



## 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
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#### 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:

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**Results analysis stage**

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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:

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**General information about the trial**

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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:

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**Population of trial subjects**

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**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:

<b>Subjects enrolled per age group</b>	
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
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<b>Arm title</b>	V565
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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

<b>Arm title</b>	Placebo
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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

<b>Number of subjects in period 1</b>	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
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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

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

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

End point type	Other pre-specified
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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		

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**Statistical analyses**

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No statistical analyses for this end point

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**Other pre-specified: Comparative assessment of endoscopic mucosal appearance**

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End point title	Comparative assessment of endoscopic mucosal appearance
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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
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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		

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**Statistical analyses**

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## 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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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### Reporting groups

Reporting group title	V565
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Reporting group description:

V565 PO 555mg TID

Reporting group title	Placebo
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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	
<b>Infections and infestations</b>			
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 %

<b>Non-serious adverse events</b>	V565	Placebo	
<b>Total subjects affected by non-serious adverse events</b>			
subjects affected / exposed	30 / 82 (36.59%)	16 / 43 (37.21%)	
<b>Investigations</b>			
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	
<b>Cardiac disorders</b>			
Tachycardia			
subjects affected / exposed	0 / 82 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
<b>Nervous system disorders</b>			
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	
<b>Blood and lymphatic system disorders</b>			

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)	0 / 82 (0.00%) 0	1 / 43 (2.33%) 1	
Personality change subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 43 (2.33%) 1	
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	1 / 82 (1.22%) 1	1 / 43 (2.33%) 1	
Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 82 (0.00%) 0	1 / 43 (2.33%) 1	
Infections and infestations Anal abscess subjects affected / exposed occurrences (all)	2 / 82 (2.44%) 2	0 / 43 (0.00%) 0	
Gastroenteritis			

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

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported