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Supplementary appendix

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Supplement to: Raymond S, Piffaut M, Bigot J, et al. Sexual transmission of an extensively drug-resistant HIV-1 strain. *Lancet HIV* 2020; **7:** e529–30.

Appendix 1

Sexual transmission of an XDR HIV-1 strain

A. Resistance genotyping of the XDR HIV-1 strain using ultra-deep sequencing

Resistance associated mutations	Transmitted virus (Month 0)		Transmitted virus (Month 1)		Transmitted virus (Month 2)		Source virus	
	VL=5.1 log10 cp/mL		VL=4 log10 cp/mL		VL=3.5 log10 cp/mL		VL=5.5 log10 cp/mL	
	Coverage	Frequency	Coverage	Frequency	Coverage	Frequency	Coverage	Frequency
Protease								
L10F	2215	>0.99	908	>0.99	627	>0.99	1792	>0.99
V11I	2252	>0.99	922	>0.99	644	>0.99	1818	>0.99
V32I	4180	**>0.99**	1431	**>0.99**	1462	**>0.99**	2949	**>0.99**
M36I	4513	>0.99	1439	1	1631	>0.99	3126	0.89
M36L	-	-	-	-	-	-	3025	0.11
M46L	5439	>0.99	1568	>0.99	1938	>0.99	3126	0.96
I54L	6012	**>0.99**	1759	**>0.99**	2049	**>0.99**	3779	**>0.99**
Q58E	6182	**>0.99**	1834	**>0.99**	2012	**1**	3866	**>0.99**
D60E	6249	0.94	1850	0.88	2010	0.81	3875	0.9
I62V	6195	>0.99	1815	>0.99	1995	1	3852	0.97
L63P	6150	>0.99	1807	0.99	1965	>0.99	3828	>0.99
A71I	6526	>0.99	1898	0.99	2091	>0.99	4012	>0.99
G73S	6629	0.95	1938	0.89	2119	0.86	4081	0.64
T74P	6544	**0.99**	1936	**>0.99**	2059	**>0.99**	4032	**>0.99**
I84V	7112	**>0.99**	2136	**>0.99**	2288	**>0.99**	4439	**>0.99**
I85V	7126	>0.99	2141	>0.99	2291	>0.99	4444	>0.99
L89V	7090	0.88	2131	0.75	2276	0.64	4462	0.9
L90M	7098	>0.99	2144	>0.99	2303	>0.99	4441	>0.99
Reverse Transcriptase								
A62V	8183	**>0.99**	2978	**>0.99**	3389	**0.99**	5812	**0.94**
D67E	1784	1	1835	>0.99	1863	0.95	1757	0.87
T69ins	1784	**1**	1835	**>0.99**	1863	**0.95**	1757	**0.87**
A98G	6964	0.99	2566	0.97	2951	>0.99	5353	0.99
V106I	6578	>0.99	2523	>0.99	2643	>0.99	4901	0.99
V179I	7199	>0.99	2922	>0.99	2829	1	5025	0.98
Y181F	7537	>0.99	3024	>0.99	2953	>0.99	5276	0.96
M184V	7206	**>0.99**	2943	**1**	2813	**>0.99**	5053	**>0.99**
Y188L	7400	**>0.99**	3004	**>0.99**	2828	**0.92**	5211	**0.95**
L210W	7379	**0.99**	2921	**0.99**	2718	**>0.99**	5321	**>0.99**
T215Y	7593	**>0.99**	3118	**0.97**	2716	**>0.99**	5445	**0.96**
Integrase								
T97A	6394	>0.99	4440	>0.99	3252	>0.99	9132	>0.99
E138K	6649	>0.99	4642	>0.99	3940	>0.99	9876	>0.99
S147G	6289	**>0.99**	4441	**>0.99**	3884	**>0.99**	9441	**>0.99**
V151I	5693	>0.99	4047	>0.99	3469	1	8415	>0.99
N155H	5144	**>0.99**	3693	**0.98**	3160	**>0.99**	7584	**>0.99**
E157Q	5186	1	3685	>0.99	3187	>0.99	7592	>0.99

Sequencing was performed using the PGM IonTorrent from the Sentosa platform (VelaDX). Coverage indicates the number of reads for each amino acid position and frequency is the percentage of mutant variant in the quasispecies. Mutations associated with resistance according to IAS (https://www.iasusa.org/resources/hiv-drug-resistance-mutations/) or Stanford HIV database (https://hivdb.stanford.edu/) have been listed. Major mutations according to IAS are indicated in bold.

B. Genotypic susceptibility of the XDR HIV-1 strain to antiretroviral drugs

	ANRS v30 (2019-11) [a]	Stanford HIVdb 8.8 [b]
Protease inhibitors		
Lopinavir/ritonavir (r)	Resistance	High-level resistance
Atazanavir/r	Resistance	High-level resistance
Tipranavir/r	Resistance	High-level resistance
Darunavir/r (QD or BID)[c]	Resistance	High-level resistance
Nucleos(t)ide RT inhibitors		
Zidovudine	Resistance	High-level resistance
Lamivudine/Emtricitabine	Resistance	High-level resistance
Abacavir	Resistance	High-level resistance
Tenofovir (TDF or TAF)	Resistance	High-level resistance
Non-nucleoside RT inhibitors		
Efavirenz	Resistance	High-level resistance
Nevirapine	Resistance	High-level resistance
Etravirine	Resistance	Intermediate resistance
Rilpivirine	Resistance	High-level resistance
Doravirine	Resistance	High-level resistance
Integrase inhibitors		
Raltegravir	Resistance	High-level resistance
Elvitegravir	Resistance	High-level resistance
Dolutegravir BID	Susceptible	Low-level resistance
Dolutegravir QD	Resistance	Low-level resistance
Cabotegravir/Bictegravir	Resistance	Low-level resistance

[a] http://www.hivfrenchresistance.org/; [b] https://hivdb.stanford.edu/

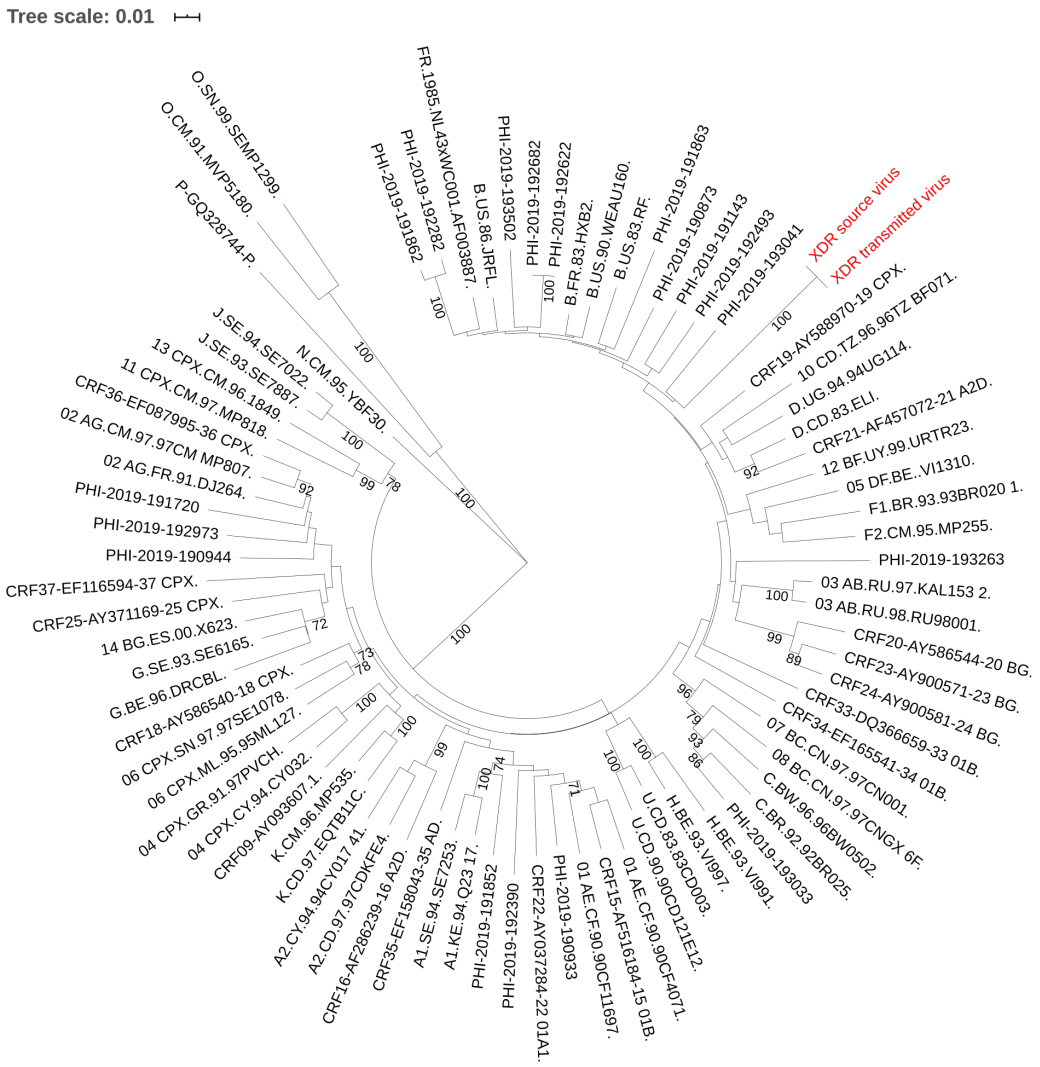
[c]QD= once daily; BID= twice daily

C. Coreceptor used for entry by the XDR HIV-1 strains

Phenotype[a]	V3 amino acids variants – frequency (%) – Genotype[b]		
Transmitted virus (Month 0)			
R5	1445 reads (MiSeq)		
	1- C T R P N N N T R K S I H I G P G Q A F Y A T G Q V I G D I R Q A H C	**95.6**	R5
	2- . . . . . Y .	**4.4**	R5
Source virus			
R5	1042 reads (MiSeq)		
	1- C T R P N N N T R K S I H I G P G Q A F Y A T G Q V I G D I R Q A H C	**73.6**	R5
	2- . . . . . I	**19.7**	R5
	3- . . . L . . . . . R . T M . . . R V . . T . . E I V . . . . K . . .	**2.7**	**X4**
	4- . . . L . . . . . R . T M . . . R V . . T . . E I . . . . . K . . .	**1.8**	**X4**
	5- . . . . . N	**0.7**	R5
	6- . . . L	**0.6**	R5
	7- . . . . . I . . . . . R . . .	**0.5**	R5
	8- . . . . . R . . .	**0.5**	R5

[a]Recombinant virus assay; [b]PyroVir genotypic algorithm (DOI: 10.1038/srep16944)

D. Neighbor-joining phylogenetic tree of HIV-1 polymerase sequences from the XDR HIV strains



Alignment of the nucleotide sequences (nucleotides 169-1176 of *pol* in HXB2) was performed with ClustalW and included sequences from the XDR viruses (red labels) and from primary HIV infections (PHI) of 2019 and reference sequences. Bootstrap values >70% are indicated on branches. The genetic relatedness of two different sequences is represented by the branch length that separates them.