(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 June 2015 (25.06.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/095572 A1

(51) **International Patent Classification**:
A61K 31/427 (2006.01) *A61K 31/7056* (2006.01)
A61K 31/4965 (2006.01) *A61P 31/14* (2006.01)
A61K 31/513 (2006.01)

(21) **International Application Number**:
PCT/US2014/071239

(22) **International Filing Date**:
18 December 2014 (18.12.2014)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:

61/918,264	19 December 2013 (19.12.2013)	US
61/972,866	31 March 2014 (31.03.2014)	US
62/008,784	6 June 2014 (06.06.2014)	US

(71) **Applicant**: **ABBVIE INC.** [US/US]; 1 North Waukegan Road, North Chicago, Illinois 60064 (US).

(72) **Inventors**: **COAKLEY, Eoin**; 1974 Kenton Lane, Green Oaks, Illinois 60048 (US). **BERNSTEIN, Barry M.**; 10829 Wyngate Trace, Mequon, Wisconsin 53092 (US). **VILCHEZ, Regis A.**; 760 Oakwood Avenue, Lake Forest, Illinois 60045 (US).

(74) **Agents**: **ZHANG, Xu** et al.; AbbVie Inc. 1 North Waukegan Road AP34-2/V377, North Chicago, Illinois 60064 (US).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

WO 2015/095572 A1

(54) **Title**: METHODS FOR TREATING LIVER TRANSPLANT RECIPIENTS

(57) **Abstract**: This application features interferon-free therapies for the prevention or treatment of HCV infection in liver transplant recipient. In one aspect, the treatment comprises administering a DAA combination to a liver transplant recipient after liver transplantation, wherein the DAA combination comprises Compound 1, ritonavir, Compound 2 and Compound 4.

METHODS FOR TREATING LIVER TRANSPLANT RECIPIENTS

FIELD OF THE TECHNOLOGY

[0001] This application relates to interferon-free treatment of liver transplant recipients for the prevention or treatment of hepatitis C virus (HCV) infection.

BACKGROUND

[0002] The HCV is an RNA virus belonging to the Hepacivirus genus in the Flaviviridae family. The enveloped HCV virion contains a positive stranded RNA genome encoding all known virus-specific proteins in a single, uninterrupted, open reading frame. The open reading frame comprises approximately 9500 nucleotides and encodes a single large polyprotein of about 3000 amino acids. The polyprotein comprises a core protein, envelope proteins E1 and E2, a membrane bound protein p7, and the non-structural proteins NS2, NS3, NS4A, NS4B, NS5A and NS5B.

[0003] Chronic HCV infection is associated with progressive liver pathology, including cirrhosis and hepatocellular carcinoma. Chronic hepatitis C may be treated with peginterferon-alpha in combination with ribavirin. Substantial limitations to efficacy and tolerability remain as many users suffer from side effects, and viral elimination from the body is often incomplete.

DETAILED DESCRIPTION

[0004] Recurrence of HCV infection after liver transplantation is universal and is a primary cause of graft loss. Current interferon-based HCV therapies have been associated with treatment-limiting toxicities and low efficacy. The application features the use of a combination of direct acting antiviral agents (DAAs), without the use of interferon, to treat liver transplant recipients for the prevention or treatment of HCV infection. The methods comprise administering a combination of DAAs to a liver transplant recipient.

[0005] In any aspect, embodiment, example, preference or feature described herein, the DAA combinations can be used, for example, with ribavirin. In any aspect, embodiment, example, preference or feature described herein, the DAA combinations can be used, for example, without ribavirin.

[0006] In any aspect, embodiment, example, preference or feature described herein, the treatment of liver transplant recipients can last from 4 to 20 weeks. For example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 4 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the

treatment lasts for 5 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 6 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 7 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 8 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 9 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 10 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 11 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 12 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 13 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 14 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 15 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 16 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 17 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 18 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 19 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 20 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 21 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 22 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 23 weeks. For another example, in any aspect, embodiment, example, preference or feature described herein, the treatment lasts for 24 weeks.

[0007] In any aspect, embodiment, example, preference or feature described herein, any DAA combination known in the art can be used to treat liver transplant recipients. Non-limiting examples of suitable DAA combinations can comprise one of the following combinations:

a combination of Compound 1, ritonavir, and Compound 4;

a combination of Compound 1, ritonavir, Compound 4 and Compound 2;

a combination of PSI-7977 and GS-5885;

a combination of PSI-7977 and TMC-435;

a combination of PSI-7977 and GS-5816;

a combination of PSI-7977 and BMS-790052;

a combination of BMS-790052 and BMS-650032;

a combination of GS-5885, GS-9190, and GS-9451; or

a combination of BI-201335 and BI-207127.

[0008] As used herein, ritonavir is not a DAA; instead, it is used to enhance the pharmacokinetics of Compound 1.

[0009] In any aspect, embodiment, example, preference or feature described herein, each DAA in the DAA combination can be, for example, dosed separately from the other DAA(s) in the DAA combination. In any aspect, embodiment, example, preference or feature described herein, each DAA in the DAA combination can be, for example, dosed together with the other DAA(s) in the DAA combination.

[0010] In any aspect, embodiment, example, preference or feature described herein, each DAA in the DAA combination can be, for example, formulated separately from the other DAA(s) in the DAA combination. In any aspect, embodiment, example, preference or feature described herein, all DAAs in the DAA combination can be, for example, formulated together in a single formulation.

[0011] In any aspect, embodiment, example, preference or feature described herein, one or more DAAs in the DAA combination can be, for example, dosed once daily (QD), and the other DAA(s) in the combination can be dosed twice daily (BID). In any aspect, embodiment, example, preference or feature described herein, all DAAs in the DAA combination can be, for example, dosed once daily.

[0012] In any aspect, embodiment, example, preference or feature described herein, a DAA can be in a pharmaceutically acceptable salt form.

[0013] Preferably, in any aspect, embodiment, example, preference or feature described herein, the DAA combination used to treat liver transplant recipients is a combination of Compound 1, ritonavir and Compound 4, all of which are formulated together in a single formulation and dosed once daily.

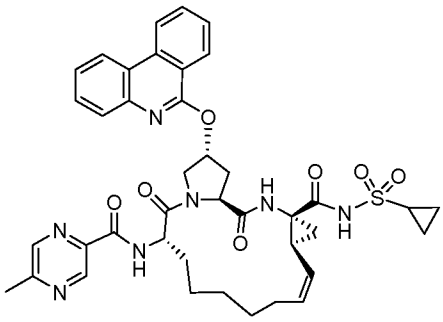
[0014] Also, preferably, in any aspect, embodiment, example, preference or feature described herein, the DAA combination used to treat liver transplant recipients is a combination of Compound 1, ritonavir and Compound 4, together with Compound 2, where Compound 1/ritonavir/Compound 4 are formulated together in a single formulation and dosed once daily, and Compound 2 is formulated separately and dosed twice daily.

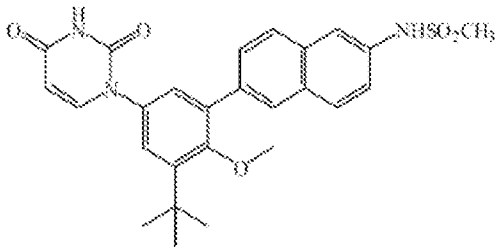
[0015] In any aspect, embodiment, example, preference or feature described herein, Compound 1 can be used, for example, from 100-200 mg QD, preferably 150 mg QD.

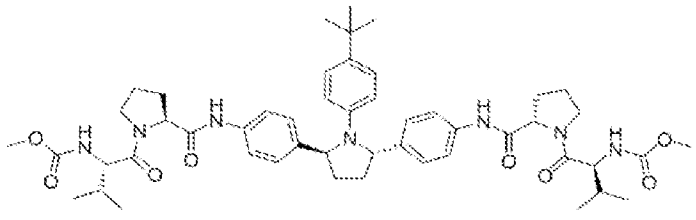
[0016] In any aspect, embodiment, example, preference or feature described herein, Compound 2 can be used, for example, from 100 to 600 mg BID, preferably 250 mg BID.

[0017] In any aspect, embodiment, example, preference or feature described herein, Compound 4 can be used, for example, from 10 to 50 mg QD, preferably 25 mg BID.

[0018] In any aspect, embodiment, example, preference or feature described herein, ritonavir can be used, for example, from 50 to 200 mg QD, preferably 100 mg QD.

[0019] Compound 1 () is known as (2R,6S,13aS,14aR,16aS,Z)-N-(cyclopropylsulfonyl)-6-(5-methylpyrazine-2-carboxamido)-5,16-dioxo-2-(phenanthridin-6-yloxy)-1,2,3,5,6,7,8,9,10,11,13a,14,14a,15,16,16a-hexadecahydrocyclopropa[e]pyrrolo[1,2-a][1,4]diazacyclopentadecine-14a-carboxamide. The synthesis and formulation of Compound 1 are described in U.S. Patent Application Publication Nos. 2010/0144608 and 2011/0312973 filed on March 8, 2011, respectively.

[0020] Compound 2 () is known as N-(6-(3-tert-butyl-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2H)-yl)-2-methoxyphenyl)naphthalen-2-yl)methanesulfonamide and is described in International Application Publication No. WO2009/039127.

[0021] Compound 4 () is known as dimethyl (2S,2'S)-1,1'-((2S,2'S)-2,2'-(4,4'-((2S,5S)-1-(4-tert-butylphenyl)pyrrolidine-2,5,diyl)bis(4,1-phenylene))bis(azanediyl)bis(oxomethylene)bis(pyrrolidine-2,1-diyl)bis(3-methyl-1-oxobutane-2,1-diyl)dicarbamate, and is described in U.S. Publication No. 2010/0317568.

[0022] In any aspect, embodiment, example, preference or feature described herein, the DAA combination can be used with ribavirin (including a pro-drug thereof). Ribavirin may include any suitable form or formulation of ribavirin. Exemplary formulations of ribavirin include COPEGUS®, REBETOL® and RIBASPHERE®. An exemplary pro-drug of ribavirin is taribavirin having the chemical name of 1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamidine. Ribavirin and taribavirin may be administered in accordance with ribavirin and taribavirin administration well known in the art. In some embodiments, COPEGUS® or REBETOL® is administered in a daily dosage amount of from about 500 mg to about 1500 mg in one dose or in divided doses. In some embodiments, COPEGUS® or REBETOL® is administered in a daily dosage amount of about 800 mg. In some embodiments, REBETOL® is administered in a daily dosage amount of about 1000 mg. In some embodiments, COPEGUS® or REBETOL® is administered in a daily dosage amount of about 1200 mg. In some embodiments, REBETOL® is administered in a daily dosage amount of about 1400 mg. Suitable dosages of ribavirin are dependent on the weight of the subject, for example about 1000-1200 mg. Suitable total daily dosages of ribavirin include, but are not limited to about 400 mg to about 1400 mg a day, alternatively about 800 mg to about 1400 mg per day, alternatively about 400 mg to about 1200 mg, alternatively about 800 mg to about 1200 mg.

[0023] In any aspect, embodiment, example, preference or feature described herein, the DAA combination can be administered to liver transplant recipients before, during, or after liver transplantation for the prevention or treatment of HCV infection.

[0024] In any aspect, embodiment, example, preference or feature described herein, the HCV infection to be treated or prevented can be, for example, genotype 1 infection. The HCV infection can also be, for example, genotype 2 infection. The HCV infection can also be, for example, genotype 3 infection. The HCV infection can also be, for example, genotype 4 infection. The HCV infection can also be, for example, genotype 5 infection. The HCV infection can also be, for example, genotype 6 infection. The HCV infection can also be, for example, genotype 1a infection. The HCV infection can also be, for example, genotype 1b infection.

[0025] Preferably, in any aspect, embodiment, example, preference or feature described herein, the DAA combination is administered to liver transplant recipients after liver transplantation.

[0026] Preferably, in any aspect, embodiment, example, preference or feature described herein, the liver transplant recipient is infected with HCV genotype 1.

[0027] In any aspect, embodiment, example, preference or feature described herein, the liver transplant recipient can be cirrhotic or non- cirrhotic.

[0028] In any aspect, embodiment, example, preference or feature described herein, the liver transplant recipient can be, for example, either HCV-free or infected with HCV prior to the liver transplantation.

[0029] In any aspect, embodiment, example, preference or feature described herein, the liver transplantation can, for example, be a transplantation of the whole liver organ or a portion thereof.

[0030] Various measures may be used to express the effectiveness of the present methods of HCV treatment. One such measure is rapid virological response (RVR), meaning that HCV is undetectable in the subject after 4 weeks of treatment, for example, after 4 weeks of administration of two or more of DAAs and ribavirin. Another measure is the presence or absence of detectable virus at the end of therapy (EOT or EOTR). Another measure is (SVR), which, as used herein, means that the virus is undetectable at the end of therapy and for at least a number of weeks after the end of therapy (i.e., SVRx, where x is the number of weeks after the end of therapy).

[0031] It should be understood that the above-described embodiments and the following examples are given by way of illustration, not limitation. Various changes and modifications within the scope of the present application will become apparent to those skilled in the art from the present description.

Example 1 Clinical Study

[0032] In an ongoing open-label phase 2 study, non-cirrhotic liver transplant recipients with recurrent HCV genotype 1 (GT1) infection received co-formulated Compound 1/ritonavir/Compound 4 (150mg/100mg/25mg QD), together with Compound 2 (250mg BID) and ribavirin, for 24 weeks. The patients were ≥12 months post-liver transplant, had not received treatment for HCV infection after transplantation, and had a screening biopsy confirmed Metavir score≤F2. Because of potential interaction between the calcineurin inhibitor(CNI) and the therapy, the CNI dose was adjusted accordingly.

[0033] Thirty-four patients were enrolled in the study. Baseline characteristics/efficacy are in the table. Treatment-emergent adverse events were observed in 88.2% of patients and were generally mild with no severe events. One patient discontinued. Three patients received erythropoietin and none underwent transfusion. There were no episodes of rejection.

[0034] The result in Table 1 showed that the interferon-free regimen of Compound 1/ritonavir/Compound 4 plus Compound 2 and ribavirin, was generally well-tolerated and achieved high RVR, EOTR, and SVR4 rates in liver transplant recipients with recurrent HCV GT1 infection. High SVR12 rate is expected.

[0035] Further analysis showed that 96.8% of patients (30 out of the total 31 patients tested) achieved SVR4 and 95% (19 out of the total 20 patients tested) achieved SVR12.

Table 1. Baseline characteristics and efficacy.

	Patients N=34
Time since transplantation- months, median (range)	39.5 (12.9-136.4)
Male, n (%)	27 (79.4)
Age- yr, median (range)	60.0 (30.0-71.0)
Race, n (%) Black race White race	 4 (11.8) 29 (85.3)
Hispanic or Latino ethnicity, n (%)	6 (17.6)
BMI- kg/m^2, median (range)	30.1 (19.3-36.9)
HCV subtype, n (%) GT 1a GT1b	 29 (85.3) 5 (14.7)
Immunosuppressive medication, n (%) Tacrolimus Cyclosporine	 29 (85.3) 5 (14.7)
IL28B CC, n (%)	8 (23.5)
Baseline HCV viral load- log_{10} IU/mL, median (range)	6.7 (5.3-7.6)
RVR, n/N (%)	34/34 (100)
EOTR, n/N (%)	13/13 (100)
SVR4, n/N (%)	12/13 (92.3)
Breakthrough, n	0
Relapse, n	1

Example 2 Dose Adjustment

[0036] Example 1 showed the safety and efficacy of 3D + RBV (i.e., co-formulated Compound 1/ritonavir/Compound 4 (150mg/100mg/25mg QD), together with Compound 2 (250mg BID) and ribavirin) in liver transplant (LT) recipients with GT1 HCV infection.

[0037] The Example summarizes the management of concentrations of the immunosuppressants, tacrolimus (TAC) and cyclosporine (CSA) during the treatment. In healthy volunteers, the TAC and CSA concentrations, 24 hours after co-dosing with 3D, showed a 17- and 16-fold increase, respectively, necessitating dose adjustment.

[0038] Patients (n=34) on stable TAC or CSA therapy, at least 12 months post-LT, fibrosis stage ≤ F2, received 3D + RBV for 24 weeks. When co-dosed with 3D, it was recommended that the prestudy total CSA daily dose be reduced to one-fifth and given QD. For TAC, a dose of 0.5 mg/7 days or 0.2 mg/3 days was recommended. Subsequent dose and dosing frequency modifications in TAC were made based on the individual TAC levels. Observed CSA trough concentrations (C_{trough})

were summarized for CSA recipients (n= 5) while TAC data (n= 29) were interrogated further to profile on-study TAC C_{trough}s. A nonlinear mixed effects model was used to characterize TAC concentration-time profiles using NONMEM software. A one compartment pharmacokinetic (PK) model with first order oral absorption and between subject variability on apparent clearance was used to describe the TAC data. The model estimated TAC PK parameters were used to predict TAC concentration-time profiles in order to evaluate TAC dosing strategies when co-dosed with 3D.

[0039] Blood concentrations of TAC (median: 4.6 ng/ml (interquartile range (IQR): 3.3-6.6 ng/ml, dose: 0.2-1 mg)) and CSA (median: 111 ng/ml (IQR: 92-138 ng/ml, dose: 25-75 mg)) were maintained when co-dosed with 3D. The median dosing interval was 10 days for TAC, and 1 day for CsA. Simulations demonstrated that subjects with a stable prestudy TAC C_{trough} of 6 ng/mL, while receiving the 3D with TAC 0.5 mg every 7 days or 14 days, would have TAC C_{trough} in the range of 6-9 ng/ml and 2-4 ng/ml, respectively. For LT recipients with GT1 HCV infection receiving 3D, the recommended CSA or TAC dose modifications yielded concentrations within the therapeutic range.

[0040] The present application also features the following:

WHAT IS CLAIMED IS:

1. A method of treatment for preventing or treating HCV infection in a liver transplant recipient, comprising administering a combination of DAAs to said recipient, wherein said treatment does not comprise the use of interferon, and said treatment last from 4 to 24 weeks.

2. The method of claim 1, wherein said combination of DAAs comprises Compound 1, ritonavir, and Compound 4.

3. The method of claim 1, wherein said combination of DAAs comprises Compound 1, ritonavir, Compound 4 and Compound 2.

4. The method according to one of claims 1-3, wherein the treatment lasts for 12 week.

5. The method according to one of claims 1-3, wherein the treatment lasts for 24 week.

6. The method according to one of claims 1-5, wherein the treatment comprises administering ribavirin to said recipient.

7. The method according to one of claims 1-6, wherein the combination of DAAs is administered to said recipient after liver transplantation on said recipient.

8. The method according to one of claims 1-7, wherein the recipient is HCV-free prior to receiving said liver transplant.

9. The method according to one of claims 1-7, wherein the recipient is infected with HCV prior to receiving said liver transplant.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/071239

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/427 A61K31/4965 A61K31/513 A61K31/7056 A61P31/14
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, BIOSIS, EMBASE, SCISEARCH, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FONTANA, R. J. ET AL.: "First ever successful use of daclatasvir and GS-7977, an interferon-free oral regimen, in a liver transplant recipient with severe recurrent hepatitis C", HEPATHOLOGY, vol. 56, 694, October 2012 (2012-10), page 524a, XP009182678,	1,9
Y	abstract	1-9

X	US 2013/102557 A1 (BERNSTEIN BARRY M [US] ET AL) 25 April 2013 (2013-04-25)	1-9
Y	paragraphs [0013] - [0018]; claims; examples	1-9

	-/--	

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 February 2015	02/03/2015

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Venturini, Francesca

2

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/071239

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2013/102558 A1 (BERNSTEIN BARRY M [US] ET AL) 25 April 2013 (2013-04-25) paragraphs [0013] - [0018]; claims; examples	1-9 1-9
X	POORDAD F ET AL: "12-WEEK INTERFERON-FREE REGIMEN OF ABT-450/R +ABT-333+RIBAVIRIN ACHIEVED SVR12 IN MORE THAN 90% OF TREATMENT-NAIVE HCV GENOTYPE-1-INFECTED SUBJECTS AND 47% OF PREVIOUS NON-RESPONDERS", JOURNAL OF HEPATOLOGY, ELSEVIER, AMSTERDAM, NL, vol. 56, no. Suppl.2, 1 April 2012 (2012-04-01), pages S549-S550, XP009172068, ISSN: 0168-8278 abstract	1-9
X,P	KWO, P.Y. ET AL.: "An Interferon-free antiviral regimen for HCV after liver transplantation", N ENGL J MED, vol. 371, no. 25, 11 November 2014 (2014-11-11), pages 2375-2382, XP009182662, the whole document	1,4,6,7, 9
A	KOSH AGARWAL ET AL: "Treatment of chronic hepatitis C virus infection after liver transplantation", DIGESTIVE AND LIVER DISEASE, vol. 45, 1 September 2013 (2013-09-01), pages S349-S354, XP055170448, ISSN: 1590-8658, DOI: 10.1016/j.dld.2013.07.014 discussion	1-9

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2014/071239

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2013102557 A1	25-04-2013	AR 088463 A1	11-06-2014
		AU 2013201406 A1	09-05-2013
		CL 2014000777 A1	05-09-2014
		CN 103826627 A	28-05-2014
		DE 112012002748 T5	31-07-2014
		DE 202012012956 U1	16-10-2014
		DE 202012012958 U1	12-08-2014
		DE 202012013111 U1	14-01-2015
		DK 2583677 T1	19-01-2015
		DO P2014000049 A	15-04-2014
		EA 201490837 A1	28-11-2014
		EP 2583677 A2	24-04-2013
		ES 2527510 T1	26-01-2015
		ES 2529143 A2	17-02-2015
		GB 2506086 A	19-03-2014
		GB 2515941 A	07-01-2015
		JP 2014532627 A	08-12-2014
		PT 107665 A	16-07-2014
		PT 107894 A	31-10-2014
		SE 1450019 A1	10-01-2014
		SE 1450130 A1	07-05-2014
		TW 201321005 A	01-06-2013
		US 2013102557 A1	25-04-2013
		US 2015024999 A1	22-01-2015
		UY 34402 A	31-05-2013
		WO 2013059630 A1	25-04-2013
US 2013102558 A1	25-04-2013	GB 2511699 A	10-09-2014
		US 2013102558 A1	25-04-2013
		US 2014057835 A1	27-02-2014
		US 2014107016 A1	17-04-2014