

Supplementary Materials

Cost-effectiveness and budget impact of dolutegravir/lamivudine for treatment of human immunodeficiency virus (HIV-1) infection in the United States

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Table 1

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Table 26

Figure 1

Figure 2

Figure 3

Table 1. Model parameters

Patient baseline characteristics	Treatment naïve	Treatment experienced	Range for DSA	Probability distribution	Varied in PSA
	Mean value (SE)	Mean value (SE)			
Average baseline age of cohort (years) ^{Error!} <small>Bookmark not defined.,Error!</small> <small>Bookmark not defined.</small>	32.50 (3.50)	40.8 (0.41)	± 20%	Normal	✓
Percentage that are female (%) ^{Error!} <small>Bookmark not defined.,Error! Bookmark not defined.</small>	14.72% (0.94%)	7.8 % (0.78%)	0%, 100%	Beta	✓
Percentage who are currently smokers (%) ^{Error!} <small>Bookmark not defined.,Error! Bookmark not defined.</small>	38.10% (1.28%)	30.63% (3.06%)	0%, 100%	Beta	✓
Average baseline total cholesterol (mg/dL) ^{Error!} <small>Bookmark not defined.,Error! Bookmark not defined.</small>	162.15 (9.34)	192.27 (1.39)	± 20%	Normal	✓
Average baseline HDL (mg/dL) ^{Error!} <small>Bookmark not defined.,Error! Bookmark not defined.</small>	43.11 (2.66)	52.85 (0.54)	± 20%	Normal	✓
Average baseline SBP (mmHg) ²²	122.99 (12.30)	122.88 (12.30)	± 20%	Normal	✓
Average baseline BMD (g/cm ²) ²³	0.93 (0.02)	0.93 (0.02)	-	Normal	✓
Average baseline eGFR (mL/min/1.73m ²) ^{Error!} <small>Bookmark not defined.,Error!</small> <small>Bookmark not defined.</small>	111.42 (11.32)	97.40 (0.62)	-	Normal	✓
Percentage with a history of diabetes (%) ^{*Error!} <small>Bookmark not defined.</small>	0.00%	4.18% (0.42%)	0%, 100%	Beta	✓
Patient distribution in CD4 categories (SE) ^{Error!} <small>Bookmark not defined.,Error! Bookmark not defined.</small>					
Viral load <50 (copies/mL)					
CD4 <50 (%)	0.00	0.00	-	Beta	✓
CD4 50-<200 (%)	0.00	1.8 (0.18)	-		
CD4 200-<350 (%)	0.00	6.7 (0.67)	-		
CD4 350-<500 (%)	0.00	14.1 (1.41)	-		
CD4 ≥ 500 (%)	0.00	75.1 (7.51)	-		
Viral load ≥ 50 (copies/mL)					
CD4 <50 (%)	1.19 (0.29)	0.00	-	Beta	✓
CD4 50-<200 (%)	6.98 (0.67)	0.00	-		

CD4 200-<350 (%)	24.08 (1.13)	0.1 (0.01)	-		
CD4 350-<500 (%)	30.15 (1.21)	0.3 (0.03)	-		
CD4 ≥ 500 (%)	37.61 (1.28)	1.7 (0.17)	-		
Other parameters					
Model time horizon	80 years	10 Years, 20 Years	NA		NA Scenario analysis
Discounting rate	3%	0%, 5%	NA		✓
Treatment duration without response	12 months	3 Months, 10 Months	NA		✓

Abbreviations: BMD, bone mineral density; CD4, cluster of differentiation 4; DSA, deterministic sensitivity analyses; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; SBP, systolic blood pressure; SE, standard error.

Treatment efficacy: Transition matrices

Transition matrices are used in the model to control patient’s movement between different viral load and CD4 cell count states. Within the first treatment line, transition rates may be specified differently for the first 11 months (proxy for 48-week time point) receiving a particular treatment and all subsequent months receiving that treatment; subsequent treatment lines utilize just one transition matrix therefore utilising the assumption that any observed movement from 48-96 weeks is representative of each subsequent 48 week period. In lieu of longer-term data this is deemed reasonable but is an identified limitation of the available data.

For each treatment line, matrices were generated by using published summary statistics of the change in CD4 cell count. The CD4 trajectories of 10,000 patients were simulated based on the baseline and change in CD4 from the clinical trial data; GEMINI 1 and 2 for treatment naïve patients and TANGO for treatment experienced patients. The simulated data was tabulated to count transitions between CD4 cell states.

An example table showing the simulated state transitions derived from the GEMINI trials (DTG/3TC arm) can be seen in Table A2.

Each row of data displayed in Table A2 has a multinomial likelihood which is combined with a flat Dirichlet prior distribution using Gibbs sampling in WinBUGS to obtain the posterior probability distribution of the transition matrix. The resulting CD4 transition matrix can be seen in Table A3.

Table 2. Simulated transitions between CD4 cell count states

		To CD4 cell count state					Row totals
		CD4 ≥500	CD4 350-<500	CD4 200-<350	CD4 50-<200	CD4 <50	
From CD4 cell count state	CD4 ≥500	74,545	128	0	0	0	74,545
	CD4 350-<500	4,074	20,718	84	0	0	4,074
	CD4 200-<350	0	2,496	11,203	34	0	0
	CD4 50-<200	0	0	1,186	4,635	11	0
	CD4 <50	0	0	0	347	539	0

CD4: cluster of differentiation 4

Each row of data displayed in Table A2 has a multinomial likelihood which is combined with a flat Dirichlet prior distribution using Gibbs sampling in WinBUGS to obtain the posterior probability distribution of the transition matrix.⁵² The resulting CD4 transition matrix can be seen in Table A3.

Table 3. Derived CD4 cell count state transition probability matrix

		To CD4 cell count state				
		CD4 ≥500	CD4 350-<500	CD4 200-<350	CD4 50-<200	CD4 <50
From CD4 cell count state	<50	0.99820	0.00173	0.00001	0.00001	0.00001
	50-<200	0.16380	0.83270	0.00341	0.00004	0.00004
	200-<350	0.00007	0.18180	0.81550	0.00255	0.00007
	350-<500	0.00017	0.00017	0.20340	0.79420	0.00206
	≥500	0.00114	0.00112	0.00113	0.39050	0.60610

CD4: cluster of differentiation 4

Over the first 11 months, the probability of moving between viral load states is determined by adjusting the 48-week suppression probability to a 1-month cycle length and is combined with the CD4 cell state transition matrix (Table A3) to produce the final state transition matrix. The default transition matrices used for each therapy line can be seen in Table A4-Table A19 below; currently, default profiles for the first 11 months are set to the same values as those for all subsequent months.

Please note that only the GEMINI trial data can inform separate matrices for the subsequent period. All other matrices are informed by 48-week endpoints.

Table 4. Transition matrix for patients receiving DTG/3TC (trial data) weeks 0 to 48

		To									
		<50					≥50				
Viral load*		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	CD4 cell count^	<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
	<50	0.6061	0.3905	0.0011	0.0011	0.0011	0.6010	0.3953	0.0012	0.0012	0.0013
	50-<200	0.0021	0.7942	0.2034	0.0002	0.0002	0.0024	0.7846	0.2126	0.0002	0.0002
	200-<350	0.0001	0.0025	0.8155	0.1818	0.0001	0.0001	0.0029	0.8150	0.1819	0.0001
	350-<500	0.0000	0.0000	0.0034	0.8327	0.1638	0.0000	0.0000	0.0039	0.8348	0.1613
≥500	0.0000	0.0000	0.0000	0.0017	0.9982	0.0000	0.0000	0.0000	0.0020	0.9980	

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 5. Transition matrix for patients receiving DTG/3TC (trial data) weeks 48 to 96

		To									
		<50					≥50				
Viral load*											
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.6159	0.3802	0.0013	0.0013	0.0013	0.6022	0.3935	0.0014	0.0014	0.0014
	50-<200	0.0041	0.7852	0.2103	0.0002	0.0002	0.0047	0.7824	0.2125	0.0002	0.0002
	200-<350	0.0001	0.0065	0.8103	0.1831	0.0001	0.0001	0.0053	0.8117	0.1829	0.0001
	350-<500	0.0000	0.0000	0.0058	0.8324	0.1617	0.0000	0.0000	0.0059	0.8363	0.1577
	≥500	0.0000	0.0000	0.0000	0.0031	0.9969	0.0000	0.0000	0.0000	0.0029	0.9971

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 6. Transition matrix for patients receiving DTG/3TC (trial data) weeks 48 to 96

		To									
		<50					≥50				
Viral load*											
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.8452	0.1510	0.0013	0.0013	0.0013	0.8402	0.1556	0.0014	0.0014	0.0014
	50-<200	0.0254	0.8993	0.0746	0.0003	0.0003	0.0209	0.8889	0.0896	0.0003	0.0003
	200-<350	0.0001	0.0178	0.8968	0.0851	0.0001	0.0001	0.0217	0.8968	0.0813	0.0001
	350-<500	0.0001	0.0001	0.0257	0.9016	0.0725	0.0001	0.0001	0.0242	0.9030	0.0726
	≥500	0.0000	0.0000	0.0000	0.0061	0.9939	0.0000	0.0000	0.0000	0.0067	0.9932

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 7. Transition matrix for patients receiving DTG+TDF/FTC (trial data) weeks 48 to 96

		To									
		<50					≥50				
Viral load*											
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.8500	0.1477	0.0008	0.0008	0.0008	0.8557	0.1419	0.0008	0.0008	0.0008
	50-<200	0.0313	0.8864	0.0818	0.0002	0.0002	0.0255	0.8951	0.0789	0.0003	0.0003
	200-<350	0.0001	0.0241	0.8957	0.0800	0.0001	0.0001	0.0253	0.8978	0.0768	0.0001
	350-<500	0.0001	0.0001	0.0286	0.8964	0.0748	0.0001	0.0001	0.0282	0.9006	0.0710
	≥500	0.0000	0.0000	0.0000	0.0073	0.9926	0.0000	0.0000	0.0000	0.0075	0.9925

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 8. Transition matrix for patients receiving DTG/ABC/3TC (NMA data) weeks 0 to 48

		To									
Viral load*		<50					≥50				
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.5899	0.4063	0.0013	0.0013	0.0013	0.5733	0.4225	0.0014	0.0014	0.0014
	50-<200	0.0031	0.7636	0.2329	0.0002	0.0002	0.0027	0.7656	0.2314	0.0002	0.0002
	200-<350	0.0001	0.0037	0.7991	0.1970	0.0001	0.0001	0.0022	0.7999	0.1978	0.0001
	350-<500	0.0000	0.0000	0.0023	0.8222	0.1754	0.0000	0.0000	0.0030	0.8240	0.1728
	≥500	0.0000	0.0000	0.0000	0.0013	0.9987	0.0000	0.0000	0.0000	0.0013	0.9986

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 9. Transition matrix for patients receiving DTG/ABC/3TC (NMA data) weeks 48 to 96

		To									
Viral load*		<50					≥50				
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.9121	0.0848	0.0010	0.0010	0.0010	0.9084	0.0880	0.0012	0.0012	0.0012
	50-<200	0.0339	0.9067	0.0586	0.0004	0.0004	0.0308	0.9063	0.0622	0.0003	0.0003
	200-<350	0.0001	0.0292	0.9160	0.0546	0.0001	0.0001	0.0347	0.9131	0.0519	0.0001
	350-<500	0.0001	0.0001	0.0383	0.9121	0.0495	0.0001	0.0001	0.0372	0.9135	0.0491
	≥500	0.0000	0.0000	0.0000	0.0103	0.9897	0.0000	0.0000	0.0000	0.0107	0.9893

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 10. Transition matrix for patients receiving BIC/TAF/FTC (NMA data) weeks 0 to 48

		To									
Viral load*		<50					≥50				
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.5837	0.4124	0.0013	0.0013	0.0013	0.5655	0.4301	0.0014	0.0014	0.0014
	50-<200	0.0026	0.7613	0.2357	0.0002	0.0002	0.0024	0.7616	0.2356	0.0002	0.0002
	200-<350	0.0001	0.0029	0.7957	0.2012	0.0001	0.0001	0.0021	0.7963	0.2015	0.0001
	350-<500	0.0000	0.0000	0.0024	0.8185	0.1790	0.0000	0.0000	0.0028	0.8203	0.1768
	≥500	0.0000	0.0000	0.0000	0.0013	0.9987	0.0000	0.0000	0.0000	0.0013	0.9987

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 11. Transition matrix for patients receiving BIC/TAF/FTC (NMA data) weeks 48 to 96

		To									
Viral load*		<50					≥50				
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.9338	0.0632	0.0010	0.0010	0.0010	0.9294	0.0675	0.0011	0.0010	0.0010
	50-<200	0.0270	0.9220	0.0504	0.0003	0.0003	0.0340	0.9072	0.0581	0.0003	0.0003
	200-<350	0.0001	0.0371	0.9192	0.0435	0.0001	0.0001	0.0376	0.9134	0.0488	0.0001
	350-<500	0.0001	0.0001	0.0401	0.9122	0.0476	0.0001	0.0001	0.0416	0.9152	0.0431
	≥500	0.0000	0.0000	0.0000	0.0121	0.9878	0.0000	0.0000	0.0000	0.0118	0.9882

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 12. Transition matrix for patients receiving DRV/r/TAF/FTC (NMA data) all time periods (assumed as DRV/c)

		To									
Viral load*		<50					≥50				
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.5949	0.4014	0.0012	0.0012	0.0013	0.5866	0.4094	0.0014	0.0014	0.0014
	50-<200	0.0036	0.7739	0.2221	0.0002	0.0002	0.0026	0.7733	0.2237	0.0002	0.0002
	200-<350	0.0001	0.0039	0.8052	0.1908	0.0001	0.0001	0.0029	0.8066	0.1904	0.0001
	350-<500	0.0000	0.0000	0.0031	0.8274	0.1694	0.0000	0.0000	0.0034	0.8300	0.1665
	≥500	0.0000	0.0000	0.0000	0.0016	0.9984	0.0000	0.0000	0.0000	0.0015	0.9985

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 13. Transition matrix for patients receiving TE: stable switch

		To									
Viral load*		<50					≥50				
CD4 cell count^		<50	50- <200	200- <350	350- <500	≥500	<50	50- <200	200- <350	350- <500	≥500
From	<50	0.8182	0.1795	0.0008	0.0008	0.0008	0.8636	0.1344	0.0006	0.0006	0.0007
	50-<200	0.0149	0.8924	0.0924	0.0002	0.0002	0.0198	0.9063	0.0736	0.0002	0.0002
	200-<350	0.0001	0.0143	0.9066	0.0790	0.0001	0.0001	0.0205	0.9144	0.0650	0.0001
	350-<500	0.0000	0.0000	0.0157	0.9151	0.0692	0.0000	0.0000	0.0232	0.9219	0.0548
	≥500	0.0000	0.0000	0.0000	0.0069	0.9931	0.0000	0.0000	0.0000	0.0116	0.9883

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 14. Transition matrix for patients receiving TE: failing switch

Viral load*		To									
		<50					≥50				
CD4 cell count^		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	<50	0.6773	0.3223	0.0001	0.0001	0.0001	0.8058	0.1940	0.0001	0.0001	0.0001
	50-<200	0.0039	0.8627	0.1334	0.0000	0.0000	0.0196	0.8949	0.0854	0.0000	0.0000
	200-<350	0.0000	0.0054	0.8924	0.1022	0.0000	0.0000	0.0250	0.9120	0.0630	0.0000
	350-<500	0.0000	0.0000	0.0075	0.9217	0.0708	0.0001	0.0001	0.0332	0.9234	0.0432
	≥500	0.0001	0.0001	0.0001	0.0091	0.9905	0.0003	0.0003	0.0003	0.0398	0.9594

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 15. Transition matrix for patients receiving salvage therapy 1

Viral load*		To									
		<50					≥50				
CD4 cell count^		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	<50	0.7540	0.2457	0.0001	0.0001	0.0001	0.8463	0.1535	0.0001	0.0001	0.0001
	50-<200	0.0065	0.9101	0.0833	0.0000	0.0000	0.0187	0.9234	0.0579	0.0000	0.0000
	200-<350	0.0000	0.0092	0.9286	0.0622	0.0000	0.0000	0.0264	0.9325	0.0410	0.0000
	350-<500	0.0001	0.0001	0.0137	0.9498	0.0364	0.0001	0.0001	0.0396	0.9369	0.0234
	≥500	0.0003	0.0003	0.0003	0.0202	0.9788	0.0009	0.0009	0.0009	0.0587	0.9387

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 16. Transition matrix for patients receiving salvage therapy 2

Viral load*		To									
		<50					≥50				
CD4 cell count^		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	<50	0.7703	0.2294	0.0001	0.0001	0.0001	0.8507	0.1491	0.0001	0.0001	0.0001
	50-<200	0.0100	0.9053	0.0847	0.0000	0.0000	0.0221	0.9178	0.0601	0.0000	0.0000
	200-<350	0.0000	0.0121	0.9275	0.0603	0.0000	0.0000	0.0294	0.9290	0.0415	0.0000
	350-<500	0.0001	0.0001	0.0180	0.9450	0.0369	0.0001	0.0001	0.0446	0.9317	0.0235
	≥500	0.0003	0.0003	0.0003	0.0224	0.9766	0.0007	0.0007	0.0007	0.0540	0.9439

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 17. Transition matrix for patients receiving salvage therapy 3

Viral load*		To									
		<50					≥50				
CD4 cell count^		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	<50	0.8411	0.1587	0.0001	0.0001	0.0001	0.9020	0.0979	0.0000	0.0000	0.0000
	50-<200	0.0092	0.9385	0.0523	0.0000	0.0000	0.0160	0.9460	0.0380	0.0000	0.0000
	200-<350	0.0000	0.0104	0.9550	0.0345	0.0000	0.0000	0.0214	0.9541	0.0245	0.0000
	350-<500	0.0001	0.0001	0.0150	0.9635	0.0213	0.0001	0.0001	0.0314	0.9533	0.0151
	≥500	0.0005	0.0005	0.0005	0.0227	0.9757	0.0008	0.0008	0.0008	0.0464	0.9512

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 18. Transition matrix for patients receiving DTG/3TC (TANGO) all time periods

Viral load*		To									
		<50					≥50				
CD4 cell count^		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	<50	0.8680	0.1293	0.0009	0.0009	0.0009	0.8733	0.1239	0.0009	0.0009	0.0009
	50-<200	0.0311	0.8882	0.0801	0.0003	0.0003	0.0261	0.8985	0.0749	0.0003	0.0003
	200-<350	0.0001	0.0260	0.9007	0.0730	0.0001	0.0001	0.0254	0.9015	0.0728	0.0001
	350-<500	0.0001	0.0001	0.0288	0.9045	0.0666	0.0001	0.0001	0.0291	0.9070	0.0637
	≥500	0.0000	0.0000	0.0000	0.0070	0.9929	0.0000	0.0000	0.0000	0.0070	0.9929

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 19. Transition matrix for patients receiving TBR (TANGO) all time periods

Viral load*		To									
		<50					≥50				
CD4 cell count^		<50	50-<200	200-<350	350-<500	≥500	<50	50-<200	200-<350	350-<500	≥500
From	<50	0.8601	0.1353	0.0015	0.0015	0.0015	0.8467	0.1481	0.0017	0.0017	0.0018
	50-<200	0.0241	0.8946	0.0805	0.0004	0.0004	0.0245	0.8938	0.0809	0.0004	0.0004
	200-<350	0.0002	0.0219	0.9018	0.0759	0.0002	0.0002	0.0218	0.8993	0.0786	0.0002
	350-<500	0.0001	0.0001	0.0263	0.9044	0.0691	0.0001	0.0001	0.0264	0.9071	0.0663
	≥500	0.0000	0.0000	0.0000	0.0064	0.9936	0.0000	0.0000	0.0000	0.0064	0.9936

CD4: cluster of differentiation 4; *Viral load in copies/mL; ^CD4 cell count in cells/mm³

Table 20. Utilities and costs

CD4 health state-based utilities and costs	Utilities		Event-based cost (\$)		Included in PSA
	Treatment naïve ^{Error!} Bookmark not defined.	Treatment experienced ^{Error!} Bookmark not defined.		Monthly maintenance cost (\$)	
CD4 health state*	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	
<50	0.894 (0.174)	0.948 (0.003)	NA	NA	✓
50-<200	0.931 (0.108)	0.948 (0.003)	NA	NA	✓
200-<350	0.950 (0.093)	0.955 (0.015)	NA	NA	✓
350-<500	0.960 (0.069)	0.956 (0.292)	NA	NA	✓
≥500	0.959 (0.086)	0.953 (0.292)	NA	NA	✓
Event based disutilities and costs	Event disutility	Maintenance disutility	Event-based cost (\$)	Monthly maintenance cost (\$)	Included in PSA
ADEs ³⁷	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	
Acute viral OI	0.141 (0.014)	NA	7,195.56 (719.56)	NA	
Acute bacterial OI	0.232 (0.023)	NA	4,622.70 (462.27)	NA	✓
Acute fungal OI	0.141 (0.014)	NA	7,877.60 (787.76)	NA	✓
Acute protozoal OI	0.232 (0.023)	NA	27,194.56 (2,719.46)	NA	✓
Other OI	0.232 (0.023)	NA	5,276.17 (527.62)	NA	✓
Long-term toxicities	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	Included in PSA
CVD ⁵³	0.283 (0.028)	0.156 (0.016)	4,069.22 (406.92)	4,069.22 (406.92)	
CKD stage 1 (eGFR >90 mL/min/1.73m ²)* ⁵⁴	NA	0.000 (0.000)	NA	0 (0)	✓
CKD stage 2 (eGFR 60-89 mL/min/1.73m ²)* ³⁷	NA	0.000 (0.000)	NA	713.53 (71.35)	✓
CKD stage 3 (eGFR 30-59 mL/min/1.73m ²)* ^{Error! Bookmark not defined.}	NA	0.030 (0.003)	NA	2,364.51 (236.45)	✓
CKD stage 4 (eGFR 15-29 mL/min/1.73m ²)* ^{Error! Bookmark not defined.}	NA	0.050 (0.005)	NA	4,207.85 (420.79)	✓
CKD stage 5 (eGFR <15 mL/min/1.73m ²)* ³⁷	NA	0.130 (0.013)	NA	8,545.83 (854.58)	✓
Hip fracture ^{Δ35}	0.581 (0.058)	0.031 (0.003)	61,447.19 (6,144.72)	NA	✓
Spine fracture ^{Δ53}	0.551 (0.055)	0.031 (0.003)	3,453.20 (345.32)	NA	✓
Forearm fracture ^{Δ53}	0.271 (0.027)	NA	2,685.18 (268.52)	NA	✓
Shoulder fracture ^{Δ53}	0.271 (0.027)	NA	5,648.80 (564.88)	NA	✓
End of life care ⁵⁵	Mean (SE)	Mean (SE)	Mean (SE)	Mean (SE)	
End of life care ^{ΔΔ}	NA	NA	77,003 (7,700)	NA	✓

ADE: AIDS defining event; CD4: cluster of differentiation 4; CKD: chronic kidney disease; CVD: cardiovascular disease; eGFR: estimated glomerular filtration rate; NA: not applicable; OI: opportunistic infection; SE: standard error

**Utility decrements were calculated assuming that CKD stage 2 utility estimates are equivalent to that of the general population (i.e. no disutility was applied for CKD stage 1 or 2 patients); disutility estimates for CKD stage 3, 4 and 5 were calculated assuming CKD stage 2 as a reference.

^Disutility estimates are calculated by subtracting the absolute utility from the baseline utility of a 40-year old (the baseline age of patients in the Nashimyumukiza et al. study).

^^Applied in the final month of life.

Table 21. AIDS-defining event incidence

Time on treatment	Opportunistic infection	Probability of experiencing an ADE (mean value)* ¹⁵					Included in PSA
		CD4 <50	CD4 50- <200	CD4 200- <350	CD4 350- <500	CD4 ≥500	
0-6 months	Acute viral OI						✓
	Acute bacterial OI	0.0071	0.0033	0.0008	0.0008	0.0008	
	Acute fungal OI	0.0070	0.0022	0.0006	0.0004	0.0004	
	Acute protozoal OI	0.0049	0.0022	0.0003	0.0001	0.0001	
	Acute protozoal OI	0.0021	0.0006	0.0002	0.0001	0.0001	
	Other OI	0.0036	0.0020	0.0000	0.0000	0.0000	
7-12 months	Acute viral OI						✓
	Acute bacterial OI	0.0039	0.0010	0.0003	0.0003	0.0002	
	Acute fungal OI	0.0027	0.0009	0.0001	0.0001	0.0001	
	Acute protozoal OI	0.0018	0.0013	0.0002	0.0002	0.0001	
	Acute protozoal OI	0.0018	0.0004	0.0001	0.0001	0.0001	
	Other OI	0.0022	0.0014	0.0007	0.0003	0.0003	
13-24 months	Acute viral OI						✓
	Acute bacterial OI	0.0019	0.0005	0.0002	0.0002	0.0001	
	Acute fungal OI	0.0022	0.0008	0.0001	0.0001	0.0001	
	Acute protozoal OI	0.0016	0.0011	0.0002	0.0002	0.0001	
	Acute protozoal OI	0.0015	0.0004	0.0001	0.0001	0.0001	
	Other OI	0.0014	0.0009	0.0004	0.0002	0.0002	
25-36 months	Acute viral OI						✓
	Acute bacterial OI	0.0005	0.0001	0.0000	0.0000	0.0000	
	Acute fungal OI	0.0012	0.0004	0.0000	0.0000	0.0000	
	Acute protozoal OI	0.0015	0.0011	0.0001	0.0001	0.0001	
	Acute protozoal OI	0.0008	0.0002	0.0000	0.0000	0.0000	
	Other OI	0.0009	0.0006	0.0003	0.0001	0.0001	
36 months+	Acute viral OI	0.0005	0.0001	0.0000	0.0000	0.0000	✓
	Acute bacterial OI	0.0012	0.0004	0.0000	0.0000	0.0000	
	Acute fungal OI	0.0015	0.0011	0.0001	0.0001	0.0001	
	Acute fungal OI	0.0008	0.0002	0.0000	0.0000	0.0000	
	Other OI	0.0009	0.0006	0.0003	0.0001	0.0001	

	Acute protozoal OI						
	Other OI						
ADE: AIDS-defining event; CD4: cluster of differentiation 4; OI: opportunistic infection SE assumed to be 10% of mean for all inputs * Lowest value for each time-point by CD4 cell count carried forward							

Table 22. ADE related mortality

Risk of death ¹⁵	Mean	SE	Included in PSA
Acute viral OI	0.0492	0.0049	✓
Acute bacterial OI	0.0460	0.0046	✓
Acute fungal OI	0.0362	0.0036	✓
Acute protozoan OI	0.2009	0.0201	✓
Other OI	0.0440	0.0044	✓
OI: opportunistic infection; SE: standard error			

Table 23. First line adverse event incidence for the treatment naïve population

AE	DTG+3TC (trial)	DTG + TDF/FTC (trial)	DTG + ABC/3TC (NMA)	BIC + TAF/FTC (NMA)	DRVr + TAF/FTC (NMA)* ^β
	Headache	0.13 (0.14)	0.19 (0.16)	0.2 (0.17)	0.12 (0.13)
Nausea	0.09 (0.11)	0.25 (0.19)	0.13 (0.14)	0.08 (0.1)	0.38 (0.23)
Diarrhoea	0.1 (0.12)	0.12 (0.13)	0.14 (0.14)	0.08 (0.11)	0.38 (0.23)
Insomnia	0.1 (0.12)	0.12 (0.13)	0.14 (0.14)	0.08 (0.11)	0.35 (0.22)
Somnolence	0.04 (0.08)	0.03 (0.07)	0.07 (0.1)	0.04 (0.07)	0.22 (0.17)
Dizziness	0.05 (0.08)	0.08 (0.11)	0.08 (0.1)	0.04 (0.08)	0.22 (0.17)
Fatigue	0.07 (0.1)	0.04 (0.07)	0.1 (0.12)	0.06 (0.09)	0.27 (0.19)
Abnormal dreams	0.03 (0.06)	0.02 (0.05)	0.04 (0.07)	0.02 (0.06)	0.19 (0.16)
Dyspepsia	0.02 (0.05)	0.03 (0.06)	0.03 (0.06)	0.02 (0.05)	0.08 (0.11)
Faeces soft	0.01 (0.04)	0.03 (0.07)	0.02 (0.05)	0.01 (0.04)	0.05 (0.09)
Increased appetite	0.03 (0.06)	0.02 (0.05)	0.04 (0.07)	0.02 (0.06)	0.11 (0.12)
Anxiety	0.07 (0.1)	0.03 (0.07)	0.1 (0.12)	0.06 (0.09)	0.22 (0.17)
Flatulence	0.01 (0.03)	0.03 (0.06)	0.01 (0.04)	0.01 (0.03)	0.08 (0.11)

3TC: lamivudine; ABC: abacavir; AE: adverse event; BIC: bictegravir; DRVr: darunavir/ritonavir; DTG: dolutegravir; EFV: efavirenz; FTC: emtricitabine; NMA: network meta-analysis; RPV: rilpivirine; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate
AE probabilities for DTG+3TC and DTG+TDF/FTC efficacy profiles based on trial data were derived directly from the GEMINI trial data; AE probabilities for all other profiles were derived using odds ratios from the NMA with the DTG+3TC arm of the GEMINI trials as the reference case
*48 week data used where 96 week data were not available
^βThe efficacy profile assigned to the DRV/c/TAF/FTC profile is informed by DRV/r/TDF/FTC where cobicistat-boosted darunavir is assumed equally efficacious as ritonavir-boosted darunavir and TAF/FTC is assumed equally efficacious to TDF/FTC

Table 24. First line adverse event incidence for the treatment switch population

AE	Monthly probability (%): mean (SE)	
	DTG + 3TC (trial)	TBR (trial)
Nausea	0.12 (0.01)	0.24 (0.02)
Diarrhoea	0.10 (0.01)	0.49 (0.05)
Insomnia	0.15 (0.02)	0.00 (0.00)
Anxiety	0.10 (0.01)	0.00 (0.00)

3TC: lamivudine; AE: adverse event; DTG: dolutegravir; TBR: tenofovir alafenamide based regimen
AE probabilities for DTG+3TC and TBR efficacy profiles based on trial data were derived directly from the TANGO trial data

Figure 1: Tornado plot of univariate sensitivity analysis in treatment naïve PLHIV

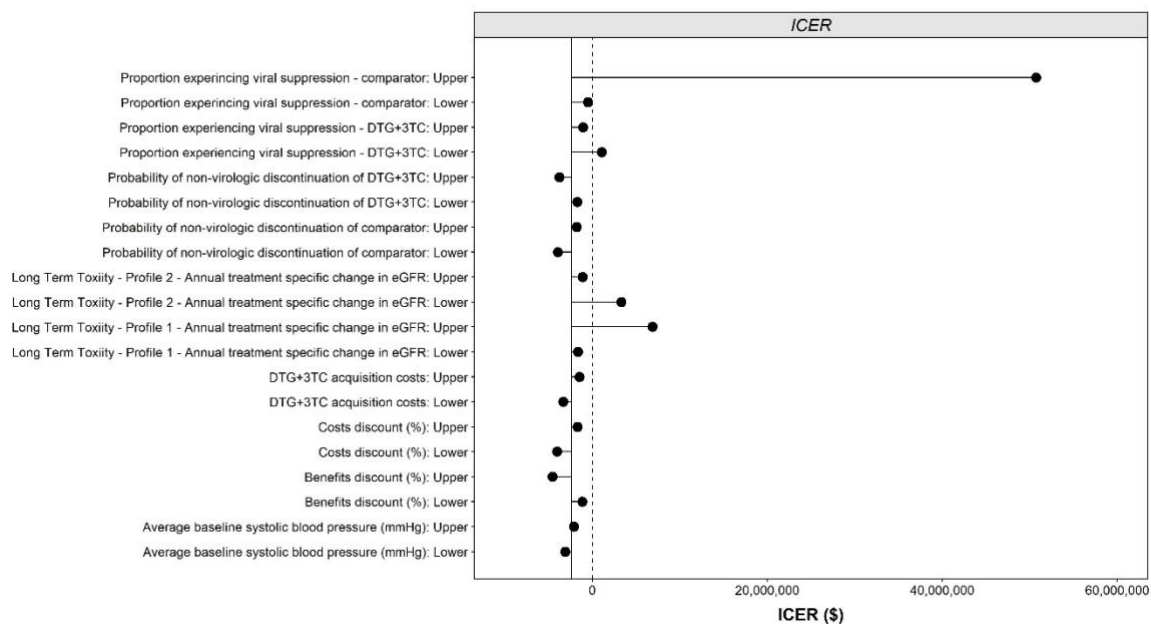
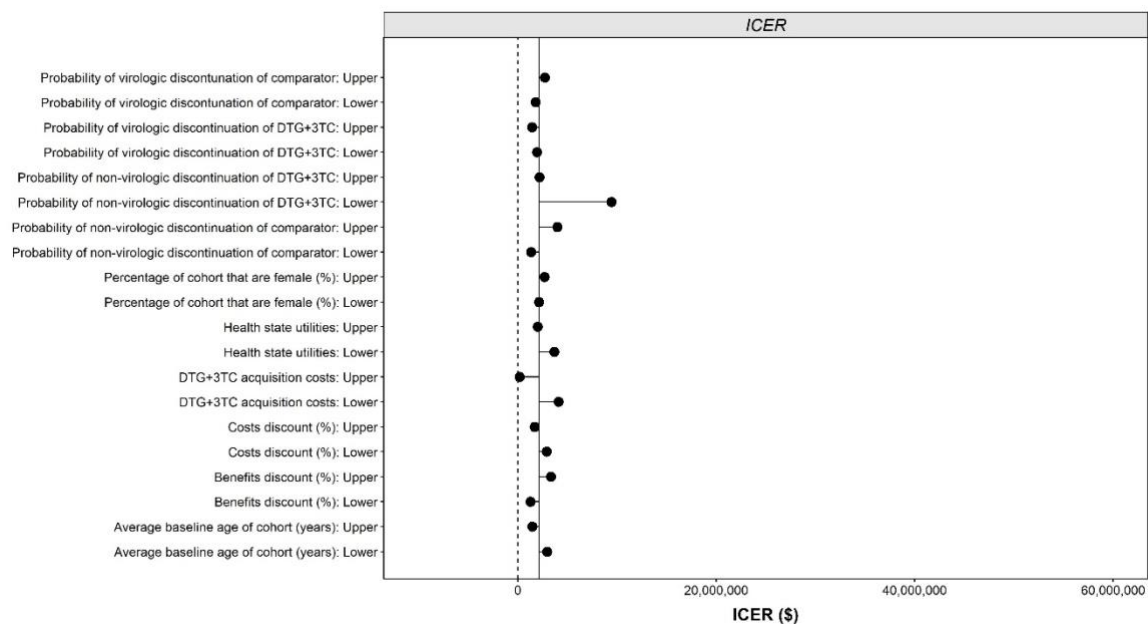


Figure 2: Tornado plot of univariate sensitivity analysis in treatment experienced PLHIV



Appendix: Evaluation of the Budget Impact of the Introduction of DTG/3TC in the US

The Budget Impact Analysis (BIA) evaluates the potential cost savings of introducing DTG/3TC in the US. To construct the BIA, the size of the population eligible for DTG/3TC was estimated, to which projected market shares of different classes of regimens in scenarios with and without DTG/3TC were applied. The difference in the total budget required between these two scenarios was then calculated.

This analysis was designed as an update to an earlier study by Girouard et al.⁴³ This modelling exercise sought to evaluate the budget impact of the introduction of dual therapy (DTG and 3TC) but was conducted prior to the results of the clinical trials evaluating DTG/3TC. Here, we sought to provide an update to this analysis given the non-inferior trial results and details of the cost of the regimen.

Perspective of the Analysis

This analysis considers only drug costs. Due to the fact this is a well-controlled population, who have a relatively low rate of events that would require additional healthcare resource use (i.e. adverse events, AIDS defining events) and a short time horizon considered in this analysis, inclusion of other healthcare costs are unlikely to significantly impact the conclusions of this analysis as the drug costs will dominate results.

Population Size Estimate

First, the size of the patient population eligible for DTG/3TC was estimated from epidemiological data. There were approximately 1.2M people with HIV in the US in 2018⁴⁴ We assume that 20% of these HIV positive people are both virally suppressed and have never experienced prior virologic failure and therefore are more likely to switch to DTG/3TC (giving an eligible population of 240,000 in year 1 for those who are treatment experienced). This is in line with the assumption made in the Girouard analysis.⁴³ From the 37,968 patients newly diagnosed each year, 37% are assumed to receive treatment in line with the earlier Girouard study and are added to the existing treatment experienced patients eligible for DTG/3TC each year (i.e. 14,048 patients are assumed to be newly eligible each year). Table A25 gives the size of the treatment naïve and treatment experienced population who are considered eligible for DTG/3TC in this analysis. It is these populations that the market share data described is applied to.

Table 25: Eligible Population Size by Year

	Year 1	Year 2	Year 3	Year 4	Year 5
Treatment Experienced Patients Eligible for DTG/3TC	240,000	254,048	268,096	282,144	296,192
Treatment Naïve Patients Eligible for DTG/3TC	14,048	14,048	14,048	14,048	14,048

Projected Market Shares and the Costs of the Regimens

The BIA compares scenarios in which DTG/3TC is available in the eligible population, with a scenario which reflects existing market share projections across drug classes in the absence of DTG/3TC. Table A26 below gives the assumed market shares in the absence of DTG/3TC. Here we track market share by drug class and apply an average cost per drug class. Current market share data suggests that INI based combinations make up the majority of regimens used by PLHIV (66%), with smaller proportions of NNRTI

(13%) and PI (8%) and other regimens (1%). The market share of INIs was assumed to increase modestly over time (4.5%), whilst NNRTIs, PIs and other regimens decline (4.3%, 0.5% and 0.3% respectively) based on market projections. The market share data presented here reflects the entirety of the treated population and these projections are applied to both the treatment naïve and treatment experienced patient groups.

The average costs of each drug class were based on the mean of the Wholesale Acquisition Cost or Average Wholesale Price of relevant individual regimens (those which are commonly used within the drug class). The cost of DTG/3TC (\$2,408.37 per month) is lower than the average regimen cost of the most widely used drug class, INIs, at \$857.28 less per month (\$10,287 less per year).

Table 26: Projected Market Shares by Regimen Class in the Absence of DTG/3TC and Average Cost of Each Regimen Class

	Year 1	Year 5	Change (Year 1- Year 5)	Average Cost of Class (per month)	Average Cost of Class (per year)
Market share INI	0.66	0.71	0.045	\$3265.65	\$39,187.80
Market share NNRTI	0.13	0.09	-0.043	\$2445.32	\$29,343.84
Market share PI	0.08	0.08	-0.005	\$3675.94	\$44,111.28
Other	0.12	0.12	0.003	\$2513.12	\$30,157.44

The Calculation of Budget Impact

To calculate the budget impact the total drug costs in the eligible population in the presence and absence of DTG/3TC were calculated. The scenario without DTG/3TC reflects the market share projections described above in Table A26. The scenario with DTG/3TC assumes that market share for DTG/3TC is taken from other drug classes proportional to their market share. Immediate scale up to the target coverage level is assumed. Three scenarios of DTG/3TC use in eligible patients were evaluated as follows: 1) 5% naïve/10% experienced; 2) 10% naïve/20% experienced; and 3) 15% naïve/30% experienced.

The total annual budget needs for each scenario were calculated as the sum of the product of the size of the eligible population, the relevant market share percentages and the associated annual regimen cost, for each regimen class or DTG/3TC. The difference in total cost between the scenarios with DTG/3TC and the scenario without DTG/3TC over 5 years was evaluated. BIA results were undiscounted.