



Clinical trial results:

A placebo-controlled, patient and investigator blinded, randomized parallel cohort study to assess pharmacodynamics, pharmacokinetics, safety, tolerability and preliminary clinical efficacy of VAY736 and CFZ533 in patients with systemic lupus erythematosus (SLE)

Summary

EudraCT number	2018-001508-12
Trial protocol	CZ DE ES FR
Global end of trial date	28 April 2025

Results information

Result version number	v1 (current)
This version publication date	07 May 2026
First version publication date	07 May 2026

Trial information

Trial identification

Sponsor protocol code	CVAY736X2208
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03656562
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	Novartis Campus, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@Novartis.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	28 April 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	28 April 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to determine the effect of VAY736 and of CFZ533 versus their respective placebo on disease activity in SLE patients at Week 29 compared to baseline. Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com> for complete trial results.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 December 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	Argentina: 3
Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	China: 9
Country: Number of subjects enrolled	Czechia: 5
Country: Number of subjects enrolled	France: 1
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 5
Country: Number of subjects enrolled	Japan: 11
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Poland: 11
Country: Number of subjects enrolled	Russian Federation: 12
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	Thailand: 8
Worldwide total number of subjects	107
EEA total number of subjects	46

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)	103
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted in 31 centers in 15 countries: Argentina (1), Australia (1), China (3), Czech Republic (1), France (1), Germany (2), Hungary (2), Israel (1), Japan (5), Korea, Republic of (1), Poland (3), Russia (3), Spain (2), Taiwan (3), Thailand (2).

Period 1

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

Blinding implementation details:

Patients, investigator staff, persons performing the assessments, and the clinical trial team (CTT) remained blind to the identity of the treatment within each cohort from the time of randomization until end of the Week 29 visit.

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1 VAY736

Arm description:

Blinded treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.

Arm type	Experimental
Investigational medicinal product name	VAY736
Investigational medicinal product code	
Other name	Ianalumab
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Blinded treatment phase:

VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Open-label treatment phase:

VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.

Arm title	Cohort 1 VAY736 Placebo
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Arm description:

Blinded treatment phase: VAY736 matching placebo administered subcutaneously (s.c.) every 4 weeks as multiple doses of placebo 0 mg until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.

Arm type	Placebo
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Investigational medicinal product name	VAY736 Placebo
Investigational medicinal product code	
Other name	Ianalumab/Placebo
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Blinded treatment phase:

VAY736 matching placebo administered subcutaneously (s.c.) every 4 weeks as multiple doses of placebo 0 mg until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Arm title	Cohort 2 CFZ533
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Arm description:

Blinded treatment phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 49.

Arm type	Experimental
Investigational medicinal product name	CFZ533
Investigational medicinal product code	
Other name	Iscalimab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Blinded treatment phase:

CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Open-label phase:

CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 49.

Arm title	Cohort 2 CFZ533 Placebo
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Arm description:

Blinded treatment phase: CFZ533 matching placebo administered intravenously (i.v) every 4 weeks as multiple doses of placebo 0 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 49.

Arm type	Placebo
Investigational medicinal product name	CFZ533 Placebo
Investigational medicinal product code	
Other name	Iscalimab/Placebo
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Blinded treatment phase:

CFZ533 matching placebo administered intravenously (i.v) every 4 weeks as multiple doses of placebo 0 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Number of subjects in period 1	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533
Started	34	33	20
Pharmacodynamic analysis set	34	33	20
Safety set	34	33	20
Pharmacokinetic analysis set	34	30	20
Completed	26	21	20
Not completed	8	12	0
Physician decision	3	5	-
Subject Decision	5	7	-

Number of subjects in period 1	Cohort 2 CFZ533 Placebo
Started	20
Pharmacodynamic analysis set	20
Safety set	20
Pharmacokinetic analysis set	16 ^[1]
Completed	17
Not completed	3
Physician decision	-
Subject Decision	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This milestone represents the PK set.

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1 VAY736
Reporting group description:	
Blinded treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.	
Reporting group title	Cohort 1 VAY736 Placebo
Reporting group description:	
Blinded treatment phase: VAY736 matching placebo administered subcutaneously (s.c.) every 4 weeks as multiple doses of placebo 0 mg until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.	
Reporting group title	Cohort 2 CFZ533
Reporting group description:	
Blinded treatment phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 49.	
Reporting group title	Cohort 2 CFZ533 Placebo
Reporting group description:	
Blinded treatment phase: CFZ533 matching placebo administered intravenously (i.v) every 4 weeks as multiple doses of placebo 0 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 49.	

Reporting group values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533
Number of subjects	34	33	20
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age $<$ 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	32	33	20
From 65-84 years	2	0	0
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	42.0	39.2	37.4
standard deviation	\pm 10.91	\pm 10.46	\pm 11.34

Sex: Female, Male			
Units: Participants			
Female	32	27	20
Male	2	6	0
Race/Ethnicity, Customized			
Units: Subjects			
Asian	9	12	7
Black or African American	0	0	1
White	25	21	12

Reporting group values	Cohort 2 CFZ533 Placebo	Total	
Number of subjects	20	107	
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)	0	0	
Adults (18-64 years)	18	103	
From 65-84 years	2	4	
85 years and over	0	0	
Age Continuous			
Units: Years			
arithmetic mean	44.7		
standard deviation	± 12.47	-	
Sex: Female, Male			
Units: Participants			
Female	19	98	
Male	1	9	
Race/Ethnicity, Customized			
Units: Subjects			
Asian	12	40	
Black or African American	0	1	
White	8	66	

End points

End points reporting groups

Reporting group title	Cohort 1 VAY736
Reporting group description:	
Blinded treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.	
Reporting group title	Cohort 1 VAY736 Placebo
Reporting group description:	
Blinded treatment phase: VAY736 matching placebo administered subcutaneously (s.c.) every 4 weeks as multiple doses of placebo 0 mg until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label treatment phase: VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.	
Reporting group title	Cohort 2 CFZ533
Reporting group description:	
Blinded treatment phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (≥ 50 kg BW) and 13 mg/kg (< 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (≥ 50 kg BW) and 13 mg/kg (< 50 kg BW)) until Week 49.	
Reporting group title	Cohort 2 CFZ533 Placebo
Reporting group description:	
Blinded treatment phase: CFZ533 matching placebo administered intravenously (i.v) every 4 weeks as multiple doses of placebo 0 mg, based on body weight (BW) of the patients (10 mg/kg (≥ 50 kg BW) and 13 mg/kg (< 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE). Open-label phase: CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (≥ 50 kg BW) and 13 mg/kg (< 50 kg BW)) until Week 49.	

Primary: Percentage of Participants With SLE Responder Index (SRI)-4 Response Status at Week 29 With Reduced Steroid Dose Maintained Between Weeks 17 and 29

End point title	Percentage of Participants With SLE Responder Index (SRI)-4 Response Status at Week 29 With Reduced Steroid Dose Maintained Between Weeks 17 and 29 ^[1]
End point description:	
The primary endpoint was a composite of SRI-4 response at Week 29 with sustained reduction in oral corticosteroid from Week 17 through Week 29. Patients taking other rescue medication or prohibited medication or drop out before Week 29 were considered non-responders.	
SRI-4 response is defined as below:	
<ul style="list-style-type: none">• having ≥ 4 points reduction from baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score (score is 0 to 105; a higher score indicating more severe disease) AND• no new British Isles Lupus Activity Group (BILAG)-2004 A organ domain score and no more than one new BILAG-2004 B organ domain scores compared with baseline AND• < 10 mm point increase from baseline with scale 0 to 100 mm in the physician's global assessment from baseline	
Sustained reduction in oral corticosteroid is defined as below:	
<ul style="list-style-type: none">• ≤ 5 mg/day or less than or equal to baseline dose, whichever was lower at Week 17 AND	
<ul style="list-style-type: none">• no increase of that dose from Week 17 through Week 29	
End point type	Primary

End point timeframe:

Baseline, Week 17 to Week 29

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 planned for this primary outcome.

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	33	20	20
Units: Participants	15	3	8	6

Statistical analyses

No statistical analyses for this end point

Secondary: Changes Between Baseline and Week 29 in the Physicians' Global Assessment (PhGA) Visual Analog Scale (VAS) Assessing Patient's Overall Disease Activity

End point title	Changes Between Baseline and Week 29 in the Physicians' Global Assessment (PhGA) Visual Analog Scale (VAS) Assessing Patient's Overall Disease Activity
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End point description:

The Physician's global assessment (PhGA-VAS) of disease activity was performed using 100 mm VAS ranging from "no disease activity" (score 0) to "maximal disease activity" (score 100), after the question on how well the patient was doing with the disease considering all aspects affected by the disease. The investigator was then measuring the distance in mm from the left edge of the scale and entering the value.

End point type	Secondary
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End point timeframe:

Baseline, Week 5, Week 9, Week 13, Week 17, Week 21, Week 25, Week 29

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	33	20	20
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Week 5 n=34,33,20,20	-7.6 (± 14.27)	-5.6 (± 13.76)	-8.3 (± 12.04)	-12.5 (± 15.94)
Week 9 n=33,33,20,19	-17.4 (± 18.72)	-10.9 (± 13.54)	-9.3 (± 15.73)	-13.7 (± 18.43)
Week 13 n=33,33,20,19	-23.0 (± 19.51)	-13.6 (± 16.72)	-19.4 (± 16.70)	-20.3 (± 19.26)
Week 17 n=34,31,20,19	-26.2 (± 19.14)	-14.2 (± 16.38)	-21.9 (± 21.81)	-22.2 (± 20.10)
Week 21 n=34,33,19,18	-28.1 (± 20.27)	-17.9 (± 16.24)	-26.1 (± 23.15)	-24.1 (± 17.71)

Week 25 n=33,32,19,18	-33.2 (± 19.63)	-18.6 (± 17.62)	-28.5 (± 22.92)	-24.6 (± 19.12)
Week 29 n=33,32,20,17	-32.8 (± 20.74)	-19.4 (± 16.04)	-28.7 (± 22.89)	-24.5 (± 19.25)

Statistical analyses

No statistical analyses for this end point

Secondary: Changes Between Baseline and Week 29 in the Patient's Global Assessment (PGA) Visual Analog Scale (VAS) Assessing Patient's Global Disease Activity

End point title	Changes Between Baseline and Week 29 in the Patient's Global Assessment (PGA) Visual Analog Scale (VAS) Assessing Patient's Global Disease Activity
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End point description:

The patient's global assessment of disease activity was performed using a Visual Analogue Scale (VAS) of 100 mm ranging from "no disease activity" (score 0) to "severe disease activity" (score 100), after the question on how well the patient was doing with the disease considering all aspects affected by the disease. The investigator was then measuring the distance in mm from the left edge of the scale and entering the value.

End point type	Secondary
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End point timeframe:

Baseline, Week 5, Week 9, Week 13, Week 17, Week 21, Week 25, Week 29

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	33	20	20
Units: Unit on a scale				
arithmetic mean (standard deviation)				
Week 5 n=34,32,20,20	-9.0 (± 23.14)	-4.8 (± 13.60)	-9.8 (± 20.63)	-3.8 (± 19.33)
Week 9 n=33,33,20,19	-12.5 (± 21.35)	-12.2 (± 15.62)	-17.9 (± 30.22)	0.1 (± 20.52)
Week 13 n=32,33,20,19	-15.7 (± 21.69)	-8.8 (± 17.75)	-21.8 (± 31.01)	-0.1 (± 22.10)
Week 17 n=34,31,20,19	-12.7 (± 24.19)	-8.0 (± 19.27)	-26.7 (± 28.92)	1.6 (± 19.05)
Week 21 n=34,32,19,18	-15.1 (± 24.82)	-9.5 (± 24.88)	-27.2 (± 31.92)	-0.5 (± 24.79)
Week 25 n=33,32,19,18	-18.0 (± 19.91)	-10.4 (± 21.33)	-27.0 (± 30.58)	1.1 (± 25.62)
Week 29 n=33,32,20,17	-18.1 (± 21.81)	-9.0 (± 24.64)	-27.8 (± 33.41)	-1.9 (± 25.06)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Flare

End point title	Percentage of Participants With Flare
End point description: Flare was defined as one new 'A' score or two or more 'B' scores using the British Isles Lupus Assessment Group Index (BILAG -2004).	
End point type	Secondary
End point timeframe: Up to 69 weeks	

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	34	33	20	20
Units: percentage of participants				
number (not applicable)				
Double-blind Treatment (<=29 Weeks) n=34,33,20,20	8.8	30.3	20	10
Open-label Treatment n=33,32,20,16	0	9.4	10	0
Post-treatment Follow-up n=32,30,20,16	3.1	3.3	5	0

Statistical analyses

No statistical analyses for this end point

Secondary: Time to First Flare

End point title	Time to First Flare
End point description: Time to first flare, with flare defined as one new 'A' score or two or more 'B' score using BILAG -2004	
End point type	Secondary
End point timeframe: Up to 69 weeks	

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	10	4	2
Units: days				
arithmetic mean (standard deviation)				
Double-blind Treatment (<=29 Weeks) n=3,10,4,2	94.7 (± 89.80)	107.7 (± 34.23)	113.0 (± 68.61)	69.0 (± 19.80)

Open-label Treatment n=0,3,2,0	999 (± 999)	301.3 (± 17.79)	379.0 (± 11.31)	999 (± 999)
Post-treatment Follow-up n=1,1,1,0	419.0 (± 999)	484.0 (± 999)	421.0 (± 999)	999 (± 999)

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetics (PK) Cohort 1 - VAY736 Free Serum Concentration

End point title	Pharmacokinetics (PK) Cohort 1 - VAY736 Free Serum Concentration ^[2]
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End point description:

Note: End of study (EoS) was a floating timepoint and did not represent a uniform timepoint across the study.

End point type	Secondary
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End point timeframe:

Weeks 29, 53, 69, and EoS (up to 69 weeks), pre-dose

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data are reported for applicable reporting groups.

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	26		
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 29 n=29,26	1.85 (± 1.17)	0 (± 0)		
Week 53 n=22,23	1.68 (± 1.30)	2.24 (± 1.45)		
Week 69 n=26,23	0.03 (± 0.14)	0 (± 0)		
EoS n=13,13	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: PK Cohort 2 - Free CFZ533 Concentration in Plasma

End point title	PK Cohort 2 - Free CFZ533 Concentration in Plasma ^[3]
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End point description:

End point type	Secondary
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End point timeframe:

Weeks 29, 53, and 69, pre-dose

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data are reported for applicable reporting groups.

End point values	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	11		
Units: µg/mL				
arithmetic mean (standard deviation)				
Week 29 n=20,7	59.9 (± 40.3)	0 (± 0)		
Week 53 n=20,9	56.9 (± 39.6)	42.5 (± 20)		
Week 69 n=18,11	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: PD Cohort 2 (CFZ533): Total Soluble CD40

End point title	PD Cohort 2 (CFZ533): Total Soluble CD40 ^[4]
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End point description:

End point type	Secondary
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End point timeframe:

Weeks 29, 53, and 69

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data are reported for applicable reporting groups.

End point values	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: ng/mL				
arithmetic mean (standard deviation)				
Week 29	143 (± 44.4)	0.365 (± 0.504)		
Week 53	158 (± 36.1)	124 (± 67)		
Week 69	3 (± 3.89)	1.38 (± 0.892)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-drug Antibodies (ADAs)

End point title	Percentage of Participants With Anti-drug Antibodies (ADAs)
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End point description:

ADAs were measured in plasma for CFZ533 and in serum for VAY736. Note: End of study (EoS) was a floating timepoint and did not represent a uniform timepoint across the study.

End point type	Secondary
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End point timeframe:

Baseline, Weeks 29, 53, 69, and EoS (up to 69 weeks)

End point values	Cohort 1 VAY736	Cohort 1 VAY736 Placebo	Cohort 2 CFZ533	Cohort 2 CFZ533 Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	20	17
Units: percentage of participants				
number (not applicable)				
Baseline n=30,29,19,17	26.5	21.2	0	0
Week 29 n=30,30,20,17	5.9	21.2	0	0
Week 53 n=29,28,20,15	0	6.3	0	0
Week 69 n=26,28,18,14	9.4	13.3	0	0
EoS n=19,16,0,0	11.8	9.1	999	999

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from first dose of study treatment until end of study treatment plus up to 2 years post treatment, up to a maximum duration of approximately 3 years.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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Reporting groups

Reporting group title	VAY736
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Reporting group description:

Blinded treatment phase:

VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Reporting group title	VAY736 Placebo
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Reporting group description:

Blinded treatment phase:

VAY736 matching placebo administered subcutaneously (s.c.) every 4 weeks as multiple doses of placebo 0 mg until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Reporting group title	CFZ533
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Reporting group description:

Blinded treatment phase:

CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Reporting group title	CFZ533 Placebo
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Reporting group description:

Blinded treatment phase:

CFZ533 matching placebo administered intravenously (i.v) every 4 weeks as multiple doses of placebo 0 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 25 + Standard of Care (SoC) for systemic lupus erythematosus (SLE).

Reporting group title	Total (Double-blind)
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Reporting group description:

Total (Double-blind)

Reporting group title	VAY736/VAY736
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Reporting group description:

Open-label treatment phase:

VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.

Reporting group title	CFZ533/CFZ533
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Reporting group description:

Open-label phase:

CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (\geq 50 kg BW) and 13 mg/kg ($<$ 50 kg BW)) until Week 49.

Reporting group title	VAY736 Placebo/VAY736
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Reporting group description:

Open-label treatment phase:

VAY736 administered subcutaneously (s.c.) every 4 weeks as multiple doses of VAY736 150 mg (total dose being VAY736 300 mg) until Week 49.

Reporting group title	CFZ533 Placebo/CFZ533
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Reporting group description:

Open-label phase:

CFZ533 administered intravenously (i.v) every 4 weeks as multiple doses of CFZ533 150 mg, based on body weight (BW) of the patients (10 mg/kg (≥ 50 kg BW) and 13 mg/kg (< 50 kg BW)) until Week 49.

Reporting group title	VAY736/VAY736 (Secondary Post-treatment Follow-up)
Reporting group description:	
Secondary Post-treatment Follow-up	
Reporting group title	Total (Open-label)
Reporting group description:	
Total (Open-label)	
Reporting group title	VAY736/VAY736 (Post-treatment Follow-up)
Reporting group description:	
Post-treatment Follow-up	
Reporting group title	VAY736 Placebo/VAY736 (Post-treatment Follow-up)
Reporting group description:	
Post-treatment Follow-up	
Reporting group title	CFZ533/CFZ533 (Post-treatment Follow-up)
Reporting group description:	
Post-treatment follow-up	
Reporting group title	CFZ533 Placebo/CFZ533 (Post-treatment Follow-up)
Reporting group description:	
Post-treatment Follow-up	
Reporting group title	Total (Post-treatment follow-up)
Reporting group description:	
Total (Post-treatment follow-up)	
Reporting group title	VAY736 Placebo/VAY736 (Secondary Post-treatment Follow-up)
Reporting group description:	
Secondary Post-treatment Follow-up	
Reporting group title	Total (Secondary Post-treatment follow-up)
Reporting group description:	
Total (Secondary Post-treatment follow-up)	

Serious adverse events	VAY736	VAY736 Placebo	CFZ533
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 34 (2.94%)	4 / 33 (12.12%)	0 / 20 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the stomach			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			

subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 34 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 34 (2.94%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 34 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumocystis jirovecii pneumonia subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis subjects affected / exposed	0 / 34 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia subjects affected / exposed	0 / 34 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CFZ533 Placebo	Total (Double-blind)	VAY736/VAY736
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 20 (5.00%)	6 / 107 (5.61%)	3 / 33 (9.09%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Carcinoid tumour of the stomach			

subjects affected / exposed	1 / 20 (5.00%)	1 / 107 (0.93%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Ear and labyrinth disorders Vertigo positional subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 0 / 107 (0.00%) 0 / 0 0 / 0	 1 / 33 (3.03%) 0 / 1 0 / 0
Gastrointestinal disorders Pancreatitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 0 / 107 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0
Reproductive system and breast disorders Ovarian cyst subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 1 / 107 (0.93%) 0 / 1 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0
Respiratory, thoracic and mediastinal disorders Respiratory failure subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 0 / 107 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0
Renal and urinary disorders Renal impairment subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 1 / 107 (0.93%) 0 / 1 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0
Musculoskeletal and connective tissue disorders Spinal stenosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 0 / 107 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0
Infections and infestations Cytomegalovirus viraemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 20 (0.00%) 0 / 0 0 / 0	 0 / 107 (0.00%) 0 / 0 0 / 0	 0 / 33 (0.00%) 0 / 0 0 / 0

Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	1 / 107 (0.93%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 107 (0.93%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 107 (0.93%)	0 / 33 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CFZ533/CFZ533	VAY736 Placebo/VAY736	CFZ533 Placebo/CFZ533
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	1 / 32 (3.13%)	2 / 16 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the stomach			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 20 (0.00%)	1 / 32 (3.13%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Cytomegalovirus viraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	VAY736/VAY736	Total (Open-label)	VAY736/VAY736
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	(Secondary Post-treatment Follow-up)		(Post-treatment Follow-up)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	6 / 101 (5.94%)	1 / 32 (3.13%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the stomach			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			

subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Spinal stenosis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			

subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	VAY736 Placebo/VAY736 (Post-treatment Follow-up)	CFZ533/CFZ533 (Post-treatment Follow-up)	CFZ533 Placebo/CFZ533 (Post-treatment Follow-up)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)	0 / 20 (0.00%)	2 / 16 (12.50%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the stomach			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			

subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia cytomegaloviral			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyelonephritis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Total (Post-treatment follow-up)	VAY736 Placebo/VAY736 (Secondary Post-treatment Follow-up)	Total (Secondary Post-treatment follow-up)
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 98 (4.08%)	1 / 25 (4.00%)	2 / 54 (3.70%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Carcinoid tumour of the stomach			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Compression fracture			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscus injury			

subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Central nervous system vasculitis			
subjects affected / exposed	0 / 98 (0.00%)	1 / 25 (4.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	1 / 54 (1.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			

subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Spinal stenosis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cytomegalovirus viraemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	VAY736	VAY736 Placebo	CFZ533
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 34 (61.76%)	21 / 33 (63.64%)	9 / 20 (45.00%)
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 34 (5.88%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	2	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	9 / 34 (26.47%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	41	2	0
Pyrexia			
subjects affected / exposed	2 / 34 (5.88%)	0 / 33 (0.00%)	2 / 20 (10.00%)
occurrences (all)	2	0	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 34 (0.00%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	0	1	0
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Investigations Cytomegalovirus test positive subjects affected / exposed occurrences (all) Blood immunoglobulin M decreased subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0 0 / 34 (0.00%) 0	0 / 33 (0.00%) 0 0 / 33 (0.00%) 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0
Injury, poisoning and procedural complications Injection related reaction subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all)	2 / 34 (5.88%) 2 0 / 34 (0.00%) 0	1 / 33 (3.03%) 1 0 / 33 (0.00%) 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	3 / 34 (8.82%) 4 1 / 34 (2.94%) 1	1 / 33 (3.03%) 1 1 / 33 (3.03%) 1	5 / 20 (25.00%) 7 1 / 20 (5.00%) 1
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Neutropenia	0 / 34 (0.00%) 0 0 / 34 (0.00%) 0	0 / 33 (0.00%) 0 1 / 33 (3.03%) 1	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0

subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	2 / 33 (6.06%) 2	0 / 20 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1 0 / 34 (0.00%) 0	0 / 33 (0.00%) 0 0 / 33 (0.00%) 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0	0 / 33 (0.00%) 0 2 / 33 (6.06%) 2 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0	0 / 20 (0.00%) 0 1 / 20 (5.00%) 1 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Dermatitis allergic subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all) Leukoplakia	0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0 / 34 (0.00%) 0 0	0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 0 / 33 (0.00%) 0 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 0 / 20 (0.00%) 0 0

subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	1 / 33 (3.03%) 1	0 / 20 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	1 / 33 (3.03%) 1	0 / 20 (0.00%) 0
Infections and infestations			
Bacteraemia subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	2 / 33 (6.06%) 2	0 / 20 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	1 / 33 (3.03%) 1	0 / 20 (0.00%) 0
Cellulitis subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	1 / 33 (3.03%) 1	0 / 20 (0.00%) 0
Cystitis subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	1 / 33 (3.03%) 2	0 / 20 (0.00%) 0
Cytomegalovirus viraemia subjects affected / exposed occurrences (all)	0 / 34 (0.00%) 0	0 / 33 (0.00%) 0	0 / 20 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	1 / 33 (3.03%) 1	0 / 20 (0.00%) 0
Herpes zoster			

subjects affected / exposed	1 / 34 (2.94%)	1 / 33 (3.03%)	0 / 20 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	7 / 34 (20.59%)	7 / 33 (21.21%)	3 / 20 (15.00%)
occurrences (all)	9	7	3
Oral fungal infection			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	1 / 20 (5.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	3 / 34 (8.82%)	1 / 33 (3.03%)	1 / 20 (5.00%)
occurrences (all)	3	2	1
Urinary tract infection			
subjects affected / exposed	1 / 34 (2.94%)	2 / 33 (6.06%)	1 / 20 (5.00%)
occurrences (all)	1	2	1
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 34 (2.94%)	2 / 33 (6.06%)	0 / 20 (0.00%)
occurrences (all)	1	2	0
Dyslipidaemia			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	1 / 34 (2.94%)	0 / 33 (0.00%)	0 / 20 (0.00%)
occurrences (all)	3	0	0

Non-serious adverse events	CFZ533 Placebo	Total (Double-blind)	VAY736/VAY736
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 20 (55.00%)	62 / 107 (57.94%)	15 / 33 (45.45%)
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 107 (1.87%) 2	0 / 33 (0.00%) 0
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	10 / 107 (9.35%) 43 4 / 107 (3.74%) 4	6 / 33 (18.18%) 53 0 / 33 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2 0 / 20 (0.00%) 0	3 / 107 (2.80%) 3 0 / 107 (0.00%) 0	0 / 33 (0.00%) 0 0 / 33 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 107 (0.93%) 1	0 / 33 (0.00%) 0
Investigations Cytomegalovirus test positive subjects affected / exposed occurrences (all) Blood immunoglobulin M decreased subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	0 / 107 (0.00%) 0 0 / 107 (0.00%) 0	0 / 33 (0.00%) 0 3 / 33 (9.09%) 3
Injury, poisoning and procedural complications Injection related reaction subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	3 / 107 (2.80%) 3 0 / 107 (0.00%) 0	1 / 33 (3.03%) 1 0 / 33 (0.00%) 0
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	10 / 107 (9.35%) 13	1 / 33 (3.03%) 1
Dizziness subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	4 / 107 (3.74%) 4	0 / 33 (0.00%) 0
Blood and lymphatic system disorders			
Leukopenia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 107 (0.93%) 1	0 / 33 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 107 (1.87%) 2	0 / 33 (0.00%) 0
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 107 (1.87%) 2	0 / 33 (0.00%) 0
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 107 (0.93%) 1	0 / 33 (0.00%) 0
Dry eye subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	5 / 107 (4.67%) 5	0 / 33 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	1 / 33 (3.03%) 1

Nausea subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 107 (0.93%) 1	0 / 33 (0.00%) 0
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Dermatitis contact subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 2	2 / 107 (1.87%) 2	0 / 33 (0.00%) 0
Leukoplakia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 107 (0.93%) 1	1 / 33 (3.03%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 107 (1.87%) 2	0 / 33 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	3 / 107 (2.80%) 3	0 / 33 (0.00%) 0
Infections and infestations			
Bacteraemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 107 (0.00%) 0	0 / 33 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	3 / 107 (2.80%) 3	1 / 33 (3.03%) 1
COVID-19 subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 107 (1.87%) 2	2 / 33 (6.06%) 2

Cellulitis			
subjects affected / exposed	2 / 20 (10.00%)	3 / 107 (2.80%)	0 / 33 (0.00%)
occurrences (all)	2	3	0
Cystitis			
subjects affected / exposed	1 / 20 (5.00%)	2 / 107 (1.87%)	1 / 33 (3.03%)
occurrences (all)	2	4	1
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 20 (0.00%)	2 / 107 (1.87%)	0 / 33 (0.00%)
occurrences (all)	0	2	0
Herpes zoster			
subjects affected / exposed	1 / 20 (5.00%)	3 / 107 (2.80%)	0 / 33 (0.00%)
occurrences (all)	1	3	0
Oral candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)	19 / 107 (17.76%)	5 / 33 (15.15%)
occurrences (all)	4	23	7
Oral fungal infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 20 (0.00%)	1 / 107 (0.93%)	0 / 33 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 20 (10.00%)	7 / 107 (6.54%)	1 / 33 (3.03%)
occurrences (all)	2	8	1
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	5 / 107 (4.67%)	1 / 33 (3.03%)
occurrences (all)	1	5	1
Metabolism and nutrition disorders			
Hypertriglyceridaemia			

subjects affected / exposed	0 / 20 (0.00%)	3 / 107 (2.80%)	1 / 33 (3.03%)
occurrences (all)	0	3	1
Dyslipidaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 107 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 107 (0.93%)	1 / 33 (3.03%)
occurrences (all)	0	3	1

Non-serious adverse events	CFZ533/CFZ533	VAY736 Placebo/VAY736	CFZ533 Placebo/CFZ533
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)	21 / 32 (65.63%)	14 / 16 (87.50%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	0 / 20 (0.00%)	12 / 32 (37.50%)	0 / 16 (0.00%)
occurrences (all)	0	69	0
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 32 (3.13%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 20 (5.00%)	2 / 32 (6.25%)	0 / 16 (0.00%)
occurrences (all)	1	2	0
Oropharyngeal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 20 (5.00%)	3 / 32 (9.38%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Investigations			

Cytomegalovirus test positive subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Blood immunoglobulin M decreased subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Injury, poisoning and procedural complications			
Injection related reaction subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	2 / 32 (6.25%) 4	0 / 16 (0.00%) 0
Procedural pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	2 / 20 (10.00%) 4	1 / 32 (3.13%) 2	1 / 16 (6.25%) 1
Dizziness subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 32 (6.25%) 2	0 / 16 (0.00%) 0
Blood and lymphatic system disorders			
Leukopenia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 32 (3.13%) 1	1 / 16 (6.25%) 1
Anaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Neutropenia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 32 (3.13%) 1	0 / 16 (0.00%) 0
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	2 / 16 (12.50%) 2
Eye disorders			

Cataract subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Dry eye subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 32 (0.00%) 0	2 / 16 (12.50%) 2
Gastrointestinal disorders			
Abdominal pain subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	2 / 32 (6.25%) 2	0 / 16 (0.00%) 0
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Leukoplakia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Eczema subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
COVID-19			
subjects affected / exposed	1 / 20 (5.00%)	1 / 32 (3.13%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Cellulitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 32 (3.13%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Cystitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 32 (3.13%)	1 / 16 (6.25%)
occurrences (all)	1	1	1
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 32 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasopharyngitis			

subjects affected / exposed occurrences (all)	4 / 20 (20.00%) 4	1 / 32 (3.13%) 1	3 / 16 (18.75%) 3
Oral fungal infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Oral herpes subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 32 (3.13%) 2	0 / 16 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 32 (3.13%) 1	0 / 16 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	0 / 16 (0.00%) 0
Metabolism and nutrition disorders Hypertriglyceridaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 32 (3.13%) 1	0 / 16 (0.00%) 0
Dyslipidaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 32 (0.00%) 0	1 / 16 (6.25%) 1

Non-serious adverse events	VAY736/VAY736 (Secondary Post- treatment Follow- up)	Total (Open-label)	VAY736/VAY736 (Post-treatment Follow-up)
Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 29 (27.59%)	57 / 101 (56.44%)	4 / 32 (12.50%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	0 / 101 (0.00%) 0	0 / 32 (0.00%) 0
General disorders and administration site conditions Injection site reaction			

subjects affected / exposed	0 / 29 (0.00%)	18 / 101 (17.82%)	0 / 32 (0.00%)
occurrences (all)	0	122	0
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 101 (1.98%)	0 / 32 (0.00%)
occurrences (all)	1	3	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 29 (0.00%)	3 / 101 (2.97%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Oropharyngeal pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 29 (0.00%)	5 / 101 (4.95%)	0 / 32 (0.00%)
occurrences (all)	0	5	0
Investigations			
Cytomegalovirus test positive			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Blood immunoglobulin M decreased			
subjects affected / exposed	0 / 29 (0.00%)	3 / 101 (2.97%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	0 / 29 (0.00%)	4 / 101 (3.96%)	0 / 32 (0.00%)
occurrences (all)	0	6	0
Procedural pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 29 (6.90%)	5 / 101 (4.95%)	0 / 32 (0.00%)
occurrences (all)	2	8	0
Dizziness			

subjects affected / exposed occurrences (all)	0 / 29 (0.00%) 0	2 / 101 (1.98%) 2	0 / 32 (0.00%) 0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 29 (0.00%)	3 / 101 (2.97%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Anaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 29 (0.00%)	2 / 101 (1.98%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 29 (3.45%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Dry eye			
subjects affected / exposed	0 / 29 (0.00%)	3 / 101 (2.97%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 29 (0.00%)	2 / 101 (1.98%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	0 / 29 (0.00%)	2 / 101 (1.98%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Dermatitis allergic			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Dermatitis contact			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Leukoplakia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 101 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Bronchitis			
subjects affected / exposed	0 / 29 (0.00%)	2 / 101 (1.98%)	1 / 32 (3.13%)
occurrences (all)	0	2	1
COVID-19			
subjects affected / exposed	3 / 29 (10.34%)	4 / 101 (3.96%)	0 / 32 (0.00%)
occurrences (all)	3	4	0
Cellulitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Cystitis			

subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 29 (0.00%)	3 / 101 (2.97%)	0 / 32 (0.00%)
occurrences (all)	0	3	0
Herpes zoster			
subjects affected / exposed	1 / 29 (3.45%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	4 / 29 (13.79%)	13 / 101 (12.87%)	1 / 32 (3.13%)
occurrences (all)	7	15	1
Oral fungal infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 29 (0.00%)	2 / 101 (1.98%)	0 / 32 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 29 (3.45%)	2 / 101 (1.98%)	1 / 32 (3.13%)
occurrences (all)	1	2	1
Dyslipidaemia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 101 (0.99%)	0 / 32 (0.00%)
occurrences (all)	0	1	0

Hyperuricaemia subjects affected / exposed occurrences (all)	1 / 29 (3.45%) 1	2 / 101 (1.98%) 2	2 / 32 (6.25%) 2
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Non-serious adverse events	VAY736 Placebo/VAY736 (Post-treatment Follow-up)	CFZ533/CFZ533 (Post-treatment Follow-up)	CFZ533 Placebo/CFZ533 (Post-treatment Follow-up)
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 30 (20.00%)	2 / 20 (10.00%)	5 / 16 (31.25%)
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
General disorders and administration site conditions Injection site reaction subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0 0 / 30 (0.00%) 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	0 / 16 (0.00%) 0 0 / 16 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1 0 / 30 (0.00%) 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	0 / 16 (0.00%) 0 1 / 16 (6.25%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Investigations Cytomegalovirus test positive subjects affected / exposed occurrences (all) Blood immunoglobulin M decreased subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0 0 / 30 (0.00%) 0	0 / 20 (0.00%) 0 0 / 20 (0.00%) 0	0 / 16 (0.00%) 0 0 / 16 (0.00%) 0

Injury, poisoning and procedural complications			
Injection related reaction			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	1 / 16 (6.25%) 1
Dyspepsia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	1 / 16 (6.25%) 1
Nausea subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Skin and subcutaneous tissue disorders			
Acne subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Leukoplakia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1	0 / 20 (0.00%) 0	1 / 16 (6.25%) 1
Infections and infestations			

Bacteraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Cystitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cytomegalovirus viraemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastroenteritis			
subjects affected / exposed	1 / 30 (3.33%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)	1 / 20 (5.00%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Oral fungal infection			
subjects affected / exposed	0 / 30 (0.00%)	0 / 20 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 30 (0.00%)	1 / 20 (5.00%)	1 / 16 (6.25%)
occurrences (all)	0	1	1

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Metabolism and nutrition disorders			
Hypertriglyceridaemia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Dyslipidaemia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0	0 / 20 (0.00%) 0	0 / 16 (0.00%) 0

Non-serious adverse events	Total (Post-treatment follow-up)	VAY736 Placebo/VAY736 (Secondary Post-treatment Follow-up)	Total (Secondary Post-treatment follow-up)
Total subjects affected by non-serious adverse events subjects affected / exposed	17 / 98 (17.35%)	5 / 25 (20.00%)	13 / 54 (24.07%)
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
General disorders and administration site conditions			
Injection site reaction subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	1 / 54 (1.85%) 1
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0

Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
Investigations Cytomegalovirus test positive subjects affected / exposed occurrences (all) Blood immunoglobulin M decreased subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0 0 / 98 (0.00%) 0	0 / 25 (0.00%) 0 0 / 25 (0.00%) 0	0 / 54 (0.00%) 0 0 / 54 (0.00%) 0
Injury, poisoning and procedural complications Injection related reaction subjects affected / exposed occurrences (all) Procedural pain subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0 0 / 98 (0.00%) 0	0 / 25 (0.00%) 0 0 / 25 (0.00%) 0	0 / 54 (0.00%) 0 0 / 54 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0 0 / 98 (0.00%) 0	0 / 25 (0.00%) 0 1 / 25 (4.00%) 1	2 / 54 (3.70%) 2 1 / 54 (1.85%) 1
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Neutropenia	0 / 98 (0.00%) 0 1 / 98 (1.02%) 1	1 / 25 (4.00%) 1 1 / 25 (4.00%) 1	1 / 54 (1.85%) 1 1 / 54 (1.85%) 1

subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Eye disorders Cataract subjects affected / exposed occurrences (all) Dry eye subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0 0 / 98 (0.00%) 0	0 / 25 (0.00%) 0 0 / 25 (0.00%) 0	1 / 54 (1.85%) 1 0 / 54 (0.00%) 0
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Dyspepsia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0 1 / 98 (1.02%) 1 1 / 98 (1.02%) 1 0 / 98 (0.00%) 0	0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0	0 / 54 (0.00%) 0 1 / 54 (1.85%) 1 0 / 54 (0.00%) 0 0 / 54 (0.00%) 0
Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) Dermatitis allergic subjects affected / exposed occurrences (all) Dermatitis contact subjects affected / exposed occurrences (all) Leukoplakia	0 / 98 (0.00%) 0 0 / 98 (0.00%) 0 0 / 98 (0.00%) 0	0 / 25 (0.00%) 0 0 / 25 (0.00%) 0 0 / 25 (0.00%) 0	0 / 54 (0.00%) 0 0 / 54 (0.00%) 0 0 / 54 (0.00%) 0

subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 2	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	2 / 98 (2.04%) 2	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
Infections and infestations			
Bacteraemia subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Bronchitis subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
COVID-19 subjects affected / exposed occurrences (all)	0 / 98 (0.00%) 0	1 / 25 (4.00%) 1	4 / 54 (7.41%) 4
Cellulitis subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
Cystitis subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Cytomegalovirus viraemia subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	0 / 25 (0.00%) 0	0 / 54 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	1 / 98 (1.02%) 1	1 / 25 (4.00%) 1	1 / 54 (1.85%) 1
Herpes zoster			

subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	1 / 54 (1.85%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	3 / 98 (3.06%)	1 / 25 (4.00%)	5 / 54 (9.26%)
occurrences (all)	3	1	8
Oral fungal infection			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	2 / 98 (2.04%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypertriglyceridaemia			
subjects affected / exposed	1 / 98 (1.02%)	0 / 25 (0.00%)	1 / 54 (1.85%)
occurrences (all)	1	0	1
Dyslipidaemia			
subjects affected / exposed	0 / 98 (0.00%)	0 / 25 (0.00%)	0 / 54 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	2 / 98 (2.04%)	0 / 25 (0.00%)	1 / 54 (1.85%)
occurrences (all)	2	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 June 2019	The key purpose of this amendment was to clarify and implement the following inclusion and exclusion criteria - Inclusion Criteria: Clarification of required pattern of autoantibodies; Allowable background therapies were expanded to include mycophenolic acid derivatives and thalidomide; Clarification of the required BILAG score index at screening added. Exclusion Criteria: Activated partial thromboplastin time was specified; Allowable background disease modifying anti-rheumatic drugs (DMARD) therapies were expanded, and the wash-out period of any B cell-depleting therapies was clarified; Clarification of the tuberculosis criterion; Lowered the threshold for thrombocytopenia from 75,000 cells/mm ³ to 50,000 cells/mm ³ ; Eastern Cooperative Oncology Group (ECOG) performance status was removed; Clarification of the proteinuria criterion was added; Hepatitis B screening and monitoring procedures were adjusted in accordance with current guidelines of the American Association for the Study of Liver Diseases; Malignancy clarified by adding squamous cell carcinoma of the skin; Permitted hormonal contraceptives extended to include progesterone-only formulations; an exploratory endpoint (Lupus Low Disease Activity State [LLDAS]) was included. Information regarding female partners of male patients was removed.
23 January 2020	The key purpose of this amendment was to mitigate the potential risk of cytomegalovirus (CMV) infection by including the screening for active and latent CMV infection and to have CMV monitoring in Cohort 2.
17 March 2021	The key purpose of this amendment was to increase the duration of contraception after VAY736 treatment from 4 to 6 months.
25 February 2022	The purpose of this amendment was to implement change in contraception requirements from "highly effective" to "effective" methods for CFZ533, to add malignancy as an important potential risk for VAY736, to remove hypogammaglobulinemia study/cohort stopping rules. Measurements of IgG and IgM at end-of-study (EoS) were added to VAY736 cohort to invite patients who met the criteria for B cell recovery for an EoS visit. Interim analysis was revised to include the revised text that provides for use of interim results to prepare for abstracts and other external communications at scientific meetings/publications.
11 February 2025	The purpose of this amendment was to reduce the follow-up period and allow the EoS visit 2 years after end of treatment (EoT, Cohort 1), independent of B cell recovery.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use <https://www.novctrd.com> for complete trial results.

Notes:

