Supplementary Materials for

A Randomized Phase III Study of Daclatasvir, Sofosbuvir and Ribavirin for Hepatitis C Virus Genotype 3 With Advanced Liver Disease: ALLY-3+.

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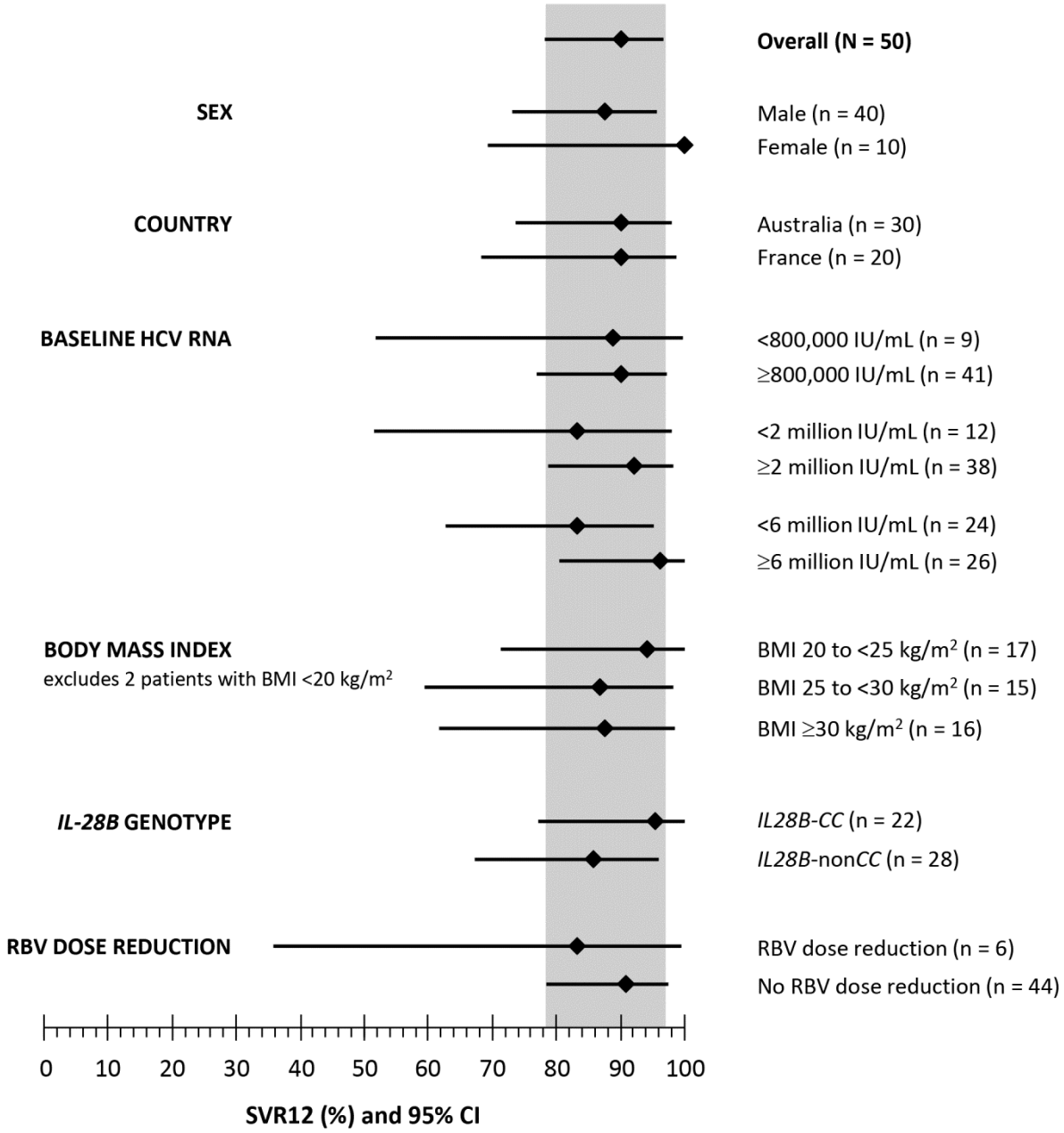
Figure S1. SVR12 in Selected Key Subgroups

12-week and 16-week treatment groups combined. Shaded region shows the 95% CI for all 50 treated patients. Data for other subgroups assessed are shown in Table S2.



BMI, body mass index; CI, confidence interval; RBV, ribavirin; SVR12, sustained virologic response at posttreatment 12.

Table S1. Baseline Characteristics of Patients with Advanced Fibrosis or Compensated Cirrhosis

Parameter	Advanced Fibrosis* (n = 14)	Cirrhosis* (n = 36)	Total (N = 50)
Age, median (range) years	53.0 (39–62)	55.5 (36–73)	53.5 (36–73)
Male, n (%)	11 (78.6)	29 (80.6)	40 (80.0)
Race, n (%)			
White	13 (92.9)	36 (100)	49 (98.0)
Asian	1 (7.1)	0	1 (2.0)
DCV-SOF-RBV treatment group, n (%)			
12 weeks	6 (42.9)	18 (50.0)	24 (48.0)
16 weeks	8 (57.1)	18 (50.0)	26 (52.0)
HCV RNA, median (range) $\log_{10}$ IU/mL	6.68 (4.6–7.8)	6.93 (4.7–7.7)	6.87 (4.6–7.8)
HCV RNA category, n (%)			
>800,000 IU/mL	9 (64.3)	32 (88.9)	41 (82.0)
>2,000,000 IU/mL	9 (64.3)	29 (80.6)	38 (76.0)
>6,000,000 IU/mL	6 (42.9)	20 (55.6)	26 (52.0)
Albumin, median (range) g/L	45 (38–48)	42 (33–46)	43 (33–48)
Platelet count, median (range) $\times 10^9$ cells/L	214 (138–324)	153 (63–299)	161 (63–324)
ALT, median (range) U/L	91 (39–227)	107 (29–326)	98 (29–326)
AST, median (range) U/L	60 (28–117)	101 (45–231)	82 (28–231)
Total bilirubin, median (range) mg/dL	0.5 (0.3–1.6)	0.5 (0.2–1.5)	0.5 (0.2–1.6)
IL28B (rs12979860) genotype, n (%)			
CC	5 (35.7)	17 (47.2)	22 (44.0)
CT	8 (57.1)	17 (47.2)	25 (50.0)
TT	1 (7.1)	2 (5.6)	3 (6.0)
Prior treatment status, n (%)			
Naive	7 (50.0)	6 (16.7)	13 (26.0)
Experienced	7 (50.0)	30 (83.3)	37 (74.0)
IFN-based	*7 (50.0)*	*24 (66.7)*	*31 (62.0)*
SOF-based[†]	*0*	*6 (16.7)*	*6 (12.0)*
Prior treatment outcome			
IFN-based			
Relapse	5 (35.7)	10 (27.8)	15 (30.0)
Null response	1 (7.1)	5 (13.9)	6 (12.0)
Partial response	0	1 (2.8)	1 (2.0)
VBT	1 (7.1)	1 (2.8)	2 (4.0)
Intolerance	0	5 (13.9)	5 (10.0)
Indeterminate	0	2 (5.6)	2 (4.0)
SOF-based			
Relapse	0	6 (16.7)	6 (12.0)
DCV-resistant NS5A polymorphisms, n (%)			
A30K	2 (14.3)	4 (11.1)	6 (12.0)
Y93H	0	2 (5.6)	2 (4.0)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; DCV, daclatasvir; IFN, interferon; RBV, ribavirin; SOF, sofosbuvir.

*Advanced fibrosis or cirrhosis was determined by biopsy in 10 patients (20%) and FibroScan in 40 patients (80%). See Methods for details.

[†]SOF-RBV (n=5); SOF-RBV-pegIFN (n=1; 12-week arm)

Table S2. SVR12 in Key Subgroups

HCV RNA measurements are excluded after the start of non-study anti-HCV medication on treatment or during follow-up. SVR12 is based on Next Value Carried Backwards approach.

Category Subgroup	DCV+SOF+RBV 12 WK N=24	DCV+SOF+RBV 16 WK N=26	Total N=50
Gender			
Male			
Responders/Treated (%)	15/18 (83.3)	20/22 (90.9)	35/40 (87.5)
95% CI	(58.6, 96.4)	(70.8, 98.9)	(73.2, 95.8)
Female			
Responders/Treated (%)	6/6 (100.0)	4/4 (100.0)	10/10 (100.0)
95% CI	(54.1, 100.0)	(39.8, 100.0)	(69.2, 100.0)
Age (Years)			
< 65			
Responders/Treated (%)	20/23 (87.0)	24/26 (92.3)	44/49 (89.8)
95% CI	(66.4, 97.2)	(74.9, 99.1)	(77.8, 96.6)
>=65			
Responders/Treated (%)	1/1 (100.0)		1/1 (100.0)
95% CI	(2.5, 100.0)		(2.5, 100.0)
Race			
White			
Responders/Treated (%)	20/23 (87.0)	24/26 (92.3)	44/49 (89.8)
95% CI	(66.4, 97.2)	(74.9, 99.1)	(77.8, 96.6)
Asian			
Responders/Treated (%)	1/1 (100.0)		1/1 (100.0)
95% CI	(2.5, 100.0)		(2.5, 100.0)
Country			
Australia			
Responders/Treated (%)	12/14 (85.7)	15/16 (93.8)	27/30 (90.0)
95% CI	(57.2, 98.2)	(69.8, 99.8)	(73.5, 97.9)
France			
Responders/Treated (%)	9/10 (90.0)	9/10 (90.0)	18/20 (90.0)
95% CI	(55.5, 99.7)	(55.5, 99.7)	(68.3, 98.8)
Baseline HHCV RNA			
< 800,000 Iu/Ml			
Responders/Treated (%)	4/4 (100.0)	4/5 (80.0)	8/9 (88.9)
95% CI	(39.8, 100.0)	(28.4, 99.5)	(51.8, 99.7)
>= 800,000 Iu/Ml			
Responders/Treated (%)	17/20 (85.0)	20/21 (95.2)	37/41 (90.2)
95% CI	(62.1, 96.8)	(76.2, 99.9)	(76.9, 97.3)
< 2,000,000 Iu/Ml			
Responders/Treated (%)	5/6 (83.3)	5/6 (83.3)	10/12 (83.3)
95% CI	(35.9, 99.6)	(35.9, 99.6)	(51.6, 97.9)
>= 2,000,000 Iu/Ml			
Responders/Treated (%)	16/18 (88.9)	19/20 (95.0)	35/38 (92.1)
95% CI	(65.3, 98.6)	(75.1, 99.9)	(78.6, 98.3)
< 6,000,000 Iu/Ml			
Responders/Treated (%)	11/13 (84.6)	9/11 (81.8)	20/24 (83.3)
95% CI	(54.6, 98.1)	(48.2, 97.7)	(62.6, 95.3)
>= 6,000,000 Iu/Ml			
Responders/Treated (%)	10/11 (90.9)	15/15 (100.0)	25/26 (96.2)
95% CI	(58.7, 99.8)	(78.2, 100.0)	(80.4, 99.9)
< Median (7404605)			
Responders/Treated (%)	11/13 (84.6)	10/12 (83.3)	21/25 (84.0)
95% CI	(54.6, 98.1)	(51.6, 97.9)	(63.9, 95.5)
>= Median (7404605)			
Responders/Treated (%)	10/11 (90.9)	14/14 (100.0)	24/25 (96.0)
95% CI	(58.7, 99.8)	(76.8, 100.0)	(79.6, 99.9)
Baseline Cirrhosis Status			
Absent			
Responders/Treated (%)	6/6 (100.0)	8/8 (100.0)	14/14 (100.0)
95% CI	(54.1, 100.0)	(63.1, 100.0)	(76.8, 100.0)
Present			
Responders/Treated (%)	15/18 (83.3)	16/18 (88.9)	31/36 (86.1)
95% CI	(58.6, 96.4)	(65.3, 98.6)	(70.5, 95.3)
Fibrotest Score Category			
0 - 0.27			
Responders/Treated (%)	1/1 (100.0)	1/1 (100.0)	2/2 (100.0)
95% CI	(2.5, 100.0)	(2.5, 100.0)	(15.8, 100.0)
>0.27 - 0.48			
Responders/Treated (%)	2/2 (100.0)	1/1 (100.0)	3/3 (100.0)
95% CI	(15.8, 100.0)	(2.5, 100.0)	(29.2, 100.0)
>0.48 - 0.58			
Responders/Treated (%)	4/4 (100.0)	3/4 (75.0)	7/8 (87.5)
95% CI	(39.8, 100.0)	(19.4, 99.4)	(47.3, 99.7)
>0.58 - 0.74			
Responders/Treated (%)	4/4 (100.0)	5/5 (100.0)	9/9 (100.0)
95% CI	(39.8, 100.0)	(47.8, 100.0)	(66.4, 100.0)
>0.74 - 1.00			
Responders/Treated (%)	9/10 (90.0)	13/14 (92.9)	22/24 (91.7)
95% CI	(55.5, 99.7)	(66.1, 99.8)	(73.0, 99.0)
Not Reported			
Responders/Treated (%)	1/3 (33.3)	1/1 (100.0)	2/4 (50.0)
95% CI	(0.8, 90.6)	(2.5, 100.0)	(6.8, 93.2)

Table S2 (cont).

Category Subgroup	DCV+SOF+RBV 12 WK N=24	DCV+SOF+RBV 16 WK N=26	Total N=50
Fibrosis Stage Stratum			
F3			
Responders/Treated (%)	6/6 (100.0)	8/8 (100.0)	14/14 (100.0)
95% CI	(54.1, 100.0)	(63.1, 100.0)	(76.8, 100.0)
F4			
Responders/Treated (%)	15/18 (83.3)	16/18 (88.9)	31/36 (86.1)
95% CI	(58.6, 96.4)	(65.3, 98.6)	(70.5, 95.3)
Prior Treatment Experience			
Naive			
Responders/Treated (%)	5/6 (83.3)	7/7 (100.0)	12/13 (92.3)
95% CI	(35.9, 99.6)	(59.0, 100.0)	(64.0, 99.8)
Experienced			
Responders/Treated (%)	16/18 (88.9)	17/19 (89.5)	33/37 (89.2)
95% CI	(65.3, 98.6)	(66.9, 98.7)	(74.6, 97.0)
Fibrosis Stage Stratum x Prior Treatment Status			
F3 - Naive			
Responders/Treated (%)	4/4 (100.0)	3/3 (100.0)	7/7 (100.0)
95% CI	(39.8, 100.0)	(29.2, 100.0)	(59.0, 100.0)
F3 - Experienced			
Responders/Treated (%)	2/2 (100.0)	5/5 (100.0)	7/7 (100.0)
95% CI	(15.8, 100.0)	(47.8, 100.0)	(59.0, 100.0)
F4 - Naive			
Responders/Treated (%)	1/2 (50.0)	4/4 (100.0)	5/6 (83.3)
95% CI	(1.3, 98.7)	(39.8, 100.0)	(35.9, 99.6)
F4 - Experienced			
Responders/Treated (%)	14/16 (87.5)	12/14 (85.7)	26/30 (86.7)
95% CI	(61.7, 98.4)	(57.2, 98.2)	(69.3, 96.2)
Baseline BMI (kg/m^2)			
< 20 Kg/M2			
Responders/Treated (%)		2/2 (100.0)	2/2 (100.0)
95% CI		(15.8, 100.0)	(15.8, 100.0)
20 -< 25 Kg/M2			
Responders/Treated (%)	9/10 (90.0)	7/7 (100.0)	16/17 (94.1)
95% CI	(55.5, 99.7)	(59.0, 100.0)	(71.3, 99.9)
25 -< 30 Kg/M2			
Responders/Treated (%)	7/7 (100.0)	6/8 (75.0)	13/15 (86.7)
95% CI	(59.0, 100.0)	(34.9, 96.8)	(59.5, 98.3)
>= 30 Kg/M2			
Responders/Treated (%)	5/7 (71.4)	9/9 (100.0)	14/16 (87.5)
95% CI	(29.0, 96.3)	(66.4, 100.0)	(61.7, 98.4)
Il28B RS1297860 Genotype			
CC			
Responders/Treated (%)	10/11 (90.9)	11/11 (100.0)	21/22 (95.5)
95% CI	(58.7, 99.8)	(71.5, 100.0)	(77.2, 99.9)
Non-CC			
Responders/Treated (%)	11/13 (84.6)	13/15 (86.7)	24/28 (85.7)
95% CI	(54.6, 98.1)	(59.5, 98.3)	(67.3, 96.0)
RBV Dose Reduction Or Interruption > 14 Days			
Yes			
Responders/Treated (%)	1/2 (50.0)	4/4 (100.0)	5/6 (83.3)
95% CI	(1.3, 98.7)	(39.8, 100.0)	(35.9, 99.6)
No			
Responders/Treated (%)	20/22 (90.9)	20/22 (90.9)	40/44 (90.9)
95% CI	(70.8, 98.9)	(70.8, 98.9)	(78.3, 97.5)
NS5A-M28 Polymorphism			
Yes			
Responders/Treated (%)		0/1 (0.0)	0/1 (0.0)
95% CI		(0.0, 97.5)	(0.0, 97.5)
No			
Responders/Treated (%)	21/24 (87.5)	24/25 (96.0)	45/49 (91.8)
95% CI	(67.6, 97.3)	(79.6, 99.9)	(80.4, 97.7)
NS5A-A30 Polymorphism			
Yes			
Responders/Treated (%)	6/6 (100.0)		6/6 (100.0)
95% CI	(54.1, 100.0)		(54.1, 100.0)
No			
Responders/Treated (%)	15/18 (83.3)	24/26 (92.3)	39/44 (88.6)
95% CI	(58.6, 96.4)	(74.9, 99.1)	(75.4, 96.2)
NS5A-L31 Polymorphism			
Yes			
Responders/Treated (%)			
95% CI			
No			
Responders/Treated (%)	21/24 (87.5)	24/26 (92.3)	45/50 (90.0)
95% CI	(67.6, 97.3)	(74.9, 99.1)	(78.2, 96.7)
NS5A-Y93 Polymorphism			
Yes			
Responders/Treated (%)	0/1 (0.0)	1/1 (100.0)	1/2 (50.0)
95% CI	(0.0, 97.5)	(2.5, 100.0)	(1.3, 98.7)
No			
Responders/Treated (%)	21/23 (91.3)	23/25 (92.0)	44/48 (91.7)
95% CI	(72.0, 98.9)	(74.0, 99.0)	(80.0, 97.7)

Table S2 (cont)

Category Subgroup	DCV+SOF+RBV 12 WK N=24	DCV+SOF+RBV 16 WK N=26	Total N=50
Baseline Steatosis Grade			
0 (None To <5%)			
Responders/Treated (%)		0/1 (0.0)	0/1 (0.0)
95% CI		(0.0, 97.5)	(0.0, 97.5)
1 (5-33%)			
Responders/Treated (%)	1/1 (100.0)		1/1 (100.0)
95% CI	(2.5, 100.0)		(2.5, 100.0)
2 (34-66%)			
Responders/Treated (%)		1/1 (100.0)	1/1 (100.0)
95% CI		(2.5, 100.0)	(2.5, 100.0)
3 (67-100%)			
Responders/Treated (%)	0/1 (0.0)		0/1 (0.0)
95% CI	(0.0, 97.5)		(0.0, 97.5)
Not Reported			
Responders/Treated (%)	20/22 (90.9)	23/24 (95.8)	43/46 (93.5)
95% CI	(70.8, 98.9)	(78.9, 99.9)	(82.1, 98.6)

Table S3. Adverse Events (All-Cause Grades 1-4) on Treatment

System Organ Class (%) Preferred Term (%)	DCV+SOF+RBV 12 WK N=24	DCV+SOF+RBV 16 WK N=26	TOTAL N=50
Total Subjects With An Event	23 (95.8)	24 (92.3)	47 (94.0)
Psychiatric Disorders	14 (58.3)	14 (53.8)	28 (56.0)
Insomnia	8 (33.3)	7 (26.9)	15 (30.0)
Irritability	5 (20.8)	2 (7.7)	7 (14.0)
Depressed Mood	1 (4.2)	2 (7.7)	3 (6.0)
Depression	1 (4.2)	2 (7.7)	3 (6.0)
Abnormal Dreams	1 (4.2)	1 (3.8)	2 (4.0)
Agitation	1 (4.2)	0	1 (2.0)
Anxiety	0	1 (3.8)	1 (2.0)
Middle Insomnia	0	1 (3.8)	1 (2.0)
General Disorders And Administration Site Conditions	9 (37.5)	13 (50.0)	22 (44.0)
Fatigue	6 (25.0)	7 (26.9)	13 (26.0)
Asthenia	2 (8.3)	5 (19.2)	7 (14.0)
Chest Pain	1 (4.2)	0	1 (2.0)
Chills	1 (4.2)	0	1 (2.0)
Influenza Like Illness	1 (4.2)	0	1 (2.0)
Mass	1 (4.2)	0	1 (2.0)
Oedema Peripheral	0	1 (3.8)	1 (2.0)
Pain	1 (4.2)	0	1 (2.0)
Nervous System Disorders	11 (45.8)	11 (42.3)	22 (44.0)
Headache	7 (29.2)	5 (19.2)	12 (24.0)
Lethargy	2 (8.3)	2 (7.7)	4 (8.0)
Disturbance In Attention	1 (4.2)	1 (3.8)	2 (4.0)
Carotid Artery Stenosis	0	1 (3.8)	1 (2.0)
Dizziness	1 (4.2)	0	1 (2.0)
Memory Impairment	1 (4.2)	0	1 (2.0)
Paraesthesia	0	1 (3.8)	1 (2.0)
Somnolence	1 (4.2)	0	1 (2.0)
Syncope	0	1 (3.8)	1 (2.0)
Gastrointestinal Disorders	7 (29.2)	12 (46.2)	19 (38.0)
Diarrhoea	1 (4.2)	4 (15.4)	5 (10.0)
Nausea	3 (12.5)	1 (3.8)	4 (8.0)
Abdominal Discomfort	0	2 (7.7)	2 (4.0)
Abdominal Pain	0	2 (7.7)	2 (4.0)
Abdominal Pain Upper	2 (8.3)	0	2 (4.0)
Gastrooesophageal Reflux Disease	1 (4.2)	1 (3.8)	2 (4.0)
Mouth Ulceration	0	2 (7.7)	2 (4.0)
Tooth Loss	1 (4.2)	1 (3.8)	2 (4.0)
Vomiting	1 (4.2)	1 (3.8)	2 (4.0)
Dry Mouth	0	1 (3.8)	1 (2.0)
Dyspepsia	0	1 (3.8)	1 (2.0)
Frequent Bowel Movements	1 (4.2)	0	1 (2.0)
Varices Oesophageal	0	1 (3.8)	1 (2.0)
Skin And Subcutaneous Tissue Disorders	9 (37.5)	4 (15.4)	13 (26.0)
Pruritus	1 (4.2)	2 (7.7)	3 (6.0)
Dry Skin	2 (8.3)	0	2 (4.0)
Hyperhidrosis	2 (8.3)	0	2 (4.0)
Photosensitivity Reaction	2 (8.3)	0	2 (4.0)
Rash	1 (4.2)	1 (3.8)	2 (4.0)
Blood Blister	1 (4.2)	0	1 (2.0)
Skin And Subcutaneous Tissue Disorders			
Eczema	0	1 (3.8)	1 (2.0)
Erythema	0	1 (3.8)	1 (2.0)
Hand Dermatitis	1 (4.2)	0	1 (2.0)
Pruritus Generalised	1 (4.2)	0	1 (2.0)
Rash Erythematous	1 (4.2)	0	1 (2.0)
Rash Maculo-Papular	0	1 (3.8)	1 (2.0)
Respiratory, Thoracic And Mediastinal Disorders	6 (25.0)	4 (15.4)	10 (20.0)
Dyspnoea	2 (8.3)	3 (11.5)	5 (10.0)
Cough	1 (4.2)	1 (3.8)	2 (4.0)
Dyspnoea Exertional	1 (4.2)	0	1 (2.0)
Productive Cough	1 (4.2)	0	1 (2.0)
Rhinorrhoea	1 (4.2)	0	1 (2.0)
Infections And Infestations	4 (16.7)	3 (11.5)	7 (14.0)
Nasopharyngitis	1 (4.2)	1 (3.8)	2 (4.0)
Upper Respiratory Tract Infection	1 (4.2)	1 (3.8)	2 (4.0)
Gastrointestinal Infection	1 (4.2)	0	1 (2.0)
Pneumonia	0	1 (3.8)	1 (2.0)
Respiratory Tract Infection	1 (4.2)	0	1 (2.0)
Viral Upper Respiratory Tract Infection	1 (4.2)	0	1 (2.0)
Musculoskeletal And Connective Tissue Disorders	2 (8.3)	5 (19.2)	7 (14.0)
Back Pain	0	3 (11.5)	3 (6.0)
Muscle Spasms	1 (4.2)	1 (3.8)	2 (4.0)

Table S3 (cont).

System Organ Class (%) Preferred Term (%)	DCV+SOF+RBV 12 WK N=24	DCV+SOF+RBV 16 WK N=26	TOTAL N=50
Musculoskeletal And Connective Tissue Disorders			
Arthralgia	0	1 (3.8)	1 (2.0)
Myalgia	1 (4.2)	0	1 (2.0)
Neck Pain	0	1 (3.8)	1 (2.0)
Pain In Extremity	0	1 (3.8)	1 (2.0)
Vascular Disorders	1 (4.2)	5 (19.2)	6 (12.0)
Hypertension	0	3 (11.5)	3 (6.0)
Arteriosclerosis	0	1 (3.8)	1 (2.0)
Arteritis	0	1 (3.8)	1 (2.0)
Haematoma	1 (4.2)	0	1 (2.0)
Blood And Lymphatic System Disorders	0	2 (7.7)	2 (4.0)
Anaemia	0	2 (7.7)	2 (4.0)
Cardiac Disorders	1 (4.2)	1 (3.8)	2 (4.0)
Congestive Cardiomyopathy	1 (4.2)	0	1 (2.0)
Palpitations	0	1 (3.8)	1 (2.0)
Ear And Labyrinth Disorders	1 (4.2)	1 (3.8)	2 (4.0)
Tinnitus	0	1 (3.8)	1 (2.0)
Vertigo	1 (4.2)	0	1 (2.0)
Metabolism And Nutrition Disorders	0	2 (7.7)	2 (4.0)
Decreased Appetite	0	2 (7.7)	2 (4.0)
Renal And Urinary Disorders	1 (4.2)	1 (3.8)	2 (4.0)
Nocturia	0	1 (3.8)	1 (2.0)
Pollakiuria	1 (4.2)	0	1 (2.0)
Reproductive System And Breast Disorders	2 (8.3)	0	2 (4.0)
Atrophic Vulvovaginitis	1 (4.2)	0	1 (2.0)
Vulval Angiokeratoma	1 (4.2)	0	1 (2.0)
Vulval Disorder	1 (4.2)	0	1 (2.0)
Eye Disorders	1 (4.2)	0	1 (2.0)
Dry Eye	1 (4.2)	0	1 (2.0)
Investigations	1 (4.2)	0	1 (2.0)
Haemoglobin Decreased	1 (4.2)	0	1 (2.0)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	0	1 (3.8)	1 (2.0)
Basal Cell Carcinoma	0	1 (3.8)	1 (2.0)