Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Wyles DL, Ruane PJ, Sulkowski MS, et al. Daclatasvir plus sofosbuvir for HCV in patients coinfected with HIV-1. N Engl J Med. DOI: 10.1056/NEJMoa1503153

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List of investigators

Leslie Bank, Kalyan Bhamidimarri, Terry Box, Thomas Campbell, Taddese Desta, Douglas Dieterich, Robin Dretler, Michael Fallon, Dawn Fishbein, Joel Gallant, Joseph Gathe, Jr., Sarah Henn, Federico Hinestrosa, Charles Huynh, Kevin Korenblat, Paul Kwo, Charles Landis, Anne Luetkemeyer, Velimir Luketic, Cheryl McDonald, Anthony Mills, Dilip Moonka, Timothy Morgan, David Morris, Edgar Turner Overton, Moti Ramgopal, Aadia Rana, Bruce Rashbaum, Natarajan Ravendhran, Peter Ruane, Anthony Scarsella, Thomas Sepe, Kenneth E Sherman, Mark Sulkowski, David Wyles (lead investigator), Joseph Yozviak, Atif Zaman.

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Full study inclusion and exclusion criteria

Inclusion Criteria

Signed Written Informed Consent

- Freely given informed consent must be obtained from all subjects prior to clinical trial participation, including informed consent for any screening procedures conducted to establish eligibility for the study.

Target Population

- Able to understand and agree to comply with the prescribed dosing regimens and procedures, report for regularly scheduled study visits, and reliably communicate with study personnel about adverse events and concomitant medications.

- Chronically infected with HCV genotypes 1, 2, 3, 4, 5 or 6, as documented by positive HCV RNA at screening and either

    - Positive anti-HCV antibody, HCV RNA , or a positive HCV genotype test at least 6 months prior to screening; or

    - Liver biopsy consistent with chronic HCV infection.

    - **Treatment-naive subjects only:** mixed, indeterminate, or other variants or genotype 1 (e.g., non-1a and non-1b) were NOT eligible.

- HCV treatment-naïve or HCV treatment-experienced with the following restrictions:

    - *Treatment-naive:*
        - No previous exposure to any interferon formulation (i.e., IFNα, peg-IFNα) or RBV

        - No previous exposure to any HCV direct acting antivirals (DAAs).

    - *Treatment-experienced:*
        - All permitted prior anti-HCV therapies be discontinued or completed at least 12 weeks prior to screening

        - **Previous exposure to NS5A inhibitors is prohibited.**

        - Previous treatment with IFNα, with or without RBV is permitted. Documentation of prior virologic response to treatment is desirable but not strictly required. Subjects who did not complete treatment due to laboratory abnormality or intolerable side effect are eligible.

        - Previous exposure to NS3 protease inhibitors including, but not limited to, telaprevir or boceprevir is permitted. Subjects who did not complete

treatment due to laboratory abnormality or intolerable side effects are eligible.

- Previous exposure to nucleoside/nucleotide and non-nucleoside inhibitors of NS5B is permitted (including sofosbuvir [SOF]). Subjects who discontinued previous treatment with SOF due to intolerance of this drug are excluded.

- Previous exposure to other classes of anti-HCV agents (e.g. cyclophilin inhibitors and inhibitors of microRNA) is permitted.

- An HCV RNA at least 10^4 IU/mL (10,000 IU/mL) at screening

- HIV-1 infected and either receiving or not receiving combination antiretroviral therapy (cART)

  - *Subjects receiving cART:*
    - Screening HIV RNA < 50 copies/mL and < 200 copies/mL for at least 8 weeks prior to screening

    - Screening CD4 cell count ≥ 100 cells/uL

  - *Subjects not receiving cART:*
    - Screening CD4 cell count must be ≥ 350 cells/uL

- Seronegative for HBsAg

- Body Mass Index (BMI) of 18 to 35 kg/m^2, inclusive at screening.

- Subjects with compensated cirrhosis are eligible

  - Determination of cirrhosis status is required prior to randomization. Up to 50% of subjects in each of the 12-week treatment arms (HCV treatment-naive and -experienced subjects) and in the 8-week arm (HCV treatment-naive only) may be cirrhotic. A biopsy is not needed for participation in this study, however;

    - A subject will be considered "cirrhotic" if they meet the following criteria:

      - Liver biopsy showing cirrhosis (i.e. Metavir > F3, Ishak > 4 or the equivalent) at any time prior to screening OR;

      - FibroScan showing cirrhosis or results >14.6 kPa within 1 year of Baseline OR;

      - A FibroTest score of ≥ 0.75 and an aspartate aminotransferase (AST): platelet ratio index (APRI) of > 2 (performed during Screening).

    - A subject will be considered "non-cirrhotic" if they meet the following criteria:

- Most recent liver biopsy (within ≤36 months of Screening) showing absence of cirrhosis (i.e. Metavir F0-F3, Ishak 0-4, or the equivalent) OR;

- FibroScan with a result of ≤ 9.6 kPa within 1 year of Baseline/Day 1 OR;

- A FibroTest score of ≤ 0.48 and APRI of ≤ 1 (performed during Screening)

▪ If a subject is evaluated by more than one testing method which provide conflicting determinations of the subject's liver status, the determination of cirrhosis will be made using the following methodology:

  - Liver biopsies (performed within the pre-specified timeframe outlined above) take precedence over either FibroScan or FibroTest/APRI.

  - In the absence of an acceptable liver biopsy, FibroScan (performed within the pre-specified timeframe outlined above) results take precedence over FibroTest/APRI.

  - The combined screening FibroTest/APRI results are adequate for enrollment and to determine cirrhosis status if an acceptable biopsy or FibroScan are not available.

  - *Note If results from both FibroScan and FibroTest/APRI, do not meet the criteria above defining the subject as "cirrhotic" or "non-cirrhotic", the subject is considered to have an "indeterminant" liver status and a liver biopsy will be required prior to Day 1 for study participation.*

- **Subject re-enrollment:** This study permits the re-enrollment of a subject that has discontinued the study as a pre-treatment failure (i.e. subject has not been randomized or has not been treated). Discussion with the BMS Medical Monitor must occur prior to subject re-enrollment. If re-enrolled, the subject must be re-consented.

Age and Reproductive Status

- Males and females ≥ 18 years of age

- Women of childbearing potential (WOCBP) must have a negative serum or urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of HCG) within 24 hours prior to the start of study drug.

- Women must not be breastfeeding.

- WOCBP must agree to follow instructions for method(s) of contraception for the duration of treatment with DCV and SOF plus 5 half-lives of study drugs (5 days) plus 30 days (duration of ovulatory cycle) for a total of 5 weeks post-treatment completion.

- Men who are sexually active with WOCBP must agree to follow instructions for method(s) of contraception for the duration of treatment with study drugs plus 5 half-lives of the study drug (5 days) plus 90 days (duration of sperm turnover) for a total of 14 weeks post-treatment completion.

- Investigators shall counsel WOCBP and male subjects who are sexually active with WOCBP on the importance of pregnancy prevention and the implications of an unexpected pregnancy Investigators shall advise WOCBP and male subjects who are sexually active with WOCBP on the use of highly effective methods of contraception. Highly effective methods of contraception have a failure rate of < 1% per year when used consistently and correctly.

- At a minimum, subjects must agree to the use of two methods of contraception, with one method being highly effective and the other method being either highly effective or less effective as listed below:

    - *Highly Effective Methods of Contraception*
        - Male condoms with spermicide.

        - Hormonal methods of contraception including combined oral contraceptive pills, vaginal ring, injectables, implants, and intrauterine devices (IUDs) such as Mirena® **by male subject's WOCBP partner**. Female partners of male subjects participating in the study may use hormone based contraceptives as one of the acceptable methods of contraception since they will not be receiving study drug.

            - **WOCBP cannot use hormonal contraception as one of the two methods of contraception** because there are no data on the effectiveness of systemic hormonal contraceptives in women taking SOF. However, WOCBP can continue to use hormonal contraceptives, if necessary, in addition to 2 other non-hormonal methods of contraception.

        - Nonhormonal IUDs, such as ParaGard®

        - Tubal Ligation

        - Vasectomy

        - Complete Abstinence

            - Defined as complete avoidance of heterosexual intercourse, and is an acceptable form of contraception for all study drugs. Subjects who choose complete abstinence are not required to use a second method of contraception, but female subjects must continue to have pregnancy tests. Acceptable alternate methods of highly effective contraception must be discussed in the event that the subject chooses to forego complete abstinence.

- *Less Effective Methods of Contraception*
    - Diaphragm with spermicide
    - Cervical cap with spermicide
    - Vaginal sponge
    - Male condom without spermicide
    - Progestin only pills
    - Female condom
        - A male and female condom must not be used together

- Azoospermic males, women who are not of childbearing potential and WOCBP who abstain from heterosexual activity on a continuous basis, are exempt from contraceptive requirements. However, WOCBP who abstain from heterosexual activity on a continuous basis must still undergo pregnancy testing.

Exclusion Criteria

Target Disease Exceptions

- Presence of AIDS-defining opportunistic infections (as defined by the Centers for Disease Control) within 12 weeks prior to study entry.
- Subjects infected with HIV-2.

Medical History and Concurrent Diseases

- Liver or any other organ transplant (including hematopoietic stem cell transplants) other than cornea and hair
- Current or known history of cancer (except in situ carcinoma of the cervix or adequately treated basal or squamous cell carcinoma of the skin) within 5 years prior to screening
- Documented or suspected HCC, as evidenced by previously obtained imaging studies or liver biopsy (or on a screening imaging study/liver biopsy if this was performed)
- Evidence of decompensated liver disease including, but not limited to, radiologic criteria, a history or presence of ascites, bleeding varices, or hepatic encephalopathy
- Evidence of an ongoing medical condition contributing to chronic liver disease other than HCV (such as, but not limited to, hemochromatosis, autoimmune hepatitis, metabolic liver disease, alcoholic liver disease, toxin exposures)
- History of chronic hepatitis B virus (HBV) as documented by HBV serologies (e.g., HBsAg-seropositive). Subjects with resolved HBV infection may participate (e.g., HBsAb-seropositive with concurrent HBsAg-seronegative)

- Any gastrointestinal disease or surgical procedure that may impact the absorption of study drug (subjects who have had cholecystectomy are permitted to enter the study).
- Known history of genetic coagulopathy including, but not limited to, hemophilia
- Uncontrolled diabetes (any subject with a confirmed screening HgA1c ≥ 8.5 must be excluded)
- Confirmed, uncontrolled hypertension (any screening systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 100 mmHg should be excluded unless discussed with the BMS medical monitor)
- Active substance abuse as defined by DSM-IV, Diagnostic Criteria for Drug and Alcohol Abuse, which in the opinion of the investigator would make the candidate inappropriate for participation in this study
- Active severe psychiatric disorders including but not limited to, schizophrenia, psychosis, bipolar disorder, post-traumatic stress disorder, mania, etc.
- Inability to tolerate oral medication
- Poor venous access that would impair the subject's ability to comply with the study protocol

Physical and Laboratory Test Findings

- Alanine aminotransferase (ALT) ≥10x ULN
- Total Bilirubin ≥ 2 mg/dL (≥ 34 μmol/L), unless due to atazanavir-ritonavir treatment or a history of Gilbert's disease
- Albumin < 3.0 g/dL (30 g/L)
- Platelets < 50 x 10^3 cells/L
- ANC < 0.75 x 10^3 cells/L
- Hemoglobin < 10 g/dL (<100 g/L)
- Creatinine Clearance (CrCl) ≤ 50 mL/min (as estimated by Cockcroft and Gault)
- Alpha fetoprotein (AFP):
  - AFP >100 ng/mL (> 82.6 IU/mL) OR
  - AFP ≥ 50 and ≤ 100 ng/mL (≥ 41.3 IU/mL and 82.6 IU/mL) requires a liver ultrasound and subjects with findings suspicious for HCC are excluded.
- QTcF or QTcB > 500 mSec

Allergies and Adverse Drug Reaction

- History of hypersensitivity to drugs with a similar biochemical structure to DCV or SOF.

- Any other criteria or known contraindication that would exclude the subject from receiving DCV or SOF per the local label.

Sex and Reproductive Status

- Those males and females who do not or cannot meet the requirements outlined in Inclusion Criteria.

- Sexually active fertile men whose partners are pregnant at screening are excluded from this study.

Prohibited Treatments and/or Therapies

- Subjects (receiving cART regimens) who had first initiated anti-retroviral therapy within 6 months prior to Day 1 (Baseline) are excluded.

- Use of prohibited cART regimens (See Supplementary Table S1) within one month of Day 1 (Baseline) and throughout the treatment period of the trial is prohibited. For subjects on prohibited cART regimens who are switched to permitted cART regimens at the discretion of their HIV care providers for the purpose of enrolling in the current study, subject must:

    - Meet all of the above inclusion and exclusion criteria, and

    - Be on the permitted cART for at least one month prior to Day 1 and

    - Demonstrate complete HIV RNA suppression (HIV RNA < 50 copies/mL) at screening and prior to Day 1

Other Exclusion Criteria

- Any other medical, psychiatric and/or social reason which, in the opinion of the investigator would make the subject inappropriate for the study

- Prisoners or subjects who are involuntarily incarcerated

- Subjects who are compulsorily detained for treatment of either a psychiatric or physical (e.g., infectious disease) illness

Figure S1. HCV RNA change from baseline on treatment with DCV + SOF

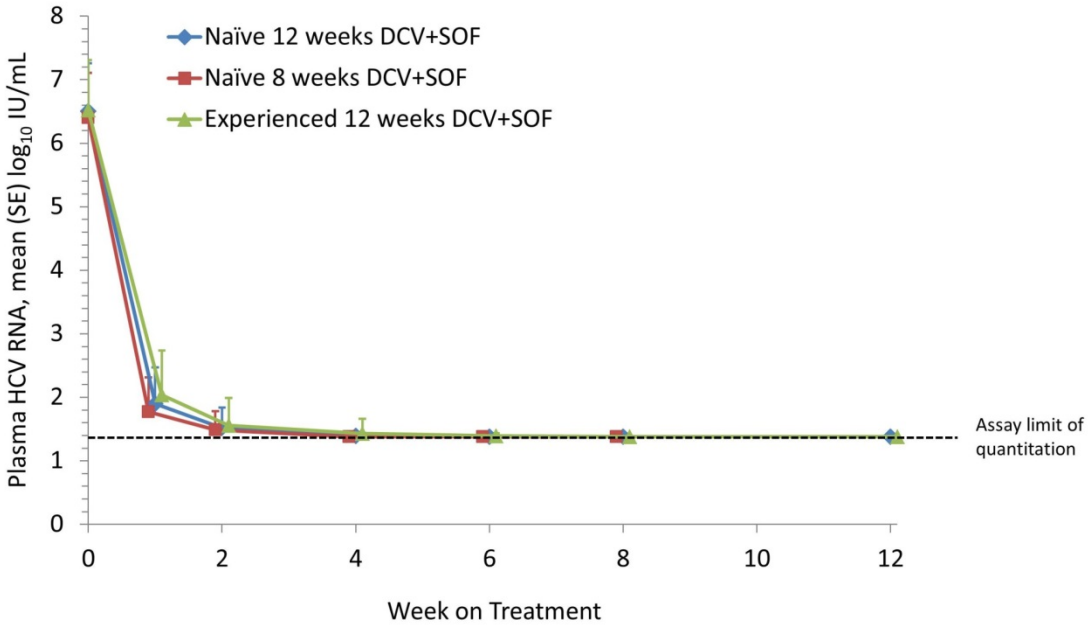
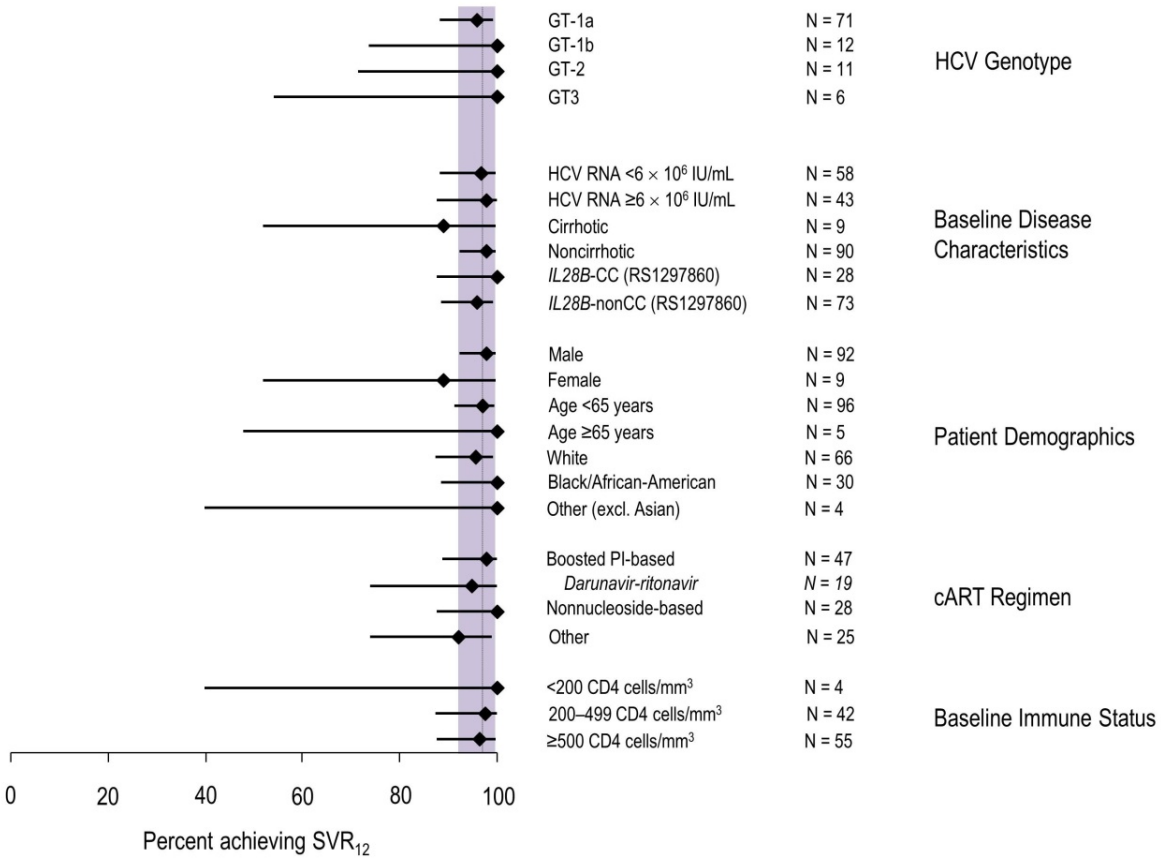


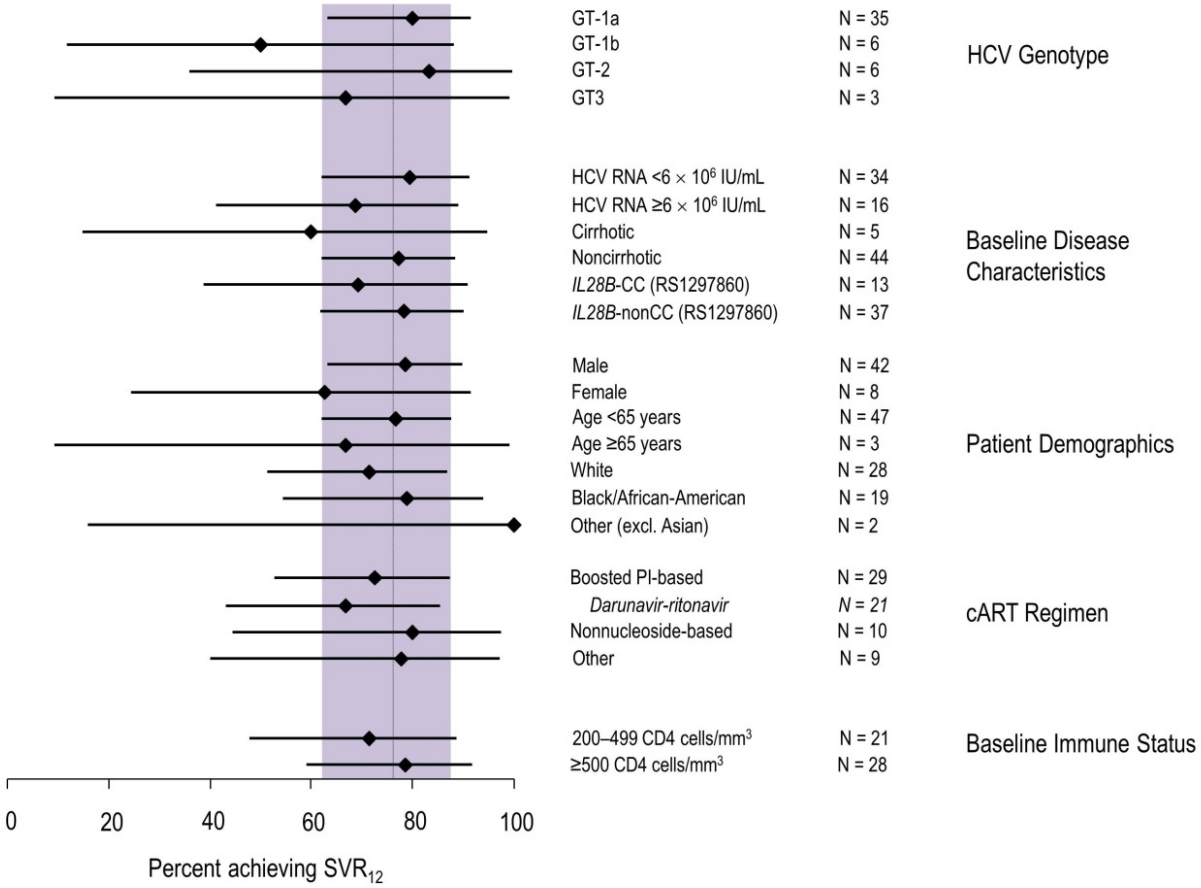
Figure S2. Sustained virologic responses and 95% confidence intervals for key subgroups by DCV + SOF treatment group (all treated patients)

Dashed vertical lines show overall SVR12 results and shaded regions show the associated overall confidence interval. Subgroups of N < 2 excluded

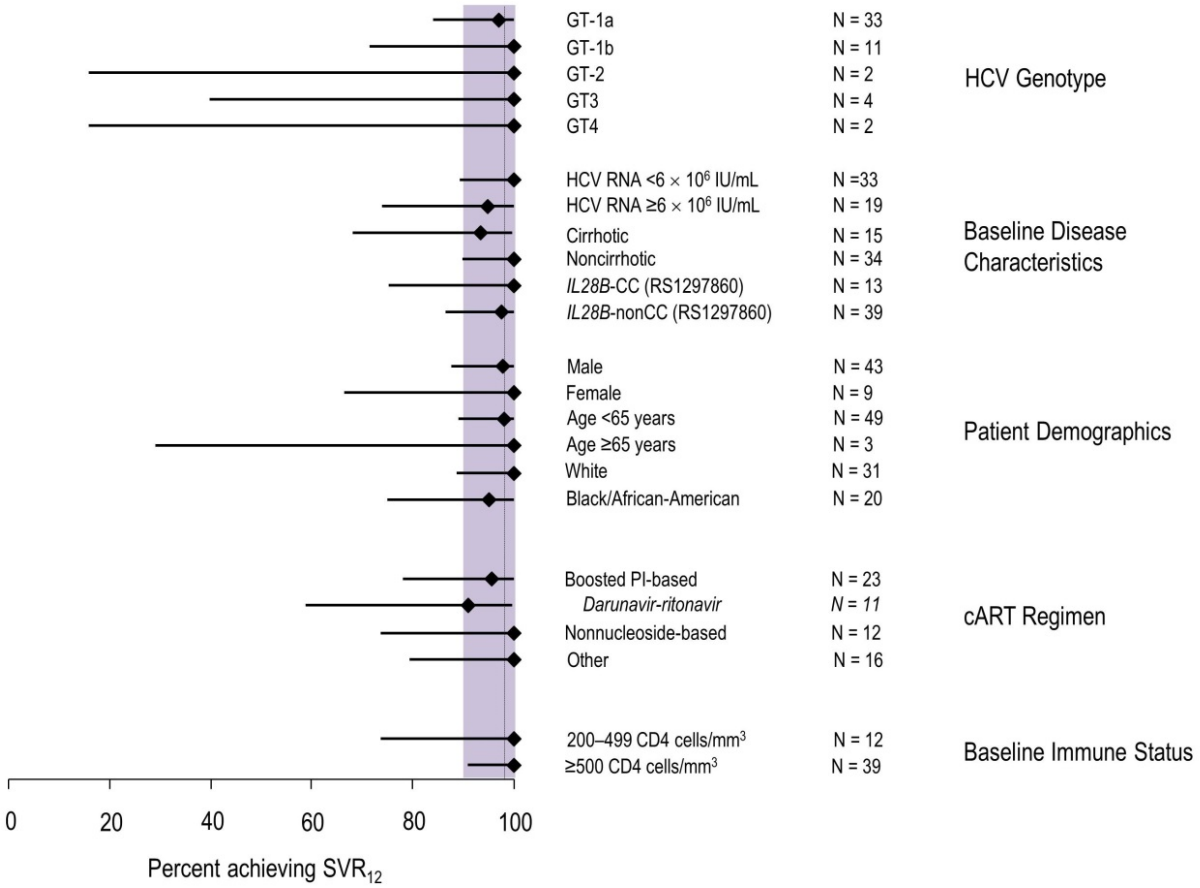
(A) Treatment-naive, 12 weeks



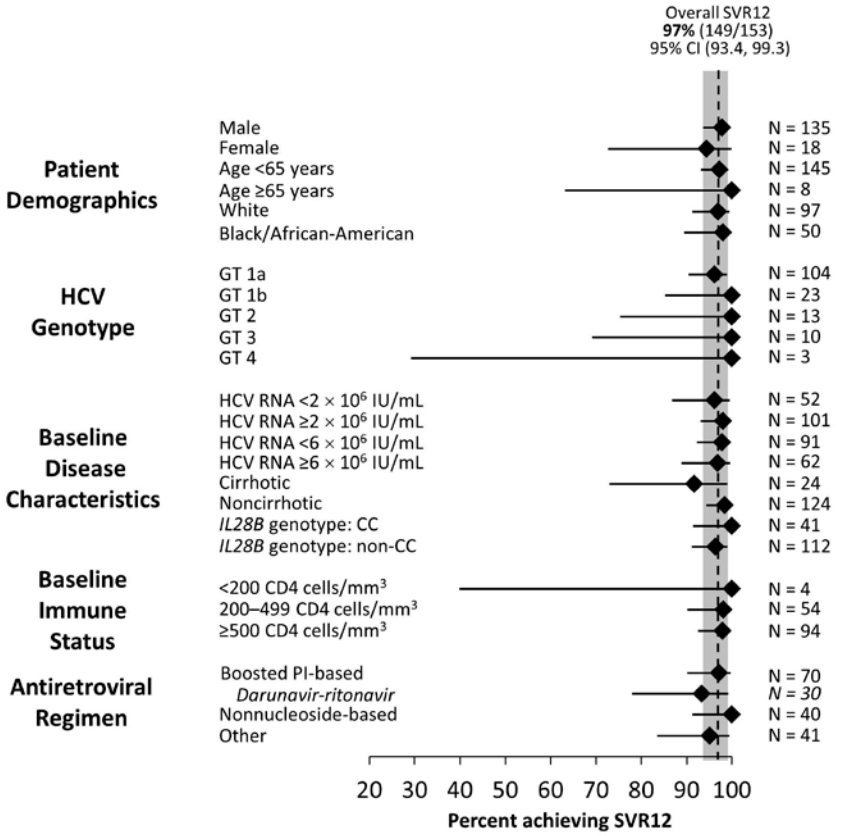
(B) Treatment-naïve, 8 weeks



(C) Treatment-experienced, 12 weeks

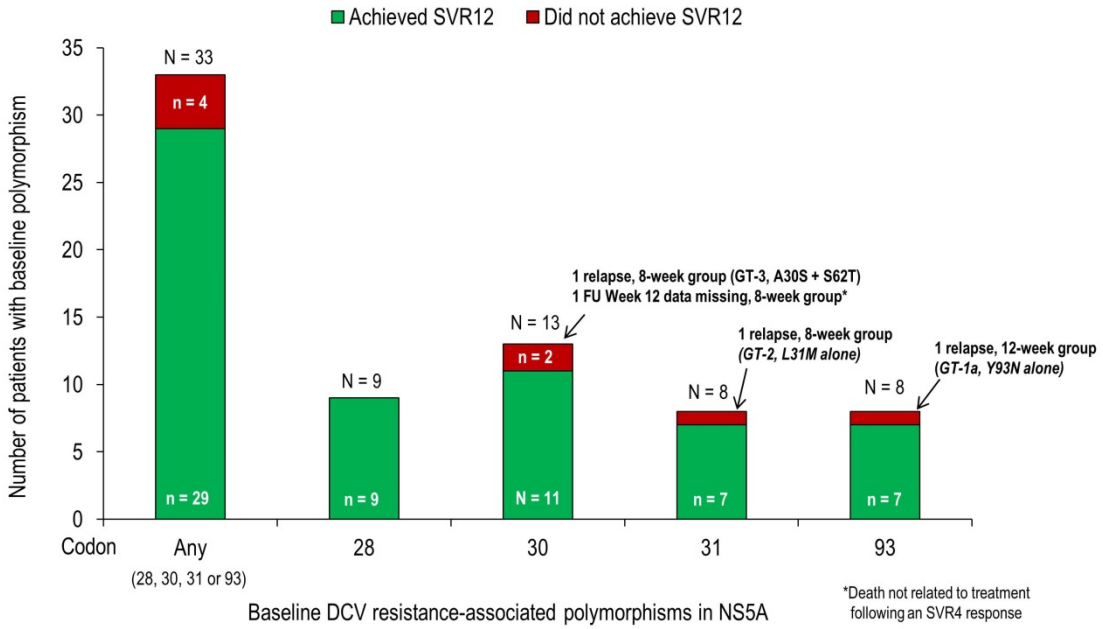


(D) Combined 12-week treatment groups *post hoc* analysis



Combined 12-week treatment groups (treatment-naive and treatment-experienced). Vertical line and shaded region represent the overall SVR12 rate and 95% confidence interval, respectively, for all patients in the combined groups.

Figure S3. Baseline DCV resistance-associated polymorphisms in NS5A and associated sustained virologic response rates to DCV + SOF (all treatment groups)



Baseline NS5A polymorphisms by HCV genotype

	GT-1a	GT-1b	GT-2	GT-3	GT-4
Codon 28	M28V	*none*	F28L	M28V	L28M
Codon 30	Q30H/L/R	R30K/Q	*none*	A30S	L30R
Codon 31	L31M	*none*	L31M	*none*	*none*
Codon 93	Y93C/H/L/S/N	Y93H	*none*	*none*	*none*

Figure S4. CD4 cell counts on treatment with DCV + SOF

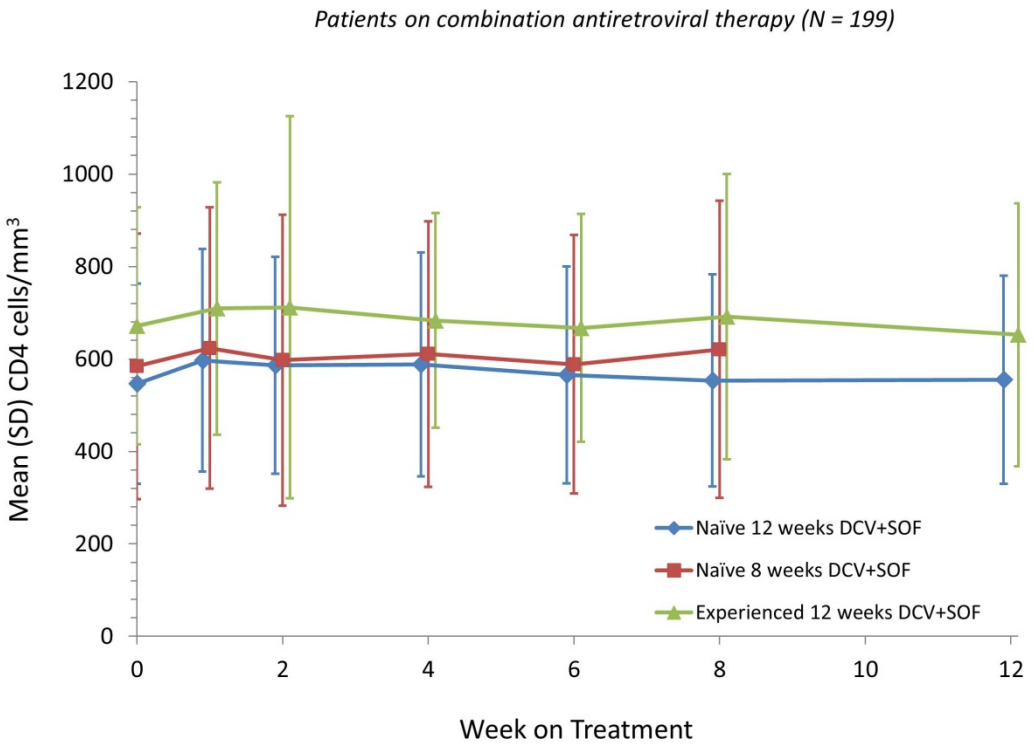


Table S1. List of permitted antiretrovirals

Allowed antiretroviral agent[a]	Concomitant daclatasvir dose (once daily)
Protease inhibitors (PIs)	
Atazanavir + ritonavir[b]	30 mg
Darunavir + ritonavir[b]	
Lopinavir + ritonavir[b]	
Nonnucleoside reverse transcriptase inhibitors (NNRTIs)	
Efavirenz	90 mg
Nevirapine	
Rilpivirine	60 mg
Integrase inhibitors	
Dolutegravir	60 mg
Raltegravir	
Entry inhibitors	
Enfuvirtide	60 mg
Maraviroc	
Nucleoside/nucleotide analogs	
Abacavir	60 mg
Emtricitabine	
Lamivudine	
Tenofovir disoproxil fumarate	
Zidovudine	

[a]Only medications listed in this column were permitted in the study. Changes to antiretroviral therapy were allowed at screening visit for subjects requiring a different regimen to meet study requirements. After regimen change, such subjects were required to remain on the new regimen for at least 1 month and have HIV RNA <50 copies/mL prior to study day 1.

[b]Pharmacokinetic booster doses of ritonavir only (subtherapeutic). All PIs **must** have been ritonavir-boosted. Unboosted PIs were disallowed. The use of alternative pharmacokinetic boosters (cobicistat) was disallowed.

The use of a protease inhibitor with any NNRTI other than rilpivirine was disallowed

Table S2. Patient demographics

	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Age (Years)				
N	101	50	52	203
Mean	50.1	50.8	55.7	51.7
Median	52.0	50.5	56.5	52.0
Min, Max	24,71	28,75	43,66	24,75
Q1, Q3	46.0,56.0	47.0,56.0	51.0,61.5	47.0,58.0
Standard Deviation	9.77	9.19	6.21	9.12
Age Categorization (%)				
< 65	96 (95.0)	47 (94.0)	49 (94.2)	192 (94.6)
≥ 65	5 (5.0)	3 (6.0)	3 (5.8)	11 (5.4)
Gender (%)				
Male	92 (91.1)	42 (84.0)	43 (82.7)	177 (87.2)
Female	9 (8.9)	8 (16.0)	9 (17.3)	26 (12.8)
Race (%)				
White	66 (65.3)	28 (56.0)	31 (59.6)	125 (61.6)
Black/African American	30 (29.7)	19 (38.0)	20 (38.5)	69 (34.0)
Asian	1 (1.0)	1 (2.0)	0	2 (1.0)
Asian Other	1 (1.0)	1 (2.0)	0	2 (1.0)
American Indian/Alaska Native	2 (2.0)	0	1 (1.9)	3 (1.5)
Native Hawaiian/Other Pacific Islander	0	2 (4.0)	0	2 (1.0)
Other	2 (2.0)	0	0	2 (1.0)
Ethnicity (%)				
Hispanic/Latino	18 (17.8)	8 (16.0)	10 (19.2)	36 (17.7)
Not Hispanic/Latino	83 (82.2)	42 (84.0)	42 (80.8)	167 (82.3)

Table S3. Baseline disease characteristics

	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
HCV RNA (log_{10} IU/mL)				
N	101	50	52	203
Mean	6.50	6.40	6.52	6.48
Median	6.74	6.44	6.68	6.65
Min, Max	3.3,7.6	4.2,7.5	3.9,7.9	3.3,7.9
Q1, Q3	6.06,7.02	6.17,6.89	6.16,7.00	6.12,7.01
Standard Deviation	0.758	0.710	0.789	0.753
HCV RNA Distribution (IU/mL) (%)				
< 800,000	22 (21.8)	6 (12.0)	8 (15.4)	36 (17.7)
≥ 800,000	79 (78.2)	44 (88.0)	44 (84.6)	167 (2.3)
< 6,000,000	58 (57.4)	34 (68.0)	33 (63.5)	125 (61.6)
≥ 6,000,000	43 (42.6)	16 (32.0)	19 (36.5)	78 (38.4)
CD4 Cell Count				
N	101	50	51	202
Mean	549.1	587.9	687.6	593.7
Median	520.0	575.0	636.0	564.5
Min, Max	122,1147	157,1430	262,1470	122,1470
Q1, Q3	400.0,692.0	339.0,814.0	500.0,816.0	406.0,750.0
Standard Deviation	216.84	282.16	277.38	255.31
CD4 (%)				
< 200	4 (4.0)	1 (2.0)	0	5 (2.5)
200 - < 500	42 (41.6)	21 (42.0)	12 (23.1)	75 (36.9)
≥ 500	55 (54.5)	28 (56.0)	39 (75.0)	122 (60.1)
Not Reported	0	0	1 (1.9)	1 (0.5)

Table S3. Baseline disease characteristics (cont.)

	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
cART Regimen (%)				
Protease Inhibitor-Based	47 (46.5)	29 (58.0)	23 (44.2)	99 (48.8)
Non-Nucleoside Reverse Transcriptase Inhibitor	28 (27.7)	10 (20.0)	12 (23.1)	50 (24.6)
Other	25 (24.8)	9 (18.0)	16 (30.8)	50 (24.6)
None	1 (1.0)	2 (4.0)	1 (1.9)	4 (2.0)
Protease Inhibitor-Based Regimen (%)				
Overall	47 (100.0)	29 (100.0)	23 (100.0)	99 (100.0)
Atazanavir/Ritonavir	19 (40.4)	5 (17.2)	12 (52.2)	36 (36.4)
Darunavir/Ritonavir	19 (40.4)	21 (72.4)	11 (47.8)	51 (51.5)
Lopinavir/Ritonavir	9 (19.1)	3 (10.3)	0	12 (12.1)
Non-Nucleoside Reverse Transcriptase Inhibitor Regimen (%)				
Overall	28 (100.0)	10 (100.0)	12 (100.0)	50 (100.0)
Efavirenz	18 (64.3)	8 (80.0)	8 (66.7)	34 (68.0)
Nevirapine	5 (17.9)	1 (10.0)	3 (25.0)	9 (18.0)
Rilpivirine	5 (17.9)	1 (10.0)	1 (8.3)	7 (14.0)
Randomization Strata (%)				
Naive Cirrhotic GT1a	10 (9.9)	5 (10.0)	0	15 (7.4)
Naive Cirrhotic GT Other	0	1 (2.0)	0	1 (0.5)
Naive Non Cirrhotic GT1a	61 (60.4)	30 (60.0)	0	91 (44.8)
Naive Non Cirrhotic GT1b	12 (11.9)	6 (12.0)	0	18 (8.9)
Naive Non Cirrhotic Other	18 (17.8)	8 (16.0)	0	26 (12.8)
Experienced	0	0	52 (100.0)	52 (25.6)

Table S3. Baseline disease characteristics (cont.)

	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
HCV Genotype Subtype (%)				
1a	71 (70.3)	35 (70.0)	33 (63.5)	139 (68.5)
1b	12 (11.9)	6 (12.0)	11 (21.2)	29 (14.3)
2, 2a or 2c, 2b	11 (10.9)	6 (12.0)	2 (3.8)	19 (9.4)
3, 3a	6 (5.9)	3 (6.0)	4 (7.7)	13 (6.4)
4, 4a/4c/4d	1 (1.0)	0	2 (3.8)	3 (1.5)
Prior Treatment Status (%)				
Naive	100 (99.0)	50 (100.0)	0	150 (73.9)
Experienced	1 (1.0)	0	52 (100.0)	53 (26.1)
Interferon-Based Anti-HCV Treatment	1 (1.0)	0	49 (94.2)	50 (24.6)
Null Responder	1 (1.0)	0	17 (32.7)	18 (8.9)
Partial Responder	0	0	7 (13.5)	7 (3.4)
Relapser	0	0	11 (21.2)	11 (5.4)
Indeterminate	0	0	3 (5.8)	3 (1.5)
Intolerance	0	0	8 (15.4)	8 (3.9)
Breakthrough	0	0	2 (3.8)	2 (1.0)
HCV RNA Never Undetectable On Treatment	0	0	1 (1.9)	1 (0.5)
HCV RNA Ever Undetectable On Treatment	0	0	0	0
Other Anti-HCV Treatment	0	0	3 (5.8)	3 (1.5)
Null Responder	0	0	0	0
Partial Responder	0	0	0	0
Relapser	0	0	3 (5.8)	3 (1.5)
Indeterminate	0	0	0	0
Intolerance	0	0	0	0
Breakthrough	0	0	0	0
HCV RNA Never Undetectable On Treatment	0	0	0	0
HCV RNA Ever Undetectable On Treatment	0	0	0	0

Table S3. Baseline disease characteristics (cont.)

	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Cirrhosis Status (%)				
Absent	90 (89.1)	44 (88.0)	34 (65.4)	168 (82.8)
Present	9 (8.9)	5 (10.0)	15 (28.8)	29 (14.3)
Not Reported	2 (2.0)	1 (2.0)	3 (5.8)	6 (3.0)
Fibrosis Stage (%)				
F0	24 (23.8)	16 (32.0)	8 (15.4)	48 (23.6)
F1	23 (22.8)	9 (18.0)	9 (17.3)	41 (20.2)
F2	10 (9.9)	2 (4.0)	7 (13.5)	19 (9.4)
F3	19 (18.8)	8 (16.0)	10 (19.2)	37 (18.2)
F4	22 (21.8)	15 (30.0)	18 (34.6)	55 (27.1)
Not Reported	3 (3.0)	0	0	3 (1.5)
Steatosis Grade (%)				
0 (None To <5%)	13 (12.9)	11 (22.0)	9 (17.3)	33 (16.3)
1 (5-33%)	7 (6.9)	5 (10.0)	3 (5.8)	15 (7.4)
2 (34-66%)	6 (5.9)	3 (6.0)	3 (5.8)	12 (5.9)
3 (67-100%)	3 (3.0)	1 (2.0)	3 (5.8)	7 (3.4)
Not Reported	72 (71.3)	30 (60.0)	34 (65.4)	136 (67.0)
IL28B RS1297860 Genotype (%)				
CC	28 (27.7)	13 (26.0)	13 (25.0)	54 (26.6)
CT	48 (47.5)	28 (56.0)	30 (57.7)	106 (52.2)
TT	25 (24.8)	9 (18.0)	9 (17.3)	43 (21.2)

Table S3. Baseline disease characteristics (cont.)

	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
HCV Source (%)				
Mother-To-Child Transmission	0	0	0	0
IV Drug Use	37 (36.6)	21 (42.0)	19 (36.5)	77 (37.9)
Sexual Contact	35 (34.7)	19 (38.0)	21 (40.4)	75 (36.9)
Transfusion	1 (1.0)	2 (4.0)	2 (3.8)	5 (2.5)
Other	6 (5.9)	0	3 (5.8)	9 (4.4)
Unknown	22 (21.8)	8 (16.0)	7 (13.5)	37 (18.2)
HIV Source (%)				
Mother-To-Child Transmission	0	0	0	0
IV Drug Use	26 (25.7)	18 (36.0)	16 (30.8)	60 (29.6)
Sexual Contact	65 (64.4)	29 (58.0)	28 (53.8)	122 (60.1)
Transfusion	1 (1.0)	0	0	1 (0.5)
Other	2 (2.0)	1 (2.0)	4 (7.7)	7 (3.4)
Unknown	7 (6.9)	2 (4.0)	4 (7.7)	13 (6.4)

Fibrosis stage is derived from baseline fibrotest scores: F0: 0 - 0.27; F1: > 0.27 - 0.48; F2: > 0.48 - 0.58; F3: > 0.58 - 0.74; F4: > 0.74 - 1.00.

Cirrhosis was determined according to a testing hierarchy: (1) liver biopsy demonstrating cirrhosis any time before or during screening, then (2)fibroscan above 14.6 kPa within one year of baseline, then(3)a screening fibrotest fibrosis score of at least 0.75 with an APRI above 2

Table S4. Details of Prior HCV treatments and outcomes

All patients received DCV + SOF for 12 weeks.

Includes one patient (genotype 1a, SVR12 responder with prior null response to peginterferon-ribavirin) randomized in error to the 12-week treatment-naïve group.

#	Prior HCV Treatment	Prior Response	SVR12 (YES/NO)	HCV GT
1	IFN	INTOLERANCE	YES	1B
2	IFN-RBV	NULL RESPONSE	YES	1A
3	PegIFN-RBV	INTOLERANCE	YES	1A
4	PegIFN-RBV	RELAPSE	YES	1B
5	PegIFN-RBV	NULL RESPONSE	YES	1A
6	PegIFN-RBV	BREAKTHROUGH	YES	1A
7	PegIFN-RBV	INTOLERANCE	YES	1B
8	PegIFN-RBV	RELAPSE	YES	1B
9	PegIFN-RBV	INDETERMINATE	YES	1A
10	PegIFN-RBV	RELAPSE	YES	1A
1	PegIFN-RBV	RELAPSE	YES	1A
12	PegIFN-RBV	RELAPSE	YES	1A
13	PegIFN-RBV	RELAPSE	YES	2
14	PegIFN-RBV	PARTIAL RESPONSE	YES	1A
15	PegIFN-RBV	NULL RESPONSE	YES	1B
16	PegIFN-RBV	NEVER UNDETECTABLE	YES	1A
17	PegIFN-RBV	NULL RESPONSE	YES	4
18	PegIFN-RBV	RELAPSE	YES	1A
19	PegIFN-RBV	NULL RESPONSE	YES	1A
20	PegIFN-RBV	PARTIAL RESPONSE	YES	1A
21	PegIFN-RBV	PARTIAL RESPONSE	YES	1B

22	PegIFN-RBV	NULL RESPONSE	YES	1A
23	PegIFN-RBV	NULL RESPONSE	YES	1A
24	PegIFN-RBV	NULL RESPONSE	NO	1A
25	PegIFN-RBV	RELAPSE	YES	1B
26	PegIFN-RBV	BREAKTHROUGH	YES	3
27	PegIFN-RBV	INTOLERANCE	YES	1B
28	PegIFN-RBV	INDETERMINATE	YES	1B
29	PegIFN-RBV	NULL RESPONSE	YES	1A
30	PegIFN-RBV	INDETERMINATE	YES	4
31	PegIFN-RBV	NULL RESPONSE	YES	1A
32	PegIFN-RBV	INTOLERANCE	YES	1B
33	PegIFN-RBV	RELAPSE	YES	2
34	PegIFN-RBV	RELAPSE	YES	1B
35	PegIFN-RBV	INTOLERANCE	YES	1A
36	PegIFN-RBV	PARTIAL RESPONSE	YES	1A
37	PegIFN-RBV	INTOLERANCE	YES	1A
38	PegIFN-RBV	NULL RESPONSE	YES	3
39	PegIFN-RBV	NULL RESPONSE	YES	1A
40	PegIFN-RBV + boceprevir	NULL RESPONSE	YES	1A
41	PegIFN-RBV + boceprevir	NULL RESPONSE	YES	1A
42	PegIFN-RBV + boceprevir	PARTIAL RESPONSE	YES	1A
43	PegIFN-RBV + boceprevir	NULL RESPONSE	YES	1A
44	PegIFN-RBV + boceprevir	PARTIAL RESPONSE	YES	1A
45	PegIFN-RBV + telaprevir	NULL RESPONSE	YES	1A
46	PegIFN-RBV + telaprevir	PARTIAL RESPONSE	YES	1A
47	PegIFN-RBV + telaprevir	NULL RESPONSE	YES	1A

48	PegIFN-RBV + telaprevir	INTOLERANCE	YES	1A
49	PegIFN-RBV + telaprevir	RELAPSE	YES	1A
50	PegIFN-RBV + faldaprevir (BI201335)	NULL RESPONSE	YES	1A
51	Sofosbuvir + RBV x 12 weeks	RELAPSE	YES	3
52	Sofosbuvir + RBV x 24 weeks	RELAPSE	YES	1A
53	Sofosbuvir + RBV x12 weeks	RELAPSE	YES	3

GT, genotype; IFN, interferon alfa; PegIFN, pegylated interferon alfa; RBV, ribavirin

Table S5. HCV RNA < 25 IU/mL (with or without target detected) by study visit

Visit	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52
Week 1			
Responder/Evaluable (%)	35/101 (34.7)	22/50 (44.0)	18/52 (34.6)
95% CI	(25.5, 44.8)	(30.0, 58.7)	(22.0, 49.1)
Week 2			
Responder/Evaluable (%)	78/101 (77.2)	39/50 (78.0)	37/52 (71.2)
95% CI	(67.8, 85.0)	(64.0, 88.5)	(56.9, 82.9)
Week 4			
Responder/Evaluable (%)	94/101 (93.1)	49/50 (98.0)	48/52 (92.3)
95% CI	(86.2, 97.2)	(89.4, 99.9)	(81.5, 97.9)
Week 6			
Responder/Evaluable (%)	100/101 (99.0)	49/50 (98.0)	51/52 (98.1)
95% CI	(94.6, 100.0)	(89.4, 99.9)	(89.7, 100.0)
Week 8			
Responder/Evaluable (%)	99/101 (98.0)	48/50 (96.0)	52/52 (100.0)
95% CI	(93.0, 99.8)	(86.3, 99.5)	(93.2, 100.0)
Week 12			
Responder/Evaluable (%)	97/101 (96.0)	1/50 (2.0)	51/52 (98.1)
95% CI	(90.2, 98.9)	(0.1, 10.6)	(89.7, 100.0)
End Of Treatment			
Responder/Evaluable (%)	100/101 (99.0)	50/50 (100.0)	52/52 (100.0)
95% CI	(94.6, 100.0)	(92.9, 100.0)	(93.2, 100.0)

Table S5. HCV RNA < 25 IU/mL (with or without target detected) by study visit (cont.)

Visit	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52
F/U Week 4			
Responder/Evaluable (%)	99/101 (98.0)	41/50 (82.0)	50/52 (96.2)
95% CI	(93.0, 99.8)	(68.6, 91.4)	(86.8, 99.5)
F/U Week 12*			
Responder/Evaluable (%)	98/101 (97.0)	38/50 (76.0)	51/52 (98.1)
95% CI	(91.6, 99.4)	(61.8, 86.9)	(89.7, 100.0)
F/U Week 24†			
Responder/Evaluable (%)	93/101 (92.1)	36/50 (72.0)	48/52 (92.3)
95% CI	(85.0, 96.5)	(57.5, 83.8)	(81.5, 97.9)

HCV RNA measurements are excluded after the start of non-study anti-HCV medication on-treatment or during follow-up.
*ITT, Next-Value-Carried-Backward †ITT, Missing=Failure

Table S6. SVR12 responses by subgroup

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Gender				
Male				
Responders/Treated (%)	90/92 (97.8)	33/42 (78.6)	42/43 (97.7)	132/135 (97.8)
95% CI	(92.4, 99.7)	(63.2, 89.7)	(87.7, 99.9)	(93.6, 99.5)
Female				
Responders/Treated (%)	8/9 (88.9)	5/8 (62.5)	9/9 (100.0)	17/18 (94.4)
95% CI	(51.8, 99.7)	(24.5, 91.5)	(66.4, 100.0)	(72.7, 99.9)
Age (Years)				
< 65				
Responders/Treated (%)	93/96 (96.9)	36/47 (76.6)	48/49 (98.0)	141/145 (97.2)
95% CI	(91.1, 99.4)	(62.0, 87.7)	(89.1, 99.9)	(93.1, 99.2)
≥ 65				
Responders/Treated (%)	5/5 (100.0)	2/3 (66.7)	3/3 (100.0)	8/8 (100.0)
95% CI	(47.8, 100.0)	(9.4, 99.2)	(29.2, 100.0)	(63.1, 100.0)
Race				
White				
Responders/Treated (%)	63/66 (95.5)	20/28 (71.4)	31/31 (100.0)	94/97 (96.9)
95% CI	(87.3, 99.1)	(51.3, 86.8)	(88.8, 100.0)	(91.2, 99.4)
Black African/American				
Responders/Treated (%)	30/30 (100.0)	15/19 (78.9)	19/20 (95.0)	49/50 (98.0)
95% CI	(88.4, 100.0)	(54.4, 93.9)	(75.1, 99.9)	(89.4, 99.9)
Asian				
Responders/Treated (%)	1/1 (100.0)	1/1 (100.0)		1/1 (100.0)
95% CI	(2.5, 100.0)	(2.5, 100.0)		(2.5, 100.0)
Other				
Responders/Treated (%)	4/4 (100.0)	2/2 (100.0)	1/1 (100.0)	5/5 (100.0)
95% CI	(39.8, 100.0)	(15.8, 100.0)	(2.5, 100.0)	(47.8, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Ethnicity				
Hispanic/Latino				
Responders/Treated (%)	18/18 (100.0)	6/8 (75.0)	10/10 (100.0)	28/28 (100.0)
95% CI	(81.5, 100.0)	(34.9, 96.8)	(69.2, 100.0)	(87.7, 100.0)
Not Hispanic/Latino				
Responders/Treated (%)	80/83 (96.4)	32/42 (76.2)	41/42 (97.6)	121/125 (96.8)
95% CI	(89.8, 99.2)	(60.5, 87.9)	(87.4, 99.9)	(92.0, 99.1)
Baseline HCV RNA				
< 800,000 IU/mL				
Responders/Treated (%)	22/22 (100.0)	6/6 (100.0)	8/8 (100.0)	30/30 (100.0)
95% CI	(84.6, 100.0)	(54.1, 100.0)	(63.1, 100.0)	(88.4, 100.0)
≥ 800,000 IU/mL				
Responders/Treated (%)	76/79 (96.2)	32/44 (72.7)	43/44 (97.7)	119/123 (96.7)
95% CI	(89.3, 99.2)	(57.2, 85.0)	(88.0, 99.9)	(91.9, 99.1)
< 2,000,000 IU/mL				
Responders/Treated (%)	33/35 (94.3)	18/18 (100.0)	17/17 (100.0)	50/52 (96.2)
95% CI	(80.8, 99.3)	(81.5, 100.0)	(80.5, 100.0)	(86.8, 99.5)
≥ 2,000,000 IU/mL				
Responders/Treated (%)	65/66 (98.5)	20/32 (62.5)	34/35 (97.1)	99/101 (98.0)
95% CI	(91.8, 100.0)	(43.7, 78.9)	(85.1, 99.9)	(93.0, 99.8)
< 6,000,000 IU/mL				
Responders/Treated (%)	56/58 (96.6)	27/34 (79.4)	33/33 (100.0)	89/91 (97.8)
95% CI	(88.1, 99.6)	(62.1, 91.3)	(89.4, 100.0)	(92.3, 99.7)
≥ 6,000,000 IU/mL				
Responders/Treated (%)	42/43 (97.7)	11/16 (68.8)	18/19 (94.7)	60/62 (96.8)
95% CI	(87.7, 99.9)	(41.3, 89.0)	(74.0, 99.9)	(88.8, 99.6)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Baseline Cirrhosis Status				
Absent				
Responders/Treated (%)	88/90 (97.8)	34/44 (77.3)	34/34 (100.0)	122/124 (98.4)
95% CI	(92.2, 99.7)	(62.2, 88.5)	(89.7, 100.0)	(94.3, 99.8)
Present				
Responders/Treated (%)	8/9 (88.9)	3/5 (60.0)	14/15 (93.3)	22/24 (91.7)
95% CI	(51.8, 99.7)	(14.7, 94.7)	(68.1, 99.8)	(73.0, 99.0)
Not Reported				
Responders/Treated (%)	2/2 (100.0)	1/1 (100.0)	3/3 (100.0)	5/5 (100.0)
95% CI	(15.8, 100.0)	(2.5, 100.0)	(29.2, 100.0)	(47.8, 100.0)
Fibrosis Stage				
F0				
Responders/Treated (%)	22/24 (91.7)	13/16 (81.3)	8/8 (100.0)	30/32 (93.8)
95% CI	(73.0, 99.0)	(54.4, 96.0)	(63.1, 100.0)	(79.2, 99.2)
F1				
Responders/Treated (%)	23/23 (100.0)	7/9 (77.8)	9/9 (100.0)	32/32 (100.0)
95% CI	(85.2, 100.0)	(40.0, 97.2)	(66.4, 100.0)	(89.1, 100.0)
F2				
Responders/Treated (%)	10/10 (100.0)	1/2 (50.0)	7/7 (100.0)	17/17 (100.0)
95% CI	(69.2, 100.0)	(1.3, 98.7)	(59.0, 100.0)	(80.5, 100.0)
F3				
Responders/Treated (%)	19/19 (100.0)	6/8 (75.0)	9/10 (90.0)	28/29 (96.6)
95% CI	(82.4, 100.0)	(34.9, 96.8)	(55.5, 99.7)	(82.2, 99.9)
F4				
Responders/Treated (%)	21/22 (95.5)	11/15 (73.3)	18/18 (100.0)	39/40 (97.5)
95% CI	(77.2, 99.9)	(44.9, 92.2)	(81.5, 100.0)	(86.8, 99.9)
Not Reported				
Responders/Treated (%)	3/3 (100.0)			3/3 (100.0)
95% CI	(29.2, 100.0)			(29.2, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Baseline BMI (kg/m^2)				
< 20				
Responders/Treated (%)	2/2 (100.0)	5/5 (100.0)	0/1 (0.0)	2/3 (66.7)
95% CI	(15.8, 100.0)	(47.8, 100.0)	(0.0, 97.5)	(9.4, 99.2)
20 - < 25				
Responders/Treated (%)	44/47 (93.6)	18/22 (81.8)	16/16 (100.0)	60/63 (95.2)
95% CI	(82.5, 98.7)	(59.7, 94.8)	(79.4, 100.0)	(86.7, 99.0)
25 - < 30				
Responders/Treated (%)	38/38 (100.0)	10/16 (62.5)	22/22 (100.0)	60/60 (100.0)
95% CI	(90.7, 100.0)	(35.4, 84.8)	(84.6, 100.0)	(94.0, 100.0)
≥ 30				
Responders/Treated (%)	14/14 (100.0)	5/7 (71.4)	13/13 (100.0)	27/27 (100.0)
95% CI	(76.8, 100.0)	(29.0, 96.3)	(75.3, 100.0)	(87.2, 100.0)
IL28B RS1297860 Genotype				
CC				
Responders/Treated (%)	28/28 (100.0)	9/13 (69.2)	13/13 (100.0)	41/41 (100.0)
95% CI	(87.7, 100.0)	(38.6, 90.9)	(75.3, 100.0)	(91.4, 100.0)
Non-CC				
Responders/Treated (%)	70/73 (95.9)	29/37 (78.4)	38/39 (97.4)	108/112 (96.4)
95% CI	(88.5, 99.1)	(61.8, 90.2)	(86.5, 99.9)	(91.1, 99.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Genotype/Subtype				
GT-1a				
Responders/Treated (%)	68/71 (95.8)	28/35 (80.0)	32/33 (97.0)	100/104 (96.2)
95% CI	(88.1, 99.1)	(63.1, 91.6)	(84.2, 99.9)	(90.4, 98.9)
Cirrhotic				
Responders/Treated (%)	8/9 (88.9)	2/4 (50.0)	10/11 (90.9)	18/20 (90.0)
95% CI	(51.8, 99.7)	(6.8, 93.2)	(58.7, 99.8)	(68.3, 98.8)
Non-Cirrhotic				
Responders/Treated (%)	58/60 (96.7)	25/30 (83.3)	20/20 (100.0)	78/80 (97.5)
95% CI	(88.5, 99.6)	(65.3, 94.4)	(83.2, 100.0)	(91.3, 99.7)
Not Reported				
Responders/Treated (%)	2/2 (100.0)	1/1 (100.0)	2/2 (100.0)	4/4 (100.0)
95% CI	(15.8, 100.0)	(2.5, 100.0)	(15.8, 100.0)	(39.8, 100.0)
GT-1b				
Responders/Treated (%)	12/12 (100.0)	3/6 (50.0)	11/11 (100.0)	23/23 (100.0)
95% CI	(73.5, 100.0)	(11.8, 88.2)	(71.5, 100.0)	(85.2, 100.0)
Cirrhotic				
Responders/Treated (%)			2/2 (100.0)	2/2 (100.0)
95% CI			(15.8, 100.0)	(15.8, 100.0)
Non-Cirrhotic				
Responders/Treated (%)	12/12 (100.0)	3/6 (50.0)	8/8 (100.0)	20/20 (100.0)
95% CI	(73.5, 100.0)	(11.8, 88.2)	(63.1, 100.0)	(83.2, 100.0)
Not Reported				
Responders/Treated (%)			1/1 (100.0)	1/1 (100.0)
95% CI			(2.5, 100.0)	(2.5, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
GT-2				
Responders/Treated (%)	11/11 (100.0)	5/6 (83.3)	2/2 (100.0)	13/13 (100.0)
95% CI	(71.5, 100.0)	(35.9, 99.6)	(15.8, 100.0)	(75.3, 100.0)
Cirrhotic				
Responders/Treated (%)			1/1 (100.0)	1/1 (100.0)
95% CI			(2.5, 100.0)	(2.5, 100.0)
Non-Cirrhotic				
Responders/Treated (%)	11/11 (100.0)	5/6 (83.3)	1/1 (100.0)	12/12 (100.0)
95% CI	(71.5, 100.0)	(35.9, 99.6)	(2.5, 100.0)	(73.5, 100.0)
GT-3				
Responders/Treated (%)	6/6 (100.0)	2/3 (66.7)	4/4 (100.0)	10/10 (100.0)
95% CI	(54.1, 100.0)	(9.4, 99.2)	(39.8, 100.0)	(69.2, 100.0)
Cirrhotic				
Responders/Treated (%)		1/1 (100.0)	1/1 (100.0)	1/1 (100.0)
95% CI		(2.5, 100.0)	(2.5, 100.0)	(2.5, 100.0)
Non-Cirrhotic				
Responders/Treated (%)	6/6 (100.0)	1/2 (50.0)	3/3 (100.0)	9/9 (100.0)
95% CI	(54.1, 100.0)	(1.3, 98.7)	(29.2, 100.0)	(66.4, 100.0)
GT-4				
Responders/Treated (%)	1/1 (100.0)		2/2 (100.0)	3/3 (100.0)
95% CI	(2.5, 100.0)		(15.8, 100.0)	(29.2, 100.0)
Cirrhotic				
Responders/Treated (%)				
95% CI				
Non-Cirrhotic				
Responders/Treated (%)	1/1 (100.0)		2/2 (100.0)	3/3 (100.0)
95% CI	(2.5, 100.0)		(15.8, 100.0)	(29.2, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
NS5A-M28 Resistance				
Yes				
Responders/Treated (%)	4/4 (100.0)	3/3 (100.0)	1/1 (100.0)	5/5 (100.0)
95% CI	(39.8, 100.0)	(29.2, 100.0)	(2.5, 100.0)	(47.8, 100.0)
No				
Responders/Treated (%)	89/92 (96.7)	34/46 (73.9)	50/51 (98.0)	139/143 (97.2)
95% CI	(90.8, 99.3)	(58.9, 85.7)	(89.6, 100.0)	(93.0, 99.2)
Not Reported				
Responders/Treated (%)	5/5 (100.0)	1/1 (100.0)		5/5 (100.0)
95% CI	(47.8, 100.0)	(2.5, 100.0)		(47.8, 100.0)
NS5A-A30 Resistance				
Yes				
Responders/Treated (%)	6/6 (100.0)	2/4 (50.0)	3/3 (100.0)	9/9 (100.0)
95% CI	(54.1, 100.0)	(6.8, 93.2)	(29.2, 100.0)	(66.4, 100.0)
No				
Responders/Treated (%)	87/90 (96.7)	35/45 (77.8)	48/49 (98.0)	135/139 (97.1)
95% CI	(90.6, 99.3)	(62.9, 88.8)	(89.1, 99.9)	(92.8, 99.2)
Not Reported				
Responders/Treated (%)	5/5 (100.0)	1/1 (100.0)		5/5 (100.0)
95% CI	(47.8, 100.0)	(2.5, 100.0)		(47.8, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
NS5A-L31 Resistance				
Yes				
Responders/Treated (%)	3/3 (100.0)	2/3 (66.7)	1/1 (100.0)	4/4 (100.0)
95% CI	(29.2, 100.0)	(9.4, 99.2)	(2.5, 100.0)	(39.8, 100.0)
No				
Responders/Treated (%)	90/93 (96.8)	35/46 (76.1)	50/51 (98.0)	140/144 (97.2)
95% CI	(90.9, 99.3)	(61.2, 87.4)	(89.6, 100.0)	(93.0, 99.2)
Not Reported				
Responders/Treated (%)	5/5 (100.0)	1/1 (100.0)		5/5 (100.0)
95% CI	(47.8, 100.0)	(2.5, 100.0)		(47.8, 100.0)
NS5A-Y93 Resistance				
Yes				
Responders/Treated (%)	5/6 (83.3)	1/1 (100.0)	1/1 (100.0)	6/7 (85.7)
95% CI	(35.9, 99.6)	(2.5, 100.0)	(2.5, 100.0)	(42.1, 99.6)
No				
Responders/Treated (%)	88/90 (97.8)	36/48 (75.0)	50/51 (98.0)	138/141 (97.9)
95% CI	(92.2, 99.7)	(60.4, 86.4)	(89.6, 100.0)	(93.9, 99.6)
Not Reported				
Responders/Treated (%)	5/5 (100.0)	1/1 (100.0)		5/5 (100.0)
95% CI	(47.8, 100.0)	(2.5, 100.0)		(47.8, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
CD4 (%)				
< 200				
Responders/Treated (%)	4/4 (100.0)	1/1 (100.0)		4/4 (100.0)
95% CI	(39.8, 100.0)	(2.5, 100.0)		(39.8, 100.0)
200 - < 500				
Responders/Treated (%)	41/42 (97.6)	15/21 (71.4)	12/12 (100.0)	53/54 (98.1)
95% CI	(87.4, 99.9)	(47.8, 88.7)	(73.5, 100.0)	(90.1, 100.0)
≥ 500				
Responders/Treated (%)	53/55 (96.4)	22/28 (78.6)	39/39 (100.0)	92/94 (97.9)
95% CI	(87.5, 99.6)	(59.0, 91.7)	(91.0, 100.0)	(92.5, 99.7)
Not Reported				
Responders/Treated (%)			0/1 (0.0)	0/1 (0.0)
95% CI			(0.0, 97.5)	(0.0, 97.5)
cART Regimen				
Protease Inhibitor-Base				
Responders/Treated (%)	46/47 (97.9)	21/29 (72.4)	22/23 (95.7)	68/70 (97.1)
95% CI	(88.7, 99.9)	(52.8, 87.3)	(78.1, 99.9)	(90.1, 99.7)
Non-Nucleoside Reverse Transcriptase Inhibitor				
Responders/Treated (%)	28/28 (100.0)	8/10 (80.0)	12/12 (100.0)	40/40 (100.0)
95% CI	(87.7, 100.0)	(44.4, 97.5)	(73.5, 100.0)	(91.2, 100.0)
Other				
Responders/Treated (%)	23/25 (92.0)	7/9 (77.8)	16/16 (100.0)	39/41 (95.1)
95% CI	(74.0, 99.0)	(40.0, 97.2)	(79.4, 100.0)	(83.5, 99.4)
None				
Responders/Treated (%)	1/1 (100.0)	2/2 (100.0)	1/1 (100.0)	2/2 (100.0)
95% CI	(2.5, 100.0)	(15.8, 100.0)	(2.5, 100.0)	(15.8, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Protease Inhibitor-Based cART Regimen				
Overall				
Responders/Treated (%)	46/47 (97.9)	21/29 (72.4)	22/23 (95.7)	68/70 (97.1)
95% CI	(88.7, 99.9)	(52.8, 87.3)	(78.1, 99.9)	(90.1, 99.7)
Atazanavir/Ritonavir				
Responders/Treated (%)	19/19 (100.0)	4/5 (80.0)	12/12 (100.0)	31/31 (100.0)
95% CI	(82.4, 100.0)	(28.4, 99.5)	(73.5, 100.0)	(88.8, 100.0)
Darunavir/Ritonavir				
Responders/Treated (%)	18/19 (94.7)	14/21 (66.7)	10/11 (90.9)	28/30 (93.3)
95% CI	(74.0, 99.9)	(43.0, 85.4)	(58.7, 99.8)	(77.9, 99.2)
Lopinavir/Ritonavir				
Responders/Treated (%)	9/9 (100.0)	3/3 (100.0)		9/9 (100.0)
95% CI	(66.4, 100.0)	(29.2, 100.0)		(66.4, 100.0)
Non-Nucleoside Reverse Transcriptase Inhibitor				
Overall				
Responders/Treated (%)	28/28 (100.0)	8/10 (80.0)	12/12 (100.0)	40/40 (100.0)
95% CI	(87.7, 100.0)	(44.4, 97.5)	(73.5, 100.0)	(91.2, 100.0)
Efavirenz				
Responders/Treated (%)	18/18 (100.0)	7/8 (87.5)	8/8 (100.0)	26/26 (100.0)
95% CI	(81.5, 100.0)	(47.3, 99.7)	(63.1, 100.0)	(86.8, 100.0)
Nevirapine				
Responders/Treated (%)	5/5 (100.0)	1/1 (100.0)	3/3 (100.0)	8/8 (100.0)
95% CI	(47.8, 100.0)	(2.5, 100.0)	(29.2, 100.0)	(63.1, 100.0)
Rilpivirine				
Responders/Treated (%)	5/5 (100.0)	0/1 (0.0)	1/1 (100.0)	6/6 (100.0)
95% CI	(47.8, 100.0)	(0.0, 97.5)	(2.5, 100.0)	(54.1, 100.0)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
Assigned DCV Dose				
30 mg				
Responders/Treated (%)	46/47 (97.9)	21/29 (72.4)	22/23 (95.7)	68/70 (97.1)
95% CI	(88.7, 99.9)	(52.8, 87.3)	(78.1, 99.9)	(90.1, 99.7)
60 mg				
Responders/Treated (%)	29/31 (93.5)	9/12 (75.0)	18/18 (100.0)	47/49 (95.9)
95% CI	(78.6, 99.2)	(42.8, 94.5)	(81.5, 100.0)	(86.0, 99.5)
90 mg				
Responders/Treated (%)	23/23 (100.0)	8/9 (88.9)	11/11 (100.0)	34/34 (100.0)
95% CI	(85.2, 100.0)	(51.8, 99.7)	(71.5, 100.0)	(89.7, 100.0)
HCV Source				
IV Drug Use				
Responders/Treated (%)	35/37 (94.6)	16/21 (76.2)	18/19 (94.7)	53/56 (94.6)
95% CI	(81.8, 99.3)	(52.8, 91.8)	(74.0, 99.9)	(85.1, 98.9)
Sexual Contact				
Responders/Treated (%)	35/35 (100.0)	16/19 (84.2)	21/21 (100.0)	56/56 (100.0)
95% CI	(90.0, 100.0)	(60.4, 96.6)	(83.9, 100.0)	(93.6, 100.0)
Transfusion				
Responders/Treated (%)	1/1 (100.0)	2/2 (100.0)	2/2 (100.0)	3/3 (100.0)
95% CI	(2.5, 100.0)	(15.8, 100.0)	(15.8, 100.0)	(29.2, 100.0)
Other				
Responders/Treated (%)	6/6 (100.0)		3/3 (100.0)	9/9 (100.0)
95% CI	(54.1, 100.0)		(29.2, 100.0)	(66.4, 100.0)
Unknown				
Responders/Treated (%)	21/22 (95.5)	4/8 (50.0)	7/7 (100.0)	28/29 (96.6)
95% CI	(77.2, 99.9)	(15.7, 84.3)	(59.0, 100.0)	(82.2, 99.9)

Table S6. SVR12 Responses By Subgroup (Cont.)

Category Subgroup	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Combined (Naive + Experienced) DCV/SOF 12 WK N=153
HIV Source				
Iv Drug Use				
Responders/Treated (%)	24/26 (92.3)	12/18 (66.7)	15/16 (93.8)	39/42 (92.9)
95% CI	(74.9, 99.1)	(41.0, 86.7)	(69.8, 99.8)	(80.5, 98.5)
Sexual Contact				
Responders/Treated (%)	64/65 (98.5)	24/29 (82.8)	28/28 (100.0)	92/93 (98.9)
95% CI	(91.7, 100.0)	(64.2, 94.2)	(87.7, 100.0)	(94.2, 100.0)
Transfusion				
Responders/Treated (%)	1/1 (100.0)			1/1 (100.0)
95% CI	(2.5, 100.0)			(2.5, 100.0)
Other				
Responders/Treated (%)	2/2 (100.0)	1/1 (100.0)	4/4 (100.0)	6/6 (100.0)
95% CI	(15.8, 100.0)	(2.5, 100.0)	(39.8, 100.0)	(54.1, 100.0)
Unknown				
Responders/Treated (%)	7/7 (100.0)	1/2 (50.0)	4/4 (100.0)	11/11 (100.0)
95% CI	(59.0, 100.0)	(1.3, 98.7)	(39.8, 100.0)	(71.5, 100.0)

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.

Table S7. Details of patients who did not achieve SVR12

#	Age	Sex	Race	Tx arm	GT	IL28	cART base	DCV dose (mg)	Cirrhotic	BL HCV RNA (million IU/mL)	Reason for no SVR	NS5A RAPs at BL	NS5A RAPs at failure
1	56	M	Black	12-wk Exp	1a	CT	Darunavir	30	Yes	14.38	Relapse	None	Q30R
2	55	M	White	12-wk Naïve	1a	CT	Darunavir	30	Yes	10.28	Relapse	Y93Y/N	Y93N
3	34	M	White	12-wk Naïve	1a	CT	Raltegravir	60	No	1.36	On-Tx failure	None	Q30Q/R*
4	49	M	Black	8-wk Naive	1a	CC	Atazanavir	30	Yes	9.38	Relapse	None	None
5	40	M	White	8-wk Naive	1a	CC	Darunavir	30	No	2.13	Relapse	None	None
6	42	F	White	8-wk Naive	1a	CT	Darunavir	30	No	2.04	Relapse	None	None
7	50	M	White	8-wk Naive	1a	CT	Darunavir	30	No	17.08	Relapse	None	None
8	55	M	Black	8-wk Naive	1a	CT	Darunavir	30	No	14.87	Relapse	None	Q30E
9	42	F	White	8-wk Naive	1a	CC	Darunavir	30	Yes	5.40	Relapse	None	None
10	50	M	Black	8-wk Naive	1a	TT	Efavirenz	90	No	2.34	Relapse	None	None
11	51	M	White	8-wk Naive	1b	TT	Darunavir	30	No	5.06	Relapse	None	None
12	75	M	Black	8-wk Naive	2	CT	Raltegravir	60	No	2.45	Relapse	L31M	L31M
13	56	M	White	8-wk Naive	3	CT	Darunavir	30	No	11.18	Relapse	A30A/S	A30S
14	24	F	White	12-wk Naïve	1a	CT	Raltegravir	60	No	1.01	Lost to follow-up	None	NA
15	52	M	White	8-wk Naive	1b	CC	Rilpivirine	90	No	7.71	Died	R30Q	NA
16	49	F	White	8-wk Naive	1b	TT	Raltegravir	60	No	2.02	Lost to follow-up	None	NA

*Noncompliant patient. Received 1.1 weeks of treatment and was <25 IU/mL with target detected at end-of-treatment measurement.

BL, baseline; cART, combination antiretroviral therapy; NA, not applicable; RAPs, daclatasvir resistance-associated polymorphisms at NS5A codons 28, 30, 31 or 93; Tx, treatment

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Total Subjects With An Event	74 (73.3)	29 (58.0)	37 (71.2)	140 (69.0)
Gastrointestinal Disorders	35 (34.7)	7 (14.0)	19 (36.5)	61 (30.0)
Nausea	14 (13.9)	4 (8.0)	8 (15.4)	26 (12.8)
Diarrhoea	11 (10.9)	1 (2.0)	3 (5.8)	15 (7.4)
Vomiting	6 (5.9)	1 (2.0)	3 (5.8)	10 (4.9)
Abdominal Pain	5 (5.0)	1 (2.0)	1 (1.9)	7 (3.4)
Constipation	3 (3.0)	0	3 (5.8)	6 (3.0)
Abdominal Distension	1 (1.0)	1 (2.0)	1 (1.9)	3 (1.5)
Dry Mouth	1 (1.0)	0	2 (3.8)	3 (1.5)
Abdominal Discomfort	2 (2.0)	0	0	2 (1.0)
Flatulence	1 (1.0)	1 (2.0)	0	2 (1.0)
Rectal Haemorrhage	1 (1.0)	0	1 (1.9)	2 (1.0)
Abdominal Pain Lower	1 (1.0)	0	0	1 (0.5)
Abdominal Pain Upper	0	0	1 (1.9)	1 (0.5)
Abnormal Faeces	1 (1.0)	0	0	1 (0.5)
Anal Skin Tags	1 (1.0)	0	0	1 (0.5)
Aphthous Stomatitis	1 (1.0)	0	0	1 (0.5)
Breath Odour	0	0	1 (1.9)	1 (0.5)
Cheilitis	1 (1.0)	0	0	1 (0.5)
Dental Caries	1 (1.0)	0	0	1 (0.5)
Faeces Soft	0	0	1 (1.9)	1 (0.5)
Frequent Bowel Movements	0	1 (2.0)	0	1 (0.5)
Gastrointestinal Hypermotility	1 (1.0)	0	0	1 (0.5)
Hemorrhoids	1 (1.0)	0	0	1 (0.5)
Mouth Ulceration	0	0	1 (1.9)	1 (0.5)
Proctalgia	1 (1.0)	0	0	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
General Disorders And Administration Site Conditions	24 (23.8)	6 (12.0)	13 (25.0)	43 (21.2)
Fatigue	19 (18.8)	5 (10.0)	10 (19.2)	34 (16.7)
Chest Pain	0	0	2 (3.8)	2 (1.0)
Influenza Like Illness	0	1 (2.0)	1 (1.9)	2 (1.0)
Oedema Peripheral	0	1 (2.0)	1 (1.9)	2 (1.0)
Pyrexia	2 (2.0)	0	0	2 (1.0)
Chills	1 (1.0)	0	0	1 (0.5)
Malaise	1 (1.0)	0	0	1 (0.5)
Oedema	0	0	1 (1.9)	1 (0.5)
Thirst	1 (1.0)	0	0	1 (0.5)
Nervous System Disorders	14 (13.9)	8 (16.0)	14 (26.9)	36 (17.7)
Headache	12 (11.9)	3 (6.0)	8 (15.4)	23 (11.3)
Dizziness	1 (1.0)	2 (4.0)	3 (5.8)	6 (3.0)
Syncope	0	1 (2.0)	1 (1.9)	2 (1.0)
Amnesia	0	0	1 (1.9)	1 (0.5)
Carpal Tunnel Syndrome	1 (1.0)	0	0	1 (0.5)
Cognitive Disorder	0	0	1 (1.9)	1 (0.5)
Disturbance In Attention	0	0	1 (1.9)	1 (0.5)
Dizziness Postural	0	1 (2.0)	0	1 (0.5)
Dysgeusia	0	1 (2.0)	0	1 (0.5)
Migraine	0	1 (2.0)	0	1 (0.5)
Neuropathy Peripheral	0	1 (2.0)	0	1 (0.5)
Presyncope	0	0	1 (1.9)	1 (0.5)
Tremor	0	0	1 (1.9)	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Infections And Infestations	17 (16.8)	7 (14.0)	3 (5.8)	27 (13.3)
Bronchitis	4 (4.0)	1 (2.0)	0	5 (2.5)
Upper Respiratory Tract Infection	2 (2.0)	1 (2.0)	1 (1.9)	4 (2.0)
Nasopharyngitis	2 (2.0)	1 (2.0)	0	3 (1.5)
Conjunctivitis	0	2 (4.0)	0	2 (1.0)
Acute Sinusitis	1 (1.0)	0	0	1 (0.5)
Cellulitis	1 (1.0)	0	0	1 (0.5)
Furuncle	0	1 (2.0)	0	1 (0.5)
Gonorrhoea	0	1 (2.0)	0	1 (0.5)
Herpes Virus Infection	1 (1.0)	0	0	1 (0.5)
Influenza	1 (1.0)	0	0	1 (0.5)
Lower Respiratory Tract Infection	1 (1.0)	0	0	1 (0.5)
Papilloma Viral Infection	0	1 (2.0)	0	1 (0.5)
Periorbital Cellulitis	1 (1.0)	0	0	1 (0.5)
Pharyngitis	1 (1.0)	0	0	1 (0.5)
Pneumonia	1 (1.0)	0	0	1 (0.5)
Sinusitis	1 (1.0)	0	0	1 (0.5)
Skin Infection	1 (1.0)	0	0	1 (0.5)
Subcutaneous Abscess	0	0	1 (1.9)	1 (0.5)
Tinea Versicolour	0	0	1 (1.9)	1 (0.5)
Tooth Abscess	0	0	1 (1.9)	1 (0.5)
Tooth Infection	1 (1.0)	0	0	1 (0.5)
Urinary Tract Infection	1 (1.0)	0	0	1 (0.5)
Viral Upper Respiratory Tract Infection	1 (1.0)	0	0	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Musculoskeletal And Connective Tissue Disorders	12 (11.9)	2 (4.0)	8 (15.4)	22 (10.8)
Arthralgia	4 (4.0)	1 (2.0)	2 (3.8)	7 (3.4)
Back Pain	1 (1.0)	1 (2.0)	2 (3.8)	4 (2.0)
Myalgia	3 (3.0)	0	0	3 (1.5)
Muscle Spasms	0	0	2 (3.8)	2 (1.0)
Pain In Extremity	1 (1.0)	0	1 (1.9)	2 (1.0)
Bone Pain	0	0	1 (1.9)	1 (0.5)
Flank Pain	1 (1.0)	0	0	1 (0.5)
Groin Pain	1 (1.0)	0	0	1 (0.5)
Joint Stiffness	1 (1.0)	0	0	1 (0.5)
Joint Swelling	0	0	1 (1.9)	1 (0.5)
Muscle Twitching	0	1 (2.0)	0	1 (0.5)
Musculoskeletal Chest Pain	1 (1.0)	0	0	1 (0.5)
Musculoskeletal Stiffness	1 (1.0)	0	0	1 (0.5)
Neck Pain	0	0	1 (1.9)	1 (0.5)
Respiratory, Thoracic And Mediastinal Disorders	10 (9.9)	7 (14.0)	4 (7.7)	21 (10.3)
Cough	3 (3.0)	3 (6.0)	1 (1.9)	7 (3.4)
Rhinitis Allergic	3 (3.0)	2 (4.0)	0	5 (2.5)
Oropharyngeal Pain	2 (2.0)	1 (2.0)	0	3 (1.5)
Dyspnoea	1 (1.0)	1 (2.0)	0	2 (1.0)
Rhinorrhoea	1 (1.0)	1 (2.0)	0	2 (1.0)
Chronic Obstructive Pulmonary Disease	0	0	1 (1.9)	1 (0.5)
Productive Cough	0	1 (2.0)	0	1 (0.5)
Pulmonary Embolism	0	0	1 (1.9)	1 (0.5)
Pulmonary Mass	0	0	1 (1.9)	1 (0.5)
Respiratory Disorder	1 (1.0)	0	0	1 (0.5)
Respiratory Tract Congestion	0	1 (2.0)	0	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Psychiatric Disorders	11 (10.9)	1 (2.0)	7 (13.5)	19 (9.4)
Insomnia	5 (5.0)	0	3 (5.8)	8 (3.9)
Abnormal Dreams	3 (3.0)	0	0	3 (1.5)
Irritability	2 (2.0)	1 (2.0)	0	3 (1.5)
Anxiety	1 (1.0)	0	0	1 (0.5)
Depression	0	0	1 (1.9)	1 (0.5)
Drug Abuse	0	0	1 (1.9)	1 (0.5)
Libido Increased	0	0	1 (1.9)	1 (0.5)
Mental Status Changes	0	0	1 (1.9)	1 (0.5)
Mood Altered	1 (1.0)	0	0	1 (0.5)
Personality Change	0	0	1 (1.9)	1 (0.5)
Sleep Disorder	1 (1.0)	0	0	1 (0.5)
Thinking Abnormal	0	0	1 (1.9)	1 (0.5)
Skin And Subcutaneous Tissue Disorders	11 (10.9)	3 (6.0)	5 (9.6)	19 (9.4)
Rash	6 (5.9)	0	3 (5.8)	9 (4.4)
Pruritus	2 (2.0)	1 (2.0)	1 (1.9)	4 (2.0)
Dermatitis Contact	2 (2.0)	0	0	2 (1.0)
Hyperhidrosis	2 (2.0)	0	0	2 (1.0)
Night Sweats	0	1 (2.0)	1 (1.9)	2 (1.0)
Alopecia	0	1 (2.0)	0	1 (0.5)
Rash Papular	0	0	1 (1.9)	1 (0.5)
Injury, Poisoning And Procedural Complications	3 (3.0)	3 (6.0)	3 (5.8)	9 (4.4)
Ligament Sprain	1 (1.0)	2 (4.0)	1 (1.9)	4 (2.0)
Contusion	0	0	1 (1.9)	1 (0.5)
Fall	1 (1.0)	0	0	1 (0.5)
Foot Fracture	0	0	1 (1.9)	1 (0.5)
Foreign Body In Eye	1 (1.0)	0	0	1 (0.5)
Laceration	0	0	1 (1.9)	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Injury, Poisoning And Procedural Complications (cont)				
Periorbital Haematoma	0	1 (2.0)	0	1 (0.5)
Investigations	3 (3.0)	1 (2.0)	3 (5.8)	7 (3.4)
Blood Creatine Phosphokinase Increased	0	0	1 (1.9)	1 (0.5)
Blood Creatinine Increased	1 (1.0)	0	0	1 (0.5)
Blood Pressure Abnormal	0	1 (2.0)	0	1 (0.5)
Body Temperature Increased	1 (1.0)	0	0	1 (0.5)
Cardiac Murmur	0	0	1 (1.9)	1 (0.5)
Creatinine Renal Clearance Decreased	1 (1.0)	0	0	1 (0.5)
Lipase Increased	1 (1.0)	0	0	1 (0.5)
Parasite Stool Test Positive	1 (1.0)	0	0	1 (0.5)
Weight Decreased	0	0	1 (1.9)	1 (0.5)
Reproductive System And Breast Disorders	3 (3.0)	3 (6.0)	1 (1.9)	7 (3.4)
Benign Prostatic Hyperplasia	0	1 (2.0)	0	1 (0.5)
Dyspareunia	0	0	1 (1.9)	1 (0.5)
Penile Pain	0	1 (2.0)	0	1 (0.5)
Penile Swelling	0	1 (2.0)	0	1 (0.5)
Priapism	1 (1.0)	0	0	1 (0.5)
Prostatitis	1 (1.0)	0	0	1 (0.5)
Scrotal Pain	1 (1.0)	0	0	1 (0.5)
Testicular Pain	1 (1.0)	0	0	1 (0.5)
Vaginal Haemorrhage	0	1 (2.0)	0	1 (0.5)
Vulvovaginal Dryness	0	0	1 (1.9)	1 (0.5)
Vascular Disorders	2 (2.0)	2 (4.0)	3 (5.8)	7 (3.4)
Hypertension	1 (1.0)	1 (2.0)	2 (3.8)	4 (2.0)
Flushing	1 (1.0)	0	0	1 (0.5)
Hypertensive Crisis	0	0	1 (1.9)	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Vascular Disorders (cont)				
Orthostatic Hypotension	0	1 (2.0)	0	1 (0.5)
Peripheral Vascular Disorder	0	0	1 (1.9)	1 (0.5)
Metabolism And Nutrition Disorders	3 (3.0)	2 (4.0)	1 (1.9)	6 (3.0)
Decreased Appetite	2 (2.0)	1 (2.0)	0	3 (1.5)
Hyperlipasaemia	1 (1.0)	0	0	1 (0.5)
Hypokalaemia	0	1 (2.0)	0	1 (0.5)
Increased Appetite	0	0	1 (1.9)	1 (0.5)
Renal And Urinary Disorders	2 (2.0)	2 (4.0)	2 (3.8)	6 (3.0)
Haematuria	1 (1.0)	0	1 (1.9)	2 (1.0)
Dysuria	1 (1.0)	0	0	1 (0.5)
Nocturia	0	0	1 (1.9)	1 (0.5)
Pollakiuria	0	1 (2.0)	0	1 (0.5)
Urethral Pain	0	1 (2.0)	0	1 (0.5)
Cardiac Disorders	1 (1.0)	2 (4.0)	2 (3.8)	5 (2.5)
Tachycardia	0	1 (2.0)	1 (1.9)	2 (1.0)
Bradycardia	0	1 (2.0)	0	1 (0.5)
Palpitations	0	0	1 (1.9)	1 (0.5)
Sinus Tachycardia	1 (1.0)	0	0	1 (0.5)
Ear And Labyrinth Disorders	2 (2.0)	0	2 (3.8)	4 (2.0)
Vertigo	0	0	2 (3.8)	2 (1.0)
Ear Pain	1 (1.0)	0	0	1 (0.5)
Tinnitus	1 (1.0)	0	0	1 (0.5)

Table S8. Adverse events (grades 1-4) on treatment with DCV + SOF (cont.)

System Organ Class (%) Preferred Term (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Blood And Lymphatic System Disorders	2 (2.0)	0	1 (1.9)	3 (1.5)
Anaemia	0	0	1 (1.9)	1 (0.5)
Lymphadenopathy	1 (1.0)	0	0	1 (0.5)
Neutropenia	1 (1.0)	0	0	1 (0.5)
Eye Disorders	1 (1.0)	0	2 (3.8)	3 (1.5)
Cataract	0	0	1 (1.9)	1 (0.5)
Conjunctival Haemorrhage	0	0	1 (1.9)	1 (0.5)
Dry Eye	1 (1.0)	0	0	1 (0.5)
Photophobia	0	0	1 (1.9)	1 (0.5)
Immune System Disorders	2 (2.0)	0	0	2 (1.0)
Hypersensitivity	1 (1.0)	0	0	1 (0.5)
Seasonal Allergy	1 (1.0)	0	0	1 (0.5)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	1 (1.0)	0	1 (1.9)	2 (1.0)
Acrochordon	1 (1.0)	0	0	1 (0.5)
Lipoma	0	0	1 (1.9)	1 (0.5)
Congenital, Familial And Genetic Disorders	0	0	1 (1.9)	1 (0.5)
Phimosis	0	0	1 (1.9)	1 (0.5)
Endocrine Disorders	1 (1.0)	0	0	1 (0.5)
Hypothyroidism	1 (1.0)	0	0	1 (0.5)

Table S9. Grade 3-4 adverse events on treatment with DCV + SOF

n (%)	**Treatment-naive 12 weeks N = 101**	**Treatment-naive 8 weeks N = 50**	**Treatment-experienced 12 weeks N = 52**	**Total N = 203**
Patients with at least 1 event	2 (2.0)	2 (4.0)	4 (7.7)	8 (3.9)
Individual events (all grade 3)				
Decreased appetite		1 (2.0)		1 (<1)
Pyrexia	1 (1.0)			1 (<1)
Hypertension			1 (1.9)	1 (<1)
Hypertensive crisis			1 (1.9)	1 (<1)
Syncope			1 (1.9)	1 (<1)
Presyncope			1 (1.9)	1 (<1)
Priapism	1 (1.0)			1 (<1)
Migraine		1 (2.0)		1 (<1)
Drug abuse			1 (1.9)	1 (<1)
Vomiting			1 (1.9)	1 (<1)

Vertical bar identifies individual events occurring in a single patient

Table S10. Serious Adverse Events

Patient identifier	Study visit	Onset (study day)	Duration (days)	Preferred term	Treatment related?	Intensity
Treatment-naive 12-week treatment group						
5-102 (62/Male/Other)	Follow-up week 12	180	Continuing	Cholangiocarcinoma	Yes	Severe
8-40 (49/Male/Caucasian)	Week 4	23	3	Priapism	No	Severe
19-74 (46/Male/Black)	Follow-up week 4	99	17	Pneumonia	No	Moderate
28-187 (53/Male/Black)	Follow-up week 4	104	1	Osteoarthritis	No	Moderate
31-93 (55/Male/Caucasian)	Pre-treatment	-9	9	Post-procedural haematoma*	No	Very severe
Treatment-naive 8-week treatment group						
30-90 (52/Male/Caucasian)	Follow-up week 4	96	1	Cardiac arrest	No	Very severe
Treatment-experienced 12-week treatment group						
2-213 (52/Male/Caucasian)	Day 1	1	-	Chest pain	No	Moderate
	Week 6	42	-	Presyncope	No	Severe
7-67 (51/Male/Black)	Week 8	51	6	Drug abuse	No	Severe
	Week 12	80	15	Pulmonary embolism	No	Severe
14-8 (60/Female/Black)	Week 8	51	2	Hypertensive crisis	No	Severe
	Week 8	54	2	Syncope	No	Severe

*Liver haematoma following biopsy

Table S11. Treatment-Emergent Laboratory Test Results By Worst Grade

Lab Test Description Toxicity Grade (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Hemoglobin	N = 101	N = 50	N = 52	N = 203
Not Emergent	101(100.0)	50(100.0)	52(100.0)	203(100.0)
Grade 1	0	0	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	0	0	0	0
Grades 3-4	0	0	0	0
Platelet Count	N = 101	N = 50	N = 51	N = 202
Not Emergent	94 (93.1)	47 (94.0)	41 (80.4)	182 (90.1)
Grade 1	4 (4.0)	2 (4.0)	9 (17.6)	15 (7.4)
Grade 2	3 (3.0)	1 (2.0)	1 (2.0)	5 (2.5)
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	7 (6.9)	3 (6.0)	10 (19.6)	20 (9.9)
Grades 3-4	0	0	0	0
Intl Normalized Ratio (INR)	N = 101	N = 50	N = 52	N = 203
Not Emergent	96 (95.0)	49 (98.0)	47 (90.4)	192 (94.6)
Grade 1	4 (4.0)	1 (2.0)	4 (7.7)	9 (4.4)
Grade 2	0	0	0	0
Grade 3	1 (1.0)	0	1 (1.9)	2 (1.0)
Grade 4	0	0	0	0
Grades 1-4	5 (5.0)	1 (2.0)	5 (9.6)	11 (5.4)
Grades 3-4	1 (1.0)	0	1 (1.9)	2 (1.0)

Table S11. Treatment-Emergent Laboratory Test Results By Worst Grade (cont.)

Lab Test Description Toxicity Grade (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Leukocytes	N = 101	N = 50	N = 52	N = 203
Not Emergent	100 (99.0)	49 (98.0)	50 (96.2)	199 (98.0)
Grade 1	1 (1.0)	1 (2.0)	2 (3.8)	4 (2.0)
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	1 (1.0)	1 (2.0)	2 (3.8)	4 (2.0)
Grades 3-4	0	0	0	0
Neutrophils + Bands (Absolute)	N = 101	N = 50	N = 52	N = 203
Not Emergent	96 (95.0)	46 (92.0)	50 (96.2)	192 (94.6)
Grade 1	3 (3.0)	3 (6.0)	1 (1.9)	7 (3.4)
Grade 2	2 (2.0)	1 (2.0)	1 (1.9)	4 (2.0)
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	5 (5.0)	4 (8.0)	2 (3.8)	11 (5.4)
Grades 3-4	0	0	0	0
Alanine Aminotransferase (ALT)	N = 101	N = 50	N = 52	N = 203
Not Emergent	100 (99.0)	49 (98.0)	51 (98.1)	200 (98.5)
Grade 1	1 (1.0)	1 (2.0)	1 (1.9)	3 (1.5)
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	1 (1.0)	1 (2.0)	1 (1.9)	3 (1.5)
Grades 3-4	0	0	0	0

Table S11. Treatment-Emergent Laboratory Test Results By Worst Grade (cont.)

Lab Test Description Toxicity Grade (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Aspartate Aminotransferase (AST)	N = 101	N = 50	N = 52	N = 203
Not Emergent	96 (95.0)	47 (94.0)	48 (92.3)	191 (94.1)
Grade 1	3 (3.0)	2 (4.0)	3 (5.8)	8 (3.9)
Grade 2	2 (2.0)	0	1 (1.9)	3 (1.5)
Grade 3	0	1 (2.0)	0	1 (0.5)
Grade 4	0	0	0	0
Grades 1-4	5 (5.0)	3 (6.0)	4 (7.7)	12 (5.9)
Grades 3-4	0	1 (2.0)	0	1 (0.5)
Alkaline Phosphatase (ALP)	N = 101	N = 50	N = 52	N = 203
Not Emergent	101(100.0)	50(100.0)	52(100.0)	203(100.0)
Grade 1	0	0	0	0
Grade 2	0	0	0	0
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	0	0	0	0
Grades 3-4	0	0	0	0
Bilirubin, Total	N = 101	N = 50	N = 52	N = 203
Not Emergent	90 (89.1)	46 (92.0)	43 (82.7)	179 (88.2)
Grade 1	1 (1.0)	0	2 (3.8)	3 (1.5)
Grade 2	5 (5.0)	3 (6.0)	5 (9.6)	13 (6.4)
Grade 3	4 (4.0)	1 (2.0)	2 (3.8)	7 (3.4)
Grade 4	1 (1.0)	0	0	1 (0.5)
Grades 1-4	11 (10.9)	4 (8.0)	9 (17.3)	24 (11.8)
Grades 3-4	5 (5.0)	1 (2.0)	2 (3.8)	8 (3.9)

Table S11. Treatment-Emergent Laboratory Test Results By Worst Grade (cont.)

Lab Test Description Toxicity Grade (%)	Naive DCV/SOF 12 WK N=101	Naive DCV/SOF 8 WK N=50	Experienced DCV/SOF 12 WK N=52	Total N=203
Albumin	N = 101	N = 50	N = 52	N = 203
Not Emergent	101(100.0)	48 (96.0)	52(100.0)	201 (99.0)
Grade 1	0	1 (2.0)	0	1 (0.5)
Grade 2	0	1 (2.0)	0	1 (0.5)
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	0	2 (4.0)	0	2 (1.0)
Grades 3-4	0	0	0	0
Lipase, Total (Colorimetric Assay)	N = 101	N = 50	N = 52	N = 203
Not Emergent	78 (77.2)	36 (72.0)	40 (76.9)	154 (75.9)
Grade 1	12 (11.9)	5 (10.0)	6 (11.5)	23 (11.3)
Grade 2	6 (5.9)	8 (16.0)	5 (9.6)	19 (9.4)
Grade 3	3 (3.0)	1 (2.0)	0	4 (2.0)
Grade 4	2 (2.0)	0	1 (1.9)	3 (1.5)
Grades 1-4	23 (22.8)	14 (28.0)	12 (23.1)	49 (24.1)
Grades 3-4	5 (5.0)	1 (2.0)	1 (1.9)	7 (3.4)
Creatinine	N = 101	N = 50	N = 52	N = 203
Not Emergent	78 (77.2)	43 (86.0)	41 (78.8)	162 (79.8)
Grade 1	14 (13.9)	5 (10.0)	8 (15.4)	27 (13.3)
Grade 2	9 (8.9)	2 (4.0)	3 (5.8)	14 (6.9)
Grade 3	0	0	0	0
Grade 4	0	0	0	0
Grades 1-4	23 (22.8)	7 (14.0)	11 (21.2)	41 (20.2)
Grades 3-4	0	0	0	0

Toxicity Scale: DAIDS Version 1.0.
Treatment Emergent laboratory abnormalities are those with a higher toxicity grade on treatment than at baseline (including missing baseline).

Table S12. SVR24 details and SVR12/SVR24 concordance

	Treatment-naive DCV + SOF 12-weeks (N = 101)	**Treatment-naive DCV + SOF 8-weeks (N = 50)**	**Treatment-experienced DCV + SOF 12-weeks (N = 52)**
SVR12, % (n/N)	97.0 (98/101)	76.0 (38/50)	98.1 (51/52)
SVR24, % (n/N)	92.1 (93/101)	72.0 (36/50)	92.3 (48/52)
SVR24 non-responders, n	**8**	**14**	**4**
Missing posttreatment week 24 data			
Previous SVR12 responder	4	1	2
Previous SVR12 non-responder	1	3	1
With posttreatment week 24 data			
Previous SVR12 non-responder	2	9	–
SVR12 response followed by relapse	–	1[b]	–
SVR12 response followed by reinfection	1[a]	–	1[c]
SVR12/SVR24 result concordance, % (n/m)[d]	99.0 (95/96)	97.8 (45/46)	98.0 (48/49)

SVR12 derived by next-observation-carried-backward. SVR24 derived by missing data = failure

[a]Available sequencing data suggest this subject (GT-2b at baseline) was reinfected with GT-3 following an SVR12 response.
[b]Relapse of baseline virus confirmed by sequencing.
[c]Available sequencing data suggest this subject (GT-1a at baseline) was reinfected with GT-1b following an SVR12 response.
[d]Includes both SVR responder and SVR non-responder concordances; m = number of patients with data available at posttreatment weeks 12 and 24.

DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
VERSION 1.0, DECEMBER, 2004; CLARIFICATION AUGUST 2009

The Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events ("DAIDS AE Grading Table") is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

This clarification of the DAIDS Table for Grading the Severity of Adult and Pediatric AE's provides additional explanation of the DAIDS AE Grading Table and clarifies some of the parameters.

I. Instructions and Clarifications

Grading Adult and Pediatric AEs

The DAIDS AE Grading Table includes parameters for grading both Adult and Pediatric AEs. When a single set of parameters is not appropriate for grading specific types of AEs for both Adult and Pediatric populations, separate sets of parameters for Adult and/or Pediatric populations (with specified respective age ranges) are given in the Table. If there is no distinction in the Table between Adult and Pediatric values for a type of AE, then the single set of parameters listed is to be used for grading the severity of both Adult and Pediatric events of that type.

> Note: In the classification of adverse events, the term "severe" is not the same as "serious." Severity is an indication of the intensity of a specific event (as in mild, moderate, or severe chest pain). The term "serious" relates to a participant/event outcome or action criteria, usually associated with events that pose a threat to a participant's life or functioning.

Addenda 1-3 Grading Tables for Microbicide Studies

For protocols involving topical application of products to the female genital tract, male genital area or rectum, strong consideration should be given to using Appendices I-III as the primary grading scales for these areas. The protocol would need to specifically state that one or more of the Appendices would be primary (and thus take precedence over the main Grading Table) for items that are listed in both the Appendix and the main Grading Table.

Addendum 1 - Female Genital Grading Table for Use in Microbicide Studies - PDF
Addendum 2 - Male Genital Grading Table for Use in Microbicide Studies - PDF
Addendum 3 - Rectal Grading Table for Use in Microbicide Studies - PDF

Grade 5

For any AE where the outcome is death, the severity of the AE is classified as Grade 5.

Estimating Severity Grade for Parameters Not Identified in the Table

In order to grade a clinical AE that is not identified in the DAIDS AE grading table, use the category "Estimating Severity Grade" located on Page 3.

Determining Severity Grade for Parameters "Between Grades"

If the severity of a clinical AE could fall under either one of two grades (e.g., the severity of an AE could be either Grade 2 or Grade 3), select the higher of the two grades for the AE. If a laboratory value that is graded as a multiple of the ULN or LLN falls between two grades, select the higher of the two grades for the AE. For example, Grade 1 is 2.5 x ULN and Grade 2 is 2.6 x ULN for a parameter. If the lab value is 2.53 x ULN (which is between the two grades), the severity of this AE would be Grade 2, the higher of the two grades.

Values Below Grade 1

Any laboratory value that is between either the LLN or ULN and Grade 1 should not be graded.

Determining Severity Grade when Local Laboratory Normal Values Overlap with Grade 1 Ranges

In these situations, the severity grading is based on the ranges in the DAIDS AE Grading Table, even when there is a reference to the local lab LLN.

For example: Phosphate, Serum, Low, Adult and Pediatric > 14 years (Page 20) Grade 1 range is 2.50 mg/dL - < LLN. A particular laboratory's normal range for Phosphate is 2.1 – 3.8 mg/dL. A participant's actual lab value is 2.5. In this case, the value of 2.5 exceeds the LLN for the local lab, but will be graded as Grade 1 per DAIDS AE Grading Table.

II. Definitions of terms used in the Table:

Basic Self-care Functions	Adult Activities such as bathing, dressing, toileting, transfer/movement, continence, and feeding. Young Children Activities that are age and culturally appropriate (e.g., feeding self with culturally appropriate eating implement).
LLN	Lower limit of normal
Medical Intervention	Use of pharmacologic or biologic agent(s) for treatment of an AE.
NA	Not Applicable
Operative Intervention	Surgical OR other invasive mechanical procedures.
ULN	Upper limit of normal
Usual Social & Functional Activities	Adult Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc. Young Children Activities that are age and culturally appropriate (e.g., social interactions, play activities, learning tasks, etc.).

DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
VERSION 1.0, DECEMBER, 2004; CLARIFICATION AUGUST 2009

PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
ESTIMATING SEVERITY GRADE				
Clinical adverse event NOT identified elsewhere in this DAIDS AE Grading Table	Symptoms causing no or minimal interference with usual social & functional activities	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activities	Symptoms causing inability to perform basic self-care functions OR Medical or operative intervention indicated to prevent permanent impairment, persistent disability, or death
SYSTEMIC				
Acute systemic allergic reaction	Localized urticaria (wheals) with no medical intervention indicated	Localized urticaria with medical intervention indicated OR Mild angioedema with no medical intervention indicated	Generalized urticaria OR Angioedema with medical intervention indicated OR Symptomatic mild bronchospasm	Acute anaphylaxis OR Life-threatening bronchospasm OR laryngeal edema
Chills	Symptoms causing no or minimal interference with usual social & functional activities	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activities	NA
Fatigue Malaise	Symptoms causing no or minimal interference with usual social & functional activities	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activities	Incapacitating fatigue/ malaise symptoms causing inability to perform basic self-care functions
Fever (nonaxillary)	37.7 – 38.6°C	38.7 – 39.3°C	39.4 – 40.5°C	> 40.5°C
Pain (indicate body site) DO NOT use for pain due to injection (See Injection Site Reactions: Injection site pain) See also Headache, Arthralgia, and Myalgia	Pain causing no or minimal interference with usual social & functional activities	Pain causing greater than minimal interference with usual social & functional activities	Pain causing inability to perform usual social & functional activities	Disabling pain causing inability to perform basic self-care functions OR Hospitalization (other than emergency room visit) indicated

Basic Self-care Functions – Adult: Activities such as bathing, dressing, toileting, transfer/movement, continence, and feeding.

Basic Self-care Functions – Young Children: Activities that are age and culturally appropriate (e.g., feeding self with culturally appropriate eating implement).

Usual Social & Functional Activities – Adult: Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc.

Usual Social & Functional Activities – Young Children: Activities that are age and culturally appropriate (e.g., social interactions, play activities, learning tasks, etc.).

DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
VERSION 1.0, DECEMBER, 2004; CLARIFICATION AUGUST 2009

PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Unintentional weight loss	NA	5 – 9% loss in body weight from baseline	10 – 19% loss in body weight from baseline	≥ 20% loss in body weight from baseline OR Aggressive intervention indicated [e.g., tube feeding or total parenteral nutrition (TPN)]
INFECTION				
Infection (any other than HIV infection)	Localized, no systemic antimicrobial treatment indicated AND Symptoms causing no or minimal interference with usual social & functional activities	Systemic antimicrobial treatment indicated OR Symptoms causing greater than minimal interference with usual social & functional activities	Systemic antimicrobial treatment indicated AND Symptoms causing inability to perform usual social & functional activities OR Operative intervention (other than simple incision and drainage) indicated	Life-threatening consequences (e.g., septic shock)
INJECTION SITE REACTIONS				
Injection site pain (pain without touching) Or Tenderness (pain when area is touched)	Pain/tenderness causing no or minimal limitation of use of limb	Pain/tenderness limiting use of limb OR Pain/tenderness causing greater than minimal interference with usual social & functional activities	Pain/tenderness causing inability to perform usual social & functional activities	Pain/tenderness causing inability to perform basic self-care function OR Hospitalization (other than emergency room visit) indicated for management of pain/tenderness
Injection site reaction (localized)				
Adult > 15 years	Erythema OR Induration of 5x5 cm – 9x9 cm (or 25 cm^2 – 81cm^2)	Erythema OR Induration OR Edema > 9 cm any diameter (or > 81 cm^2)	Ulceration OR Secondary infection OR Phlebitis OR Sterile abscess OR Drainage	Necrosis (involving dermis and deeper tissue)
Pediatric ≤ 15 years	Erythema OR Induration OR Edema present but ≤ 2.5 cm diameter	Erythema OR Induration OR Edema > 2.5 cm diameter but < 50% surface area of the extremity segment (e.g., upper arm/thigh)	Erythema OR Induration OR Edema involving ≥ 50% surface area of the extremity segment (e.g., upper arm/thigh) OR Ulceration OR Secondary infection OR Phlebitis OR Sterile abscess OR Drainage	Necrosis (involving dermis and deeper tissue)

Basic Self-care Functions – Adult: Activities such as bathing, dressing, toileting, transfer/movement, continence, and feeding.

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Usual Social & Functional Activities – Adult: Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc.

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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Pruritis associated with injection See also Skin: Pruritis (itching - no skin lesions)	Itching localized to injection site AND Relieved spontaneously or with < 48 hours treatment	Itching beyond the injection site but not generalized OR Itching localized to injection site requiring ≥ 48 hours treatment	Generalized itching causing inability to perform usual social & functional activities	NA
SKIN – DERMATOLOGICAL				
Alopecia	Thinning detectable by study participant (or by caregiver for young children and disabled adults)	Thinning or patchy hair loss detectable by health care provider	Complete hair loss	NA
Cutaneous reaction – rash	Localized macular rash	Diffuse macular, maculopapular, or morbilliform rash OR Target lesions	Diffuse macular, maculopapular, or morbilliform rash with vesicles or limited number of bullae OR Superficial ulcerations of mucous membrane limited to one site	Extensive or generalized bullous lesions OR Stevens-Johnson syndrome OR Ulceration of mucous membrane involving two or more distinct mucosal sites OR Toxic epidermal necrolysis (TEN)
Hyperpigmentation	Slight or localized	Marked or generalized	NA	NA
Hypopigmentation	Slight or localized	Marked or generalized	NA	NA
Pruritis (itching – no skin lesions) (See also Injection Site Reactions: Pruritis associated with injection)	Itching causing no or minimal interference with usual social & functional activities	Itching causing greater than minimal interference with usual social & functional activities	Itching causing inability to perform usual social & functional activities	NA
CARDIOVASCULAR				
Cardiac arrhythmia (general) (By ECG or physical exam)	Asymptomatic AND No intervention indicated	Asymptomatic AND Non-urgent medical intervention indicated	Symptomatic, non-life-threatening AND Non-urgent medical intervention indicated	Life-threatening arrhythmia OR Urgent intervention indicated
Cardiac-ischemia/infarction	NA	NA	Symptomatic ischemia (stable angina) OR Testing consistent with ischemia	Unstable angina OR Acute myocardial infarction

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DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Hemorrhage (significant acute blood loss)	NA	Symptomatic AND No transfusion indicated	Symptomatic AND Transfusion of ≤ 2 units packed RBCs (for children ≤ 10 cc/kg) indicated	Life-threatening hypotension OR Transfusion of > 2 units packed RBCs (for children > 10 cc/kg) indicated
Hypertension				
Adult > 17 years (with repeat testing at same visit)	140 – 159 mmHg systolic OR 90 – 99 mmHg diastolic	160 – 179 mmHg systolic OR 100 – 109 mmHg diastolic	**≥** 180 mmHg systolic OR **≥** 110 mmHg diastolic	Life-threatening consequences (e.g., malignant hypertension) OR Hospitalization indicated (other than emergency room visit)
Correction: in Grade 2 to 160 - 179 from > 160-179 (systolic) and to ≥ 100 -109 from > 100-109 (diastolic) and in Grade 3 to ≥ 180 from > 180 (systolic) and to ≥ 110 from > 110 (diastolic).				
Pediatric ≤ 17 years (with repeat testing at same visit)	NA	91st – 94th percentile adjusted for age, height, and gender (systolic and/or diastolic)	≥ 95th percentile adjusted for age, height, and gender (systolic and/or diastolic)	Life-threatening consequences (e.g., malignant hypertension) OR Hospitalization indicated (other than emergency room visit)
Hypotension	NA	Symptomatic, corrected with oral fluid replacement	Symptomatic, IV fluids indicated	Shock requiring use of vasopressors or mechanical assistance to maintain blood pressure
Pericardial effusion	Asymptomatic, small effusion requiring no intervention	Asymptomatic, moderate or larger effusion requiring no intervention	Effusion with non-life threatening physiologic consequences OR Effusion with non-urgent intervention indicated	Life-threatening consequences (e.g., tamponade) OR Urgent intervention indicated
Prolonged PR interval				
Adult > 16 years	PR interval 0.21 – 0.25 sec	PR interval > 0.25 sec	Type II 2nd degree AV block OR Ventricular pause > 3.0 sec	Complete AV block
Pediatric ≤ 16 years	1st degree AV block (PR > normal for age and rate)	Type I 2nd degree AV block	Type II 2nd degree AV block	Complete AV block

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DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Prolonged QTc				
Adult > 16 years	Asymptomatic, QTc interval 0.45 – 0.47 sec OR Increase interval < 0.03 sec above baseline	Asymptomatic, QTc interval 0.48 – 0.49 sec OR Increase in interval 0.03 – 0.05 sec above baseline	Asymptomatic, QTc interval ≥ 0.50 sec OR Increase in interval ≥ 0.06 sec above baseline	Life-threatening consequences, e.g. Torsade de pointes or other associated serious ventricular dysrhythmia
Pediatric ≤ 16 years	Asymptomatic, QTc interval 0.450 – 0.464 sec	Asymptomatic, QTc interval 0.465 – 0.479 sec	Asymptomatic, QTc interval ≥ 0.480 sec	Life-threatening consequences, e.g. Torsade de pointes or other associated serious ventricular dysrhythmia
Thrombosis/embolism	NA	Deep vein thrombosis AND No intervention indicated (e.g., anticoagulation, lysis filter, invasive procedure)	Deep vein thrombosis AND Intervention indicated (e.g., anticoagulation, lysis filter, invasive procedure)	Embolic event (e.g., pulmonary embolism, life-threatening thrombus)
Vasovagal episode (associated with a procedure of any kind)	Present without loss of consciousness	Present with transient loss of consciousness	NA	NA
Ventricular dysfunction (congestive heart failure)	NA	Asymptomatic diagnostic finding AND intervention indicated	New onset with symptoms OR Worsening symptomatic congestive heart failure	Life-threatening congestive heart failure
GASTROINTESTINAL				
Anorexia	Loss of appetite without decreased oral intake	Loss of appetite associated with decreased oral intake without significant weight loss	Loss of appetite associated with significant weight loss	Life-threatening consequences OR Aggressive intervention indicated [e.g., tube feeding or total parenteral nutrition (TPN)]
Comment: Please note that, while the grading scale provided for Unintentional Weight Loss may be used as a guideline when grading anorexia, this is not a requirement and should not be used as a substitute for clinical judgment.				
Ascites	Asymptomatic	Symptomatic AND Intervention indicated (e.g., diuretics or therapeutic paracentesis)	Symptomatic despite intervention	Life-threatening consequences

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VERSION 1.0, DECEMBER, 2004; CLARIFICATION AUGUST 2009

PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Cholecystitis	NA	Symptomatic AND Medical intervention indicated	Radiologic, endoscopic, or operative intervention indicated	Life-threatening consequences (e.g., sepsis or perforation)
Constipation	NA	Persistent constipation requiring regular use of dietary modifications, laxatives, or enemas	Obstipation with manual evacuation indicated	Life-threatening consequences (e.g., obstruction)
Diarrhea				
Adult and Pediatric ≥ 1 year	Transient or intermittent episodes of unformed stools OR Increase of ≤ 3 stools over baseline per 24-hour period	Persistent episodes of unformed to watery stools OR Increase of 4 – 6 stools over baseline per 24-hour period	Bloody diarrhea OR Increase of ≥ 7 stools per 24-hour period OR IV fluid replacement indicated	Life-threatening consequences (e.g., hypotensive shock)
Pediatric < 1 year	Liquid stools (more unformed than usual) but usual number of stools	Liquid stools with increased number of stools OR Mild dehydration	Liquid stools with moderate dehydration	Liquid stools resulting in severe dehydration with aggressive rehydration indicated OR Hypotensive shock
Dysphagia-Odynophagia	Symptomatic but able to eat usual diet	Symptoms causing altered dietary intake without medical intervention indicated	Symptoms causing severely altered dietary intake with medical intervention indicated	Life-threatening reduction in oral intake
Mucositis/stomatitis (clinical exam) Indicate site (e.g., larynx, oral) See Genitourinary for Vulvovaginitis See also Dysphagia-Odynophagia and Proctitis	Erythema of the mucosa	Patchy pseudomembranes or ulcerations	Confluent pseudomembranes or ulcerations OR Mucosal bleeding with minor trauma	Tissue necrosis OR Diffuse spontaneous mucosal bleeding OR Life-threatening consequences (e.g., aspiration, choking)
Nausea	Transient (< 24 hours) or intermittent nausea with no or minimal interference with oral intake	Persistent nausea resulting in decreased oral intake for 24 – 48 hours	Persistent nausea resulting in minimal oral intake for > 48 hours OR Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)

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DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Pancreatitis	NA	Symptomatic AND Hospitalization not indicated (other than emergency room visit)	Symptomatic AND Hospitalization indicated (other than emergency room visit)	Life-threatening consequences (e.g., circulatory failure, hemorrhage, sepsis)
Proctitis (functional-symptomatic) Also see Mucositis/stomatitis for clinical exam	Rectal discomfort AND No intervention indicated	Symptoms causing greater than minimal interference with usual social & functional activities OR Medical intervention indicated	Symptoms causing inability to perform usual social & functional activities OR Operative intervention indicated	Life-threatening consequences (e.g., perforation)
Vomiting	Transient or intermittent vomiting with no or minimal interference with oral intake	Frequent episodes of vomiting with no or mild dehydration	Persistent vomiting resulting in orthostatic hypotension OR Aggressive rehydration indicated (e.g., IV fluids)	Life-threatening consequences (e.g., hypotensive shock)
NEUROLOGIC				
Alteration in personality-behavior or in mood (e.g., agitation, anxiety, depression, mania, psychosis)	Alteration causing no or minimal interference with usual social & functional activities	Alteration causing greater than minimal interference with usual social & functional activities	Alteration causing inability to perform usual social & functional activities	Behavior potentially harmful to self or others (e.g., suicidal and homicidal ideation or attempt, acute psychosis) OR Causing inability to perform basic self-care functions
Altered Mental Status For Dementia, see Cognitive and behavioral/attentional disturbance (including dementia and attention deficit disorder)	Changes causing no or minimal interference with usual social & functional activities	Mild lethargy or somnolence causing greater than minimal interference with usual social & functional activities	Confusion, memory impairment, lethargy, or somnolence causing inability to perform usual social & functional activities	Delirium OR obtundation, OR coma
Ataxia	Asymptomatic ataxia detectable on exam OR Minimal ataxia causing no or minimal interference with usual social & functional activities	Symptomatic ataxia causing greater than minimal interference with usual social & functional activities	Symptomatic ataxia causing inability to perform usual social & functional activities	Disabling ataxia causing inability to perform basic self-care functions

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Usual Social & Functional Activities – Adult: Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc.

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DIVISION OF AIDS TABLE FOR GRADING THE SEVERITY OF ADULT AND PEDIATRIC ADVERSE EVENTS
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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Cognitive and behavioral/attentional disturbance (including dementia and attention deficit disorder)	Disability causing no or minimal interference with usual social & functional activities OR Specialized resources not indicated	Disability causing greater than minimal interference with usual social & functional activities OR Specialized resources on part-time basis indicated	Disability causing inability to perform usual social & functional activities OR Specialized resources on a full-time basis indicated	Disability causing inability to perform basic self-care functions OR Institutionalization indicated
CNS ischemia (acute)	NA	NA	Transient ischemic attack	Cerebral vascular accident (CVA, stroke) with neurological deficit
Developmental delay – **Pediatric ≤ 16 years**	Mild developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Moderate developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Severe developmental delay, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting	Developmental regression, either motor or cognitive, as determined by comparison with a developmental screening tool appropriate for the setting
Headache	Symptoms causing no or minimal interference with usual social & functional activities	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activities	Symptoms causing inability to perform basic self-care functions OR Hospitalization indicated (other than emergency room visit) OR Headache with significant impairment of alertness or other neurologic function
Insomnia	NA	Difficulty sleeping causing greater than minimal interference with usual social & functional activities	Difficulty sleeping causing inability to perform usual social & functional activities	Disabling insomnia causing inability to perform basic self-care functions
Neuromuscular weakness (including myopathy & neuropathy)	Asymptomatic with decreased strength on exam OR Minimal muscle weakness causing no or minimal interference with usual social & functional activities	Muscle weakness causing greater than minimal interference with usual social & functional activities	Muscle weakness causing inability to perform usual social & functional activities	Disabling muscle weakness causing inability to perform basic self-care functions OR Respiratory muscle weakness impairing ventilation

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Usual Social & Functional Activities – Adult: Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc.

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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Neurosensory alteration (including paresthesia and painful neuropathy)	Asymptomatic with sensory alteration on exam or minimal paresthesia causing no or minimal interference with usual social & functional activities	Sensory alteration or paresthesia causing greater than minimal interference with usual social & functional activities	Sensory alteration or paresthesia causing inability to perform usual social & functional activities	Disabling sensory alteration or paresthesia causing inability to perform basic self-care functions
Seizure: (new onset) **– Adult ≥ 18 years** See also Seizure: (known pre-existing seizure disorder)	NA	1 seizure	2 – 4 seizures	Seizures of any kind which are prolonged, repetitive (e.g., status epilepticus), or difficult to control (e.g., refractory epilepsy)
Seizure: (known pre-existing seizure disorder) **– Adult ≥ 18 years** For worsening of existing epilepsy the grades should be based on an increase from previous level of control to any of these levels.	NA	Increased frequency of pre-existing seizures (non-repetitive) without change in seizure character OR Infrequent break-through seizures while on stable medication in a previously controlled seizure disorder	Change in seizure character from baseline either in duration or quality (e.g., severity or focality)	Seizures of any kind which are prolonged, repetitive (e.g., status epilepticus), or difficult to control (e.g., refractory epilepsy)
Seizure **– Pediatric < 18 years**	Seizure, generalized onset with or without secondary generalization, lasting < 5 minutes with < 24 hours post ictal state	Seizure, generalized onset with or without secondary generalization, lasting 5 – 20 minutes with < 24 hours post ictal state	Seizure, generalized onset with or without secondary generalization, lasting > 20 minutes	Seizure, generalized onset with or without secondary generalization, requiring intubation and sedation
Syncope (not associated with a procedure)	NA	Present	NA	NA
Vertigo	Vertigo causing no or minimal interference with usual social & functional activities	Vertigo causing greater than minimal interference with usual social & functional activities	Vertigo causing inability to perform usual social & functional activities	Disabling vertigo causing inability to perform basic self-care functions

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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
RESPIRATORY				
Bronchospasm (acute)	FEV1 or peak flow reduced to 70 – 80%	FEV1 or peak flow 50 – 69%	FEV1 or peak flow 25 – 49%	Cyanosis OR FEV1 or peak flow < 25% OR Intubation
Dyspnea or respiratory distress				
Adult ≥ 14 years	Dyspnea on exertion with no or minimal interference with usual social & functional activities	Dyspnea on exertion causing greater than minimal interference with usual social & functional activities	Dyspnea at rest causing inability to perform usual social & functional activities	Respiratory failure with ventilatory support indicated
Pediatric < 14 years	Wheezing OR minimal increase in respiratory rate for age	Nasal flaring OR Intercostal retractions OR Pulse oximetry 90 – 95%	Dyspnea at rest causing inability to perform usual social & functional activities OR Pulse oximetry < 90%	Respiratory failure with ventilatory support indicated
MUSCULOSKELETAL				
Arthralgia See also Arthritis	Joint pain causing no or minimal interference with usual social & functional activities	Joint pain causing greater than minimal interference with usual social & functional activities	Joint pain causing inability to perform usual social & functional activities	Disabling joint pain causing inability to perform basic self-care functions
Arthritis See also Arthralgia	Stiffness or joint swelling causing no or minimal interference with usual social & functional activities	Stiffness or joint swelling causing greater than minimal interference with usual social & functional activities	Stiffness or joint swelling causing inability to perform usual social & functional activities	Disabling joint stiffness or swelling causing inability to perform basic self-care functions
Bone Mineral Loss				
Adult ≥ 21 years	BMD t-score -2.5 to -1.0	BMD t-score < -2.5	Pathological fracture (including loss of vertebral height)	Pathologic fracture causing life-threatening consequences
Pediatric < 21 years	BMD z-score -2.5 to -1.0	BMD z-score < -2.5	Pathological fracture (including loss of vertebral height)	Pathologic fracture causing life-threatening consequences
Myalgia (non-injection site)	Muscle pain causing no or minimal interference with usual social & functional activities	Muscle pain causing greater than minimal interference with usual social & functional activities	Muscle pain causing inability to perform usual social & functional activities	Disabling muscle pain causing inability to perform basic self-care functions

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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Osteonecrosis	NA	Asymptomatic with radiographic findings AND No operative intervention indicated	Symptomatic bone pain with radiographic findings OR Operative intervention indicated	Disabling bone pain with radiographic findings causing inability to perform basic self-care functions
GENITOURINARY				
Cervicitis (symptoms) (For use in studies evaluating topical study agents) For other cervicitis see Infection: Infection (any other than HIV infection)	Symptoms causing no or minimal interference with usual social & functional activities	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activities	Symptoms causing inability to perform basic self-care functions
Cervicitis (clinical exam) (For use in studies evaluating topical study agents) For other cervicitis see Infection: Infection (any other than HIV infection)	Minimal cervical abnormalities on examination (erythema, mucopurulent discharge, or friability) OR Epithelial disruption < 25% of total surface	Moderate cervical abnormalities on examination (erythema, mucopurulent discharge, or friability) OR Epithelial disruption of 25 – 49% total surface	Severe cervical abnormalities on examination (erythema, mucopurulent discharge, or friability) OR Epithelial disruption 50 – 75% total surface	Epithelial disruption > 75% total surface
Inter-menstrual bleeding (IMB)	Spotting observed by participant OR Minimal blood observed during clinical or colposcopic examination	Inter-menstrual bleeding not greater in duration or amount than usual menstrual cycle	Inter-menstrual bleeding greater in duration or amount than usual menstrual cycle	Hemorrhage with life-threatening hypotension OR Operative intervention indicated
Urinary tract obstruction (e.g., stone)	NA	Signs or symptoms of urinary tract obstruction without hydronephrosis or renal dysfunction	Signs or symptoms of urinary tract obstruction with hydronephrosis or renal dysfunction	Obstruction causing life-threatening consequences

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PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Vulvovaginitis (symptoms) (Use in studies evaluating topical study agents) For other vulvovaginitis see Infection: Infection (any other than HIV infection)	Symptoms causing no or minimal interference with usual social & functional activities	Symptoms causing greater than minimal interference with usual social & functional activities	Symptoms causing inability to perform usual social & functional activities	Symptoms causing inability to perform basic self-care functions
Vulvovaginitis (clinical exam) (Use in studies evaluating topical study agents) For other vulvovaginitis see Infection: Infection (any other than HIV infection)	Minimal vaginal abnormalities on examination OR Epithelial disruption < 25% of total surface	Moderate vaginal abnormalities on examination OR Epithelial disruption of 25 - 49% total surface	Severe vaginal abnormalities on examination OR Epithelial disruption 50 - 75% total surface	Vaginal perforation OR Epithelial disruption > 75% total surface
OCULAR/VISUAL				
Uveitis	Asymptomatic but detectable on exam	Symptomatic anterior uveitis OR Medical intervention indicated	Posterior or pan-uveitis OR Operative intervention indicated	Disabling visual loss in affected eye(s)
Visual changes (from baseline)	Visual changes causing no or minimal interference with usual social & functional activities	Visual changes causing greater than minimal interference with usual social & functional activities	Visual changes causing inability to perform usual social & functional activities	Disabling visual loss in affected eye(s)
ENDOCRINE/METABOLIC				
Abnormal fat accumulation (e.g., back of neck, breasts, abdomen)	Detectable by study participant (or by caregiver for young children and disabled adults)	Detectable on physical exam by health care provider	Disfiguring OR Obvious changes on casual visual inspection	NA
Diabetes mellitus	NA	New onset without need to initiate medication OR Modification of current medications to regain glucose control	New onset with initiation of medication indicated OR Diabetes uncontrolled despite treatment modification	Life-threatening consequences (e.g., ketoacidosis, hyperosmolar non-ketotic coma)

Basic Self-care Functions – Adult: Activities such as bathing, dressing, toileting, transfer/movement, continence, and feeding.

Basic Self-care Functions – Young Children: Activities that are age and culturally appropriate (e.g., feeding self with culturally appropriate eating implement).

Usual Social & Functional Activities – Adult: Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc.

Usual Social & Functional Activities – Young Children: Activities that are age and culturally appropriate (e.g., social interactions, play activities, learning tasks, etc.).

PARAMETER	GRADE 1 MILD	GRADE 2 MODERATE	GRADE 3 SEVERE	GRADE 4 POTENTIALLY LIFE-THREATENING
Gynecomastia	Detectable by study participant or caregiver (for young children and disabled adults)	Detectable on physical exam by health care provider	Disfiguring OR Obvious on casual visual inspection	NA
Hyperthyroidism	Asymptomatic	Symptomatic causing greater than minimal interference with usual social & functional activities OR Thyroid suppression therapy indicated	Symptoms causing inability to perform usual social & functional activities OR Uncontrolled despite treatment modification	Life-threatening consequences (e.g., thyroid storm)
Hypothyroidism	Asymptomatic	Symptomatic causing greater than minimal interference with usual social & functional activities OR Thyroid replacement therapy indicated	Symptoms causing inability to perform usual social & functional activities OR Uncontrolled despite treatment modification	Life-threatening consequences (e.g., myxedema coma)
Lipoatrophy (e.g., fat loss from the face, extremities, buttocks)	Detectable by study participant (or by caregiver for young children and disabled adults)	Detectable on physical exam by health care provider	Disfiguring OR Obvious on casual visual inspection	NA

Basic Self-care Functions – Adult: Activities such as bathing, dressing, toileting, transfer/movement, continence, and feeding.

Basic Self-care Functions – Young Children: Activities that are age and culturally appropriate (e.g., feeding self with culturally appropriate eating implement).

Usual Social & Functional Activities – Adult: Adaptive tasks and desirable activities, such as going to work, shopping, cooking, use of transportation, pursuing a hobby, etc.

Usual Social & Functional Activities – Young Children: Activities that are age and culturally appropriate (e.g., social interactions, play activities, learning tasks, etc.).

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LABORATORY				
PARAMETER	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
HEMATOLOGY	***Standard International Units are listed in italics***			
Absolute CD4+ count **– Adult and Pediatric > 13 years** (HIV NEGATIVE ONLY)	300 – 400/mm^3 *300 – 400/µL*	200 – 299/mm^3 *200 – 299/µL*	100 – 199/mm^3 *100 – 199/µL*	< 100/mm^3 *< 100/µL*
Absolute lymphocyte count **– Adult and Pediatric > 13 years** (HIV NEGATIVE ONLY)	600 – 650/mm^3 *0.600 x 10^9 – 0.650 x 10^9/L*	500 – 599/mm^3 *0.500 x 10^9 – 0.599 x 10^9/L*	350 – 499/mm^3 *0.350 x 10^9 – 0.499 x 10^9/L*	< 350/mm^3 *< 0.350 x 10^9/L*
Comment: Values in children ≤ 13 years are not given for the two parameters above because the absolute counts are variable.				
Absolute neutrophil count (ANC)				
Adult and Pediatric, > 7 days	1,000 – 1,300/mm^3 *1.000 x 10^9 – 1.300 x 10^9/L*	750 – 999/mm^3 *0.750 x 10^9 – 0.999 x 10^9/L*	500 – 749/mm^3 *0.500 x 10^9 – 0.749 x 10^9/L*	< 500/mm^3 *< 0.500 x 10^9/L*
Infant*†, 2 – ≤ 7 days	1,250 – 1,500/mm^3 *1.250 x 10^9 – 1.500 x 10^9/L*	1,000 – 1,249/mm^3 *1.000 x 10^9 – 1.249 x 10^9/L*	750 – 999/mm^3 *0.750 x 10^9 – 0.999 x 10^9/L*	< 750/mm^3 *< 0.750 x 10^9/L*
Infant*†, ≤1 day	4,000 – 5,000/mm^3 *4.000 x 10^9 – 5.000 x 10^9/L*	3,000 – 3,999/mm^3 *3.000 x 10^9 – 3.999 x10^9/L*	1,500 – 2,999/mm^3 *1.500 x 10^9 – 2.999 x 10^9/L*	< 1,500/mm^3 *< 1.500 x 10^9/L*
Comment: Parameter changed from "Infant, < 1 day" to "Infant, ≤1 day"				
Fibrinogen, decreased	100 – 200 mg/dL *1.00 – 2.00 g/L* OR 0.75 – 0.99 x LLN	75 – 99 mg/dL *0.75 – 0.99 g/L* OR 0.50 – 0.74 x LLN	50 – 74 mg/dL *0.50 – 0.74 g/L* OR 0.25 – 0.49 x LLN	< 50 mg/dL *< 0.50 g/L* OR < 0.25 x LLN OR Associated with gross bleeding

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† Use age and sex appropriate values (e.g., bilirubin).

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LABORATORY				
PARAMETER	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
Hemoglobin (Hgb)				
Comment: The Hgb values in mmol/L have changed because the conversion factor used to convert g/dL to mmol/L has been changed from 0.155 to 0.6206 (the most commonly used conversion factor). For grading Hgb results obtained by an analytic method with a conversion factor other than 0.6206, the result must be converted to g/dL using the appropriate conversion factor for that lab.				
Adult and Pediatric ≥ 57 days (HIV POSITIVE ONLY)	8.5 – 10.0 g/dL *5.24 – 6.23 mmol/L*	7.5 – 8.4 g/dL *4.62–5.23 mmol/L*	6.50 – 7.4 g/dL *4.03–4.61 mmol/L*	< 6.5 g/dL *< 4.03 mmol/L*
Adult and Pediatric ≥ 57 days (HIV NEGATIVE ONLY)	10.0 – 10.9 g/dL *6.18 – 6.79 mmol/L* OR Any decrease 2.5 – 3.4 g/dL *1.58 – 2.13 mmol/L*	9.0 – 9.9 g/dL *5.55 - 6.17 mmol/L* OR Any decrease 3.5 – 4.4 g/dL *2.14 – 2.78 mmol/L*	7.0 – 8.9 g/dL *4.34 - 5.54 mmol/L* OR Any decrease ≥ 4.5 g/dL *> 2.79 mmol/L*	< 7.0 g/dL *< 4.34 mmol/L*
Comment: The decrease is a decrease from baseline				
Infant*†, 36 – 56 days (HIV POSITIVE OR NEGATIVE)	8.5 – 9.4 g/dL *5.24 – 5.86 mmol/L*	7.0 – 8.4 g/dL *4.31 – 5.23 mmol/L*	6.0 – 6.9 g/dL *3.72 – 4.30 mmol/L*	< 6.00 g/dL *< 3.72 mmol/L*
Infant*†, 22 – 35 days (HIV POSITIVE OR NEGATIVE)	9.5 – 10.5 g/dL *5.87 - 6.54 mmol/L*	8.0 – 9.4 g/dL *4.93 – 5.86 mmol/L*	7.0 – 7.9 g/dL *4.34 – 4.92 mmol/L*	< 7.00 g/dL *< 4.34 mmol/L*
Infant*†, ≤ 21 days (HIV POSITIVE OR NEGATIVE)	12.0 – 13.0 g/dL *7.42 – 8.09 mmol/L*	10.0 – 11.9 g/dL *6.18 – 7.41 mmol/L*	9.0 – 9.9 g/dL *5.59- 6.17 mmol/L*	< 9.0 g/dL *< 5.59 mmol/L*
Correction: Parameter changed from "Infant < 21 days" to "Infant ≤ 21 days"				
International Normalized Ratio of prothrombin time (INR)	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	2.1 – 3.0 x ULN	> 3.0 x ULN
Methemoglobin	5.0 – 10.0%	10.1 – 15.0%	15.1 – 20.0%	> 20.0%
Prothrombin Time (PT)	1.1 – 1.25 x ULN	1.26 – 1.50 x ULN	1.51 – 3.00 x ULN	> 3.00 x ULN
Partial Thromboplastin Time (PTT)	1.1 – 1.66 x ULN	1.67 – 2.33 x ULN	2.34 – 3.00 x ULN	> 3.00 x ULN
Platelets, decreased	100,000 – 124,999/mm^3 *100.000 x 10^9 – 124.999 x 10^9/L*	50,000 – 99,999/mm^3 *50.000 x 10^9 – 99.999 x 10^9/L*	25,000 – 49,999/mm^3 *25.000 x 10^9 – 49.999 x 10^9/L*	< 25,000/mm^3 *< 25.000 x 10^9/L*
WBC, decreased	2,000 – 2,500/mm^3 *2.000 x 10^9 – 2.500 x 10^9/L*	1,500 – 1,999/mm^3 *1.500 x 10^9 – 1.999 x 10^9/L*	1,000 – 1,499/mm^3 *1.000 x 10^9 – 1.499 x 10^9/L*	< 1,000/mm^3 *< 1.000 x 10^9/L*

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† Use age and sex appropriate values (e.g., bilirubin).

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LABORATORY				
PARAMETER	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
CHEMISTRIES	***Standard International Units are listed in italics***			
Acidosis	NA	pH < normal, but ≥ 7.3	pH < 7.3 without life-threatening consequences	pH < 7.3 with life-threatening consequences
Albumin, serum, low	3.0 g/dL – < LLN *30 g/L – < LLN*	2.0 – 2.9 g/dL *20 – 29 g/L*	< 2.0 g/dL *< 20 g/L*	NA
Alkaline Phosphatase	1.25 – 2.5 x ULN†	2.6 – 5.0 x ULN†	5.1 – 10.0 x ULN†	> 10.0 x ULN†
Alkalosis	NA	pH > normal, but ≤ 7.5	pH > 7.5 without life-threatening consequences	pH > 7.5 with life-threatening consequences
ALT (SGPT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	> 10.0 x ULN
AST (SGOT)	1.25 – 2.5 x ULN	2.6 – 5.0 x ULN	5.1 – 10.0 x ULN	> 10.0 x ULN
Bicarbonate, serum, low	16.0 mEq/L – < LLN *16.0 mmol/L – < LLN*	11.0 – 15.9 mEq/L *11.0 – 15.9 mmol/L*	8.0 – 10.9 mEq/L *8.0 – 10.9 mmol/L*	< 8.0 mEq/L *< 8.0 mmol/L*
Comment: Some laboratories will report this value as Bicarbonate (HCO_3) and others as Total Carbon Dioxide (CO_2). These are the same tests; values should be graded according to the ranges for Bicarbonate as listed above.				
Bilirubin (Total)				
Adult and Pediatric > 14 days	1.1 – 1.5 x ULN	1.6 – 2.5 x ULN	2.6 – 5.0 x ULN	> 5.0 x ULN
Infant*†, ≤ 14 days (non-hemolytic)	NA	20.0 – 25.0 mg/dL *342 – 428 µmol/L*	25.1 – 30.0 mg/dL *429 – 513 µmol/L*	> 30.0 mg/dL *> 513.0 µmol/L*
Infant*†, ≤ 14 days (hemolytic)	NA	NA	20.0 – 25.0 mg/dL *342 – 428 µmol/L*	> 25.0 mg/dL *> 428 µmol/L*
Calcium, serum, high				
Adult and Pediatric ≥ 7 days	10.6 – 11.5 mg/dL *2.65 – 2.88 mmol/L*	11.6 – 12.5 mg/dL *2.89 – 3.13 mmol/L*	12.6 – 13.5 mg/dL *3.14 – 3.38 mmol/L*	> 13.5 mg/dL *> 3.38 mmol/L*
Infant*†, < 7 days	11.5 – 12.4 mg/dL *2.88 – 3.10 mmol/L*	12.5 – 12.9 mg/dL *3.11 – 3.23 mmol/L*	13.0 – 13.5 mg/dL *3.245 – 3.38 mmol/L*	> 13.5 mg/dL *> 3.38 mmol/L*
Calcium, serum, low				
Adult and Pediatric ≥ 7 days	7.8 – 8.4 mg/dL *1.95 – 2.10 mmol/L*	7.0 – 7.7 mg/dL *1.75 – 1.94 mmol/L*	6.1 – 6.9 mg/dL *1.53 – 1.74 mmol/L*	< 6.1 mg/dL *< 1.53 mmol/L*
Infant*†, < 7 days	6.5 – 7.5 mg/dL *1.63 – 1.88 mmol/L*	6.0 – 6.4 mg/dL *1.50 – 1.62 mmol/L*	5.50 – 5.90 mg/dL *1.38 – 1.51 mmol/L*	< 5.50 mg/dL *< 1.38 mmol/L*
Comment: Do not adjust Calcium, serum, low or Calcium, serum, high for albumin				

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LABORATORY				
PARAMETER	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
Cardiac troponin I (cTnI)	NA	NA	NA	Levels consistent with myocardial infarction or unstable angina as defined by the manufacturer
Cardiac troponin T (cTnT)	NA	NA	NA	≥ 0.20 ng/mL OR Levels consistent with myocardial infarction or unstable angina as defined by the manufacturer
Cholesterol (fasting)				
Adult ≥ 18 years	200 – 239 mg/dL *5.18 – 6.19 mmol/L*	240 – 300 mg/dL *6.20 – 7.77 mmol/L*	> 300 mg/dL *> 7.77 mmol/L*	NA
Pediatric < 18 years	170 – 199 mg/dL *4.40 – 5.15 mmol/L*	200 – 300 mg/dL *5.16 – 7.77 mmol/L*	> 300 mg/dL *> 7.77 mmol/L*	NA
Creatine Kinase	3.0 – 5.9 x ULN†	6.0 – 9.9 x ULN†	10.0 – 19.9 x ULN†	≥ 20.0 x ULN†
Creatinine	1.1 – 1.3 x ULN†	1.4 – 1.8 x ULN†	1.9 – 3.4 x ULN†	≥ 3.5 x ULN†
Glucose, serum, high				
Nonfasting	116 – 160 mg/dL *6.44 – 8.88 mmol/L*	161 – 250 mg/dL *8.89 – 13.88 mmol/L*	251 – 500 mg/dL *13.89 – 27.75 mmol/L*	> 500 mg/dL *> 27.75 mmol/L*
Fasting	110 – 125 mg/dL *6.11 – 6.94 mmol/L*	126 – 250 mg/dL *6.95 – 13.88 mmol/L*	251 – 500 mg/dL *13.89 – 27.75 mmol/L*	> 500 mg/dL *> 27.75 mmol/L*
Glucose, serum, low				
Adult and Pediatric ≥ 1 month	55 – 64 mg/dL *3.05 – 3.55 mmol/L*	40 – 54 mg/dL *2.22 – 3.06 mmol/L*	30 – 39 mg/dL *1.67 – 2.23 mmol/L*	< 30 mg/dL *< 1.67 mmol/L*
Infant*†, < 1 month	50 – 54 mg/dL *2.78 – 3.00 mmol/L*	40 – 49 mg/dL *2.22 – 2.77 mmol/L*	30 – 39 mg/dL *1.67 – 2.21 mmol/L*	< 30 mg/dL *< 1.67 mmol/L*
Lactate	ULN - < 2.0 x ULN without acidosis	≥ 2.0 x ULN without acidosis	Increased lactate with pH < 7.3 without life-threatening consequences	Increased lactate with pH < 7.3 with life-threatening consequences
Comment: Added ULN to Grade 1 parameter				

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† Use age and sex appropriate values (e.g., bilirubin).

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LABORATORY				
PARAMETER	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
LDL cholesterol (fasting)				
Adult ≥ 18 years	130 – 159 mg/dL *3.37 – 4.12 mmol/L*	160 – 190 mg/dL *4.13 – 4.90 mmol/L*	≥ 190 mg/dL *≥ 4.91 mmol/L*	NA
Pediatric > 2 - < 18 years	110 – 129 mg/dL *2.85 – 3.34 mmol/L*	130 – 189 mg/dL *3.35 – 4.90 mmol/L*	≥ 190 mg/dL *≥ 4.91 mmol/L*	NA
Lipase	1.1 – 1.5 x ULN	1.6 – 3.0 x ULN	3.1 – 5.0 x ULN	> 5.0 x ULN
Magnesium, serum, low	1.2 – 1.4 mEq/L *0.60 – 0.70 mmol/L*	0.9 – 1.1 mEq/L *0.45 – 0.59 mmol/L*	0.6 – 0.8 mEq/L *0.30 – 0.44 mmol/L*	< 0.60 mEq/L *< 0.30 mmol/L*
Pancreatic amylase	1.1 – 1.5 x ULN	1.6 – 2.0 x ULN	2.1 – 5.0 x ULN	> 5.0 x ULN
Phosphate, serum, low				
Adult and Pediatric > 14 years	2.5 mg/dL – < LLN *0.81 mmol/L – < LLN*	2.0 – 2.4 mg/dL *0.65 – 0.80 mmol/L*	1.0 – 1.9 mg/dL *0.32 – 0.64 mmol/L*	< 1.00 mg/dL *< 0.32 mmol/L*
Pediatric 1 year – 14 years	3.0 – 3.5 mg/dL *0.97 – 1.13 mmol/L*	2.5 – 2.9 mg/dL *0.81 – 0.96 mmol/L*	1.5 – 2.4 mg/dL *0.48 – 0.80 mmol/L*	< 1.50 mg/dL *< 0.48 mmol/L*
Pediatric < 1 year	3.5 – 4.5 mg/dL *1.13 – 1.45 mmol/L*	2.5 – 3.4 mg/dL *0.81 – 1.12 mmol/L*	1.5 – 2.4 mg/dL *0.48 – 0.80 mmol/L*	< 1.50 mg/dL *< 0.48 mmol/L*
Potassium, serum, high	5.6 – 6.0 mEq/L *5.6 – 6.0 mmol/L*	6.1 – 6.5 mEq/L *6.1 – 6.5 mmol/L*	6.6 – 7.0 mEq/L *6.6 – 7.0 mmol/L*	> 7.0 mEq/L *> 7.0 mmol/L*
Potassium, serum, low	3.0 – 3.4 mEq/L *3.0 – 3.4 mmol/L*	2.5 – 2.9 mEq/L *2.5 – 2.9 mmol/L*	2.0 – 2.4 mEq/L *2.0 – 2.4 mmol/L*	< 2.0 mEq/L *< 2.0 mmol/L*
Sodium, serum, high	146 – 150 mEq/L *146 – 150 mmol/L*	151 – 154 mEq/L *151 – 154 mmol/L*	155 – 159 mEq/L *155 – 159 mmol/L*	≥ 160 mEq/L *≥ 160 mmol/L*
Sodium, serum, low	130 – 135 mEq/L *130 – 135 mmol/L*	125 – 129 mEq/L *125 – 129 mmol/L*	121 – 124 mEq/L *121 – 124 mmol/L*	≤ 120 mEq/L *≤ 120 mmol/L*
Triglycerides (fasting)	NA	500 – 750 mg/dL *5.65 – 8.48 mmol/L*	751 – 1,200 mg/dL *8.49 – 13.56 mmol/L*	> 1,200 mg/dL *> 13.56 mmol/L*

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† Use age and sex appropriate values (e.g., bilirubin).

LABORATORY				
PARAMETER	**GRADE 1 MILD**	**GRADE 2 MODERATE**	**GRADE 3 SEVERE**	**GRADE 4 POTENTIALLY LIFE-THREATENING**
Uric acid	7.5 – 10.0 mg/dL *0.45 – 0.59 mmol/L*	10.1 – 12.0 mg/dL *0.60 – 0.71 mmol/L*	12.1 – 15.0 mg/dL *0.72 – 0.89 mmol/L*	> 15.0 mg/dL *> 0.89 mmol/L*
URINALYSIS	***Standard International Units are listed in italics***			
Hematuria (microscopic)	6 – 10 RBC/HPF	> 10 RBC/HPF	Gross, with or without clots OR with RBC casts	Transfusion indicated
Proteinuria, random collection	1 +	2 – 3 +	4 +	NA
Proteinuria, 24 hour collection				
Adult and Pediatric ≥ 10 years	200 – 999 mg/24 h *0.200 – 0.999 g/d*	1,000 – 1,999 mg/24 h *1.000 – 1.999 g/d*	2,000 – 3,500 mg/24 h *2.000 – 3.500 g/d*	> 3,500 mg/24 h *> 3.500 g/d*
Pediatric > 3 mo - < 10 years	201 – 499 mg/m^2/24 h *0.201 – 0.499 g/d*	500 – 799 mg/m^2/24 h *0.500 – 0.799 g/d*	800 – 1,000 mg/m^2/24 h *0.800 – 1.000 g/d*	> 1,000 mg/ m^2/24 h *> 1.000 g/d*

* Values are for term infants. Preterm infants should be assessed using local normal ranges.

† Use age and sex appropriate values (e.g., bilirubin).