SUPPLEMENTARY MATERIAL FOR:

Cabotegravir and Rilpivirine Long-Acting Antiretroviral Therapy Administered Every 2 Months Is Cost-Effective for the Treatment of HIV-1 in Spain

Santiago Moreno,[1] Antonio Rivero,[2] Pere Ventayol,[3] Vicenç Falcó,[4] Miguel Torralba,[5] Melanie Schroeder,[6] Victoria Neches,[7] Laura Amanda Vallejo-Aparicio,[7] Isaac Mackenzie,[8] Matthew Turner,[8] Cale Harrison[8]

[1]Hospital Ramón y Cajal, CIBERINFEC, Universidad de Alcalá, IRYCIS, Madrid, Spain; [2]Hospital Reina Sofía, Córdoba, Spain; [3]Hospital Son Espases, Palma de Mallorca, Spain; [4]Hospital Vall d'Hebron, Barcelona, Spain; [5]Hospital de Guadalajara, Guadalajara, Spain; [6]ViiV Healthcare, Brentford, UK; [7]GSK, Madrid, Spain; [8]HEOR Ltd, Cardiff, UK

Correspondence and reprint requests to:

Victoria Neches

E-mail: victoria.x.neches@gsk.com

Figure S1. Treatment switching decision processes.

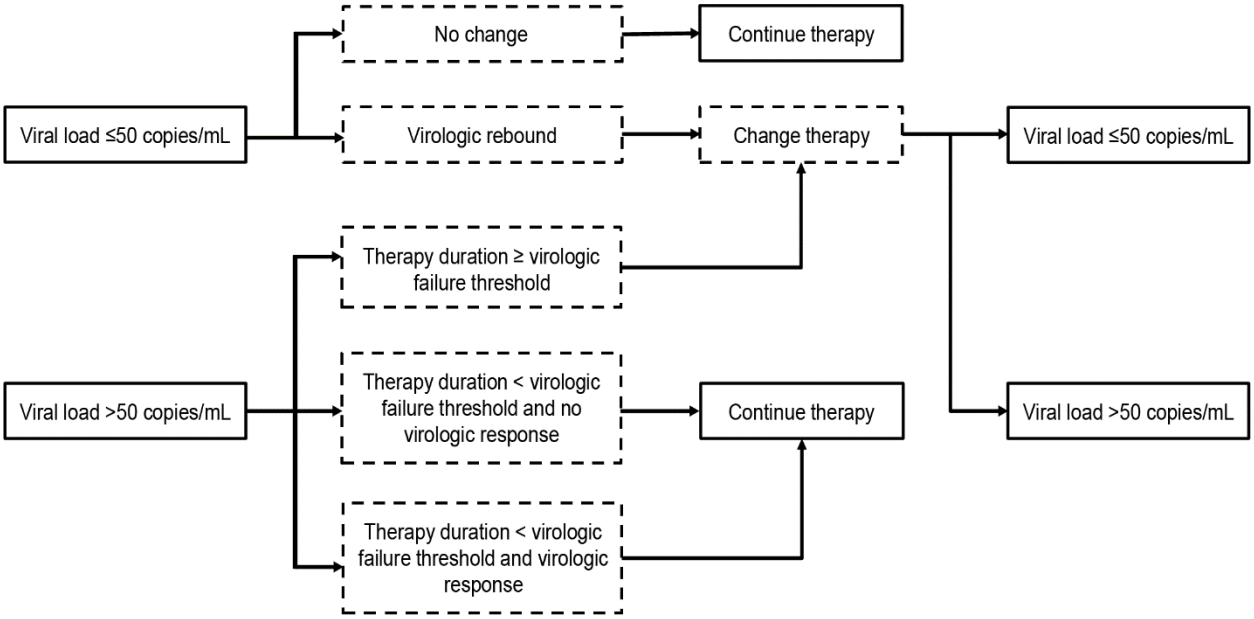

Figure S2. Health state utility values from Kauf et al. [1], as applied in the model. HSUV, health state utility value.

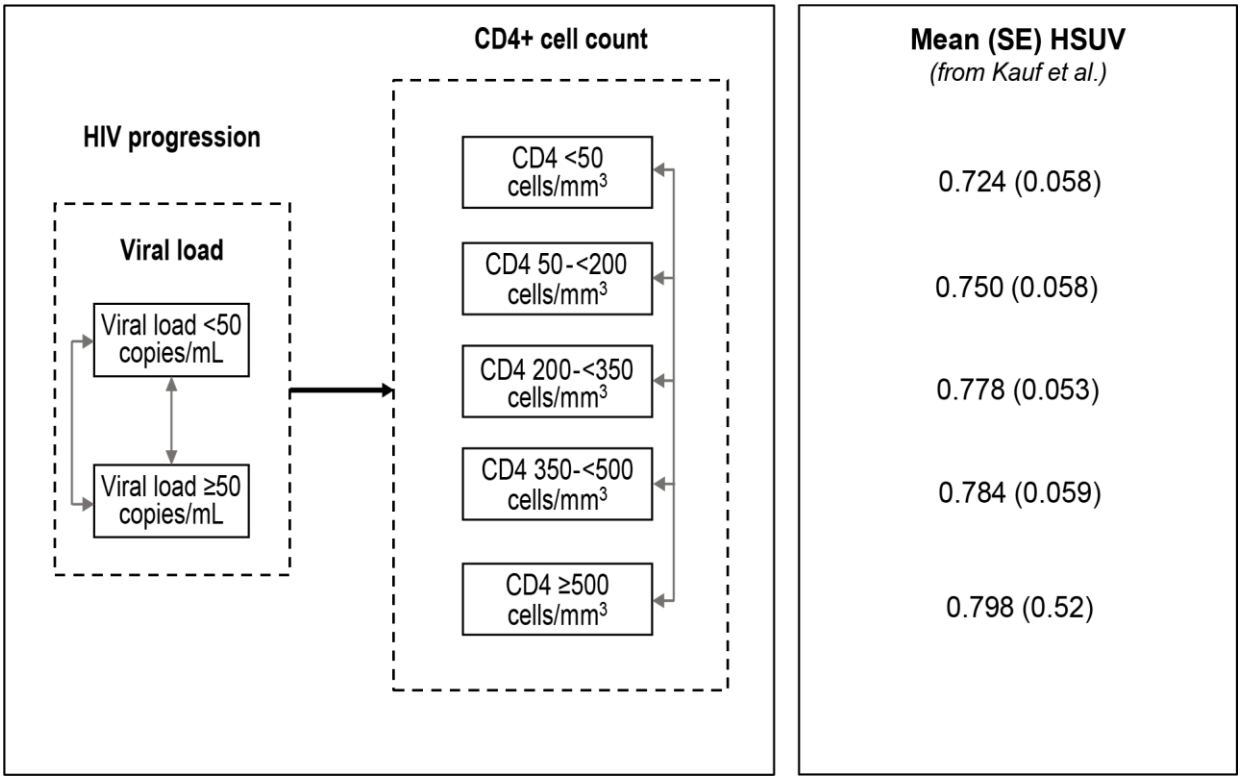

Table S1. Probabilities of Virologic and Non-virologic Discontinuations Based on Literature

			Monthly discontinuation (Weeks 0-48)		Monthly discontinuation (Weeks 48-96 and >96)	
Efficacy profile	**Source**	**Notes**	**Virologic discontinuation, mean (SE)**	**Non-virologic discontinuation, mean (SE)**	**Virologic discontinuation, mean (SE)**	**Non-virologic discontinuation, mean (SE)**
Treatment-experienced: stable switch	Baril et al, 2016 [2]	Weighted mean of included studies reporting variable of interest; same rates assumed for each time period	0.0053 (0.0003)	0.0079 (0.0004)	0.0053 (0.0003)	0.0079 (0.0004)
Treatment-experienced: failing switch	Kanters et al, 2017 [3]		0.0165 (0.0008)	0.0024 (0.0001)	0.0165 (0.0008)	0.0024 (0.0001)
CAB+RPV LA Q2M (ATLAS-2M ITC) trial analysis	ATLAS-2M	Q2M group of ATLAS-2M	0.0016 (0.0017)	0.0037 (0.0027)	0.0016 (0.0017)	0.0037 (0.0027)

cART (ATLAS-2M ITC; equivalent efficacy to CAB+RPV LA Q2M) trial analysis	ATLAS-2M	Q2M group of ATLAS-2M (comparator efficacy assumed equivalent based on ITC)	0.0016 (0.0017)	0.0037 (0.0027)	0.0016 (0.0017)	0.0037 (0.0027)

CAB, cabotegravir; cART, combination antiretroviral therapy; ITC, indirect treatment comparison; LA, long-acting; Q2M, every 2 months; RPV, rilpivirine; SE, standard error.

Table S2. AIDS-defining event incidence from the ARAMIS technical report

		Monthly probability of experiencing an AIDS-defining event, mean				
Time on treatment	**Opportunistic infection**	**CD4+ <50 cells/mm^3**	**CD4+ 50-200 cells/mm^3**	**CD4+ 200-350 cells/mm^3**	**CD4+ 350-500 cells/mm^3**	**CD4+ >500 cells/mm^3**
0-6 months	Acute viral	0.0071	0.0033	0.0008	0.0008	0.0008
	Acute bacterial	0.0070	0.0022	0.0006	0.0004	0.0004
	Acute fungal	0.0049	0.0022	0.0003	0.0001	0.0001
	Acute protozoal	0.0021	0.0006	0.0002	0.0001	0.0001
	Other	0.0036	0.0020	0.0000	0.0000	0.0000
7-12 months	Acute viral	0.0039	0.0010	0.0003	0.0003	0.0002
	Acute bacterial	0.0027	0.0009	0.0001	0.0001	0.0001
	Acute fungal	0.0018	0.0013	0.0002	0.0002	0.0001
	Acute protozoal	0.0018	0.0004	0.0001	0.0001	0.0001
	Other	0.0022	0.0014	0.0007	0.0003	0.0003
13-24 months	Acute viral	0.0019	0.0005	0.0002	0.0002	0.0001
	Acute bacterial	0.0022	0.0008	0.0001	0.0001	0.0001
	Acute fungal	0.0016	0.0011	0.0002	0.0002	0.0001

	Acute protozoal	0.0015	0.0004	0.0001	0.0001	0.0001
	Other	0.0014	0.0009	0.0004	0.0002	0.0002
	Acute viral	0.0005	0.0001	0.0000	0.0000	0.0000
	Acute bacterial	0.0012	0.0004	0.0000	0.0000	0.0000
25-36 months	Acute fungal	0.0015	0.0011	0.0001	0.0001	0.0001
	Acute protozoal	0.0008	0.0002	0.0000	0.0000	0.0000
	Other	0.0009	0.0006	0.0003	0.0001	0.0001
	Acute viral	0.0005	0.0001	0.0000	0.0000	0.0000
	Acute bacterial	0.0012	0.0004	0.0000	0.0000	0.0000
>36 months	Acute fungal	0.0015	0.0011	0.0001	0.0001	0.0001
	Acute protozoal	0.0008	0.0002	0.0000	0.0000	0.0000
	Other	0.0009	0.0006	0.0003	0.0001	0.0001

Standard error assumed to be 10% of mean for all inputs. Lowest value for each time-point CD4+ cell count carried forward.

Table S3. Efficacy parameters for available efficacy profiles

Therapy line	Treatment arm	Source	Virologic suppression at Week 48, Mean (SE), %	Baseline CD4+ cell count, mean (SD)	Change in CD4+ cell count at Week 48, mean (SD)
Initial modelled line	CAB+RPV LA	Q2M arm from ATLAS-2M	94.3%	681.8 (259.9)	5.3 (168.62)
	Comparators	Assumed equivalent to Q2M arm from ATLAS-2M			
Second modelled (Symtuza)	Stable switch[a]	Baril (2016) [2]	74.8% (3.7)	540.0 (232.5)	69.3 (149.1)
	Failing switch[a]	Kanters (2017) [3]	73.8% (3.7)	168.7 (155.1)	176.4 (149.3)
Third modelled line (DTG+Prescobix)	Stable switch[a]	Baril (2016) [2]	74.8% (3.7)	540.0 (232.5)	69.3 (149.1)
	Failing switch[a]	Kanters (2017) [3]	73.8% (3.7)	168.7 (155.1)	176.4 (149.3)
Fourth modelled line (Salvage)	No ART resistance	Cooper (2008) [4]; Steigbigel (2008) [5]	71.0% (7.1)	151.0 (141.0)	119.0 (132.7)
	Resistance to 1 ART class	Cooper (2008) [4]; Steigbigel (2008) [5]	60.6% (6.1)	151.0 (141.0)	111.0 (146.3)
	Resistance to 2 ART classes	Cooper (2008) [4]; Steigbigel (2008) [5]	50.8% (5.1)	151.0 (141.0)	71.0 (100.8)

[a]Failing switch refers to people who switched for virologic reasons. Stable switch refers to people who switched for non-virologic reasons

Table S4. Probabilistic Sensitivity Analysis Sampling Distributions

Parameter	Distribution	Mean	SE
Participant baseline characteristics			
Age, y	Normal	42.7	0.489
Female, %	Beta	0.26	0.019
Smokers, %	Beta	0.34	0.014
Total cholesterol, mg/dL	Normal	171.3	0.135
HDL cholesterol, mg/dL	Normal	49.3	0.016
Systolic blood pressure, mmHg	Normal	121.7	0.554
Bone mineral density, g/cm^2	Normal	0.96	0.021
eGFR, mL/min/1.73m^2	Normal	96.1	0.746
Distribution of participants across starting health states			
Viral load ≤50 copies/mL, %			
CD4+ cell count ≤50 cells/mm^3	Beta	0	0
CD4+ cell count ≤50 cells/mm^3	Beta	0	0
CD4+ cell count 200-350 cells/mm^3	Beta	0.067	0.011
CD4+ cell count 350-500 cells/mm^3	Beta	0.184	0.017
CD4+ cell count >500 cells/mm^3	Beta	0.749	0.019
Viral load >50 copies/mL, %			
CD4+ cell count ≤50 cells/mm^3	Beta	0	0
CD4+ cell count 50-200 cells/mm^3	Beta	0	0
CD4+ cell count 200-350 cells/mm^3	Beta	0	0
CD4+ cell count 350-500 cells/mm^3	Beta	0	0
CD4+ cell count >500 cells/mm^3	Beta	0	0
Participants with history of diabetes, %	—	0.194	0.006
Utility			
CD4+ cell count ≤50 cells/mm^3	Beta	0.742	0.058

CD4+ cell count 50-200 cells/mm^3	Beta	0.750	0.058
CD4+ cell count 200-350 cells/mm^3	Beta	0.778	0.053
CD4+ cell count 350-500 cell/mm^3	Beta	0.784	0.059
CD4+ cell count >500 cells/mm^3	Beta	0.798	0.052
Acute viral OI utility decrement	Beta	0.141	0.014
Acute bacterial OI utility decrement	Beta	0.232	0.023
Acute fungal OI utility decrement	Beta	0.141	0.014
Acute protozoal OI utility decrement	Beta	0.232	0.023
Other OI utility decrement	Beta	0.232	0.023
Costs			
HCRU			
CD4+ cell count ≤50 cells/mm^3	Gamma	€2627.42	€262.74
CD4+ cell count 50-200 cells/mm^3	Gamma	€1020.16	€102.02
CD4+ cell count 200-350 cells/mm^3	Gamma	€745.48	€74.55
CD4+ cell count 350-500 cells/mm^3	Gamma	€202.28	€20.23
CD4+ cell count >500 cells/mm^3	Gamma	€136.9	€13.69
Diarrhea	Gamma	€38.74	€3.87
Injection site reaction, grade 3-4	Gamma	€102.86	€10.29
End-of-life cost, last 3 months	Gamma	€34,489.71	€3448.97

eGFR, estimated glomerular filtration rate; HCRU, healthcare resource utilization; HDL, high-density lipoprotein; OI, opportunistic infection; SE, standard error.

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