

Table S1. AVIATOR 2D with RBV study design and treatment outcome

	Arm	2D Regimen ^a + RBV	Paritaprevir dose mg ^a	SVR ₂₄		Virologic failures ^b (n)			
				% (n/N)		Breakthrough		Relapse	
				1a	1b	1a	1b	1a	1b
Treatment-naive	B	Dasabuvir	150	75.9 (22/29)	100 (12/12)	1		3	
	C	Ombitasvir	100	76.9 (20/26)	100 (13/13)			6	
	D	Ombitasvir	200	88.5 (23/26)	100 (14/14)	1		1	
Treatment-experienced null-responders	J	Ombitasvir	200	80.8 (21/26)	100 (19/19)			5	

2D, paritaprevir/r + (ombitasvir or dasabuvir)

^a The daily dose of paritaprevir (plus 100 mg of ritonavir) in each arm is indicated; ombitasvir = 25 mg once daily; dasabuvir = 400 mg twice daily; RBV = 1000 mg if the body was less than 75 kg or 1200 mg if body weight was 75 kg or more. The treatment duration was 12 weeks across all 2D arms.

^b Patients not achieving SVR₂₄ due to non-virologic reasons, e.g. early discontinuations, missing SVR₂₄ data etc., are not considered as VFs.

Table S2. RAVs relative to reference sequence in NS3, NS5A and NS5B at the time of VF in AVIATOR 2D with RBV arms

Study Population	Arm	GT	VF Type	NS3		NS5A		NS5B	
				Baseline	Time of VF	Baseline	Time of VF	Baseline	Time of VF
Treatment-naïve	B	1a	Relapse at PTW4	none ^a	D168V	none	nd	none	M414T
	B	1a	Breakthrough at Week 8	none	R155K + A156G	none	nd	none	D559N
	B	1a	D/C	none	none	none	nd	none	none
	B	1a	Relapse at PTW12	none	R155K, D168H/V	none	nd	none	none
	B	1a	Relapse at PTW2	none	Y56H + D168V/S	none	nd	none	none
	C	1a	Relapse at PTW2	none	D168V	none	Q30R	none	nd
	C	1a	Relapse at PTW8	none	D168V	none	M28T	none	nd
	C	1a	Relapse at PTW24	NA	D168V	NA	Q30L + Y93H	NA	nd
	C	1a	Relapse at PTW4	none	D168V	M28M/V	M28V	none	nd
	C	1a	Relapse at PTW24	none	none	none	H58D	none	nd
	C	1a	Relapse at PTW2	none	D168A	none	M28T, Q30R	none	nd
	D	1a	Breakthrough at Week 4	none	V36A/M + Y56H + D168V	M28T	M28T/V	none	nd
	D	1a	Relapse at PTW2	none	V36A + D168V	none	Q30R	none	nd
	D	1a	D/C	none	none	none	M28V, L31V, H58D	none	nd
Treatment-experienced Null-responders	J	1a	Relapse at PTW2	none	Y56H + D168V	M28M/V	M28V	none	nd
	J	1a	Relapse at PTW2	none	D168V	none	Q30R	none	nd
	J	1a	Relapse at PTW2	none	D168V/Y	Q30Q/R, Y93Y/N	M28T, Q30R	none	nd
	J	1a	Relapse at PTW4	none	A156V + D168V	none	M28T	none	nd
	J	1a	Relapse at PTW4	none	D168V	none	Q30R	none	nd

GT, genotype; D/C, premature study drug discontinuation; NA, sequence not available due to technical difficulties; nd, not determined as 2D regimen did not include drug target; PTW, Post-Treatment Week; VF, virologic failure; +, indicates linked variants; /, indicates mixture of variants

^a none = variants at resistance-associated amino acid positions were not detected by clonal sequencing.