



Clinical trial results:

Open-Label, Single-Arm Trial to Evaluate the Pharmacokinetics, Safety and Efficacy of Daclatasvir (DCV) in Combination with Sofosbuvir (SOF) in Children from 3 to less than 18 Years of Age with GT-1 to -6 Chronic Hepatitis C (CHC) Infection

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2017-003338-94 |
| Trial protocol | DE ES PL Outside EU/EEA |
| Global end of trial date | 17 September 2020 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 28 March 2021 |
| First version publication date | 28 March 2021 |

Trial information

Trial identification

| | |
|-----------------------|-----------|
| Sponsor protocol code | AI444-423 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-001191-PIP01-11 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 12 November 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 17 September 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To Evaluate the Pharmacokinetics, Safety and Efficacy of Daclatasvir (DCV) in Combination with Sofosbuvir (SOF) in Children from 3 to less than 18 Years of Age with GT-1 to -6 Chronic Hepatitis C (CHC) Infection

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 25 June 2018 |
| 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 | Spain: 2 |
| Country: Number of subjects enrolled | Australia: 3 |
| Worldwide total number of subjects | 5 |
| EEA total number of subjects | 2 |

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) | 5 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

5 participants were enrolled and treated

Period 1

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

Arms

| | |
|------------------|--------------------------------------|
| Arm title | Daclatasvir (DCV) + Sofosbuvir (SOF) |
|------------------|--------------------------------------|

Arm description:

DCV 60 mg QD + SOF 400 mg QD for 12 weeks

| | |
|--|--------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Sofosbuvir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

400 mg QD

| | |
|--|--------------------|
| Investigational medicinal product name | Daclatasvir |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg QD

| | |
|---------------------------------------|--------------------------------------|
| Number of subjects in period 1 | Daclatasvir (DCV) + Sofosbuvir (SOF) |
| Started | 5 |
| Completed | 4 |
| Not completed | 1 |
| Lost to follow-up | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Daclatasvir (DCV) + Sofosbuvir (SOF) |
|-----------------------|--------------------------------------|

Reporting group description:

DCV 60 mg QD + SOF 400 mg QD for 12 weeks

| Reporting group values | Daclatasvir (DCV) + Sofosbuvir (SOF) | Total | |
|---|---|-------|--|
| Number of subjects | 5 | 5 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 5 | 5 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 13.6 | | |
| standard deviation | ± 1.3 | - | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 2 | 2 | |
| Male | 3 | 3 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 0 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 4 | 4 | |
| More than one race | 0 | 0 | |
| Other | 1 | 1 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 0 | 0 | |
| Unknown or Not Reported | 5 | 5 | |

End points

End points reporting groups

| | |
|---|--------------------------------------|
| Reporting group title | Daclatasvir (DCV) + Sofosbuvir (SOF) |
| Reporting group description: DCV 60 mg QD + SOF 400 mg QD for 12 weeks | |

Primary: Minimum (Trough) Observed Plasma Concentration (Cmin) for Daclatasvir

| | |
|-----------------|--|
| End point title | Minimum (Trough) Observed Plasma Concentration (Cmin) for Daclatasvir ^[1] |
|-----------------|--|

End point description:

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: Day 10 after first dose | |

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: No statistical analysis was performed for this endpoint.

| | | | | |
|---|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 152.94 (\pm 48.3) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Maximum Observed Plasma Concentration (Cmax) for Daclatasvir

| | |
|-----------------|---|
| End point title | Maximum Observed Plasma Concentration (Cmax) for Daclatasvir ^[2] |
|-----------------|---|

End point description:

| | |
|---|---------|
| End point type | Primary |
| End point timeframe: Day 10 after first dose | |

Notes:

[2] - 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: No statistical analysis was performed for this endpoint.

| | | | | |
|---|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 1215.32 (\pm 37.2) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Time of Maximum Observed Plasma Concentration (Tmax) for Daclatasvir

| | |
|-----------------|---|
| End point title | Time of Maximum Observed Plasma Concentration (Tmax) for Daclatasvir ^[3] |
|-----------------|---|

End point description:

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

End point timeframe:

Day 10 after first dose

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: No statistical analysis was performed for this endpoint.

| | | | | |
|-------------------------------|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: Hours | | | | |
| median (full range (min-max)) | 2.00 (1.0 to 4.0) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Concentration-Time Curve (AUC(TAU)) for Daclatasvir

| | |
|-----------------|---|
| End point title | Area Under the Concentration-Time Curve (AUC(TAU)) for Daclatasvir ^[4] |
|-----------------|---|

End point description:

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

End point timeframe:

Day 10 after first dose

Notes:

[4] - 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: No statistical analysis was performed for this endpoint.

| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
|---|--------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: h*ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 11535.45 (\pm 26.6) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Apparent Total Body Clearance (CLT/F) for Daclatasvir

| | |
|-----------------|--|
| End point title | Apparent Total Body Clearance (CLT/F) for Daclatasvir ^[5] |
|-----------------|--|

End point description:

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

End point timeframe:

Day 10 after first dose

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: No statistical analysis was performed for this endpoint.

| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
|---|--------------------------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: mL/min | | | | |
| geometric mean (geometric coefficient of variation) | 86.69 (\pm 22.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events

| | |
|-----------------|--|
| End point title | Number of Participants Experiencing Adverse Events |
|-----------------|--|

End point description:

This outcome describes the number of participants experiencing different types of any grade adverse events.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| From first dose to last dose (12 weeks) | |

| | | | | |
|--------------------------------|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: Participants | | | | |
| Adverse Events (AEs) | 4 | | | |
| Serious Adverse Events (SAEs) | 0 | | | |
| AEs leading to discontinuation | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Laboratory Abnormalities - On-treatment analysis

| | |
|---|--|
| End point title | Number of Participants Experiencing Laboratory Abnormalities - On-treatment analysis |
| End point description: | |
| Laboratory tests abnormalities were analyzed in the following categories: | |
| -Hematology (hemoglobin, platelets, international normalized ratio (INR), white blood cell count (WBC), lymphocytes (absolute), neutrophils + bands (absolute; ANC)). | |
| -Hepatobiliary enzymes (ALT, AST, alkaline phosphatase, total bilirubin, albumin). | |
| -Pancreatic enzymes (lipase, creatinine). | |
| Tests results were reported by worst toxicity grade (0 to 4) based on the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events (2017). | |
| Only laboratory abnormalities with a worst toxicity grade 3 or higher in any of the above-mentioned tests, experienced during the on-treatment period, are reported here. | |
| End point type | Secondary |
| End point timeframe: | |
| From the day after first dose to last dose (approximately 12 weeks) | |

| | | | | |
|-----------------------------|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: Participants | | | | |
| Lipase, Total | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Laboratory Abnormalities - Follow-up analysis

| | |
|-----------------|---|
| End point title | Number of Participants Experiencing Laboratory Abnormalities - Follow-up analysis |
|-----------------|---|

End point description:

Laboratory tests abnormalities were analyzed in the following categories:

-Hematology (hemoglobin, platelets, international normalized ratio (INR), white blood cell count (WBC), lymphocytes (absolute), neutrophils + bands (absolute; ANC)).

-Hepatobiliary enzymes (ALT, AST, alkaline phosphatase, total bilirubin, albumin).

-Pancreatic enzymes (lipase, creatinine).

Tests results were reported by worst toxicity grade (0 to 4) based on the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events (2017).

Only laboratory abnormalities with a worst toxicity grade 3 or higher in any of the above-mentioned tests, experienced during the follow-up period, are reported here.

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

End point timeframe:

From the day after last dose to end of follow-up period (up to approximately 96 weeks)

| | | | | |
|-----------------------------|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: Participants | | | | |
| Glomerular Filtration Rate | 2 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Hepatitis C Virus (HCV) RNA Levels Below the Lower Limit of Quantitation (LLOQ) at Post-Treatment Follow-Up Week 12

| | |
|-----------------|---|
| End point title | Percentage of Participants with Hepatitis C Virus (HCV) RNA Levels Below the Lower Limit of Quantitation (LLOQ) at Post-Treatment Follow-Up Week 12 |
|-----------------|---|

End point description:

HCV RNA levels were measured by using the Roche COBAS® AmpliPrep/COBAS® TaqMan® HCV Test v2.0. This assay has limit of detection = 15 IU/mL, LLOQ = 15 IU/mL.

The outcome includes both results where Target was Detected (TD) but below LLOQ and results were

Target was Not Detected (TND)

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 12 weeks after last dose | |

| | | | | |
|----------------------------------|--------------------------------------|--|--|--|
| End point values | Daclatasvir (DCV) + Sofosbuvir (SOF) | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 5 | | | |
| Units: Percent of Participants | | | | |
| number (confidence interval 95%) | 100 (50 to 100) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose to 30 days following last dose

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

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Daclatasvir (DCV) + Sofosbuvir (SOF) |
|-----------------------|--------------------------------------|

Reporting group description:

DCV 60 mg QD + SOF 400 mg QD for 12 weeks

| Serious adverse events | Daclatasvir (DCV) + Sofosbuvir (SOF) | | |
|---|--------------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 5 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Daclatasvir (DCV) + Sofosbuvir (SOF) | | |
|---|--------------------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 4 / 5 (80.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 2 / 5 (40.00%) | | |
| occurrences (all) | 5 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |

| | | | |
|---|---|--|--|
| subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 | | |
| Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 1 / 5 (20.00%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 18 December 2019 | <ul style="list-style-type: none">- Early termination of the study- No participants enrolled in Cohorts 2 and 3- Reduction of the Long-term follow-up period- Removal of analysis for some secondary and exploratory endpoints- Removal of interim analysis |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported