  |  |  |
| MSM | 5826 | 23.2 [21.8-24.6] | 1 | <0.0001 |  | 1 | <0.0001 |
| Other | 5839 | 38.3 [36.7-39.9] | 1.88 [1.73-2.04] |  |  | 1.44 [1.29-1.60] |  |
| **Geographic origin** |  |  |  |  |  |  |  |
| Sub-Saharan Africa | 2939 | 40.0 [37.8-42.2] | 1.53 [1.41-1.67] | <0.0001 |  | 1.08 [0.98-1.20] | 0.13 |
| Other | 8726 | 27.7 [26.5-28.9] | 1 |  |  | 1 |  |
| **BMI (kg/m2)** |  |  |  |  |  |  |  |
| Underweight (< 18.5) | 696 | 49.0 [44.3-53.9] | 2.05 [1.79-2.34] | <0.0001 |  | 1.76 [1.54-2.02] | <0.0001 |
| Normal [18.5-25[ | 7303 | 30.4 [29.1-31.8] | 1 |  |  | 1 |  |
| Overweight [25-30[ | 2676 | 29.2 [27.0-31.5] | 0.86 [0.78-0.95] |  |  | 0.76 [0.69-0.84] |  |
| Obese (≥ 30) | 990 | 26.6 [23.3-30.4] | 0.77 [0.66-0.90] |  |  | 0.63 [0.54-0.74] |  |
| **CD4 (cells/mm3)** |  |  |  |  |  |  |  |
| < 200 | 2018 | 56.2 [53.4-59.1] | 4.06 [3.64-4.53] | <0.0001 |  | 2.42 [2.13-2.73] | <0.0001 |
| 200-350 | 2785 | 35.2 [33.0-37.6] | 1.90 [1.70-2.13] |  |  | 1.49 [1.32-1.68] |  |
| 350-500 | 3099 | 24.5 [22.6-26.5] | 1.24 [1.10-1.40] |  |  | 1.13 [1.00-1.27] |  |
| ≥ 500 | 3763 | 20.2 [18.7-21.9] | 1 |  |  | 1 |  |
| **Viral load (copies/ml)** |  |  |  |  |  |  |  |
| ]50-30 000] | 4892 | 22.7 [21.3-24.2] | 1 | <0.0001 |  | 1 | <0.0001 |
| ]30 000-100 000] | 2928 | 29.4 [27.3-31.5] | 1.34 [1.21-1.49] |  |  | 1.20 [1.08-1.34] |  |
| ]100 000-500 000] | 2598 | 41.0 [38.6-43.6] | 2.18 [1.97-2.42] |  |  | 1.62 [1.45-1.81] |  |
| > 500 000 | 1247 | 51.0 [47.1-55.0] | 3.24 [2.87-3.65] |  |  | 2.17 [1.90-2.48] |  |

**Figure S1. Patterns of BMI categories over time (months) according to the third**

**agent for PWH presenting early (at primary infection or with CD4 > 350/mm3 and VL < 100 000 copies/mL, without AIDS)**

**a)** **Integrase inhibitor** **(INSTI: integrase strand-transfer inhibitor)**

 

**b)** **Protease inhibitor (PI)**



**c) Non-nucleoside reverse transcriptase inhibitor (NNRTI)**



**Figure S2. Patterns of BMI categories over time (months) according to the third agent for PWH presenting with advanced HIV disease (with AIDS or with CD4 < 200/mm3, not during primary infection)**

**a)** **Integrase inhibitor** **(INSTI: integrase strand-transfer inhibitor)**

 

**b)** **Protease inhibitor (PI)**



**c) Non-nucleoside reverse transcriptase inhibitor (NNRTI)**

