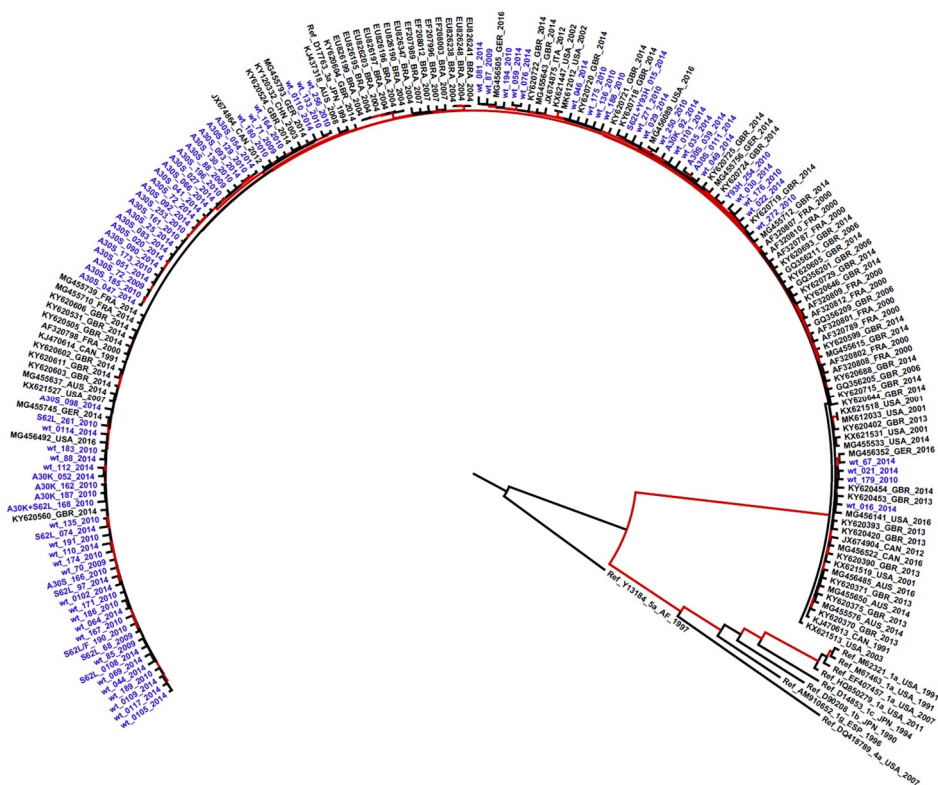


**b**



Supplementary Figure S2. Phylogenetic tree for HCV 1b (a) and HCV 3a (b) NS5A sequences (1126 nucleotides, positions 6330–7455 according to HCV 1a reference strain H77 (GenBank NC004102)), built under a GTR model; branches with group reliability >90% are indicated in red; sequences from this study are indicated in blue; the type of RAS or wild-type (WT) are indicated for each sequence.

Supplementary Table S1. Prevalence of resistance-associated amino acid substitutions in NS5A protein of HCV genotype 1a, 1b and 3a derived from the territory of the Russian Federation

HCV genotype (nn of sequences)	Prevalence of NS5a resistance associated substitutions			
	Substitution	nn found	%	Resistance to*
1a (n=19)	<b>M28V</b>	11	57.9%	<b>OBV, LDV, VEL</b>
1b (n=93)	L28M	1	1.1%	EBR
	R30Q	7	7.5%	DCV, OBV, EBR
	<b>L31M</b>	5	5.4%	<b>DCV, LDV, EBR, OBV, VEL</b>
	P58S	4	4.4%	DCV, OBV
	P58T	1	1.1%	VEL
	A92T	1	1.1%	LDV, OBV
	<b>Y93H</b>	5	5.4%	<b>DCV, LDV, EBR, OBV, VEL</b>
3a (n=90)	<b>A30K</b>	5	5.7%	<b>PIB**, DCV, VEL</b>
	A30S	26	31.0%	DCV, VEL
	S62L	8	8.9%	DCV
	<b>Y93H</b>	2	2.2%	<b>PIB**, DCV, VEL</b>

DCV, daclatasvir; LDV, ledipasvir; EBR, elbasvir; OBV, ombitasvir; PIB, pibrentasvir; VEL, velpatasvir

Substitutions associated with > 10% of virologic failures are marked in bold.

\*Resistance demonstrated both *in vitro* and *in vivo*.

\*\* Dual variant A30K+Y93H results in significant resistance to PIB.

Supplementary Table S2. The list of HCV NS5A sequences from DAA treatment naïve patients retrieved from Gene Bank

#	Country of origin	Year	Gene bank accession number
<b>HCV-1a RAS M28V</b>			
1	USA/EU	before 2013	KC127126.1
2	USA/EU	before 2013	KC127209.1
3	USA/EU	before 2013	KC127211.1
4	USA/EU	before 2013	KC127219.1
5	USA/EU	before 2013	KC127232.1
6	USA/EU	before 2013	KC127235.1
7	USA/EU	before 2013	KC127280.1
8	USA/EU	before 2013	KC127305.1
9	USA/EU	before 2013	KC127394.1
10	USA/EU	before 2013	KC127568.1
11	USA/EU	before 2013	KC127573.1
12	USA/EU	before 2013	KC127592.1
13	USA/EU	before 2013	KC127608.1
14	Japan	2014	LC209876
15	Japan	2016	LC209874.1
16	Thailand	2007	HM042039
17	USA	2001	EU155285.2
18	USA	2001	EU155289.2
19	Germany	2003	EU155379.1
20	USA	2007	EU255935.1
21	USA	2003	EU255956.1
22	USA	1990	EU255982.1
23	USA	2005	EU256058.1
24	USA	2004	EU482847.1
25	Germany	2003	EU862823.1
26	Germany	2004	EU862824.1
27	USA	2008	FJ410172.1
28	USA	before 2008	EU781746.1
29	USA	before 2007	EF407456.1
30	Brazil or USA	before 2007	EF032884.1
<b>HCV-1a M28 (wild-type)</b>			
1	USA	1993	EU862827.1
2	USA	1989	EU862826.1
3	USA	1992	EU255992.1
4	USA	1989	EU255991.1
5	USA	1995	EU255988.1
6	USA	1989	EU255987.1

7	USA	1989	EU255986.1
8	USA	1991	EU255985.1
9	USA	1990	EU255983.1
10	USA	1990	EU255981.1
11	USA	1990	EU255980.1
12	USA	1991	EU255979.1
13	USA	1991	EU255978.1
14	USA	1991	EU255977.1
15	USA	1992	EU255976.1
16	Switzerland	2005	EU255930.1
17	Switzerland	2004	EU255929.1
18	Switzerland	2003	EU255928.1
19	Switzerland	2003	EU255927.1
20	Switzerland	2003	EU660385.1
21	Switzerland	2005	EU529681.1
22	USA	2004	EU529676.1
23	USA	1990	EU234065.2
24	Germany	2004	EU155380.2
25	Germany	2003	EU155378.2
26	Switzerland	2006	EU155355.2
27	Switzerland	2005	EU155354.2
28	Switzerland	2005	EU155353.2
29	Switzerland	2004	EU155352.2
30	Switzerland	2003	EU155351.2
31	Switzerland	2005	EU155349.2
32	Switzerland	2005	EU155348.2
33	Switzerland	2005	EU155346.2
34	Germany	2003	EU482873.1
35	Switzerland	2004	EU482872.1
36	USA	2002	EU482871.1
37	Switzerland	2001	EU482854.1
38	Switzerland	2005	EU482853.1
39	USA	1989	EU482852.1
40	USA	1990	EU482850.1
41	USA	2005	EU482848.1
42	Germany	2004	EU482832.1
43	Germany	2003	EU482831.1
44	Switzerland	2003	EU255959.1
45	Switzerland	2007	EU687195.1
46	Switzerland	2004	EU687194.1
47	Switzerland	2005	EU687193.1
48	Switzerland	2004	EU256107.1
49	Switzerland	2003	EU862836.1
50	Germany	2004	EU862834.1
<b>HCV-1b RAS Q30R</b>			
1	Japan	before 2007	AB285065.1

2	Japan	before2012	AB518783.1
3	Japan	before 2011	AB602003.1
4	Japan	before 1994	D63857.1
5	USA	2003	EU155228.2
6	USA	2006	EU155258.2
7	USA	2001	EU155262.2
8	Switzerland	2004	EU155361.2
9	Switzerland	2005	EU155374.2
10	USA	1992	EU234062.2
11	Switzerland	2003	EU256085.1
12	USA	2003	EU256088.1
13	USA	2006	EU256091.1
14	USA	2001	EU862835.1
15	USA	1996	HQ110091.1
16	China	before 2016	HQ639947
17	Germany	2008	HQ908333.1
18	Estonia	2007	JX022771.1
19	USA	2004	KC439485.1
20	Italy	2009	KX688410.1
21	Italy	2014	KX688434.1
22	USA	before 2007	EF407502
23	USA	before 2007	EF407472
24	USA	before 2007	EF407487
25	USA	before 2007	EF407501
26	Japan	before 2001	AB049100
27	Japan	before 2000	AF207756
28	USA/EU	before 2013	KC124806.1
29	USA/EU	before 2013	KC124813.1
30	USA/EU	before 2013	KC124839.1
31	USA/EU	before 2013	KC124845.1
32	USA/EU	before 2013	KC124886.1
33	USA/EU	before 2013	KC124903.1
34	USA/EU	before 2013	KC124927.1
35	USA/EU	before 2013	KC124940.1
36	USA/EU	before 2013	KC124945.1
37	USA/EU	before 2013	KC124951.1
38	USA/EU	before 2013	KC124960.1
39	USA/EU	before 2013	KC124978.1
40	USA/EU	before 2013	KC124983.1
<b>HCV-1b Q30 (wild-type)</b>			
1	USA/EU	before 2013	KC124769.1
2	USA/EU	before 2013	KC124770.1
3	USA/EU	before 2013	KC124772.1
4	USA/EU	before 2013	KC124776.1
5	USA/EU	before 2013	KC124778.1
6	USA/EU	before 2013	KC124779.1

7	USA/EU	before 2013	KC124781.1
8	USA/EU	before 2013	KC124786.1
9	USA/EU	before 2013	KC124787.1
10	USA/EU	before 2013	KC124789.1
11	USA/EU	before 2013	KC124790.1
12	USA/EU	before 2013	KC124791.1
13	USA/EU	before 2013	KC124792.1
14	USA/EU	before 2013	KC124794.1
15	USA/EU	before 2013	KC124796.1
16	USA/EU	before 2013	KC124798.1
17	USA/EU	before 2013	KC124799.1
18	USA/EU	before 2013	KC124800.1
19	USA/EU	before 2013	KC124802.1
20	USA/EU	before 2013	KC124804.1
21	USA	before 2006	EF407473.1
22	USA	before 2006	EF407474.1
23	USA	before 2006	EF407475.1
24	USA	before 2006	EF407476.1
25	USA	before 2006	EF407477.1
26	USA	before 2006	EF407478.1
27	USA	before 2006	EF407479.1
28	USA	before 2006	EF407480.1
29	USA	before 2006	EF407481.1
30	USA	before 2006	EF407482.1
31	USA	before 2006	EF407483.1
32	USA	before 2006	EF407484.1
33	USA	before 2006	EF407485.1
34	USA	before 2006	EF407486.1
35	USA	before 2006	EF407488.1
36	USA	before 2006	EF407489.1
37	USA	before 2006	EF407490.1
38	USA	before 2006	EF407491.1
39	USA	before 2006	EF407492.1
40	USA	before 2006	EF407493.1
41	USA	before 2006	EF407494.1
42	USA	before 2006	EF407495.1
43	USA	before 2006	EF407496.1
44	USA	before 2006	EF407497.1
45	USA	before 2006	EF407498.1
46	USA	before 2006	EF407499.1
47	USA	before 2006	EF407500.1
48	Switzerland	2006	EU255960.1
49	USA	1991	EU255961.1
50	USA	1991	EU255962.1
<b>HCV-3a RAS A30S</b>			

1	Australia	2007	KX621499.1
2	USA	before2013	JX674929.1
3	United Kingdom	2013	KY620378.1
4	United Kingdom	2013	KY620410.1
5	United Kingdom	2014	KY620528.1
6	United Kingdom	2014	KY620753.1
7	United Kingdom	2014	KY620757.1
8	United Kingdom	2014	KY620781.1
9	United Kingdom	2014	KY620851.1
10	United Kingdom	2014	KY620854.1
11	United Kingdom	2003	GQ356216.1
12	United Kingdom	2006	GQ356217.1
13	Pakistan	2012	KC415734.1
14	Pakistan	2012	KC415735.1
<b>HCV-3a A30 (wild-type)</b>			
1	United Kingdom	2006	GQ356200.1
2	United Kingdom	2006	GQ356201.1
3	United Kingdom	2006	GQ356202.1
4	United Kingdom	2006	GQ356203.1
5	United Kingdom	2005	GQ356204.1
6	United Kingdom	2006	GQ356205.1
7	United Kingdom	2006	GQ356207.1
8	United Kingdom	2006	GQ356208.1
9	United Kingdom	2006	GQ356209.1
10	United Kingdom	2006	GQ356210.1
11	United Kingdom	2006	GQ356211.1
12	United Kingdom	2007	GQ356212.1
13	United Kingdom	2006	GQ356213.1
14	United Kingdom	2006	GQ356214.1
15	United Kingdom	2006	GQ356215.1
16	United Kingdom	2003	GQ356216.1
17	United Kingdom	2006	GQ356217.1
18	Pakistan	2012	KC415734.1
19	Pakistan	2012	KC415735.1
20	Pakistan	2012	KC415736.1
21	Pakistan	2012	KC415737.1
22	Pakistan	2012	KC415739.1
23	Pakistan	2012	KC415740.1
24	Pakistan	2012	KC415743.1
25	Pakistan	2012	KC415748.1
26	Pakistan	2012	KC415753.1
27	Pakistan	2012	KC415754.1
28	Pakistan	2012	KC415756.1
29	France	before 2002	AF320787.1
30	France	before 2002	AF320788.1



31	France	before 2002	AF320789.1
32	France	before 2002	AF320791.1
33	France	before 2002	AF320792.1
34	France	before 2002	AF320793.1
35	France	before 2002	AF320794.1
36	France	before 2002	AF320795.1
37	France	before 2002	AF320796.1
38	France	before 2002	AF320797.1
39	France	before 2002	AF320798.1
40	France	before 2002	AF320799.1
41	France	before 2002	AF320800.1
42	France	before 2002	AF320801.1
43	France	before 2002	AF320802.1
44	France	before 2002	AF320803.1
45	France	before 2002	AF320804.1
46	France	before 2002	AF320805.1
47	France	before 2002	AF320806.1
48	France	before 2002	AF320807.1
49	France	before 2002	AF320809.1
50	France	before 2002	AF320811.1



