**Supplementary materials**

Supplementary Table 1. Search terms used to identify relevant citations from PubMed and Embase

|  | **PubMed** | **Embase** |
| --- | --- | --- |
| **General search terms** | HIV-1 [mesh] OR HIV infections [mesh]) NOT pregnancy [mesh]  | ('human immunodeficiency virus 1'/exp OR 'human immunodeficiency virus infection'/exp NOT 'pregnancy'/exp) |
| **Treatment-specific search terms** | ((dolutegravir OR GSK1349572) OR (efavirenz OR Sustiva OR Stocrin OR DMP-266) OR (raltegravir OR Isentress OR MK-0518) OR (elvitegravir OR GS-9137 OR JTK-303) OR (rilpivirine OR Edurant OR TMC 278) OR (darunavir OR Prezista OR TMC-114) OR (atazanavir OR Reyataz OR BMS-232632) OR (lopinavir OR ABT-378 OR Aluviran OR Kaletra) OR (etravirine OR Intelence OR TMC-125) OR Atripla OR Quad OR Stribild OR Eviplera OR Complera OR bictegravir OR GS-9883))  | 'dolutegravir'/exp OR 'efavirenz'/exp OR 'raltegravir'/exp OR 'elvitegravir'/exp OR 'rilpivirine'/exp OR 'darunavir'/exp OR 'darunavir plus ritonavir'/exp OR 'atazanavir'/exp OR 'atazanavir plus ritonavir'/exp OR 'lopinavir'/exp OR 'lopinavir plus ritonavir'/exp OR 'etravirine'/exp OR 'efavirenz plus emtricitabine plus tenofovir disoproxil'/exp OR 'emtricitabine plus rilpivirine plus tenofovir disoproxil'/exp OR 'cobicistat'/exp OR ‘bictegravir’/exp |
| **Limits** | Humans, Randomized Controlled Trial, English, Adults and Adolescents (≥13 years of age), systematic reviews, meta-analyses |

HIV, human immunodeficiency virus.

**Supplementary Table 2.** Summary of NMA inputs for the 14 studies in treatment-naïve patients included in the NMA

| **Study** | **Treatments** | **N** | **% male** | **Mean age, y** | **Baseline CD4+, cells/mL**  | **Baseline viral load, log10 RNA copies/mL** | **VS HIV RNA <50 copies/mL (n/N)** | **CD4+ change, cells/µL (SD)** | **AEs (n/N)** | **SAE (n/N)** | **Drug-related AEs (n/N)** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| AMBER [1] | DRV/c + TAF/FTC | 362 | 88 | 34† | 462 | 4.44 | 331/362 | 190.49 (10.47) | 312/362 | 17/362 | 126/362 |
| DRV/c + TDF/FTC\* | 363 | 89 | 34† | 440 | 4.57 | 321/363 | 172.01 (10.46) | 307/363 | 21/363 | 151/363 |
| ECHO [2] | EFV + TDF/FTC | 344 | 80 | 36† | 257 | 5 | 285/344 | 181.6 (156.9) | 317/344 | 31/344 | 108/344 |
| RPV + TDF/FTC | 346 | 77 | 36† | 240 | 5 | 287/346 | 195.5 (151.7) | 303/346 | 23/346 | 55/346 |
| FLAMINGO [3] | DRV/r + ABC/3TC | 242 | 83 | 34† | 400 | 4.48 | 68/80 | 200.3 (26.9) | 69/79 | 6/80 | 39/80 |
| DRV/r + TDF/FTC\* | 132/162 | 240.3 (15.21) | 137/163 | 7/162 | 77/162 |
| DTG + ABC/3TC | 242 | 87 | 34† | 390 | 4.49 | 71/79 | 255.1 (25.49) | 67/80 | 10/79 | 27/79 |
| DTG + TDF/FTC | 146/163 | 255.1 (14.69) | 138/162 | 16/163 | 53/163 |
| GEMINI-1 [4] | DTG + 3TC | 716‡ | 84‡ | 32‡ | 462‡ | 4.42‡ | 320/356 | 222.2 (10.31) | 276/356 | 21/356 | 71/356 |
| DTG + TDF/FTC | 717‡ | 86‡ | 33‡ | 461‡ | 4.45‡ | 332/358 | 217.7 (10.22) | 295/358 | 22/358 | 94/358 |
| GEMINI-2 [4] | DTG + 3TC | 716‡ | 84‡ | 32‡ | 462‡ | 4.42‡ | 335/360 | 225.9 (9.42) | 267/360 | 29/360 | 55/360 |
| DTG + TDF/FTC | 717‡ | 86‡ | 33‡ | 461‡ | 4.45‡ | 337/359 | 216.9 (9.48) | 284/359 | 33/359 | 75/359 |
| GS-236-0102 (QUAD) [5-7] | EFV + TDF/FTC | 352 | 64 | 38† | 382 | 4.78 | 296/352 | 206 (153.4) | 376/352 | 50/352 | ‒ |
| EVG/c + TDF/FTC | 348 | 59 | 37† | 391 | 4.73 | 305/348 | 239 (167.2) | 382/348 | 69/348 | ‒ |
| GS-US-292-0104/0111 [8] | EVG/c + TAF/FTC | 866 | 85 | 33† | 404 | 4.58 | 800/866 | 230 (177.3) | 795/866 | 97/866 | ‒ |
| EVG/c + TDF/FTC | 867 | 85 | 35† | 406 | 4.58 | 784/867 | 211 (170.7) | 765/867 | 87/867 | ‒ |
| GS-US-380-1489 [9] | BIC + TAF/FTC | 314 | 91 | 31† | 443 | 4.42 | 290/314 | 233 (185.2) | 265/314 | 19/314 | 82/314 |
| DTG + ABC/3TC | 315 | 90 | 32† | 450 | 4.51 | 293/315 | 229 (188.8) | 283/315 | 25/315 | 127/315 |
| GS-US-380-1490 [10, 11] | BIC + TAF/FTC | 320 | 88 | 33† | 440 | 4.43 | 286/320 | 180 (166.6) | 264/320 | 39/320 | 57/320 |
| DTG + TAF/FTC | 325 | 89 | 34† | 441 | 4.45 | 302/325 | 201 (166.4) | 272/325 | 23/325 | 83/325 |
| SINGLE [12] | DTG + ABC/3TC | 414 | 84 | 36† | 335 | 4.67 | 364/414 | 267.06 (9.05) | 369/414 | 37/414 | 180/414 |
| EFV + TDF/FTC | 419 | 85 | 35† | 339 | 4.70 | 338/419 | 208.16 (9.31) | 387/419 | 35/419 | 278/419 |
| SPRING-2 [13] | DTG + ABC/3TC | 411 | 85 | 37† | 359 | 4.52 | 145/169 | 275.3 (16.36) | 135/169 | 11/169 | 51/169 |
| DTG + TDF/FTC | 216/242 | 240 (11.87) | 204/242 | 18/242 | 65/242 |
| RAL + ABC/3TC | 411 | 86 | 35† | 362 | 4.58 | 142/164 | 258.2 (16.38) | 137/164 | 14/164 | 51/164 |
| RAL + TDF/FTC | 209/247 | 283.8 (12.45) | 203/247 | 17/247 | 68/247 |
| STaR (GS-US-264-0110) [14, 15] | EFV + TDF/FTC | 392 | 93 | 35† | 385 | 4.8 | 320/392 | 191 (144.3) | 370/392 | 48/392 | ‒ |
| RPV + TDF/FTC | 394 | 93 | 37† | 396 | 4.8 | 338/394 | 200 (158.6) | 336/394 | 36/394 | ‒ |
| STARTMRK [16] | EFV + TDF/FTC | 282 | 82 | 37 | 217 | 5.0 | 230/282 | 163.3 (7.7) | 272/282 | 27/282 | 217/282 |
| RAL + TDF/FTC | 281 | 81 | 38 | 219 | 5.0 | 241/281 | 189.1 (7.8) | 253/281 | 28/281 | 124/281 |

\*In the NMA, date from these groups (DRV/c + TDF/FTC and DRV/r + TDF/FTC) were combined into a single group DRV/b (boosted). †Median. ‡Baseline demographics and clinical characteristics reported for GEMINI-1 and GEMINI-2 pooled population [4].

3TC, Lamivudine; ABC, Abacavir; AE, adverse event; BIC, bictegravir; DTG, dolutegravir; DRV/c, cobicistat -boosted darunavir DRV/r, ritonavir-boosted darunavir; EFV, efavirenz; EVG/c, cobicistat-boosted elvitegravir; HIV, human immunodeficiency virus; FTC, emtricitabine; NMA, network meta-analysis; RAL, raltegravir; RNA, ribonucleic acid; RPV, rilpivirine; SAE, serious adverse event; SD, standard deviation; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VL, viral load; VS, virologic suppression; y, year.

**Supplementary Table 3. EPHPP quality assessment ratings (1: strong; 2: moderate; 3: weak) for the 14 studies included in the NMA**

| Study (Source) | Selection bias | Study design | Confounders | Blinding | Data collection method | Withdrawals and dropout | Global rating |
| --- | --- | --- | --- | --- | --- | --- | --- |
| AMBER [1] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| ECHO [2] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| FLAMINGO [3] | 1 | 1 | 1 | 3 | 1 | 1 | **2** |
| GEMINI-I and GEMINI-II [4] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| GS-US-236-0102 [6] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| GS-US-292-0104/0111 [8] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| GS-US-380-1489 [9] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| GS-US-380-1490 [10] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |
| SINGLE [12] | 2 | 1 | 1 | 1 | 1 | 1 | **1** |
| SPRING-2 [13] | 2 | 1 | 1 | 1 | 1 | 1 | **1** |
| STaR (GS-US-264-0110) [14] | 1 | 1 | 1 | 3 | 1 | 1 | **2** |
| STARTMRK [16] | 1 | 1 | 1 | 1 | 1 | 1 | **1** |

EPHPP, Effective Public Health Practice Project Quality Assessment; NMA, network meta-analysis.

**References**

1. Eron JJ, Orkin C, Gallant J, Molina JM, Negredo E, Antinori A*, et al.* **A week-48 randomized phase-3 trial of darunavir/cobicistat/emtricitabine/tenofovir alafenamide in treatment-naive HIV-1 patients**. *AIDS* 2018; **32**:1431–1442.

2. Molina JM, Cahn P, Grinsztejn B, Lazzarin A, Mills A, Saag M*, et al.* **Rilpivirine versus efavirenz with tenofovir and emtricitabine in treatment-naive adults infected with HIV-1 (ECHO): a phase 3 randomised double-blind active-controlled trial**. *Lancet* 2011; **378**:238–246.

3. Clotet B, Feinberg J, van Lunzen J, Khuong-Josses MA, Antinori A, Dumitru I*, et al.* **Once-daily dolutegravir versus darunavir plus ritonavir in antiretroviral-naive adults with HIV-1 infection (FLAMINGO): 48 week results from the randomised open-label phase 3b study**. *Lancet* 2014; **383**:2222–2231.

4. Cahn P, Madero JS, Arribas JR, Antinori A, Ortiz R, Clarke AE*, et al.* **Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials**. *Lancet* 2018; **393**:143–155.

5. ClinicalTrials.gov. **Abacavir/Lamivudine Versus Emtricitabine/Tenofovir Both In Combination With Lopinavir/Ritonavir For The Treatment Of HIV (HEAT) (NCT00244712)**. <https://clinicaltrials.gov/ct2/show/results/NCT00244712>; Accessed on: 11 February 2019.

6. Sax PE, DeJesus E, Mills A, Zolopa A, Cohen C, Wohl D*, et al.* **Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks**. *Lancet* 2012; **379**:2439–2448.

7. Zolopa A, Sax PE, DeJesus E, Mills A, Cohen C, Wohl D*, et al.* **A randomized double-blind comparison of coformulated elvitegravir/cobicistat/emtricitabine/tenofovir disoproxil fumarate versus efavirenz/emtricitabine/tenofovir disoproxil fumarate for initial treatment of HIV-1 infection: analysis of week 96 results**. *J Acquir Immune Defic Syndr* 2013; **63**:96-100.

8. Sax PE, Wohl D, Yin MT, Post F, DeJesus E, Saag M*, et al.* **Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials**. *Lancet* 2015; **385**:2606–2615.

9. Gallant J, Lazzarin A, Mills A, Orkin C, Podzamczer D, Tebas P*, et al.* **Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial**. *Lancet* 2017; **390**:2063–2072.

10. Sax PE, Pozniak A, Montes ML, Koenig E, DeJesus E, Stellbrink HJ*, et al.* **Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380-1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial**. *Lancet* 2017; **390**:2073–2082.

11. Canadian Drug Expert Committee. **CADTH Canadian Drug Expert Committee Recommendation – BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE (BIKTARVY — GILEAD SCIENCES CANADA, INC.)**. <https://www.cadth.ca/sites/default/files/cdr/complete/SR0567%20Biktarvy%20-%20CDEC%20Final%20Recommendation%20October%2029%2C%202018.pdf>; Accessed on: 11 February 2019.

12. Walmsley SL, Antela A, Clumeck N, Duiculescu D, Eberhard A, Gutierrez F*, et al.* **Dolutegravir plus abacavir-lamivudine for the treatment of HIV-1 infection**. *N Engl J Med* 2013; **369**:1807–1818.

13. Raffi F, Rachlis A, Stellbrink HJ, Hardy WD, Torti C, Orkin C*, et al.* **Once-daily dolutegravir versus raltegravir in antiretroviral-naive adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority SPRING-2 study**. *Lancet* 2013; **381**:735–743.

14. Cohen C, Wohl D, Arribas JR, Henry K, Van Lunzen J, Bloch M*, et al.* **Week 48 results from a randomized clinical trial of rilpivirine/emtricitabine/tenofovir disoproxil fumarate vs. efavirenz/emtricitabine/tenofovir disoproxil fumarate in treatment-naive HIV-1-infected adults**. *AIDS* 2014; **28**:989–997.

15. van Lunzen J, Antinori A, Cohen CJ, Arribas JR, Wohl DA, Rieger A*, et al.* **Rilpivirine vs. efavirenz-based single-tablet regimens in treatment-naive adults: week 96 efficacy and safety from a randomized phase 3b study**. *AIDS* 2016; **30**:251-259.

16. Lennox JL, DeJesus E, Lazzarin A, Pollard RB, Madruga JV, Berger DS*, et al.* **Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naive patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial**. *Lancet* 2009; **374**:796–806.