

Supporting Information for

Review

Approved HIV reverse transcriptase inhibitors in the past decade

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Received 12 August 2021; received in revised form 13 October 2021; accepted

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Table S1-1 The frequency of adverse events of RTI-based regimens in phase 2/3 clinical trials.

Regimen	ClinicalTrials.gov Identifier	Ref.	Phase	Patients	Drug-related adverse events	Grade 3-4 adverse events	Diarrhoea
TDF+FTC+RPV	NCT02345252	[1]	3	VS	12% (37/314)	3% (10/314)	8% (26/314)
	NCT00540449	[2]	3	TN	NA	NA	NA
	NCT01309243	[3]	3	TN	NA	NA	NA
TAF+FTC+RPV	NCT02345226	[4]	3	VS	13% (56/438)	6% (27/438)	5% (21/438)
	NCT02345252	[1]	3	VS	6% (20/316)	5% (17/316)	7% (23/316)
DTG+RPV	NCT02429791 NCT02422797	[5]	3	VS	19% (97/513)	6% (32/513)	6% (32/513)
RPV+CAB (monthly)	NCT02951052	[6]	3	VS	29% (88/308)	5% (14/308)	1% (2/308)
	NCT02938520	[7]	3	VS	28% (79/283)	8% (22/283)	11% (32/283)
	NCT02120352	[8]	3	VS	NA	NA	NA
	NCT03299049	[9]	3	VS	NA	9.4% (49/523)	7% (37/523)
DOR+TDF+3TC	NCT02275780	[10]	3	TN	NA	NA	5% (21/333)
	NCT02403674	[11]	3	TN	31% (113/364)	NA	11% (39/364)
	NCT02397096	[12]	3	VS	19.5% (87/447)	NA	NA
TAF+FTC+EVG/c	NCT01497899	[13]	2	TN	NA	NA	16% (18/112)
	NCT01780506 NCT01797445	[14]	3	TN	40%	NA	17% (147/866)
	NCT01705574	[15]	3	VS	11.3% (18/159)	6.3% (10/159)	NA
	NCT01815736	[16]	3	VS	21% (204/959)	9% (84/959)	10% (96/959)
	NCT02616783	[17]	3	VS	20% (22/110)	9% (9/110)	7% (8/110)
TAF+FTC+BIC	NCT02603120	[18]	3	VS	8% (23/282)	6% (16/282)	9% (24/282)
	NCT02652624	[19]	3	VS	9% (20/234)	5% (11/234)	NA
	NCT03110380	[20]	3	VS	14% (41/284)	8% (23/284)	8% (23/284)
	NCT02603107	[21]	3	VS	19% (54/290)	4% (13/290)	8% (24/290)
	NCT02607956	[22]	3	TN	18% (57/320)	NA	12% (37/320)
	NCT02607930	[23]	3	TN	26% (82/314)	7% (23/314)	13% (40/314)
	NCT02397694	[24]	2	TN	NA	NA	12% (8/65)
TAF+FTC+DRV/c	NCT02269917	[25]	3	VS	18% (138/763)	7% (52/763)	8% (60/763)
	NCT01565850	[26]	2	TN	NA	NA	21% (22/103)
	NCT02431247	[27]	3	TN	35% (126/362)	5% (19/362)	20% (71/362)
TAF+FTC+DTG	NCT03122262	[28]	3	TN	NA	NA	NA
	NCT02397694	[24]	2	TN	NA	NA	12% (4/33)
	NCT02607956	[22]	3	TN	26% (83/325)	NA	12% (39/325)
	NCT03110380	[20]	3	VS	10% (28/281)	5% (13/281)	11% (32/281)
TDF+FTC+EVG/c	NCT01095796	[29]	3	TN	NA	NA	23% (80/348)
	NCT01106586	[30]	3	TN	NA	NA	22% (77/353)
	NCT01780506 NCT01797445	[14]	3	TN	42%	NA	19% (164/867)
	NCT01497899	[13]	2	TN	NA	NA	16% (9/58)
	NCT02616783	[17]	3	VS	2% (1/56)	2% (1/56)	4% (2/56)
DTG+3TC	NCT02831673 NCT02831764	[31]	3	TN	18% (126/716)	NA	9% (68/716)
	NCT02263326	[32]	3	VS	NA	NA	NA
	NCT03446573	[33]	3	VS	12.2% (45/369)	NA	8.1% (30/369)
ABC+3TC+DTG	NCT01263015	[34]	3	TN	NA	NA	5% (21/414)
	NCT02607930	[23]	3	TN	40% (127/315)	8% (24/315)	13% (41/315)

	NCT02603120	[18]	3	VS	16% (44/281)	4% (10/281)	5% (14/281)
	NCT02938520	[7]	3	VS	10% (28/283)	4% (11/283)	9% (25/283)
	NCT02105987	[35]	3	VS	22% (60/275)	3% (9/275)	7% (20/275)

Table S1-2 The frequency of adverse events of RTI-based regimens in phase 2/3 clinical trials.

Regimen	ClinicalTrials.gov Identifier	Ref.	Upper respiratory tract infection	Nasopharyngitis	Bronchitis	Headache	Insomnia
TDF+FTC+RPV	NCT02345252	[1]	8% (26/314)	8% (24/314)	6% (18/314)	5% (17/314)	NA
	NCT00540449	[2]	NA	NA	NA	NA	NA
	NCT01309243	[3]	NA	NA	NA	12% (49/394)	9.6% (38/394)
TAF+FTC+RPV	NCT02345226	[4]	10% (44/438)	8% (34/438)	NA	6% (24/438)	NA
	NCT02345252	[1]	9% (27/316)	7% (22/316)	4% (12/316)	5% (15/316)	NA
DTG+RPV	NCT02429791 NCT02422797	[5]	5% (24/513)	10% (49/513)	4% (23/513)	8% (41/513)	3% (17/513)
RPV+CAB (monthly)	NCT02951052	[6]	0% (0/308)	0% (0/308)	NA	4% (11/308)	NA
	NCT02938520	[7]	13% (38/283)	20% (56/283)	NA	14% (39/283)	NA
	NCT02120352	[8]	NA	NA	NA	NA	NA
	NCT03299049	[9]	14% (71/523)	14% (74/523)	NA	7% (36/523)	NA
DOR+TDF+3TC	NCT02275780	[10]	NA	NA	NA	6% (23/333)	NA
	NCT02403674	[11]	9% (33/364)	11% (39/364)	NA	13% (47/364)	5% (19/364)
	NCT02397096	[12]	NA	7.4% (33/447)	NA	6.5% (29/447)	NA
TAF+FTC+EVG/c	NCT01497899	[13]	15% (17/112)	6% (7/112)	6% (7/112)	10% (11/112)	4% (4/112)
	NCT01780506 NCT01797445	[14]	11% (99/866)	9% (78/866)	NA	14% (124/866)	7% (57/866)
	NCT01705574	[15]	12% (19/159)	NA	NA	9.4% (15/159)	NA
	NCT01815736	[16]	16% (151/959)	9% (88/959)	6% (58/959)	7% (69/959)	5% (50/959)
	NCT02616783	[17]	NA	NA	4% (4/110)	NA	NA
TAF+FTC+BIC	NCT02603120	[18]	10% (29/282)	7% (20/282)	NA	7% (19/282)	3% (8/282)
	NCT02652624	[19]	6% (15/234)	8% (18/234)	NA	6% (13/234)	NA
	NCT03110380	[20]	7% (20/284)	11% (32/284)	5% (14/284)	5% (13/284)	6% (18/284)
	NCT02603107	[21]	7% (21/290)	7% (21/290)	NA	12% (35/290)	NA
	NCT02607956	[22]	5% (15/320)	7% (22/320)	NA	13% (40/320)	5% (16/320)
	NCT02607930	[23]	6% (20/314)	7% (23/314)	3% (10/314)	11% (36/314)	4% (14/314)
	NCT02397694	[24]	8% (5/65)	NA	NA	8% (5/65)	NA
TAF+FTC+DRV/c	NCT02269917	[25]	11% (81/763)	11% (81/763)	NA	8% (58/763)	NA
	NCT01565850	[26]	16% (16/103)	5% (5/103)	9% (9/103)	7% (7/103)	6% (6/103)
	NCT02431247	[27]	6% (20/362)	11% (40/362)	4% (14/362)	13% (47/362)	NA
TAF+FTC+DTG	NCT03122262	[28]	NA	NA	NA	NA	NA
	NCT02397694	[24]	0% (0/33)	NA	NA	3% (1/33)	NA
	NCT02607956	[22]	7% (23/325)	10% (31/325)	NA	12% (40/325)	4% (14/325)
	NCT03110380	[20]	11% (30/281)	10% (28/281)	4% (11/281)	8% (23/281)	4% (11/281)
TDF+FTC+EVG/c	NCT01095796	[29]	14% (48/348)	NA	NA	14% (49/348)	9% (30/348)
	NCT01106586	[30]	15% (54/353)	NA	NA	15% (53/353)	NA
	NCT01780506 NCT01797445	[14]	13% (109/867)	9% (80/867)	NA	13% (108/867)	6% (48/867)
	NCT01497899	[13]	21% (12/58)	3% (2/58)	5% (3/58)	14% (8/58)	7% (4/58)
	NCT02616783	[17]	NA	NA	11% (6/56)	NA	NA

DTG+3TC	NCT02831673 NCT02831764	[31]	8% (56/716)	8% (55/716)	4% (28/716)	10% (71/716)	4% (27/716)
	NCT02263326	[32]	NA	NA	NA	NA	NA
	NCT03446573	[33]	8.4% (31/369)	12% (43/369)	2.2% (8/369)	6.5% (24/369)	NA
ABC+3TC+DTG	NCT01263015	[34]	NA	NA	2% (8/414)	3% (12/414)	4% (17/414)
	NCT02607930	[23]	11% (34/315)	9% (29/315)	5% (16/315)	14% (43/315)	6% (20/315)
	NCT02603120	[18]	10% (27/281)	8% (22/281)	NA	7% (21/281)	5% (14/281)
	NCT02938520	[7]	10% (28/283)	17% (48/283)	NA	7% (21/283)	NA
	NCT02105987	[35]	13% (35/275)	5% (13/275)	NA	6% (17/275)	5% (14/275)

Table S1-3 The frequency of adverse events of RTI-based regimens in phase 2/3 clinical trials.

Regimen	ClinicalTrials.gov Identifier	Ref.	Fatigue	Arthralgia	Back pain	Rash
TDF+FTC+RPV	NCT02345252	[1]	NA	NA	NA	NA
	NCT00540449	[2]	NA	NA	NA	NA
	NCT01309243	[3]	NA	NA	NA	6.1% (24/394)
TAF+FTC+RPV	NCT02345226	[4]	NA	5% (20/438)	NA	NA
	NCT02345252	[1]	NA	NA	NA	NA
DTG+RPV	NCT02429791 NCT02422797	[5]	NA	4% (21/513)	3% (15/513)	NA
RPV+CAB (monthly)	NCT02951052	[6]	4% (11/308)	NA	1% (2/308)	NA
	NCT02938520	[7]	NA	NA	8% (22/283)	NA
	NCT02120352	[8]	NA	NA	NA	NA
	NCT03299049	[9]	6% (33/523)	NA	6% (29/523)	NA
DOR+TDF+3TC	NCT02275780	[10]	5% (18/333)	NA	NA	2% (8/333)
	NCT02403674	[11]	6% (21/364)	NA	NA	5% (17/364)
	NCT02397096	[12]	NA	NA	NA	NA
TAF+FTC+EVG/c	NCT01497899	[13]	14% (16/112)	NA	3% (3/112)	8% (9/112)
	NCT01780506 NCT01797445	[14]	8% (71/866)	7% (61/866)	7% (60/866)	6% (55/866)
	NCT01705574	[15]	NA	NA	6.9% (11/159)	NA
	NCT01815736	[16]	NA	6% (59/959)	5% (52/959)	NA
	NCT02616783	[17]	NA	6% (7/110)	NA	NA
TAF+FTC+BIC	NCT02603120	[18]	NA	7% (19/282)	NA	NA
	NCT02652624	[19]	NA	NA	NA	NA
	NCT03110380	[20]	7% (21/284)	6% (16/284)	5% (15/284)	NA
	NCT02603107	[21]	NA	4% (12/290)	4% (13/290)	NA
	NCT02607956	[22]	6% (19/320)	5% (16/320)	3% (11/320)	NA
	NCT02607930	[23]	6% (19/314)	4% (11/314)	NA	NA
	NCT02397694	[24]	6% (4/65)	6% (4/65)	6% (4/65)	NA
TAF+FTC+DRV/c	NCT02269917	[25]	NA	NA	7% (54/763)	NA
	NCT01565850	[26]	14% (14/103)	9% (9/103)	1% (1/103)	12% (12/103)
	NCT02431247	[27]	5% (19/362)	NA	NA	9% (32/362)
TAF+FTC+DTG	NCT03122262	[28]	NA	NA	NA	NA
	NCT02397694	[24]	6% (2/33)	6% (2/33)	0% (0/33)	NA
	NCT02607956	[22]	8% (26/325)	3% (9/325)	6% (20/325)	NA
	NCT03110380	[20]	3% (8/281)	6% (17/281)	4% (11/281)	NA
TDF+FTC+EVG/c	NCT01095796	[29]	11% (40/348)	NA	NA	6% (22/348)

	NCT01106586	[30]	14% (50/353)	NA	NA	NA
	NCT01780506 NCT01797445	[14]	8% (71/867)	5% (39/867)	7% (57/867)	5% (46/867)
	NCT01497899	[13]	9% (5/58)	NA	10% (6/58)	5% (3/58)
	NCT02616783	[17]	NA	7% (4/56)	NA	NA
DTG+3TC	NCT02831673 NCT02831764	[31]	NA	2% (15/716)	5% (35/716)	NA
	NCT02263326	[32]	NA	NA	NA	NA
	NCT03446573	[33]	5.4% (20/369)	NA	5.7% (21/369)	NA
ABC+3TC+DTG	NCT01263015	[34]	NA	NA	NA	1% (3/414)
	NCT02607930	[23]	9% (27/315)	6% (19/315)	NA	NA
	NCT02603120	[18]	NA	4% (10/281)	NA	NA
	NCT02938520	[7]	NA	NA	5% (13/283)	NA
	NCT02105987	[35]	8% (22/275)	NA	NA	NA

TN: treatment-naïve, VS: virologically suppressed.

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