

Experiment	Treatment group	Mouse ID	At time of HIV exposure	
			Peripheral blood humanization	
			%CD45 ⁺	%CD4 ⁺
#1	Control vehicle	1	57.4	76.2
		2	40.8	64.8
		3	49.7	70.4
		4	51.8	51.4
		5	54	68
		6	54.7	67.2
		Mean ± s.e.m	51.4% ± 2.4%	66.3% ± 3.4%
	AZD5582	7	55.7	77.5
		8	54.4	68.5
		9	57.2	76.9
		10	51.9	70.8
		11	41.8	73.1
12		47.9	50.4	
	Mean ± s.e.m	51.5% ± 2.3%	69.5% ± 4.1%	
#2	Control vehicle	13	72.5	88.1
		14	49.1	90.1
		15	41.3	86.1
		16	31.3	74.0
		Mean ± s.e.m	48.6% ± 8.8%	84.6% ± 3.62%
	AZD5582	17	74.9	72.8
		18	42.2	79.5
		19	38.3	78.6
		20	37.2	82.8
		Mean ± s.e.m	48.15 ± 10%	78.43 ± 2.1%

Supplementary Table 1: Levels of human cells in BLT mice at the time of HIV-1_{JR-CSF}

exposure as determined by flow cytometry analysis of peripheral blood. BLT mice in

experiment 1 are shown in Fig. 2b,c left panels and BLT mice in experiment 2 are shown in Fig.

2b,c right panels. s.e.m: standard error mean. Gating strategy=Live→human CD45

(%CD45⁺)→human CD3→human CD4 (%CD4⁺).

Experiment	Treatment group	Mouse ID	Viral load (copies/mL plasma)		
			0 h	24 h	48 h
#1	Control vehicle	1	< LOQ	< LOQ	< LOQ
		2	< LOQ	< LOQ	< LOQ
		3	< LOQ	< LOQ	< LOQ
		4	< LOQ	< LOQ	< LOQ
		5	< LOQ	< LOQ	< LOQ
		6	< LOQ	< LOQ	< LOQ
	AZD5582	7	< LOQ	< LOQ	< LOQ
		8	< LOQ	< LOQ	< LOQ
		9	< LOQ	< LOQ	< LOQ
		10	< LOQ	< LOQ	553
		11	< LOQ	< LOQ	773
		12	< LOQ	< LOQ	876
#2	Control vehicle	13	< LOQ	< LOQ	< LOQ
		14	< LOQ	< LOQ	< LOQ
		15	< LOQ	< LOQ	< LOQ
		16	< LOQ	< LOQ	< LOQ
	AZD5582	17	< LOQ	< LOQ	< LOQ
		18	< LOQ	< LOQ	573
		19	< LOQ	< LOQ	953
		20	< LOQ	< LOQ	1,574

Supplementary Table 2: Detectable plasma viremia in HIV-infected, ART-suppressed BLT mice following a single dose of AZD5582 (3 mg/kg). The limit of quantification (LOQ) for this assay is 350 copies/mL.

Treatment group	Tissue	Copies HIV-DNA/ 10 ⁵ resting CD4+ T cells	Fold difference between control and AZD5582
Control vehicle	Lung	369.303	1.3
	Bone marrow	49.988	-0.59
	Thymic organoid	17.58	-1.56
AZD5582	Lung	272.822	
	Bone marrow	84.33	
	Thymic organoid	27.43	

Supplementary Table 3: Cell-associated HIV-DNA levels in the tissues of ART-suppressed BLT mice following a single dose of AZD5582 (3 mg/kg).

Analyte	Serum concentration			Comparison of serum concentrations		
	0 h	24 h	5 d	0 h vs 24 h	0 h vs 5 d	24 h vs 5 d
Albumin	3.2 ± 0.18	3.85 ± 0.55	2.63 ± 0.10	p=0.5000	p=0.1250	p=0.2500
Alkaline phosphatase	61.33 ± 30.02	58.5 ± 3.1	17.75 ± 3.17	p=0.7500	p=0.5000	p=0.1250
Alanine aminotransferase	118.50 ± 57.40	702 ± 170.71	33.50 ± 12.87	p=0.1250	p=0.2500	p=0.1250
Amylase	593.50 ± 21.85	607 ± 38.54	397 ± 101.04	p>0.9999	p=0.2500	p=0.2500
Aspartate aminotransferase	235.67 ± 106.18	709 ± 216.11	92 ± 10.03	p=0.2500	p=0.2500	p=0.1250
Blood urea nitrogen	23 ± 1.78	11.5 ± 0.96	15 ± 1	p=0.1250	p=0.1250	p=0.2500
Calcium	6.38 ± 1.57	10.75 ± 0.22	11.7 ± 0.26	p=0.2500	p=0.1250	p=0.2500
Creatinine	0.29 ± 0.06	0.11 ± 0.02	0.46 ± 0.04	p=0.1250	p=0.2500	p=0.1250
Phosphorus	4.45 ± 1.4	5.45 ± 0.25	4.90 ± 0.44	p>0.9999	p=0.8750	p=0.3750
Total bilirubin	2.15 ± 0.95	1.15 ± 0.22	0.80 ± 0.14	p=0.5000	p=0.2500	p=0.3750
Total protein	5.27 ± 0.24	5.90 ± 0.97	6.45 ± 0.33	p>0.9999	p=0.2500	p=0.8750

Supplementary Table 4: Levels of serum indicators for organ drug toxicity. Serum was collected from BALB/c mice (n=4) immediately prior to, 24 h after, and five days after administration of a single dose of AZD5582. Shown are the mean concentrations (\pm standard error mean) of serum albumin (g/dL), alkaline phosphatase (U/L), alanine aminotransferase (U/L), amylase (U/L), aspartate aminotransferase (U/L), blood urea nitrogen (mg/dL), calcium (mg/dL), creatinine (mg/dL), phosphorus (mg/dL), total bilirubin (mg/dL) and total protein (g/dL). A two-sided Wilcoxon matched-pairs signed ranks T test was used to evaluate statistical significance.

	Tissue	Treatment group		p value
		Control vehicle	AZD5582	
%CD38+HLA-DR+ of CD4+ T cells	Bone marrow	0.85 ± 0.35	1.15 ± 0.68	0.8593
	Thymic organoid	2.7 ± 1.13	2.78 ± 1.03	0.6991
	Lymph nodes	1.23 ± 0.50	1.40 ± 0.57	0.9372
	Spleen	0.71 ± 0.31	0.63 ± 0.21	0.8593
	Liver	1.08 ± 0.38	1.04 ± 0.36	0.8939
	Lung	0.56 ± 0.23	0.89 ± 0.40	0.8139
%CD38+HLA-DR+ of CD8+ T cells	Bone marrow	1.8 ± 0.43	1.69 ± 0.99	0.3874
	Thymic organoid	0.30 ± 0.11	0.23 ± 0.08	0.8030
	Lymph nodes	0.35 ± 0.25	0.53 ± 0.24	0.6991
	Spleen	1.87 ± 0.50	0.62 ± 0.36	0.0260
	Liver	0.23 ± 0.08	0.34 ± 0.21	0.4827
	Lung	0.35 ± 0.19	0.86 ± 0.47	0.4177

Supplementary Table 5: AZD5582 does not activate T cells in the tissues of HIV-infected, ART-suppressed BLT mice. Shown is the mean percentage (\pm standard error mean) of CD4⁺ and CD8⁺ T cells co-expressing CD38 and HLA-DR from the bone marrow, thymic organoid, lymph nodes, spleen, liver and lung of HIV-infected, ART-suppressed BLT mice (n=6/group) 24 h after treatment with control vehicle or AZD5582. A two-sided Mann-Whitney test was used to evaluate statistical significance.

Cytokine/chemokine	Control (pg/mL)	AZD5582 (pg/mL)	Difference between means	p value
EGF	< LOQ	< LOQ	NA	NA
FGF-2	616.1 ± 192	626.6 ± 218	10.5 ± 26	0.7835
Eotaxin	< LOQ	< LOQ	NA	NA
TGFα	< LOQ	< LOQ	NA	NA
G-CSF	< LOQ	< LOQ	NA	NA
Flt-3L	3.205 ± 1.605	< LOQ	NA	NA
GM-CSF	34.53 ± 16.31	32.30 ± 16.1	-2.23 ± 0.21	0.9221
Fractalkine	26.82 ± 25.22	18.67 ± 17.07	-8.15 ± 8.15	>0.9999
IFNα2	6.038 ± 3.193	4.069 ± 2.469	-1.969 ± 0.724	0.7273
IFNγ	130.1 ± 41.68	130.1 ± 41.34	0 ± 0.34	>0.9999
GRO	55.12 ± 18.23	68.16 ± 19.85	13.04 ± 1.62	0.6234
IL-10	40.39 ± 11.51	40.37 ± 11.05	-0.02 ± 0.46	0.9372
MCP-3	< LOQ	< LOQ	NA	NA
IL-12p40	21.64 ± 6.422	22.23 ± 9.533	0.59 ± 3.111	0.974
MDC	166.6 ± 12.84	145.9 ± 16.25	-20.73 ± 3.41	0.3939
IL-12p70	< LOQ	< LOQ	NA	NA
PDGF-AA	1,325 ± 505.5	1,303 ± 463.8	-22 ± 41.70	>0.9999
IL-13	4.649 ± 2.096	5.444 ± 2.569	0.795 ± 0.473	0.8485
PDGF-AB/BB	201 ± 32.67	169.7 ± 36.58	-31.30 ± 3.91	0.4848
IL-15	2.825 ± 1.225	< LOQ	NA	NA
sCD40L	65.34 ± 8.32	63.31 ± 9.24	-2.03 ± 0.92	>0.9999
IL-17A	15.32 ± 4.241	14.75 ± 4.141	-0.57 ± 0.100	0.9372
IL-1RA	2.170 ± 0.5698	3.619 ± 2.019	1.449 ± 1.4492	>0.9999
IL-1α	33.93 ± 15.72	38.85 ± 21	4.92 ± 5.280	0.8139
IL-9	< LOQ	< LOQ	NA	NA
IL-1β	< LOQ	< LOQ	NA	NA
IL-2	1.907 ± 0.3074	2.066 ± 0.4656	0.159 ± 0.1582	>0.9999
IL-3	< LOQ	< LOQ	NA	NA
IL-4	24.58 ± 9.935	24.64 ± 8.402	0.06 ± 1.533	0.8939
IL-5	10.10 ± 7.984	9.210 ± 7.268	-0.8900 ± 0.716	0.8485
IL-6	9.847 ± 5.244	10.43 ± 5.650	0.5830 ± 0.4060	0.8485
IL-7	< LOQ	< LOQ	NA	NA
IL-8	60.04 ± 27.66	66.50 ± 31.76	6.46 ± 4.1	0.7381
IP-10	1,071 ± 448.9	1,076 ± 434.3	5.000 ± 14.60	>0.9999
MCP-1	461.5 ± 114.8	465.4 ± 120.3	3.9 ± 5.500	>0.9999
MIP-1α	< LOQ	< LOQ	NA	NA
MIP-1β	9.593 ± 3.152	10.22 ± 3.037	0.6270 ± 0.1150	0.7792
RANTES	840.3 ± 364.8	764.3 ± 329.8	-76 ± 35.00	0.5887
TNFα	21.41 ± 10.45	22.6 ± 9.11	1.190 ± 1.340	0.9805
TNFβ	< LOQ	< LOQ	NA	NA
VEGF	9.014 ± 7.414	9.655 ± 5.33	0.641 ± 2.084	0.5455

Supplementary Table 6: Plasma cytokine analysis from mice treated with vehicle control or AZD5582. BLT mice were administered vehicle control (n=6) or AZD5582 (n=6) and peripheral blood plasma collected 24 h later to analyze the levels of 41 human cytokines/chemokines that are commonly associated with cell activation. Shown is the mean concentration (pg/mL) ± standard error mean of each cytokine/chemokine analyzed, the difference between the mean concentrations of each cytokine/chemokine between groups and the corresponding p value as

determined with a two-sided Mann-Whitney U test. Assay range: $3.2-1 \times 10^4$ pg/mL. LOQ: limit of quantification. NA: not applicable. For statistical analysis, values <LOQ were set at 1.6 pg/ml.

RM ID	Group	Sex	Date of birth	Age at first dose (years)
RDm16	AZD5582	Male	4/19/2014	3.8
RDl16	AZD5582	Male	4/12/2014	3.8
RKn16	AZD5582	Male	4/26/2014	3.8
RFk16	AZD5582	Male	4/08/2014	3.8
RNp16	AZD5582	Male	4/08/2014	3.8
RLu16	AZD5582	Male	6/10/2014	3.6
RQs16	AZD5582	Male	5/28/2014	4.0
RAr16	AZD5582	Male	5/17/2014	4.0
RKp16	AZD5582	Male	5/06/2014	4.1
RLy15	AZD5582	Male	5/02/2013	5.1
RKl16	AZD5582	Male	4/14/2014	4.1
RYs16	AZD5582	Male	5/30/2014	4.0
RAj16	Control	Male	3/29/2014	3.9
RDF16	Control	Male	6/27/2013	4.6
RNq16	Control	Male	5/15/2014	3.8
RQd16	Control	Male	6/11/2013	4.7
RFv15	Control	Male	4/20/2013	5.2
RKw16	Control	Male	7/07/2014	3.9
RUl16	Control	Male	5/29/2014	4.0
RKz15	Control	Male	5/06/2013	5.1
RZe15	Control	Female	4/22/2012	6.2

Supplementary Table 7: Sex and age of AZD5582-treated and control SIV-infected, ART-suppressed RMs.