2.0 Synopsis

AbbVie GK	**Individual Study Table Referring to Part of Dossier:** **Volume:** **Page:**	**(For National Authority Use Only)**
Name of Study Drug: ABT-493/ABT-530		
Name of Active Ingredient: ABT-493: (3aR,7S,10S,12R,21E,24aR)-7-tert-butyl-N-{(1R,2R)-2-(difluoromethyl)-1-[(1-methylcyclopropane-1-sulfonyl)carbamoyl]cyclopropyl}-20,20-difluoro-5,8-dioxo-2,3,3a,5,6,7,8,11,12,20,23,24a-dodecahydro-1H,10H-9,12-methanocyclopenta[18,19][1,10,17,3,6]trioxadiazacyclononadecino[11,12-b]quinoxaline-10-carboxamide hydrate ABT-530: Methyl {(2*S*,3*R*)-1-[(2*S*)-2-{5-[(2*R*,5*R*)-1-{3,5-difluoro-4-[4-(4-fluorophenyl)piperidin-1-yl]phenyl}-5-(6-fluoro-2-{(2*S*)-1-[*N*-(methoxycarbonyl)-*O*-methyl-L-threonyl]pyrrolidin-2-yl}-1*H*-benzimidazol-5-yl)pyrrolidin-2-yl]-6-fluoro-1*H*-benzimidazol-2-yl}pyrrolidin-1-yl]-3-methoxy-1-oxobutan-2-yl}carbamate		
Title of Study: A Randomized, Open-Label, Multicenter Study to Evaluate the Efficacy and Safety of ABT-493/ABT-530 in Japanese Adults with Chronic Hepatitis C Virus Infection (CERTAIN-1)		
Coordinating Investigator: [redacted]		
Study Sites: A total of 62 investigative sites were approved to receive drug supplies on behalf of AbbVie and screen and enroll subjects into the study.		
Publications: Not applicable		

Studied Period (Years): First Subject First Visit: 22 February 2016 Last Subject Last Visit: 09 February 2017	**Phase of Development:** 3

Objectives:

The primary objectives of this study were to assess:

- The safety of 8 weeks of treatment with the combination regimen ABT-493/ABT-530 compared to 12 weeks of treatment with ombitasvir/paritaprevir/ritonavir (OBV/PTV/r) in hepatitis C virus (HCV) genotype (GT)1-infected Japanese adults without cirrhosis;
- The efficacy of 8 weeks of treatment with the combination regimen ABT-493/ABT-530 compared to 12 weeks of treatment with OBV/PTV/r in HCV GT1-infected Japanese adults without cirrhosis and without Y93H polymorphism.

The secondary objectives were to assess:

- The percentages of subjects achieving sustained virologic response 12 weeks post dosing (SVR_{12}) in HCV GT1-infected Japanese adults without cirrhosis treated with the ABT-493/ABT-530 combination regimen;
- The percentages of subjects achieving SVR_{12} for each subpopulation in Substudy 2 (HCV GT1-infected cirrhotic subjects, HCV GT2-infected cirrhotic subjects, prior direct-acting antiviral agent (DAA)-experienced subjects, HCV GT3-, GT4-, GT5- or GT6-infected subjects, and subjects with severe renal impairment);
- The percentages of subjects with on-treatment virologic failure;
- The percentages of subjects with post-treatment relapse.

Additional objectives were to assess pharmacokinetic (PK) and emergence and persistence of viral variants in these treatment regimens.

Methodology:

This was a Phase 3, multicenter study to evaluate efficacy, safety, and PK of coformulated ABT-493/ABT-530 (300 mg/120 mg) once daily (QD) in chronic HCV-infected, HCV DAA treatment-naïve, and DAA treatment-experienced Japanese adult subjects. The study consisted of 2 substudies that enrolled in parallel.

Substudy 1 was randomized, open-label, and active-controlled, wherein HCV treatment-naïve or interferon (IFN)-experienced (i.e., DAA treatment-naïve), GT1-infected subjects without cirrhosis were enrolled. Prior to randomization, the HCV from eligible subjects was tested for the Y93H polymorphism. Subjects whose HCV tested negative for Y93H were randomized 2:1 to Arm A or Arm B. Randomization was stratified by prior IFN-experience (naïve versus experienced), and Screening HCV ribonucleic acid (RNA) viral load ($< \text{or} \geq 6$ million International Units [IU]/mL). All subjects whose HCV tested positive for Y93H were assigned to Arm A. All subjects in Arm A received treatment with 8 weeks of ABT-493/ABT-530 QD, and subjects in Arm B received 12 weeks of OBV/PTV/r QD.

Methodology (Continued):

Substudy 2 was nonrandomized, open label, and enrolled special populations of HCV-infected subjects. Hepatitis C virus GT1- or GT2-infected subjects with compensated cirrhosis, HCV GT3-, 4-, 5- and 6-infected subjects (with compensated cirrhosis or without cirrhosis), HCV GT1- and GT2-infected subjects who had failed prior DAA treatments (with compensated cirrhosis or without cirrhosis), and HCV GT1- or GT2-infected subjects with severe renal impairment and compensated cirrhosis were assigned to Arm C and received treatment with ABT-493/ABT-530 (300 mg/120 mg) QD for 12 weeks. Hepatitis C virus GT1- or GT2-infected subjects with severe renal impairment and without cirrhosis were assigned to Arm D and received ABT-493/ABT-530 (300 mg/120 mg) QD for 8 weeks.

This study consisted of a treatment period and post-treatment period, as described below:

Treatment Period: Subjects enrolled into Substudy 1 received 8 weeks of ABT-493/ABT-530 or 12 weeks of OBV/PTV/r. Subjects enrolled in Substudy 2 received 8 or 12 weeks of ABT-493/ABT-530.

Post-Treatment Period: Subjects who completed the Treatment Period, experienced on-treatment virologic failure, or prematurely discontinued the Treatment Period were followed for 24 weeks after receipt of the last dose of study drug to monitor safety, HCV RNA levels, and to evaluate efficacy and the emergence and persistence of viral resistance-associated variants.

Number of Subjects (Planned and Analyzed):

The study was designed to enroll 245 subjects to meet scientific and regulatory objectives without enrolling an undue number of subjects in alignment with ethical considerations. A total of 295 subjects were enrolled in the study at 62 study sites.

Diagnosis and Main Criteria for Inclusion:

Main Inclusion Criteria

Subjects were Japanese males or females at least 18 years of age.

Females were postmenopausal for at least 2 years; surgically sterile or had a vasectomized partner; or, if of childbearing potential and sexually active with a male partner, were currently using at least 1 effective method of birth control at the time of Screening and agreed to practice 1 effective method of birth control from Screening through 30 days after stopping study drug. Sexually active males were surgically sterile or, if sexually active with a female partner of childbearing potential, agreed to practice 1 effective form of birth control from Screening through 30 days after stopping study drug.

All subjects had chronic HCV infection with a single GT; positive results for anti-HCV antibody; and a plasma HCV RNA viral load of $\geq$ 1000 IU/mL at Screening.

Subjects were defined as HCV DAA treatment-naïve if they had not received a single dose of any approved or investigational DAA. Subjects were defined as HCV DAA treatment-experienced if they had received any approved, commercially available HCV DAA treatment in Japan. All previous HCV DAA and/or IFN treatment must have been completed at least 2 months prior to Screening.

Diagnosis and Main Criteria for Inclusion (Continued):

Noncirrhotic Subjects were Included as Follows:

The absence of cirrhosis was demonstrated by the results of a liver biopsy within 24 months prior to or during Screening (e.g., a Meta-analysis of Histological Data in Viral Hepatitis [METAVIR], Batts-Ludwig, Knodell, International Association for the Study of Liver [IASL], Scheuer, New Inuyama, or Laennec fibrosis score of ≤ 3 or an Ishak fibrosis score of ≤ 4); a FibroScan® score of < 12.5 kPa within 6 months of or during Screening; a Screening FibroTest score of score of ≤ 0.72 and aspartate aminotransferase/platelet ratio index (APRI) ≤ 2; or a Screening Discriminant Score less than 0.

Subjects with Compensated Cirrhosis were Included as Follows:

The presence of cirrhosis was demonstrated by the results of a liver biopsy within 24 months prior to or during Screening (e.g., a METAVIR, Batts-Ludwig, Knodell, IASL, Scheuer, or New Inuyama fibrosis score > 3 [including 3 – 4 or 3/4]; a Laennec fibrosis score of > 3; or an Ishak fibrosis score of > 4); a FibroScan score of ≥ 14.6 kPa within 6 months of or during Screening; a FibroTest score of ≥ 0.73 and APRI > 2; or a Screening Discriminant Score greater than 0. Subjects with compensated cirrhosis were required to have absence of hepatocellular carcinoma, as indicated by ultrasound, computed tomography scan, or magnetic resonance imaging within 3 months prior to or during Screening.

Subjects with Severe Renal Impairment were Included as Follows:

The presence of severe renal impairment was demonstrated by an estimated glomerular filtration rate of < 30 mL/min/1.73 m^2.

Main Exclusion Criteria

- Females who were pregnant or planned to become pregnant, or breastfeeding or males whose partner was pregnant or planning to become pregnant during the study.
- Subjects coinfected with hepatitis B virus or human immunodeficiency virus.
- Use of contraindicated medications or supplements within 2 weeks or 10 half-lives (if known), whichever was longer, prior to the first dose of any study drug.
- Any cause of liver disease other than chronic HCV infection, including (but not limited to) hemochromatosis, alpha-1 antitrypsin deficiency, Wilson's disease, autoimmune hepatitis, alcoholic liver disease, or steatohepatitis considered to be the primary cause of the liver disease rather than concomitant/incidental with HCV infection.
- Any current or past clinical evidence of Child-Pugh B or C classification or clinical history of decompensated liver disease (e.g., ascites noted on physical exam, hepatic encephalopathy, or variceal bleeding).
- Any of the following laboratory abnormalities:
    - Estimated glomerular filtration rate < 30 mL/min/1.73 m^2 (except for subjects with severe renal impairment in Substudy 2)
    - Albumin < lower limit of normal (for noncirrhotic subjects) or < 2.8 g/dL (for subjects with compensated cirrhosis)
    - International normalized ratio ≥ 1.2 (for noncirrhotic subjects) or ≥ 1.8 (for subjects with compensated cirrhosis)
    - Hemoglobin < 10 g/dL
    - Platelets < 90,000 cells/mm^3 (for noncirrhotic subjects) or < 50,000 cells/mm^3 (for subjects with compensated cirrhosis)

Test Product, Dose/Strength/Concentration, Mode of Administration and Lot Number:

Investigational Product	Manufacturer	Mode of Administration	Dosage Form	Strength	Bulk Lot Number
ABT-493/ ABT-530	AbbVie	Oral	Tablet	100 mg/ 40 mg	15-006595

Duration of Treatment:

Subjects received ABT-493/ABT-530 (300/120 mg) for 8 or 12 weeks or OBV/PTV/r for 12 weeks.

Reference Therapy, Dose/Strength/Concentration and Mode of Administration and Lot Number:

Investigational Product	Manufacturer	Mode of Administration	Dosage Form	Strength	Bulk Lot Number
ombitasvir/ paritaprevir/ ritonavir	AbbVie	Oral	Tablet	12.5 mg/ 75 mg/ 50 mg	14-005707

Criteria for Evaluation

Efficacy:

Virologic response was assessed by plasma HCV RNA levels in IU/mL at various time points from Day 1 through 24 weeks after completion of treatment.

The primary efficacy variable was SVR_{12} (HCV RNA < lower limit of quantification 12 weeks after the last actual dose of study drug).

The secondary efficacy variables were on-treatment virologic failure and post-treatment relapse.

Resistance:

For all subjects receiving ABT-493/ABT-530, the variants at signature amino acid positions at baseline identified by population or deep sequencing and comparison to the appropriate prototypic reference sequence were analyzed.

The following resistance information was analyzed for subjects receiving ABT-493/ABT-530 who did not achieve SVR_{12} and who had a post-baseline sample with HCV RNA ≥ 1000 IU/mL:

- The amino acid variants in available post-baseline samples identified by population or deep sequencing and comparison to the baseline sequence
- The amino acid variants in available post-baseline samples at signature resistance-associated positions identified by population or deep sequencing and comparison to the appropriate prototypic reference sequence, and
- The persistence of viral resistance by population or deep sequencing.

Safety:

The following safety evaluations were performed during the study: adverse events (AEs), which include common AEs, serious AEs, AEs that cause treatment discontinuation and deaths, changes in vital signs, physical examination findings, and laboratory tests assessments.

Criteria for Evaluation (Continued)

Pharmacokinetic:

Individual plasma concentrations of ABT-493, ABT-530, ombitasvir, paritaprevir, ritonavir, and possible metabolites were tabulated and summarized.

Pharmacogenetic:

Interleukin 28B status was determined for each subject and analyzed as a factor contributing to the subject's response to study treatment.

Quality of Life:

The following patient-reported outcomes (PROs) were evaluated: EuroQol 5 Dimensions 3 Levels Health State Instrument (EQ-5D-3L), visual analogue scale (VAS), and Fatigue Severity Scale (FSS).

Statistical Methods

All analyses were performed on randomized subjects who received at least 1 dose of study drug, unless otherwise specified. The primary analysis presented in this clinical study report occurred after all subjects had completed the Post-Treatment Week 12 Visit or prematurely discontinued from the study. No data were imputed for any efficacy or safety analysis except for analyses of sustained virologic response (SVR) endpoints (HCV RNA data) and the PRO questionnaires.

Efficacy:

Plasma HCV RNA levels were determined for each sample collected by the central laboratory using the Roche COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Test, v2.0. In addition to the analyses of the primary and secondary endpoints described below, sensitivity and subgroup analyses of efficacy were performed on prespecified subject populations.

Primary Efficacy Endpoint

The following primary efficacy analysis for Substudy 1 was performed on the intent-to-treat (ITT) subset of HCV-infected subjects without the Y93H polymorphism at Screening, denoted as the ITT primary subset (ITT-PS) population.

For the primary efficacy endpoint in Substudy 1, to show noninferiority in SVR_{12} rates of the 8-week regimen (Arm A) compared with the 12-week regimen (Arm B), the percentage of subjects achieving SVR_{12} was calculated for each arm. A 2-sided 95% confidence interval (CI) for the difference in SVR_{12} rates (Arm A minus Arm B) was calculated using the normal approximation to the binomial distribution. All subjects in the ITT-PS population were used when calculating SVR_{12}. If the lower bound of the CI for the difference was above the noninferiority margin of –10%, then the 8-week regimen (ABT-493/ABT-530) was considered noninferior to the 12-week regimen (OBV/PTV/r).

Secondary Endpoints

The percentage of subjects in Arm A achieving SVR_{12} in the ITT population, the percentage of subjects achieving SVR_{12} for each subpopulation in Substudy 2, the percentage of subjects with on-treatment virologic failure, and the percentage of subjects with post-treatment relapse were summarized along with 95% CIs, where applicable, using the normal approximation to the binomial distribution or the Wilson score methods.

Statistical Methods (Continued)

Patient-Reported Outcomes:

The mean change from baseline to each applicable post-baseline time point in the FSS total score, EQ-5D-3L health index score, and VAS score was summarized descriptively at each visit and for change from baseline to each visit by treatment arm. For each of these scores, mean change from Baseline to the Final Treatment Visit and from Baseline to Post-Treatment Week 12 was compared between treatment Arms A and B using an analysis of covariance model with treatment arm as a factor and baseline score as a covariate.

Resistance:

The following resistance information was analyzed for all baseline samples from subjects: 1) the prevalence of variants at signature amino acid positions at baseline identified by next-generation sequencing (NGS) were compared to the appropriate subtype specific prototypic reference sequence; and, (2) a comparison of SVR_{12} rates in subjects with or without baseline variants was conducted. For subjects experiencing virologic failure, variants at postbaseline time points identified by NGS were compared to the respective baseline sequence and to a subtype-specific reference sequence.

HCV Genotype/Subtype:

Phylogenetic analysis was conducted on all available HCV sequences from baseline samples in order to accurately determine HCV subtype.

Safety:

The number and percentage of subjects in each arm with treatment-emergent AEs (TEAEs; defined as any event that began or worsened in severity after initiation of study drug through 30 days post-study drug dosing) were tabulated by primary Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class (SOC) and preferred term and compared between arms using Fisher's exact test. The number of subjects with TEAEs by severity grade and relationship to study drug was also tabulated. Subjects reporting more than 1 AE for a given MedDRA preferred term or SOC were counted only once for that term or SOC using the most severe grade for the severity grade table and the most related for the relationship to study drug tables.

Clinical laboratory tests values and changes from baseline were summarized by arm at each visit. Mean changes from baseline to each post-baseline visit were compared between arms using contrasts within an analysis of variance (ANOVA) model with treatment arm as the factor. The number and percentage of subjects with post-baseline shifts or a maximum of at least grade 3 for the laboratory parameters were summarized by arm. Laboratory abnormalities (by toxicity grade) for each parameter were compared using Fisher's exact tests.

Mean changes in vital signs from baseline to each post-baseline visit were summarized descriptively by arm and compared using contrasts within an ANOVA model with treatment arm as the factor. Frequencies and percentages of subjects with post-baseline values meeting pre-defined criteria for potentially clinically significant vital signs values were summarized and compared using Fisher's exact tests.

Pharmacokinetic:

Plasma concentrations of and PK parameter values for ABT-493, ABT-530, ombitasvir, paritaprevir, ritonavir, and, if applicable, their possible metabolites were tabulated for each subject and group. Summary statistics were computed for each time and visit.

Summary/Conclusions

Efficacy Results:

High SVR_{12} rates were observed in subjects enrolled in Substudy 1 as follows:

- HCV GT1-infected, DAA treatment-naïve, Japanese subjects without cirrhosis (including 23 subjects with the Y93H polymorphism in nonstructural viral protein 5A [NS5A]) treated with 8 weeks of ABT-493/ABT-530 (300 mg/120 mg) QD achieved an SVR_{12} rate of 99.2% (128/129).
  - The 8-week regimen of ABT-493/ABT-530 (SVR_{12} rate: 99.1%) was noninferior to 12 weeks of OBV/PTV/r (SVR_{12} rate: 100%) in subjects without the Y93H polymorphism in NS5A, as the difference between arms was –0.9% (95% CI: –2.8%, 0.9%; lower confidence bound above the noninferiority margin –10%).
  - All 23 subjects with the Y93H polymorphism in NS5A achieved SVR_{12} following 8 weeks of treatment with ABT-493/ABT-530, indicating the presence of this polymorphism at baseline had no impact on treatment outcome.
  - There were no virologic failures in subjects treated with 8 weeks of ABT-493/ABT-530.

High SVR_{12} rates were also observed across all special populations enrolled in Substudy 2, including the following:

- A 100% SVR_{12} rate was achieved in DAA treatment-naïve subjects with HCV GT1 (38 subjects) or GT2 (18 subjects) infection with compensated cirrhosis treated with 12 weeks of ABT-493/ABT-530.
- A 93.9% SVR_{12} rate (31/33) was achieved in subjects who failed prior treatment with a DAA and were treated with 12 weeks of ABT-493/ABT-530.
- 93.3% (28/30) of subjects previously treated with both an NS5A inhibitor and a protease inhibitor (PI) achieved SVR_{12}.
- An 83.3% SVR_{12} rate (10/12) was achieved in HCV GT3-infected subjects with compensated cirrhosis or without cirrhosis and with or without prior pegylated IFN/ribavirin experience who were treated with 12 weeks of ABT-493/ABT-530.
- A 100% SVR_{12} rate was achieved in HCV GT1- and GT2-infected subjects with severe renal impairment with either 8 weeks (10 subjects without cirrhosis) or 12 weeks (2 subjects with compensated cirrhosis) of ABT-493/ABT-530.

No subject who achieved SVR_{12} relapsed between Post-Treatment Week 12 and Post-Treatment Week 24.

Patient-Reported Outcomes Results:

Overall, regardless of cirrhosis status or renal impairment, treatment with ABT-493/ABT-530 had little impact on health state at end of treatment (mean changes in EQ-5D-3L of 0.02 – 0.03), quality of life (mean changes of 0.10 – 8.91), or fatigue (mean changes of –0.20 – 0.20).

Summary/Conclusions (Continued)

Resistance Results:

Based on phylogenetic analysis of 288 HCV nonstructural viral protein 3/4A (NS3/4A) and/or NS5A sequences, the number of subjects infected with each of the following HCV subtypes was 4 GT1a, 246 GT1b (including 50 in Arm B), 14 GT2a, 12 GT2b, 7 GT3a, 4 GT3b, and 1 GT3k.

The prevalence of baseline polymorphisms was similar at 2% and 15% detection thresholds. At the 15% detection threshold, among GT1b-infected DAA treatment-naïve subjects in Arms A, C, and D, the prevalence of nonstructural viral protein 3 (NS3) D168E was 1.2% (2/162), NS5A L31M was 3.7% (6/161), and NS5A Y93H was 18.0% (29/161); 1 of these subjects had L31M + Y93H in NS5A. Among GT1b-infected DAA-experienced subjects in Arm C, the prevalence of NS3 D168E/T/V was 48.4% (15/31), NS5A L31F/I/M/V was 81.3% (26/32), and NS5A Y93H was 59.4% (19/32). Of these, 13 subjects had NS3 D168E/T/V in combination with NS5A L31F/I/M/V or with Y93H, and 19 subjects had L31F/I/M/V + Y93H in NS5A.

Among DAA treatment-naïve subjects, there were no virologic failures in subjects infected with GT1 or GT2. Two GT3-infected subjects experienced virologic failure. As the total number of GT3-infected subjects in this study was low (N = 12) and the subtypes were diverse, the impact of baseline polymorphisms on treatment outcome could not be assessed. Among DAA treatment-experienced subjects in Arm C, 2 GT1b-infected subjects who were previously treated with PI + NS5A inhibitors experienced virologic failure. Baseline polymorphisms in NS3 and/or NS5A including subjects with polymorphisms at amino acid position 168 in NS3 or positions 31 or 93 in NS5A had no impact on SVR_{12}. The 2 DAA treatment-experienced GT1b-infected subjects who experienced virologic failure both had P32deletion in NS5A at baseline. P32deletion confers high level resistance to ABT-530. Both of these subjects had previously been treated with a regimen containing asunaprevir and daclatasvir. P32deletion is an uncommon treatment-emergent substitution in patients who have been treated with a daclatasvir-containing regimen.

Among the NS5A-inhibitor and PI-experienced GT1b-infected virologic failure subjects, treatment-emergent substitutions A156D/V in NS3 were detected in 1 of the 2 subjects (D168V was also present at baseline and post-baseline in this subject). In NS5A, P32L/P32deletion and L31F/P32deletion were each present at both baseline and post-baseline in 1 DAA-experienced virologic failure subjects. Among GT3 virologic failures, NS3 sequences were not available for analyses; treatment-emergent substitutions L28F and/or Y93H were detected in NS5A (with G92E and V31M in NS5A each present at baseline and post-baseline in 1 subject). Among subjects with available data, treatment-emergent A156D/V in NS3 did not persist through Post-Treatment Week 24. Amino acid substitutions in NS5A remained detectable through Post-Treatment Week 24.

Pharmacokinetic Results:

ABT-493 and ABT-530 concentrations were comparable between the 8-week and 12-week treatment durations, irrespective of prior HCV treatment history or the presence of severe renal impairment. ABT-493 concentrations in HCV-infected subjects with compensated cirrhosis were higher compared to subjects without cirrhosis, while ABT-530 concentrations were comparable between subjects without cirrhosis and subjects with compensated cirrhosis.

Summary/Conclusions (Continued)

Safety Results:

- The fixed-dose combination of ABT-493/ABT-530 300 mg/120 mg QD administered for 8 and 12 weeks was well tolerated by Japanese subjects including those without cirrhosis, with compensated cirrhosis, and with severe renal impairment, including those on dialysis.
- A similar safety profile was observed between HCV GT1-infected, DAA treatment-naïve, Japanese subjects treated with either ABT-493/ABT-530 300 mg/120 mg QD administered for 8 weeks or OBV/PTV/r QD for 12 weeks.
- Overall, among subjects treated with ABT-493/ABT-530, the most common (≥ 5.0% of subjects) TEAEs were nasopharyngitis, pruritus, and headache.
- The majority of subjects who experienced TEAEs had a maximum severity of grade 1 (mild) or grade 2 (moderate).
- The 1 treatment-related TEAE that was reported in ≥ 5% of subjects treated with ABT-493/ABT-530 was pruritus and most events were mild.
- No unique safety concerns related to ABT-493/ABT-530 were identified among subjects with compensated cirrhosis or severe renal impairment.
- The overall safety profile of ABT-493/ABT-530 was similar in cirrhotics and noncirrhotics.
- The overall safety profile of ABT-493/ABT-530 was similar in subjects with severe renal impairment and in those without.
- No treatment-related serious AEs were reported in subjects treated with ABT-493/ABT-530, and treatment discontinuations were rare (< 1%).
- No significant pattern of laboratory abnormalities was observed.
- No cases consistent with drug-induced liver injury or hepatic decompensation were identified. One case of hepatocellular carcinoma (HCC) was identified in a cirrhotic, treatment-naïve subject treated with ABT-493/ABT-530 (without severe renal impairment) approximately 3 months after the last dose of study drug.
- No deaths were reported in the study.

Conclusions:

- The fixed-dose regimen of ABT-493/ABT-530 300 mg/120 mg QD for 8 weeks achieved high efficacy in HCV GT1-infected, DAA treatment-naïve, Japanese subjects without cirrhosis, achieved high efficacy (SVR_{12} rate of 99.2%) regardless of the presence of baseline polymorphisms in NS3 and/or NS5A (including those at positions 31 and 93). ABT-493/ABT-530 for 8 weeks was noninferior to OBV/PTV/r for 12 weeks (100%).
- ABT-493/ABT-530 for 12 weeks achieved high efficacy in GT1 and GT2 DAA-naïve cirrhotics (100%), prior DAA failures including subjects who had previously failed NS5A inhibitors and/or a PI (93.9%), and GT3 with or without cirrhosis (83.3%). In addition, 100% of subjects with severe renal impairment achieved SVR_{12} with 8 or 12 weeks in noncirrhotics and cirrhotics, respectively.
- The fixed-dose combination of ABT-493/ABT-530 300 mg/120 mg QD was well-tolerated by Japanese HCV-infected subjects and demonstrated a favorable safety profile, with most AEs being mild to moderate in severity. The only related TEAE that occurred in ≥ 5% of subjects was pruritus. No unique safety concerns were observed in subjects with compensated cirrhosis, without cirrhosis or those with severe renal impairment.