



Clinical trial results:

A Follow-up Study to Assess Resistance and Durability of Response to AbbVie Direct-Acting Antiviral Agent (DAA) Therapy (ABT-493 and/or ABT-530) in Subjects Who Participated in Phase 2 or 3 Clinical Studies for the Treatment of Chronic Hepatitis C Virus (HCV) Infection

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2015-000452-24 |
| Trial protocol | BE DE |
| Global end of trial date | 04 December 2019 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 09 October 2020 |
| First version publication date | 09 October 2020 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | M13-576 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02441283 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | AbbVie |
| Sponsor organisation address | AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United Kingdom, SL6-4UB |
| Public contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |
| Scientific contact | Global Medical Services, AbbVie, 001 8006339110, abbvieclinicaltrials@abbvie.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 04 December 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 04 December 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This was a long-term, Phase 2/3, multicenter, follow-up study to evaluate the durability of sustained virologic response (SVR), persistence of direct-acting antiviral agent (DAA) resistance, and clinical outcomes for subjects who received glecaprevir (ABT-493) and/or pibrentasvir (ABT-530) in prior AbbVie Phase 2 or 3 clinical studies for the treatment of chronic hepatitis C virus (HCV) infection. The subject must have completed the follow-up period of the prior eligible AbbVie study. To be included in the analyses, the subject must not have been retreated prior to enrolling in this study. Subjects were followed for a total of approximately 3 years after their last dose of DAA in the previous HCV clinical study. The 3 years were inclusive of any post-treatment period in the prior study, as well as any gaps between the end of the prior study and enrollment in this study.

Protection of trial subjects:

Subject read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 22 June 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 39 |
| Country: Number of subjects enrolled | Canada: 18 |
| Country: Number of subjects enrolled | New Zealand: 12 |
| Country: Number of subjects enrolled | Puerto Rico: 24 |
| Country: Number of subjects enrolled | United States: 222 |
| Country: Number of subjects enrolled | United Kingdom: 26 |
| Country: Number of subjects enrolled | Belgium: 30 |
| Country: Number of subjects enrolled | Germany: 6 |
| Worldwide total number of subjects | 377 |
| EEA total number of subjects | 62 |

Notes:

Subjects enrolled per age group

| | |
|----------|---|
| In utero | 0 |
|----------|---|

| | |
|---|-----|
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 320 |
| From 65 to 84 years | 57 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Full Analysis Set (FAS): subjects who rcvd ABT-493 and/or ABT-530 in a prior Phase 2/3 study and weren't retreated prior to enrolling in this study. 3 subjects were retreated prior to enrollment in this study and 4 didn't receive ABT-493 and/or ABT-540 in prior study and were excluded from the FAS. Baseline data= values at time of prior study start.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|---------------------------|
| Arm title | HCV-infected Participants |
|-----------|---------------------------|

Arm description:

Hepatitis C virus (HCV)-infected participants who received ABT-493 and/or ABT-530 in prior Phase 2 or 3 clinical studies with these agents for the treatment of chronic HCV and were not retreated prior to entering this study. No AbbVie study drug was administered in this study.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Glecaprevir |
| Investigational medicinal product code | |
| Other name | ABT-493 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-493 was not administered in this study. This study was a follow-up for participants who received the drug in prior studies.

| | |
|--|--------------|
| Investigational medicinal product name | Pibrentasvir |
| Investigational medicinal product code | |
| Other name | ABT-530 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

ABT-530 was not administered in this study. This study was a follow-up for participants who received the drug in prior studies.

| Number of subjects in period 1 | HCV-infected Participants |
|---------------------------------------|------------------------------|
| Started | 377 |
| Completed | 287 |
| Not completed | 90 |
| Death | 1 |
| Other, not specified | 32 |
| Withdrew consent | 15 |
| Lost to follow-up | 42 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------|
| Reporting group title | Overall Study |
|-----------------------|---------------|

Reporting group description:

Full Analysis Set (FAS): all subjects who received ABT-493 and/or ABT-530 in a prior Phase 2/3 study and were not retreated prior to enrolling in this study. Three subjects who received retreatment prior to enrollment in this study and four subjects who did not receive ABT-493 and/or ABT-540 in a prior study were excluded from the FAS.

| Reporting group values | Overall Study | Total | |
|---|-----------------|-------|--|
| Number of subjects | 377 | 377 | |
| Age categorical Units: Subjects | | | |
| Age continuous Units: years arithmetic mean standard deviation | 54.1 ± 10.96 | - | |
| Gender categorical Units: Subjects | | | |
| Female | 172 | 172 | |
| Male | 205 | 205 | |

End points

End points reporting groups

| | |
|---|---------------------------|
| Reporting group title | HCV-infected Participants |
| Reporting group description: Hepatitis C virus (HCV)-infected participants who received ABT-493 and/or ABT-530 in prior Phase 2 or 3 clinical studies with these agents for the treatment of chronic HCV and were not retreated prior to entering this study. No AbbVie study drug was administered in this study. | |

Primary: Percentage of Participants Who Maintained a Sustained Virologic Response (SVR) Out of Those Who Achieved SVR12 in a Prior Study With an ABT-493- and/or ABT-530-containing Regimen

| | |
|-----------------|---|
| End point title | Percentage of Participants Who Maintained a Sustained Virologic Response (SVR) Out of Those Who Achieved SVR12 in a Prior Study With an ABT-493- and/or ABT-530-containing Regimen ^[1] |
|-----------------|---|

End point description:

Maintaining a sustained virologic response (SVR) is defined as having Hepatitis C virus ribonucleic acid (HCV RNA) value consistently below the lower limit of quantification (< LLOQ) from the end of treatment in the previous study throughout Study M13-576 (this study).

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the end of treatment in the previous study up to 3 years post-treatment

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable for this endpoint.

| End point values | HCV-infected Participants | | | |
|-----------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 376 ^[2] | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | 99.5 | | | |

Notes:

[2] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants Who Relapsed or Had a New Hepatitis C Virus (HCV) Infection at Any Time up to the Last Follow-up in This Study Among Participants Who Achieved SVR12 in a Prior Study With an ABT-493- and/or ABT-530-containing Regimen

| | |
|-----------------|--|
| End point title | Percentage of Participants Who Relapsed or Had a New Hepatitis C Virus (HCV) Infection at Any Time up to the Last Follow-up in This Study Among Participants Who Achieved SVR12 in a Prior Study With an ABT-493- and/or ABT-530-containing Regimen ^[3] |
|-----------------|--|

End point description:

Relapse was defined as confirmed Hepatitis C virus ribonucleic acid (HCV RNA) greater than or equal to the lower limit of quantification (\geq LLOQ) between end of treatment and up to and including the last

HCV RNA measurement collected in this study for a participant with HCV RNA < LLOQ at Final Treatment Visit who completed treatment, excluding reinfection. HCV reinfection was defined as confirmed HCV RNA ≥ LLOQ after the end of treatment in a participant who had HCV RNA < LLOQ at Final Treatment Visit, along with the post-treatment detection of a different HCV genotype, subtype, or clade compared with baseline, as determined by phylogenetic analysis of the NS3 or NS5A, and/or NS5B gene sequences.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From the end of treatment in the previous study up to 3 years post-treatment

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable for this endpoint.

| | | | | |
|-----------------------------------|---------------------------|--|--|--|
| End point values | HCV-infected Participants | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 376 ^[4] | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Relapse overall | 0.3 | | | |
| Reinfection overall | 0.3 | | | |

Notes:

[4] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Persistence of Resistance-Associated Amino Acid Variants Among Those Experiencing Virologic Failure

| | |
|-----------------|--|
| End point title | Number of Participants With Persistence of Resistance-Associated Amino Acid Variants Among Those Experiencing Virologic Failure ^[5] |
|-----------------|--|

End point description:

Plasma samples for HCV resistance testing were collected at study visits. The variants in nonstructural viral protein 3 (NS3) and nonstructural viral protein 5A (NS5A) at amino acid positions of interest were analyzed by next generation sequencing relative to baseline and prototypic reference sequences.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Day 1 to Month 12

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable for this endpoint.

| | | | | |
|--------------------------------------|---------------------------|--|--|--|
| End point values | HCV-infected Participants | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 1 ^[6] | | | |
| Units: participants | | | | |
| NS3 Variants at Months 3, 6, and 12 | 1 | | | |
| NS5A Variants at Months 3, 6, and 12 | 1 | | | |

Notes:

[6] - Subjects w/ virologic failure in prior/current study and NS3/4A and/or NS5A sequencing data

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Medical Events Related to Progression of Liver Disease or Hepatitis C Virus Infection

| | |
|-----------------|---|
| End point title | Number of Participants With Medical Events Related to Progression of Liver Disease or Hepatitis C Virus Infection |
|-----------------|---|

End point description:

Any events (i.e., diagnoses) related to liver disease progression and/or HCV infection considered to be clinically significant by the investigator that began or worsened after Day 1 were documented until the end of the study or initiation of re-treatment for HCV (if applicable). Significant events related to liver disease progression include the development of cirrhosis, events indicative of hepatic decompensation, (including: variceal bleeding, new ascites, spontaneous bacterial peritonitis, hepatic encephalopathy, hepato-renal syndrome, hepatic hydrothorax or other evidence of hepatic decompensation considered to be significant by the investigator), change in the Child-Pugh category (e.g., change from Child-Pugh Class A to Child-Pugh Class B), the occurrence of hepatocellular carcinoma, liver transplantation and/or death.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

After Day 1 up to 3 years post-treatment

| End point values | HCV-infected Participants | | | |
|--|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 377 ^[7] | | | |
| Units: participants | | | | |
| Medical events related to liver disease or HCV inf | 7 | | | |
| Development of cirrhosis | 0 | | | |
| Liver decompensation (Variceal bleeding) | 0 | | | |
| Liver decompensation (Ascites) | 0 | | | |
| Liver decomp (spontaneous bacterial peritonitis) | 0 | | | |
| Liver decompensation (hepatic encephalopathy) | 0 | | | |
| Liver decompensation (hepatorenal syndrome) | 0 | | | |
| Liver decompensation (hepatic hydrothorax) | 0 | | | |
| Liver decompensation (other [PI's discretion]) | 0 | | | |
| Change in Child-Pugh Score in subject w/cirrhosis | 0 | | | |
| Hepatocellular carcinoma (HCC) | 5 | | | |

| | | | | |
|--|---|--|--|--|
| Liver transplantation occurred | 0 | | | |
| Death | 0 | | | |
| Regenerated node in the liver | 1 | | | |
| Cholangiocarcinoma/differentiated adenocarcinoma | 1 | | | |

Notes:

[7] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Concentration of Interferon Gamma-induced Protein 10 (IP-10) Over Time

| | |
|-----------------|---|
| End point title | Mean Concentration of Interferon Gamma-induced Protein 10 (IP-10) Over Time |
|-----------------|---|

End point description:

A plasma sample for IP-10 testing was collected at study visits for all participants, until the end of the study or initiation of re-treatment for HCV (if applicable). IP-10 is used to assess liver fibrosis in participants with chronic liver disease. Values of 999 in the standard deviation fields in the table below indicate not calculable due to n=1 subject.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Day 1 up to 3 years post-treatment

| End point values | HCV-infected Participants | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 374 ^[8] | | | |
| Units: ng/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (n=374) | 146.884 (± 116.6272) | | | |
| Month 3 (n=363) | 147.606 (± 118.5143) | | | |
| Month 6 (n=336) | 148.959 (± 119.0047) | | | |
| Month 12 (n=1) | 224.400 (± 999) | | | |
| Month 18 (n=7) | 133.300 (± 50.2647) | | | |
| Month 24 (n=234) | 140.185 (± 97.2769) | | | |
| Month 30 (n=88) | 164.244 (± 276.9176) | | | |
| Month 36 (n=1) | 120.600 (± 999) | | | |

Notes:

[8] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

Secondary: Mean FibroTest Score Over Time

| | |
|---|--------------------------------|
| End point title | Mean FibroTest Score Over Time |
| End point description: | |
| A serum sample for FibroTest evaluation was collected at study visits for all participants, until the end of the study or initiation of re treatment for HCV (if applicable). FibroTest uses six biomarkers to generate a score that correlates to the degree of liver damage in participants. Scores range from 0 to 1, with higher scores indicating more severe liver fibrosis. The value of 999 in the standard deviation field in the table below indicates not calculable due to n=1 subject. | |
| End point type | Secondary |
| End point timeframe: | |
| From Day 1 up to 3 years post-treatment | |

| End point values | HCV-infected Participants | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 367 ^[9] | | | |
| Units: units on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (n=367) | 0.354 (± 0.2341) | | | |
| Month 3 (n=347) | 0.363 (± 0.2383) | | | |
| Month 6 (n=333) | 0.353 (± 0.2311) | | | |
| Month 12 (n=2) | 0.405 (± 0.0919) | | | |
| Month 18 (n=5) | 0.272 (± 0.1281) | | | |
| Month 24 (n=227) | 0.321 (± 0.2156) | | | |
| Month 30 (n=68) | 0.261 (± 0.1667) | | | |
| Month 36 (n=1) | 0.190 (± 999) | | | |

Notes:

[9] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Aspartate Transaminase to Platelet Ratio Index (APRI) Over Time

| | |
|---|--|
| End point title | Mean Aspartate Transaminase to Platelet Ratio Index (APRI) Over Time |
| End point description: | |
| A serum sample for aspartate transaminase evaluation and platelets were collected at study visits for all participants, until the end of the study or initiation of re-treatment for HCV (if applicable). The aspartate transaminase to platelet ratio index (APRI) is used to assess liver fibrosis in participants with chronic liver disease. Scores range from 0 to ≥ 2.0, with scores < 0.5 predictive of no liver fibrosis; scores > 1.5 significant fibrosis; and scores > 2.0 indicative of cirrhosis. The value of 999 in the standard deviation field in the table below indicates not calculable due to n=1 subject. | |
| End point type | Secondary |

End point timeframe:
From Day 1 up to 3 years post-treatment

| End point values | HCV-infected Participants | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 367 ^[10] | | | |
| Units: ratio | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (n=367) | 0.317 (± 0.2268) | | | |
| Month 3 (n=352) | 0.303 (± 0.2171) | | | |
| Month 6 (n=333) | 0.298 (± 0.2101) | | | |
| Month 12 (n=1) | 0.230 (± 999) | | | |
| Month 18 (n=5) | 0.262 (± 0.0589) | | | |
| Month 24 (n=232) | 0.275 (± 0.1620) | | | |
| Month 30 (n=69) | 0.227 (± 0.1084) | | | |
| Month 36 (n=2) | 0.215 (± 0.1768) | | | |

Notes:

[10] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

No statistical analyses for this end point

Secondary: Mean FibroScan scores over time

| | |
|---|---------------------------------|
| End point title | Mean FibroScan scores over time |
| End point description: | |
| The FibroScan test is used to assess liver fibrosis in participants with chronic liver disease. This was not performed as a study procedure, but any available results from source documents were summarized. For participants with Hepatitis C infection, a Fibroscan score of 2-7 kPa indicates no liver scarring or mild scarring; a score of 8 or 9 is associated with moderate liver scarring ; 9-14 indicates severe liver scarring; and 14 or higher is indicative of advanced liver scarring, cirrhosis. The value of 999 in the standard deviation field in the table below indicates not calculable due to n=1 subject. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 3 years post-treatment | |

| End point values | HCV-infected Participants | | | |
|--------------------------------------|---------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 23 ^[11] | | | |
| Units: kPa | | | | |
| arithmetic mean (standard deviation) | | | | |
| Day 1 (n=7) | 13.014 (± 12.6850) | | | |
| Month 3 (n=5) | 6.880 (± 4.6677) | | | |
| Month 6 (n=10) | 10.780 (± 5.9260) | | | |
| Month 12 (n=10) | 7.700 (± 4.2208) | | | |
| Month 18 (n=8) | 6.913 (± 2.8002) | | | |
| Month 24 (n=23) | 6.757 (± 3.1564) | | | |
| Month 30 (n=1) | 9.400 (± 999) | | | |

Notes:

[11] - Subjects rcvd ABT-493 +/- ABT-530 in prior Phase 2/3 study and weren't retreated before this study

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

SAEs reasonably related to interventional study procedures or to ABT-530 and/or ABT-493 Tx in the prior study were collected from Day 1 through the last study procedure or discontinuation from study, whichever was later, up to 3 years post-treatment.

Adverse event reporting additional description:

An adverse event is any untoward medical occurrence as a result of a study procedure or considered by the investigator to be reasonably related to exposure to ABT-493 and/or ABT-530 in the prior study. Deaths were collected as a medical event from consent until study end. SAEs outside of the study time frame and nonserious AEs were not collected.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 22.0 |

Reporting groups

| | |
|-----------------------|---------------------------------|
| Reporting group title | HCV-infected Participants-- FAS |
|-----------------------|---------------------------------|

Reporting group description:

Full Analysis Set (FAS): all participants who received ABT-493 and/or ABT-530 in a prior Phase 2 /3 study and were not retreated prior to enrolling in this study. Three participants who received retreatment prior to enrollment in this study and four participants who did not receive ABT-493 and/or ABT-530 in a prior study were excluded from the FAS.

| Serious adverse events | HCV-infected Participants-- FAS | | |
|---|------------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 377 (0.00%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | HCV-infected Participants-- FAS | | |
|---|------------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 0 / 377 (0.00%) | | |

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Nonserious adverse events were not collected for this study.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 03 April 2015 | <p>Amendment 1</p> <ul style="list-style-type: none">• Included the reporting of any SAEs considered by the investigator to be reasonably related to exposure to ABT-530 and/or ABT-493 in the prior study because it was possible that a subject enrolled in this study may have experienced a SAE that the investigator believed to be reasonably related to their exposure to ABT-530 and/or ABT-493 in the prior study• Included the requirement to record, in the CRF, the concomitant medications used to treat SAEs considered to be related to the subject's exposure to ABT-530 and/or ABT-493 in the previous study• Clarified the use of the Roche COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative Test, v2.0 and provided a revised LLOQ of 15 IU/mL for all HCV genotypes using this assay• Added Protocol M15-410 to Appendix C• Added the Child-Pugh classification definitions to Appendix D |
| 19 July 2016 | <p>Amendment 2</p> <ul style="list-style-type: none">• Changed Phase from 2 to 2/3 to reflect addition of subjects from Phase 3 studies• Revised Secondary Objectives to include all laboratory tests/scores: those required by study to be presented in final analysis• Changed anticipated no. of subjects/sites to reflect potential enrollment from Phase 3 studies• Clarified that all subjects failing Tx in prior study would be offered this study if they had not/would not be receiving immediate Tx in AbbVie Study M15-942• Added Exclusion Criterion 3 (Subjects experiencing non-virologic treatment failure due to premature discontinuation of study drug in prior study of ABT-493/ABT-530 may not participate), to exclude any non-virologic treatment failure who did not complete study drug• Added Exclusion Criterion 4 (Subjects enrolling in Study M15-942 for retreatment are not eligible for Study M13-576), to specify that subjects who were re-treated in Study M15-942 could not enroll because they could not be in both studies• Appendix D: expanded list of Phase 3 studies from which subjects could be enrolled• Revised to allow for re-treatment with commercially available HCV medications any time after treatment with study drugs in prior AbbVie HCV Phase 2/3 studies (prior to/during participation in Study M13-576). Subjects who were re-treated were to be followed to SVR12, to assess posttreatment Wk 12 (SVR12) outcomes of HCV re-treatment among subjects who experienced a virology failure in a prior study• Added requirement for a posttreatment Wk 12 (SVR12) visit for all re-treated VFs, since SVR12 assessment is generally accepted standard for SVR• Added requirement for Child-Pugh Score and Classification for all cirrhotic subjects at Day 1 and every 6 mos• Removed archived serum sample requirement• Updated sequencing method for resistance analysis to more sensitive deep sequencing |

| | |
|-----------------|--|
| 09 October 2017 | Amendment 3 <ul style="list-style-type: none"> • Removed collection of alpha fetoprotein, as it is an unreliable test for screening for liver disease including HCC and was no longer recommended in the AASLD HCV guidelines current at the time • Clarified Inclusion Criterion 3 by adding a sentence to note that subjects who had been re-treated with a commercially available anti-HCV treatment were able to enroll in the study greater than 2 years after the last dose of the AbbVie DAA therapy from the previous AbbVie clinical study. The 2-year timeframe did not apply to subjects who had been re-treated, for whom blood samples were not to be collected to evaluate the persistence of resistance substitutions • Screening for HCC by liver ultrasound was added to the final study visit for cirrhotic subjects, in order to screen them for development of HCC as part of long-term follow-up |
|-----------------|--|

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported