



Clinical trial results:

A Phase 2 study to investigate the efficacy, safety, and tolerability of six weeks treatment with V565 in subjects with active Crohn's disease.

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2016-002939-15 |
| Trial protocol | CZ DE AT HU SK NL NO GB |
| Global end of trial date | 08 March 2019 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 12 November 2021 |
| First version publication date | 12 November 2021 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | V56502 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02976129 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | VHsquared |
| Sponsor organisation address | 1 Lower Court, Cambridge, United Kingdom, CB22 3GN |
| Public contact | Clinical Trial Information Desk, VHsquared Ltd, 0044 1223837650, info@vhsquared.com |
| Scientific contact | Clinical Trial Information Desk, VHsquared Ltd, 0044 1223837650, info@vhsquared.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 | 08 March 2019 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 March 2019 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 March 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To investigate the efficacy, safety and tolerability of 6 weeks treatment with V565 in subjects with active Crohn's Disease.

Protection of trial subjects:

The study protocol, all study protocol amendments, written study subject information, informed consent form (ICF), Investigator's Brochure and any other relevant documents were reviewed and approved by an Independent Ethics Committee (IEC) and Institutional Review Board (IRB) at each study site.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 15 February 2017 |
| 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 | United Kingdom: 9 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | United States: 7 |
| Country: Number of subjects enrolled | Ukraine: 34 |
| Country: Number of subjects enrolled | Serbia: 6 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Poland: 14 |
| Country: Number of subjects enrolled | Slovakia: 8 |
| Country: Number of subjects enrolled | Austria: 3 |
| Country: Number of subjects enrolled | Czech Republic: 29 |
| Country: Number of subjects enrolled | Germany: 6 |
| Country: Number of subjects enrolled | Hungary: 5 |
| Worldwide total number of subjects | 125 |
| EEA total number of subjects | 76 |

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) | 121 |
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

125 subjects were recruited from 13 countries in North America and Europe.

Pre-assignment

Screening details:

Out of 330 screened subjects, 205 were considered screen failures. A total of 125 subjects were randomised and treated in the study.

Period 1

| | |
|------------------------------|--|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|------|
| Arm title | V565 |
|------------------|------|

Arm description:

V565 PO 555mg TID

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | V565 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

V565 PO 555mg TID

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

Placebo PO 3 capsules TID

| | |
|--|----------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Placebo 3 capsules TID

| Number of subjects in period 1 | V565 | Placebo |
|---------------------------------------|------|---------|
| Started | 82 | 43 |
| Completed | 77 | 41 |
| Not completed | 5 | 2 |
| Physician decision | - | 2 |
| Adverse event, non-fatal | 2 | - |
| Missed primary endpoint visit | 1 | - |
| Pregnancy | 1 | - |
| Lost to follow-up | 1 | - |

Baseline characteristics

Reporting groups

| | |
|---|---------|
| Reporting group title | V565 |
| Reporting group description: V565 PO 555mg TID | |
| Reporting group title | Placebo |
| Reporting group description: Placebo PO 3 capsules TID | |

| Reporting group values | V565 | Placebo | Total |
|---|------------|------------|-------|
| Number of subjects | 82 | 43 | 125 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 78 | 43 | 121 |
| From 65-84 years | 4 | 0 | 4 |
| Age continuous Units: years | | | |
| arithmetic mean | 37.7 | 37.2 | - |
| standard deviation | ± 14.05 | ± 12.08 | - |
| Gender categorical Units: Subjects | | | |
| Female | 32 | 19 | 51 |
| Male | 50 | 24 | 74 |
| CDAI score Units: Score on a scale | | | |
| arithmetic mean | 316.34 | 296.69 | - |
| standard deviation | ± 71.283 | ± 64.344 | - |
| Baseline CRP | | | |
| Baseline CRP value for those subjects qualifying for the study based on CRP | | | |
| Units: mg/L | | | |
| arithmetic mean | 21.9 | 18.7 | - |
| standard deviation | ± 18.43 | ± 14.56 | - |
| Baseline FCP | | | |
| Baseline FCP for those subjects qualifying for the study on FCP | | | |
| Units: µg/g | | | |
| arithmetic mean | 1082.619 | 1091.217 | - |
| standard deviation | ± 804.2154 | ± 974.0855 | - |

End points

End points reporting groups

| | |
|------------------------------|---------------------------|
| Reporting group title | V565 |
| Reporting group description: | V565 PO 555mg TID |
| Reporting group title | Placebo |
| Reporting group description: | Placebo PO 3 capsules TID |

Primary: Proportion of responders at Day 42, defined as subjects achieving both CDAI \geq 70-point reduction from Baseline or CDAI score $<$ 150, and a reduction of \geq 40% from the baseline value of CRP or FCP.

| | |
|------------------------|---|
| End point title | Proportion of responders at Day 42, defined as subjects achieving both CDAI \geq 70-point reduction from Baseline or CDAI score $<$ 150, and a reduction of \geq 40% from the baseline value of CRP or FCP. |
| End point description: | |
| End point type | Primary |
| End point timeframe: | Day 42 |

| End point values | V565 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 82 | 43 | | |
| Units: Number of responders | 29 | 16 | | |

Statistical analyses

| | |
|---|----------------------|
| Statistical analysis title | Statistical analysis |
| Comparison groups | Placebo v V565 |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Regression, Logistic |

Secondary: Proportion of subjects achieving a \geq 100-point reduction in CDAI score and a concomitant reduction of at least 50% in CRP or FCP at Day 42

| | |
|-----------------|--|
| End point title | Proportion of subjects achieving a \geq 100-point reduction in CDAI score and a concomitant reduction of at least 50% in CRP |
|-----------------|--|

or FCP at Day 42

End point description:

End point type Secondary

End point timeframe:

Day 42

| End point values | V565 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 82 | 43 | | |
| Units: Number of responders | 20 | 9 | | |

Statistical analyses

| Statistical analysis title | Statistical analysis |
|---|----------------------|
| Comparison groups | V565 v Placebo |
| Number of subjects included in analysis | 125 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | > 0.05 |
| Method | Regression, Logistic |

Other pre-specified: Proportion of subjects achieving CRP levels within normal limits at Day 14 and 42

End point title Proportion of subjects achieving CRP levels within normal limits at Day 14 and 42

End point description:

End point type Other pre-specified

End point timeframe:

Day 14 and 42

| End point values | V565 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 58 | 31 | | |
| Units: Number of patients | 11 | 4 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Proportion of subjects achieving FCP levels within normal limits at Day 14 and 42

| | |
|-----------------|---|
| End point title | Proportion of subjects achieving FCP levels within normal limits at Day 14 and 42 |
|-----------------|---|

End point description:

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 14 and 42

| End point values | V565 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 23 | 10 | | |
| Units: Number of subjects | 7 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Comparative assessment of endoscopic mucosal appearance

| | |
|-----------------|---|
| End point title | Comparative assessment of endoscopic mucosal appearance |
|-----------------|---|

End point description:

Subjects with a pre-treatment endoscopy SES-CD of at least 7 (4 if disease was confined to ileum) had a post-treatment endoscopy to evaluate changes in mucosal appearance. The central reader of the endoscopies, blinded to treatment and sequence, was asked to grade if video A was better or worse than video B. Pre- and post-treatment videos were randomly assigned to A and B. The endpoint is the number of subjects whose post-treatment endoscopy was better than their pre-treatment endoscopy.

| | |
|----------------|---------------------|
| End point type | Other pre-specified |
|----------------|---------------------|

End point timeframe:

Day 42

| End point values | V565 | Placebo | | |
|-------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 32 | 10 | | |
| Units: Proportion of subjects | 18 | 3 | | |

Statistical analyses

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of IMP on Day 1 until the follow-up visit 2 weeks after the final dose, at Day 56.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------|
| Reporting group title | V565 |
|-----------------------|------|

Reporting group description:

V565 PO 555mg TID

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Placebo PO 3 capsules TID

| Serious adverse events | V565 | Placebo | |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 82 (3.66%) | 2 / 43 (4.65%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Crohn's disease | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Anal abscess | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | 0 / 43 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | V565 | Placebo | |
|--|------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 30 / 82 (36.59%) | 16 / 43 (37.21%) | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 2 / 82 (2.44%) | 1 / 43 (2.33%) | |
| occurrences (all) | 2 | 1 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 82 (2.44%) | 0 / 43 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Urine analysis abnormal | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 1 | |
| Cardiac disorders | | | |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | 1 / 43 (2.33%) | |
| occurrences (all) | 1 | 1 | |
| Seizure | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 1 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---|----------------|--|
| Anaemia | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | 1 / 43 (2.33%) | |
| occurrences (all) | 1 | 1 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 1 | |
| Neutrophilia | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 0 | |
| General disorders and administration site conditions | | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 4 / 82 (4.88%) | 4 / 43 (9.30%) | |
| occurrences (all) | 6 | 4 | |
| Crohn's disease | Additional description: Three of five cases occurred after end of treatment. One further case was a patient with improvement in lower GI CD, resulting in oesophageal CD becoming the primary problem and therefore an AE | | |
| subjects affected / exposed | 5 / 82 (6.10%) | 0 / 43 (0.00%) | |
| occurrences (all) | 5 | 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 82 (2.44%) | 2 / 43 (4.65%) | |
| occurrences (all) | 2 | 2 | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 82 (1.22%) | 2 / 43 (4.65%) | |
| occurrences (all) | 1 | 2 | |
| Dyspepsia | | | |
| subjects affected / exposed | 2 / 82 (2.44%) | 0 / 43 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nausea | | | |
| subjects affected / exposed | 2 / 82 (2.44%) | 0 / 43 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Abdominal distension | | | |
| subjects affected / exposed | 0 / 82 (0.00%) | 1 / 43 (2.33%) | |
| occurrences (all) | 0 | 1 | |

| | | | |
|---|--|--|--|
| Gastrointestinal haemorrhage subjects affected / exposed occurrences (all) | 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 0 | |
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 1 | |
| Proctalgia subjects affected / exposed occurrences (all) | 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 1 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 1 | |
| Skin and subcutaneous tissue disorders Dry skin subjects affected / exposed occurrences (all) | 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 1 | |
| Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Personality change subjects affected / exposed occurrences (all) | 0 / 82 (0.00%) 0 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 | |
| Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all) Nephrolithiasis subjects affected / exposed occurrences (all) | 1 / 82 (1.22%) 1 0 / 82 (0.00%) 0 | 1 / 43 (2.33%) 1 1 / 43 (2.33%) 1 | |
| Infections and infestations Anal abscess subjects affected / exposed occurrences (all) Gastroenteritis | 2 / 82 (2.44%) 2 | 0 / 43 (0.00%) 0 | |

| | | | |
|--|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 2 / 82 (2.44%) 2 | 0 / 43 (0.00%) 0 | |
| Influenza subjects affected / exposed occurrences (all) | 2 / 82 (2.44%) 3 | 0 / 43 (0.00%) 0 | |
| Pulpitis dental subjects affected / exposed occurrences (all) | 2 / 82 (2.44%) 2 | 0 / 43 (0.00%) 0 | |
| Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) | 1 / 82 (1.22%) 1 | 1 / 43 (2.33%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported