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Sponsor

Novartis Pharmaceuticals

Generic Drug Name

lanalumab

Trial Indication(s)

Rheumatoid arthritis (RA)

Protocol Number

CVAY736A2101

Protocol Title

A randomized, open label, multiple dose, parallel group study to assess the safety and pharmacokinetic comparability of two VAY736 drug products in patients with rheumatoid arthritis

Clinical Trial Phase

Phase 1

Phase of Drug Development

Phase III

Study Start/End Dates

Study Start Date: December 19, 2018 (Actual)
Primary Completion Date: July 18, 2024 (Actual)

Study Completion Date: July 18, 2024 (Actual)

Reason for Termination (If applicable)

Not applicable

Study Design/Methodology

This was a non-confirmatory, randomized, open label, multicenter, parallel group trial in 48 participants with mild-to-moderate RA. The study was divided into 4 periods:

- Period 1 - Screening: Up to 5 weeks to assess participant eligibility. Participants could be re-screened twice.
- Period 2 - Treatment: At baseline, eligible participants were randomized to one of two treatment arms in a ratio of 1:1 (ianalumab Test drug product (DP) or Reference DP). Study drug was administered as subcutaneous (s.c.) injection of ianalumab 300 mg, every 4 weeks (Q4W) for a total of 3 doses on Day 1, on Day 29 (Week 4) and finally on Day 57 (Week 8). The End of Treatment (EOT) visit was on Day 85 (Week 12), 4 weeks after the last study drug administration.

Post-treatment safety follow-up period consisted of:

- Period 3 - Mandatory Follow up: Starting from four weeks after the EOT visit, mandatory follow-up visits occurred every four weeks until Week 28. If B-cell recovery was achieved at the Week 24 visit, i.e. B-cell levels returned to ≥ 50 cells/µL or at least 80% of baseline value, then the End of Study (EOS) visit would be performed 4 weeks later (at the Week 28 visit) for a total follow-up time of 20 weeks after the last dose of ianalumab.
- Period 4 - Conditional Follow up: Starting from 12 weeks after the last mandatory follow up visit, conditional follow up visits occurred at 12-week intervals until either approximately 2 years after the last administration of ianalumab (Week 112), or until B-cell recovery, whichever would occur first.

Centers

2 centers in 2 countries: Jordan(1), Germany(1)

Objectives

Primary objectives

- To assess the steady state pharmacokinetic comparability of two ianalumab drug products in RA participants.
- To evaluate the safety and tolerability of s.c. administration of two ianalumab drug products in RA participants.

Secondary objectives

- To assess the pharmacokinetic (PK) comparability of s.c. doses of two ianalumab drug products in RA participants.
- To assess the pharmacodynamic (PD) effect (B cell depletion/recovery) of s.c. doses of two ianalumab drug products
- To assess the immunogenicity (IG) following s.c. doses of two ianalumab drug products in RA participants

Test Product (s), Dose(s), and Mode(s) of Administration

- Reference DP: VAY736 150 mg as a powder for solution for injection/infusion, administered as 300 mg subcutaneously Q4W for a total of 3 doses
- Test DP: VAY736 150 mg/1 mL as a solution for injection, administered as 300 mg subcutaneously Q4W for a total of 3 doses

Statistical Methods

The statistical analyses were performed at the end of the study by Novartis. No hypothesis testing was done. Data was summarized using descriptive statistics (continuous data) and/or contingency tables (categorical data) for demographic and baseline characteristics, safety measurements, and all relevant PK, PD and immunogenicity measurements.

Analysis sets: For all analysis sets, participants were analyzed according to the study treatment received. The safety analysis set included all participants that received any study drug. The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data. The PD analysis set included all participants with no protocol deviations with relevant impact on PD data. The IG analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) anti-drug antibodies (ADA) measurement, who received any study drug and with no protocol deviations that impacted on IG data.

Analysis of the primary endpoints: The primary objectives of the study were to assess the pharmacokinetic comparability, safety, and tolerability of two ianalumab drug products (Test DP and Reference DP).

Pharmacokinetic comparability: The primary PK endpoints are AUCtau and Cmax of ianalumab in serum on Day 85 (i.e. 4 weeks after the last dose).

Safety and tolerability: Primary endpoints of safety and tolerability included adverse events, vital signs (blood pressure, pulse rate, body temperature), ECG intervals, clinical laboratory measurements, as well as participant demographics, baseline characteristics, and treatment information. Treatment-emergent adverse events (TEAEs) defined as events that started on or after the time and date of first dose of study medication that were absent prior to start of treatment, or events present prior to start of treatment but that increased in severity after the start of treatment based on preferred term were reported/analyzed. All AE data in the clinical database was analyzed for all study periods.

Analysis of the secondary endpoints: The secondary objectives were to assess the additional pharmacokinetics, pharmacodynamic effect (B-cell depletion/recovery), and immunogenicity associated with ianalumab (Test DP and Reference DP).

Pharmacokinetics: The following secondary PK parameters were determined using non-compartmental methods:

- After the first dose: AUCtau, Cmax, Tmax
- After the last dose: AUClast, AUCinf, Tmax, T1/2
- At the end of each dosing interval (Day 29, 57, 85): Ctrough

Pharmacodynamic effects: The PD variable of interest was circulating B cells ($CD19^{+}$). The change from baseline in circulating B-cells over time was assessed

Immunogenicity: All ADA results were listed by treatment group, and visit/time.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria

- Fulfilled the 2010 ACR/EULAR criteria for RA Aletaha et al 2010 at Screening.
- Had active disease defined as ≥ 2 swollen joints (of 58 evaluable joints) and ≥ 2 tender joints (of 60 evaluable joints) despite stable MTX ≤ 25 mg/week and/or hydroxychloroquine ≤ 400 mg/day treatment for at least 2 months prior to randomization.

Key Exclusion Criteria

- Had prior or previous use of (specific dosages and intervals prior to study start may apply): other investigational drugs, B-cell depleting therapy (e.g., rituximab), monoclonal antibodies (mAb), i.v. / s.c. Ig, thymoglobulin, i.v. or oral cyclophosphamide, oral cyclosporine, soluble cytokine receptors, azathioprine.
- Were currently receiving prednisone >10 mg/day (or equivalent oral glucocorticoid) or had a dose adjustment within 2 weeks prior to randomization.
- Had active viral, bacterial, or other infections requiring systemic treatment at the time of screening or enrollment, or had a history of recurrent clinically significant infection or bacterial infections with encapsulated organisms.
- Had received a live/attenuated vaccine within a 2-month period before randomization.
- Were pregnant or nursing (lactating) women.
- Were women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, unless they were using highly effective methods of contraception from screening and for 4 months after stopping the investigational drug.

Participant Flow Table

Treatment

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**	**Total**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses	
Started	23	25	48
Completed	22	23	45
Not Completed	1	2	3
Sponsor decision	1	2	3

Post-Treatment Follow-up

	Ianalumab- Reference Drug Product (DP)	Ianalumab - Test Drug Product (DP)	Total
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses	
Started	23	25	48
Completed	21	23	44
Not Completed	2	2	4
Death	1	0	1
Participant Decision	1	2	3

Baseline Characteristics

	Ianalumab- Reference Drug Product (DP)	Ianalumab - Test Drug Product (DP)	Total
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses	
Number of Participants [units: participants]	23	25	48

Baseline Analysis Population Description			
Age Continuous (units: Years) Analysis Population Type: Participants Mean ± Standard Deviation			
	50.3±9.28	45.9±12.75	48.0±11.33
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
Female	18	15	33
Male	5	10	15
Race/Ethnicity, Customized (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)			
White	23	25	48

Primary Outcome Result(s)

Number of participants with Adverse Events (AEs)

Description	The number of participants with AEs after repeated subcutaneous injections of ianalumab. The number of participants with at least one event in the category is reported
Time Frame	From start of treatment up to end of study, assessed up to Week 112
Analysis Population Description	The safety analysis set included all participants that received any study drug.

	Ianalumab- Reference Drug Product (DP)	Ianalumab - Test Drug Product (DP)
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Number of participants with Adverse Events (AEs) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
AEs- All intensities	22 (95.65%)	25 (100%)
AEs- Mild intensity	22 (95.65%)	25 (100%)
AEs- Moderate intensity	12 (52.17%)	16 (64%)
AEs- Severe intensity	3 (13.04%)	3 (12%)
Study drug-related AEs	21 (91.3%)	22 (88%)
Serious AEs	5 (21.74%)	3 (12%)
AEs leading to discontinuation of study treatment	0 (%)	0 (%)
Study-drug related AEs leading to discontinuation of study treatment	0 (%)	0 (%)

Pharmacokinetic (PK) comparability at steady state - AUCtau

Description The area under the serum ianalumab concentration-time curve from time zero to the end of the dosing interval (AUCtau)

Time Frame From Week 8 to Week 12

Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Pharmacokinetic (PK) comparability at steady state - AUCtau (units: day*ug/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	213 ± 96.1	203 ± 88.3

Statistical Analysis

Groups	Ianalumab- Reference Drug Product (DP), Ianalumab - Test Drug Product (DP)
Type of Statistical Test	Other
Other Geometric mean ratio	1.01
90 % Confidence Interval 2-Sided	0.82 to 1.24

Pharmacokinetic comparability at steady state - Cmax

Description	Observed maximum serum concentration of ianalumab following drug administration (Cmax)
Time Frame	From Week 8 to 12

Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Pharmacokinetic comparability at steady state - Cmax (units: ug/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	18.3 ± 6.43	16.8 ± 7.13

Statistical Analysis

Groups	Ianalumab- Reference Drug Product (DP), Ianalumab - Test Drug Product (DP)
Type of Statistical Test	Other
Other Geometric mean ratio	0.92
90 % Confidence Interval 2-Sided	0.76 to 1.12

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Secondary Outcome Result(s)

Pharmacokinetic comparability after the first dose - AUCtau

Description	The area under the serum ianalumab concentration-time curve from time zero to the end of the dosing interval (AUCtau)
Time Frame	From Week 0 to Week 4
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Pharmacokinetic comparability after the first dose - AUCtau (units: day*ug/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	167 ± 81.9	155 ± 50.8

Pharmacokinetic comparability after the first dose - Cmax

Description	Observed maximum serum concentration of ianalumab following drug administration (Cmax)
Time Frame	From Week 0 to Week 4
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**

Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Pharmacokinetic comparability after the first dose - Cmax (units: ug/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	15.3 ± 6.26	14.3 ± 4.41

Pharmacokinetic comparability after the first dose - Tmax

Description	Time to reach the maximum concentration after drug administration (Tmax)
Time Frame	From Week 0 to 4
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Pharmacokinetic comparability after the first dose - Tmax (units: day)	**Median (Full Range)**	**Median (Full Range)**
	3.00 (2.91 to 7.94)	3.01 (2.89 to 6.02)

Pharmacokinetic comparability of two ianalumab drug products after the last dose - AUCinf

Description	The area under the serum ianalumab concentration-time curve from time zero to infinity (AUCinf)
Time Frame	From Week 8 to 12
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	22	23
Pharmacokinetic comparability of two ianalumab drug products after the last dose - AUCinf (units: day*ug/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	248 ± 132	235 ± 112

Pharmacokinetic comparability after the last dose - Tmax

Description	Time to reach the maximum concentration after drug administration (Tmax)
Time Frame	From Week 8 to 12
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**

Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	22	23
Pharmacokinetic comparability after the last dose - Tmax (units: day)	**Median (Full Range)**	**Median (Full Range)**
	3.01 (2.93 to 6.10)	3.01 (2.93 to 5.94)

Pharmacokinetic comparability after the last dose - T1/2

Description	The terminal elimination half-life (T1/2)
Time Frame	From Week 8 to 12
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	22	23
Pharmacokinetic comparability after the last dose - T1/2 (units: day)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
	10.1 ± 3.57	10.5 ± 3.40

Pharmacokinetic comparability at the end of each dosing interval - Ctrough

Description	Observed minimum serum ianalumab concentration following drug administration (Ctrough)
Time Frame	From Week 0 to Week 12
Analysis Population Description	The PK analysis set included all participants with at least one available valid (i.e. not flagged for exclusion) PK concentration measurement, who received any study drug and experienced no protocol deviations with relevant impact on PK data

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	22	25
Pharmacokinetic comparability at the end of each dosing interval - Ctrough (units: ug/mL)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
After the first dose	1.46 ± 1.36	1.17 ± 0.599
After the second dose	2.11 ± 1.82	2.03 ± 1.09
After the third dose	2.08 ± 1.77	1.92 ± 1.23

Change from baseline in circulating B cells (CD19+) concentrations over time

Description	Pharmacodynamic (PD) effect as measured by CD19+ B cells level. The change from baseline in circulating B cells (CD19+) concentrations was assessed. CD19+ B cells levels were assessed by flow cytometry. Baseline is defined as the last non-missing value before first dose.
Time Frame	From baseline to Week 100
Analysis Population Description	The PD analysis set included all participants with no protocol deviations with relevant impact on PD data. At each post-baseline time point, only participants with a value at both baseline and that time point are included.

	Ianalumab- Reference Drug Product (DP)	Ianalumab - Test Drug Product (DP)
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Change from baseline in circulating B cells (CD19+) concentrations over time (units: 10E6/L)	**Mean ± Standard Deviation**	**Mean ± Standard Deviation**
Week 0 Day 1 6H Postdose (n=22, 24)	-236.09 ± 155.154	-200.92 ± 124.784
Week 0 Day 2 (n=20, 23)	-244.90 ± 154.320	-181.26 ± 113.893
Week 0 Day 4 (n=22, 24)	-214.64 ± 143.910	-188.13 ± 123.572
Week 0 Day 7 (n=21, 23)	-221.57 ± 154.183	-197.48 ± 119.838
Week 0 Day 14 (n=23, 23)	-241.65 ± 153.802	-199.78 ± 125.779
Week 4 Day 29 (n=20, 25)	-230.50 ± 126.674	-216.72 ± 133.033
Week 8 Day 57 predose (n=21, 24)	-253.95 ± 159.126	-215.17 ± 136.335
Week 8 Day 60 (n=22, 25)	-246.23 ± 159.821	-217.60 ± 134.012
Week 8 Day 63 (n=21, 24)	-253.24 ± 157.659	-216.58 ± 137.113
Week 9 Day 70 (n=20, 24)	-255.15 ± 161.858	-217.25 ± 137.278
Week 12 EOT (n=20, 24)	-236.55 ± 151.006	-223.96 ± 132.358
Week 16 (n=22, 24)	-241.77 ± 156.346	-216.71 ± 137.047
Week 20 (n=23, 24)	-247.13 ± 154.847	-215.50 ± 135.812
Week 24 (n=22, 25)	-251.59 ± 149.204	-210.96 ± 130.345
Week 28 (n=22, 25)	-235.50 ± 135.973	-200.12 ± 126.719
Week 40 (n=17, 22)	-187.76 ± 116.517	-175.05 ± 121.779
Week 52 (n=13, 14)	-174.54 ± 128.905	-135.50 ± 99.118

Week 64 (n=10, 12)	-158.20 ± 98.841	-136.00 ± 113.080
Week 76 (n=8, 8)	-112.13 ± 53.421	-109.00 ± 85.108
Week 88 (n=8, 7)	-131.38 ± 83.519	-127.57 ± 132.199
Week 100 (n=6, 8)	-117.17 ± 98.129	-147.50 ± 135.571

Incidence of treatment-induced Anti-Drug Antibodies (ADA)

Description	Percentage of participants with treatment-induced ADA positive results.
Time Frame	From Week 0 to Week 112
Analysis Population Description	The safety analysis set included all participants that received any study drug.

	Ianalumab- Reference Drug Product (DP)	**Ianalumab - Test Drug Product (DP)**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses
Number of Participants Analyzed [units: participants]	23	25
Incidence of treatment-induced Anti-Drug Antibodies (ADA) (units: Participants)	**Count of Participants (Not Applicable)**	**Count of Participants (Not Applicable)**
	1 (4.35%)	1 (4%)

Other Pre-Specified Outcome Result(s)

No data identified.

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Post-Hoc Outcome Result(s)

No data identified.

Safety Results

Time Frame	From baseline up to Week 112
Additional Description	The safety analyses were conducted in the safety set, including all participants that received any study drug.
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

All-Cause Mortality

	Ianalumab- Reference Drug Product (DP) N = 23	**Ianalumab - Test Drug Product (DP) N = 25**	**Total N = 48**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses	Total
Total Number Affected	1	0	1
Total Number At Risk	23	25	48

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Serious Adverse Events

Time Frame	From baseline up to Week 112
Additional Description	The safety analyses were conducted in the safety set, including all participants that received any study drug.
Source Vocabulary for Table Default	MedDRA (27.0)
Collection Approach for Table Default	Systematic Assessment

	Ianalumab- Reference Drug Product (DP) N = 23	**Ianalumab - Test Drug Product (DP) N = 25**	**Total N = 48**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses	Total
Total # Affected by any Serious Adverse Event	5	3	8
Total # at Risk by any Serious Adverse Event	23	25	48
Gastrointestinal disorders			
Large intestinal ulcer	1 (4.35%)	0 (0.00%)	1 (2.08%)
General disorders and administration site conditions			
Gait disturbance	1 (4.35%)	0 (0.00%)	1 (2.08%)

Medical device site joint inflammation	0 (0.00%)	1 (4.00%)	1 (2.08%)
Infections and infestations			
COVID-19	1 (4.35%)	0 (0.00%)	1 (2.08%)
Respiratory tract infection	0 (0.00%)	1 (4.00%)	1 (2.08%)
Musculoskeletal and connective tissue disorders			
Chondropathy	1 (4.35%)	0 (0.00%)	1 (2.08%)
Intervertebral disc protrusion	1 (4.35%)	0 (0.00%)	1 (2.08%)
Osteoarthritis	0 (0.00%)	1 (4.00%)	1 (2.08%)
Rheumatoid arthritis	2 (8.70%)	0 (0.00%)	2 (4.17%)
Spinal instability	1 (4.35%)	0 (0.00%)	1 (2.08%)
Spinal stenosis	1 (4.35%)	0 (0.00%)	1 (2.08%)
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease	0 (0.00%)	1 (4.00%)	1 (2.08%)
Pulmonary toxicity	1 (4.35%)	0 (0.00%)	1 (2.08%)

Other (Not Including Serious) Adverse Events

Time Frame	From baseline up to Week 112
Additional Description	The safety analyses were conducted in the safety set, including all participants that received any study drug.
Source Vocabulary for Table Default	MedDRA (27.0)

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Collection Approach for Table Default Systematic Assessment

Frequent Event Reporting Threshold 5%

	Ianalumab- Reference Drug Product (DP) N = 23	**Ianalumab - Test Drug Product (DP) N = 25**	**Total N = 48**
Arm/Group Description	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a powder for solution for injection or infusion (reference DP), every 4 weeks for a total of 3 doses	Participants received a subcutaneous administration of 300 mg of ianalumab, formulated as a solution for injection (Test DP), every 4 weeks for a total of 3 doses	Total
Total # Affected by any Other Adverse Event	22	25	47
Total # at Risk by any Other Adverse Event	23	25	48
Eye disorders			
Dry eye	2 (8.70%)	1 (4.00%)	3 (6.25%)
Gastrointestinal disorders			
Abdominal pain upper	2 (8.70%)	0 (0.00%)	2 (4.17%)
Diarrhoea	1 (4.35%)	2 (8.00%)	3 (6.25%)
General disorders and administration site conditions			
Fatigue	2 (8.70%)	3 (12.00%)	5 (10.42%)

Injection site reaction	17 (73.91%)	12 (48.00%)	29 (60.42%)
Infections and infestations			
Bronchitis	1 (4.35%)	2 (8.00%)	3 (6.25%)
Conjunctivitis	4 (17.39%)	0 (0.00%)	4 (8.33%)
COVID-19	1 (4.35%)	2 (8.00%)	3 (6.25%)
Nasopharyngitis	5 (21.74%)	5 (20.00%)	10 (20.83%)
Oral herpes	2 (8.70%)	2 (8.00%)	4 (8.33%)
Upper respiratory tract infection	3 (13.04%)	0 (0.00%)	3 (6.25%)
Urinary tract infection	0 (0.00%)	4 (16.00%)	4 (8.33%)
Injury, poisoning and procedural complications			
Injection related reaction	10 (43.48%)	13 (52.00%)	23 (47.92%)
Investigations			
Low density lipoprotein increased	2 (8.70%)	0 (0.00%)	2 (4.17%)
Musculoskeletal and connective tissue disorders			
Arthralgia	4 (17.39%)	1 (4.00%)	5 (10.42%)
Back pain	2 (8.70%)	2 (8.00%)	4 (8.33%)
Rheumatoid arthritis	2 (8.70%)	5 (20.00%)	7 (14.58%)
Nervous system disorders			
Headache	3 (13.04%)	4 (16.00%)	7 (14.58%)
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain	2 (8.70%)	2 (8.00%)	4 (8.33%)
Skin and subcutaneous tissue disorders			

Alopecia	0 (0.00%)	2 (8.00%)	2 (4.17%)
Vascular disorders			
Haematoma	0 (0.00%)	3 (12.00%)	3 (6.25%)
Hypertension	1 (4.35%)	2 (8.00%)	3 (6.25%)

Conclusion

Overall, the Test Drug Product results were comparable to the Reference Drug Product ones in terms of pharmacokinetics, pharmacodynamics, immunogenicity, and safety.

Date of Clinical Trial Report

24-Apr-2025