ABT-450/ritonavir/ABT-267 in combination with ABT-333 for chronic genotype-1 hepatitis C infection

SUMMARY

ABT-450/ritonavir/ABT-267 (ABT-267/r/ABT-450) and ABT-333 is a combination therapy for the treatment of chronic hepatitis C virus genotype-1 in treatment-naïve and treatment-experienced adults. If licensed, it will offer an oral, interferon-free treatment option for these patients. ABT-450 is a small molecule NS3/4A serine protease inhibitor; ritonavir is a HIV aspartic protease inhibitor; ABT-267 is a HCV non-structural 5A (NS5A) inhibitor; and ABT-333 is a non-nucleoside inhibitor of the HCV NS5B RNA-dependent RNA polymerase.

The true incidence of HCV infection is difficult to establish, however recent estimates suggest that in the UK there are around 216,000 individuals who are chronically infected with HCV, of whom approximately 30,240 are diagnosed (in the UK, about 86% of infected individuals are unaware of their infection status, of whom 45% are genotype 1). Prevalence in England and Wales is in the range of 0.6-1.2% of the population and in 2010, there were 10,380 new diagnoses in the UK. In 2011-12, there were 2,404 hospital admissions due to HCV infection in England, resulting in 2,650 finished consultant episodes and 3,332 bed days. In 2010, there were 166 deaths registered in England and Wales.

The choice of therapy for HCV is influenced by genotype. Patients with genotype 1 are treated with triple combination therapy for a duration influenced by pre-treatment factors (including cirrhosis) and response to therapy. ABT-267/r/ABT-450 is currently in seven phase III clinical trials comparing its effect on sustained virologic response at 12 and 24 weeks against treatment with placebo, with or without ribavirin and pegylated interferon. These trials are expected to complete by Q3 2016.
TARGET GROUP

• Chronic hepatitis C infection: genotype 1 – treatment naïve and treatment experienced.

TECHNOLOGY

DESCRIPTION

ABT-450/ritonavir/ABT-267 (ABT-267/ritonavir/ABT-450) and ABT-333 is a combination therapy for the treatment of chronic hepatitis C virus (HCV) genotype-1 in treatment-naïve and treatment-experienced adults. ABT-450 is a small molecule NS3/4A serine protease inhibitor; ritonavir is a HIV aspartic protease inhibitor; ABT-267 is a HCV non-structural 5A (NS5A) inhibitor; and ABT-333 is a nono-nucleoside inhibitor of the HCV NS5B RNA-dependent RNA polymerase.

ABT-450/ritonavir/ABT-267 is co-administered orally at 150mg/100mg/25mg once daily in combination with oral ABT-333 250mg twice daily for 12 weeks.

INNOVATION and/or ADVANTAGES

If licensed, ABT-450/ritonavir/ABT-267 in combination with ABT-333 will offer an oral, interferon-free treatment option for patients with chronic HCV genotype 1, treatment naïve and treatment experienced adults.

DEVELOPER

AbbVie Ltd.

AVAILABILITY, LAUNCH OR MARKETING

In Phase III clinical trials.

PATIENT GROUP

BACKGROUND

HCV is a member of the flaviviridae family of spherical, enveloped, positive-strand RNA viruses. There are six different HCV genotypes; genotype 1 is the most common and the most resistant to treatment. The virus is acquired primarily through percutaneous exposure to contaminated blood. Most acute infections with HCV are asymptomatic with only 20% developing overt hepatitis. Approximately 80% of people who are infected go on to develop chronic HCV, symptoms of which include malaise, weakness and anorexia. Chronic HCV is categorised as mild, moderate or severe depending on the extent of liver damage. Approximately 30% of infected people develop cirrhosis within 20-30 years, and some of these develop hepatocellular carcinoma. End stage-liver disease or hepatocellular carcinoma may require liver transplantation. Factors known to increase the rate of progression include age, ethnicity, male sex, excessive alcohol consumption and HIV co-infection.
This topic is relevant to:

The true incidence of HCV infection is difficult to establish, however recent estimates suggest that in the UK there are around 216,000 individuals who are chronically infected with HCV, of whom approximately 30,240 are diagnosed (in the UK, about 86% of infected individuals are unaware of their infection status, of whom 45% are genotype 1). Prevalence in England and Wales is in the range of 0.6-1.2% of the population and in 2010, there were 10,380 new diagnoses in the UK. Estimates suggest that by 2020, around 15,840 individuals will be living with HCV-related cirrhosis or HCC in England and more than 4,200 of these are predicted to be living with severe decompensated liver disease or HCC. An estimated 30.6% of people with HCV infection currently receive antiviral treatment. In 2011-12, there were 2,404 hospital admissions due to HCV infection (ICD10 B17.1, B18.2) in England, resulting in 2,650 finished consultant episodes and 3,332 bed days. In 2010, there were 166 deaths registered in England and Wales.

NICE Guidance
- NICE clinical guideline in development. Hepatitis C. Expected date of issue to be confirmed.
- NICE public health guidance. Hepatitis B and C – ways to promote and offer testing to people at risk of infection (PH43). December 2012.
Other Guidance

- Department of Health. Hepatitis C: quick reference guide for primary care. 2009\textsuperscript{16}.
- Royal College of General Practitioners. Guidance for the prevention, testing, treatment and management of hepatitis C in primary care. 2007\textsuperscript{3}.
- Scottish Intercollegiate Guidelines Network. Management of hepatitis C. (92). 2006\textsuperscript{17}.
- British Association of Sexual Health and HIV. United Kingdom national guideline on the management of the viral hepatitides A, B & C. 2005\textsuperscript{18}.
- British Society of Gastroenterology. Guidance on the treatment of hepatitis C incorporating the use of pegylated interferon. 2003\textsuperscript{19}.

EXISTING COMPARATORS and TREATMENTS

The choice of therapy for HCV is influenced by genotype. Patients with genotype 2 or 3 are usually treated with 24 weeks of peginterferon alfa (peg IFNα) and ribavirin (RBV). Patients with genotype 1 are treated with triple combination therapy for a duration influenced by pre-treatment factors (including cirrhosis) and response to therapy\textsuperscript{20}. All patients with chronic HCV (irrespective of the stage of the disease) are considered for therapy\textsuperscript{3}.

Current treatment options include\textsuperscript{3,10,11}:
- A combination of ribavirin and pegIFNα-2a or 2b.
- Telaprevir in combination with pegIFN and RBV.
- Boceprevir in combination with pegIFNα and RBV.

Successful treatment is usually indicated by a sustained virologic response (SVR), which is defined as undetectable serum HCV RNA 6 months after the end of treatment\textsuperscript{2}. The proportion of people with HCV genotype 1 who show SVR after finishing a course of treatment with pegIFN and RBV is about 40% to 50%, compared to approximately 75% to 85% of people with HCV genotype 2 or 3, and 50% to 75% for other genotypes (4, 5, and 6)\textsuperscript{2,21}.

EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>SAPPHIRE-I, NCT01716585; ABT-450/r/ABT-267 in combination with RBV and ABT-333 vs placebo; phase III.</th>
<th>SAPPHIRE-II, NCT01715415; ABT-450/r/ABT-267 in combination with RBV and ABT-333 vs placebo; phase III.</th>
<th>TURQUOISE-II, NCT01704755, M13-099, 2012-003088-23; ABT-450/r/ABT-267 in combination with ABT-333 and RBV; phase III.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>AbbVie.</td>
<td>AbbVie.</td>
<td>AbbVie.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry\textsuperscript{22}.</td>
<td>Trial registry\textsuperscript{22}.</td>
<td>Trial registry\textsuperscript{24}.</td>
</tr>
<tr>
<td>Location</td>
<td>EU (incl UK), USA, Canada, Australia and New Zealand.</td>
<td>EU (incl UK), USA, Canada, Australia and Puerto Rico.</td>
<td>EU (incl UK), USA, Canada and Puerto Rico.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=600 (planned); aged 18-70 years; chronic HCV genotype 1; treatment naïve.</td>
<td>n=400 (planned); aged 18-70 years; chronic HCV genotype 1; failed previous treatment with pegIFN and RBV.</td>
<td>n=360 (planned); aged 18-70 years; chronic HCV genotype 1; compensated cirrhosis.a</td>
</tr>
<tr>
<td>Schedule</td>
<td>Randomised to: Arm 1: ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg oral twice daily, and RBV 1,000-1,200mg b oral twice daily for 12 weeks. Arm 2: placebo (for ABT-450/r/ABT-267, ABT-333 and RBV) oral once and placebo twice daily for 12 weeks; then ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg oral twice daily, and RBV 1,000-1,200mg c oral twice daily for 12 weeks.</td>
<td>Randomised to: Arm 1: ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg oral twice daily, and RBV 1,000-1,200mg c oral twice daily for 12 weeks.</td>
<td>Randomised to ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg oral twice daily and RBV 1,000-1,200mg c oral for 12 or 24 weeks.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment period 12 weeks, follow-up 48 weeks.</td>
<td>Active treatment period 12 weeks, follow-up 48 weeks.</td>
<td>Active treatment period 12 or 24 weeks, follow-up 48 weeks.</td>
</tr>
<tr>
<td>Secondary outcome/s</td>
<td>Number of subjects with alanine aminotransferase (ALT) normalisation; SVR12 in genotype 1a; SVR12 in genotype 1b; on-treatment virologic failure; post-treatment relapse.</td>
<td>Number of subjects with ALT normalisation; SVR12 in genotype 1a; SVR12 in genotype 1b; on-treatment virologic failure; post-treatment relapse.</td>
<td>SVR12 in the 24 week arm vs 12 week arm; number of subjects with on-treatment virologic failure during treatment period; number of subject in each arm with post-treatment relapse.</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Primary completion date reported as Sept 2013.</td>
<td>Primary completion date reported as Sept 2013.</td>
<td>Primary completion date reported as Dec 2013.</td>
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<td>Sponsor</td>
<td>AbbVie.</td>
<td>AbbVie.</td>
<td>AbbVie.</td>
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<tr>
<td>Location</td>
<td>EU (inc UK), USA, Canada and other countries.</td>
<td>EU (not inc UK), USA and Puerto Rico.</td>
<td>USA.</td>
</tr>
</tbody>
</table>

a Defined as a Child-Pugh score (used to assess the prognosis of chronic liver disease) of less than or equal to 6. 
b RBV dose is determined by weight.
| Participants | n=500 (planned); chronic HCV; received at least one dose of ABT-450/r, ABT-333, or ABT-267 in a prior AbbVie HCV phase II/III trial. | n=210 (planned); 18-70 years; chronic HCV genotype 1b; failed treatment with PegIFN and RBV. | n=400 (planned); 18-70 years; chronic HCV genotype 1b; treatment naive. |
| Schedule | Continue on previous treatment. | Randomised to ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg oral twice daily, with or without RBV 1,000-1,200mg c oral. | Randomised to: Arm 1: ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg and RBV 1,000-1,200mg³ oral once daily, in combination with ABT-333 250mg and RBV 1,000-1,200mg³ oral and twice daily for 12 weeks. Arm 2: ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg and placebo, both oral and twice daily for 12 weeks. |
| Follow-up | Follow-up 3 years. | Active treatment period 12 weeks, follow-up 48 weeks. | Active treatment period 12 weeks, follow-up 48 weeks. |
| Primary outcome/s | Durability of treatment response d; persistence of resistance mutations e. | SVR12. | SVR12. |
| Expected reporting date | Primary completion date reported as May 2016. | Primary completion date reported as Mar 2014. | Study completion date reported as Aug 2014. |
| Sponsor | AbbVie. | AbbVie. | AbbVie. |
| Location | USA. | USA. | EU (inc UK), USA, Canada, Australia, Puerto Rico and New Zealand. |

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c RBV dose is determined by weight.
d Defined as the percentage of subjects who relapse or have new HCV at any time up to the last follow-up in this study out of subjects who achieved a SVR12 post-treatment in the previous study.
e The persistence of specific hepatitis C amino acid variants associated with drug resistance in subjects who experience virologic failure.
| Participants | n=300 (planned); 18-70 years; chronic HCV genotype 1b; treatment naive. | n=30 (planned); aged 18-70 years old; chronic HCV genotype 1; liver transplantation as a consequence of HCV infection; patient on an immunosuppressant regimen based on either tacrolimus or cyclosporin. | n=560 (planned); aged 18-70 years; chronic HCV genotype 1; treatment naïve or prior non-responders to previous treatment with pegIFN and RBV. |
| Schedule | Randomised to: Arm 1: ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg and RBV 1,000-1,200mg, both oral and twice daily for 12 weeks. Arm 2: ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg and placebo, both oral and twice daily for 12 weeks. | Participants receive ABT-450/r/ABT-267 150mg/100mg/25mg oral once daily, in combination with ABT-333 250mg oral twice daily, and RBV 1,000-1,200mg for 24 weeks. | Treatment naïve Randomised to: Arm 1: ABT-450/r 150/100mg oral once daily, with ABT-267 25mg oral once daily, and ABT-333 400mg oral twice daily in combination with RBV 1,000-1,200mg oral twice daily for 8 wks. Arm 2: ABT-450/r 150/100mg oral once daily, with ABT-333 400mg oral twice daily, in combination with RBV 1,000-1,200mg oral twice daily for 12 wks. Arm 3: ABT-450/r 100/100mg or 200/100mg oral once daily, with ABT-267 25mg oral once daily, in combination with RBV 1,000-1,200mg oral twice daily for 12 wks. Arm 4: ABT-450/r 150/100mg oral once daily, with ABT-267 25mg oral once daily, and ABT-333 400mg oral twice daily for 12 wks. Arm 5: ABT-450/r 100/100mg or 150/100mg oral once daily, with ABT-267 25mg oral once daily, and ABT-333 400mg oral twice daily in combination with RBV 1,000-1,200mg oral twice daily for 12 wks. Arm 6: ABT-450/r 100/100mg or 150/100mg oral once daily, with ABT-267 25mg oral once daily, and ABT-333 400mg oral twice daily in combination with RBV 1,000-1,200mg oral twice daily for 24 wks. |
|注 | RBV dose is determined by weight. Dose received determined by random assignment. |
Prior non-responders
Randomised to:
Arm 1: ABT-450/r 200/100mg oral once daily and ABT-267 25mg oral once daily, in combination with RBV 1,000-1,200mg oral twice daily for 12 weeks.
Arm 2: ABT-450/r 100/100mg or 150/100mg oral once daily, with ABT-267 25mg oral once daily, and ABT-333 400mg oral twice daily in combination with RBV 1,000-1,200mg oral twice daily for 12 weeks.
Arm 3: ABT-450/r 100/100mg or 150/100mg oral once daily, with ABT-267 25mg oral once daily, and ABT-333 400mg oral twice daily in combination with RBV 1,000-1,200mg oral twice daily for 24 weeks.

Follow-up
Active treatment period 12 weeks, follow-up 48 weeks.
Active treatment period 24 weeks, follow-up 48 weeks.
Active treatment period 8, 12 or 24 weeks, follow-up 48 weeks.

Primary outcome/s
SVR12.
SVR12.
SVR24 in treatment naïve subjects; safety.

Secondary outcome/s
Haemoglobin; virologic failure during treatment; virologic response after treatment.
SVR 24 weeks post treatment (SVR24); virologic failure during treatment; post-treatment relapse.
SVR24 in non-responders; any emerged or enriched mutations.

Key results
- Treatment naïve
SVR12 for arm number: 1, 89%; 2, 85%; 3, 91%; 4, 90%; 5, 99%; 6, 93%. SVR 24 for arm number: 1, 88%; 2, 83%; 3, 89%; 4, 87%; 5, 96%, 6, 90%.
Prior-non responders
SVR12 for arm number: 1, 89%; 2, 93%; 3, 98%. SVR24 for arm number: 1, 89%; 2, 93%; 3, 95%.

Adverse effects (AEs)
- AEs include: fatigue, headache, insomnia, nausea, bilirubin increase.

Expected reporting date
Study completion date reported as Nov 2014.
Primary completion date reported as Mar 2014.

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h Dose received determined by random assignment.
i RBV dose is determined by weight.
<table>
<thead>
<tr>
<th>Trial</th>
<th>Trial PEARK I, NCT01665203, M13-393, 2011-005762-38; ABT-450/r in combination with ABT-267; phase II.</th>
<th>Navigator, NCT01458535, M12-998; ABT-450/r and ABT-267 with or without RBV; phase II.</th>
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</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>AbbVie.</td>
<td>AbbVie.</td>
</tr>
<tr>
<td>Status</td>
<td>Ongoing.</td>
<td>Ongoing.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry.</td>
<td>Presentation; trial registry.</td>
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<tr>
<td>Location</td>
<td>EU (not inc UK), USA and Puerto Rico.</td>
<td>USA and Puerto Rico.</td>
</tr>
<tr>
<td>Design</td>
<td>Randomised, active-controlled.</td>
<td>Non-randomised, active-controlled.</td>
</tr>
<tr>
<td>Participants</td>
<td>n=320 (planned); aged 18-70 years; chronic HCV genotype 1b with or without cirrhosis, or HCV genotype 4 without cirrhosis for at least 6 months prior to study; treatment-naïve or treatment experienced.</td>
<td>n=60 (planned); aged 18-65 years; chronic HCV genotype 1, 2, or 3; treatment naïve.</td>
</tr>
<tr>
<td>Schedule</td>
<td>Randomised to: Arm 1 treatment naïve genotype 1b: ABT-450/r 150mg/100mg in combination with ABT-267 25mg, both oral and once daily for 12 weeks. Arm 2 treatment experienced genotype 1b: ABT-450/r 150mg/100mg and ABT-267 25mg, both oral and once daily for 12 weeks. Arm 3 treatment naïve genotype 1b with compensated cirrhosis: ABT-450/r 150mg/100mg in combination with ABT-267 25mg, both oral and once daily for 12 weeks. Arm 4 treatment experienced genotype 1b with compensated cirrhosis: ABT-450/r 150mg/100mg and ABT-267 25mg, both oral and once daily for 12 weeks.</td>
<td>Participants receive ABT-450/r 200mg/100mg and ABT-267 25mg, both oral once daily, with or without RBV 1,000-1,200mg oral for 12 weeks.</td>
</tr>
<tr>
<td>Follow-up</td>
<td>Active treatment period 8, 12 or 14 weeks, follow-up 48 weeks.</td>
<td>Active treatment period 12 weeks, follow-up 48 weeks.</td>
</tr>
<tr>
<td>Primary outcome/s</td>
<td>Adverse effects; SVR12.</td>
<td>Safety.</td>
</tr>
<tr>
<td>Secondary outcome/s</td>
<td>SVR24; number of subject in each treatment group with on-treatment virologic failure; number of subjects in each treatment group with post-treatment relapse.</td>
<td>SVR12; SVR24; number of subject with HCV RNA &lt;1000IU/mL; number of subjects with HCV RNA &lt; lower limit of quantification (LLCQ); time to failure; suppress, rebound or relapse.</td>
</tr>
<tr>
<td>Key results</td>
<td>-</td>
<td>SVR24 with and without RBV respectively: 100% vs 60%.</td>
</tr>
<tr>
<td>Adverse effects (AEs)</td>
<td>-</td>
<td>AEs include fatigue, nausea, headache, diarrhoea, arthralgia, cough, depression.</td>
</tr>
<tr>
<td>Expected reporting date</td>
<td>Primary completion date reported as Sept 2013.</td>
<td>Previously reported as May 2013.</td>
</tr>
</tbody>
</table>

1 RBV dose is determined by weight.
2 HCV ribonucleic acid greater than lower limit of quantification.
3 Defined as a confirmed increase of at least 1 log10IU/ML above nadir or confirmed HCV RNA > LLCQ for subjects who previously achieved HCV RNA < LLOQ.
ESTIMATED COST and IMPACT

COST

The cost of ABT-450/r/ABT-267 in combination with ABT-333 is not yet known. The costs of selected currently licensed treatments for HCV are summarised below:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>12 week cost</th>
<th>48 week cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peginterferon alfa-2a (Pegasys)</td>
<td>180µg subcutaneous once weekly</td>
<td>£1,492.80</td>
<td>£5,971.20</td>
</tr>
<tr>
<td>Peginterferon alfa-2b (ViraferonPeg)</td>
<td>100µg subcutaneous once weekly</td>
<td>£1,595.04</td>
<td>£6,380.16</td>
</tr>
<tr>
<td>Ribavirin (Rebetol)</td>
<td>1,000mg daily</td>
<td>£803.43</td>
<td>£3,213.80</td>
</tr>
<tr>
<td>Telaprevir (Incivo)</td>
<td>2,250mg daily</td>
<td>£22,398.00</td>
<td>n/a</td>
</tr>
<tr>
<td>Bopeprevir (Victrelis)</td>
<td>2,400mg daily</td>
<td>n/a</td>
<td>£22,400†</td>
</tr>
</tbody>
</table>

IMPACT - SPECULATIVE

Impact on Patients and Carers
- Reduced mortality/increased length of survival
- Reduced symptoms or disability
- No impact identified

Impact on Services
- Increased use of existing services
- Decreased use of existing services: successful HCV therapy may reduce the burden to the NHS associated with liver transplantation service and healthcare costs associated with management of decompensated cirrhosis or hepatocellular carcinoma. Oral therapy will be more straightforward to deliver outside clinic than IFN based regimens.
- Re-organisation of existing services
- Need for new services
- None identified

Impact on Costs
- Increased drug treatment costs
- Reduced drug treatment costs
- Other increase in costs:
- Other reduction in costs:
- Other: uncertain unit cost compared to existing treatments
- None identified

Other Issues
- Clinical uncertainty or other research question identified:
- None identified

m Based on an average weight of 77.9kg (men and women).
† Indicated for 32 weeks’ treatment.
o Information provided by company.
REFERENCES

23. ClinicalTrials.gov. A randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of ABT-450/Ritonavir/ABT-267 (ABT-450/ri/ABT-267) and ABT-333 co-administered with ribavirin (RBV) in treatment-experienced adults with genotype 1 chronic hepatitis C virus (HCV) infection (SAPPHIRE-II).
ClinicalTrials.gov. A randomized, open-label study to evaluate the safety and efficacy of ABT-450/Ritonavir/ABT-267 (ABT-450/ir/ABT-267) and ABT-333 coadministered with ribavirin (RBV) in adults with genotype 1 chronic hepatitis C virus (HCV) infection and cirrhosis (TURQUOISE-II).
http://clinicaltrials.gov/ct2/show/study/NCT01704755?term=NCT01704755&rank=1

ClinicalTrials.gov. A follow-up study to assess resistance and durability of response to abbott direct-acting antiviral agent (DAA) therapy in subjects who participated in phase 2 or 3 clinical studies for the treatment of chronic hepatitis C virus (HCV) infection.
http://clinicaltrials.gov/ct2/show/NCT01773070?term=NCT01773070&rank=1

ClinicalTrials.gov. A randomized, open-label, multicenter study to evaluate the safety and antiviral activity of the combination of ABT-450/Ritonavir/ABT-267 (ABT 450/r/ABT-267) and ABT-333 with and without ribavirin in treatment-experienced subjects with genotype 1b chronic hepatitis C virus (HCV) infection (PEARL-II).
http://clinicaltrials.gov/ct2/show/study/NCT01674725?term=NCT01674725&rank=1

ClinicalTrials.gov. A randomized, double-blind, controlled study to evaluate the efficacy and safety of the combination of ABT-450/ritonavir/ABT-267 (ABT-450/r/ABT-267) and ABT-333 with and without ribavirin (RBV) in treatment-naive adults with genotype 1b chronic hepatitis C virus (HCV) infection (PEARL-III).
http://clinicaltrials.gov/ct2/show/NCT01767116?term=NCT01767116&rank=1

ClinicalTrials.gov. Open-label, single arm, phase 2 study to evaluate the safety and efficacy of the combination of ABT-450/ritonavir/ABT-267 (ABT-450/ir/ABT-267) and ABT-333 coadministered with ribavirin (RBV) in adult liver transplant recipients with genotype 1 hepatitis C virus (HCV) infection.
http://clinicaltrials.gov/ct2/show/NCT01782495


ClinicalTrials.gov. A randomized, open-label, multicenter study to evaluate the antiviral activity, safety, and pharmacokinetics, of ABT-450 with ritonavir (ABT-450/ir) in combination with ABT-267 and/or ABT-333 with and without ribavirin (RBV) for 8, 12 or 24 weeks in treatment-naive and null responder subjects with genotype 1 chronic hepatitis C virus infection.
http://clinicaltrials.gov/ct2/show/NCT01464827

ClinicalTrials.gov. A randomized, open-label study to evaluate the safety and efficacy of coadministration of ABT-450 with ritonavir (ABT-450/ir) and ABT-267 in adults with chronic hepatitis C virus infection (PEARL-I).
http://clinicaltrials.gov/ct2/show/NCT01685203


ClinicalTrials.gov. An open-label, sequential arm, multicenter study to evaluate the antiviral activity, safety and pharmacokinetics of ABT-450 with ritonavir (ABT-450/ir) dosed in combination with ABT-267 with and without ribavirin (RBV) in treatment-naive subjects with genotype 1, 2 or 3 chronic hepatitis C virus (HCV) infection.
http://clinicaltrials.gov/ct2/show/NCT01458535