Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Dapirolizumab Pegol in Study Participants With Moderately to Severely Active Systemic Lupus Erythematosus

Summary

EudraCT number	2019-003406-27
Trial protocol	BE PL DE BG HU ES AT GR PT GB FR CZ IT DK RO
Global end of trial date	04 June 2024

Results information

Result version number	v1 (current)
This version publication date	19 April 2025
First version publication date	19 April 2025

Trial information

Trial identification

Sponsor protocol code	SL0043

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04294667
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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	23 July 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 May 2024
Global end of trial reached?	Yes
Global end of trial date	04 June 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the ability of DZP as an add-on treatment to SOC medication to achieve clinically relevant long-term improvement of moderate to severe disease activity

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	12 August 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 12
Country: Number of subjects enrolled	Australia: 1
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Bulgaria: 11
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	Colombia: 30
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Greece: 6
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Mexico: 21
Country: Number of subjects enrolled	Peru: 25
Country: Number of subjects enrolled	Philippines: 2
Country: Number of subjects enrolled	Poland: 40
Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Serbia: 12
Country: Number of subjects enrolled	Korea, Republic of: 4

Country: Number of subjects enrolled	Spain: 12
Country: Number of subjects enrolled	Taiwan: 17
Country: Number of subjects enrolled	United States: 65
Worldwide total number of subjects	321
EEA total number of subjects	114

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)	1
Adults (18-64 years)	307
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in August 2020 and concluded in June 2024.

Pre-assignment

Screening details:

Participant flow refers to the Randomized Set (RS).

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	PBO+SOC

Arm description:

Participants received placebo (PBO) as an intravenous (iv) infusion every 4 weeks (Q4W) in combination with Standard of Care (SOC) during 48 weeks Treatment Period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	PBO
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received placebo at prespecified time-points.

Arm title	DZP+SOC

Arm description:

Participants received Dapirolizumab pegol (DZP) 24 milligrams/kilogram (mg/kg) as an iv infusion Q4W in combination with SOC during 48 weeks Treatment Period.

Arm type	Experimental
Investigational medicinal product name	Dapriolizumab pegol
Investigational medicinal product code	
Other name	CDP7657, DZP
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received Dapirolizumab pegol at prespecified time-points.

Number of subjects in period 1	PBO+SOC	DZP+SOC
Started	108	213
Completed	91	192
Not completed	17	21
Subject Decision due to Personal Reason	-	1
Adverse event, serious fatal	-	1
PI closed Site – Subject Early Withdrawal	-	1
Consent Withdrawal by Study Participant	9	7
Adverse event, non-fatal	3	4
Patient has a Renal Flare	1	-
SLE Worsening	-	1
Subject Moved to Another State	-	1
Subject Withdrew due to Personal Reason	-	1
Lack of efficacy	4	4

Baseline characteristics

Reporting groups	
Reporting group title	PBO+SOC
Reporting group description:	
Participants received placebo (PBO) as an intravenous (iv) infusion every 4 weeks (Q4W) in combination with Standard of Care (SOC) during 48 weeks Treatment Period.	
Reporting group title	DZP+SOC
Reporting group description:	
Participants received Dapirolizumab pegol (DZP) 24 milligrams/kilogram (mg/kg) as an iv infusion Q4W in combination with SOC during 48 weeks Treatment Period.	

Reporting group values	PBO+SOC	DZP+SOC	Total
Number of subjects	108	213	321
Age Categorical Units: participants			
12 to <18 Years	0	1	1
18 to <65 Years	106	201	307
65 to <85 Years	2	11	13
Age Continuous Units: Years			
arithmetic mean	41.5	43.8	
standard deviation	± 12.3	± 12.4	-
Sex: Female, Male Units: participants			
Female	101	198	299
Male	7	15	22

End points

End points reporting groups

Reporting group title	PBO+SOC
Reporting group description:	
Participants received placebo (PBO) as an intravenous (iv) infusion every 4 weeks (Q4W) in combination with Standard of Care (SOC) during 48 weeks Treatment Period.	
Reporting group title	DZP+SOC
Reporting group description:	
Participants received Dapirolizumab pegol (DZP) 24 milligrams/kilogram (mg/kg) as an iv infusion Q4W in combination with SOC during 48 weeks Treatment Period.	

Primary: Percentage of Participants with Achievement of BILAG 2004-based Composite Lupus Assessment (BICLA) response at Week 48

End point title	Percentage of Participants with Achievement of BILAG 2004-based Composite Lupus Assessment (BICLA) response at Week 48

End point description:

Participants were considered to be BILAG 2004-BICLA responder if all of following were fulfilled:

• BILAG 2004 improvement without worsening (A scores at Baseline improved to B, C or D; B scores improved to C or D; no new A scores and less than or equal to [≤] 1 new B.); Here, score A ("Active"): Severely active disease; score B ("Beware"): Moderately active disease; score C ("Contentment"): Mild stable disease; score D ("Discount"): Inactive now but previously active; and
• No worsening in the SLEDAI-2K total score compared to Baseline Visit (defined as no increase in SLEDAI-2K total score); and
• No worsening in the Physician's Global Assessment of Disease (PGA) compared to Baseline Visit defined as ≤ 10 millimeter (mm) increase on a 100 mm visual analog scale (VAS).

Full Analysis Set (FAS) consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Primary
End point timeframe:	
Week 48	

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	34.6	49.5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in proportion responding between SOC+DZP 24mg/kg and SOC+PBO was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate controlling for the randomization stratification factors, Pooled Region (North America vs Western Europe/Asia-Pacific vs

Latin America/Eastern Europe), Screening disease activity (chronic active vs acute flaring) and Screening SLEDAI score (<10 vs >=10).

Comparison groups	DZP+SOC v PBO+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.011
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportions (%)
Point estimate	14.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.3
upper limit	25.8

Secondary: Percentage of Participants with Achievement of BICLA response at Week 24

End point title	Percentage of Participants with Achievement of BICLA response at Week 24

End point description:

Study participants were considered to be a BICLA responder if all of the following were fulfilled:

• British Isles Lupus Assessment Group Disease Activity Index 2004 (BILAG 2004) improvement without worsening (A scores at Baseline improved to B, C or D; B scores improved to C or D; no new A scores and ≤ 1 new B.); Here, score A ("Active"): Severely active disease; score B ("Beware"): Moderately active disease; score C ("Contentment"): Mild stable disease; score D ("Discount"): Inactive now but previously active; and
• No worsening in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) total score compared to Baseline Visit (defined as no increase in SLEDAI-2K total score); and
• No worsening in the PGA compared to Baseline Visit defined as ≤ 10 mm increase on a 100 mm VAS.

The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

Week 24

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	38.3	46.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in proportion responding between SOC+DZP 24mg/kg and SOC+PBO was estimated and tested using the CMH risk difference estimate controlling for the randomization stratification factors, Pooled Region (North America vs Western Europe/Asia-Pacific vs Latin America/Eastern Europe), Screening disease activity (chronic active vs acute flaring) and Screening SLEDAI score (<10 vs >=10).

Comparison groups	PBO+SOC v DZP+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1776
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportions (%)
Point estimate	7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	19.4

Secondary: Percentage of Participants with Achievement of BICLA response at Week 12

End point title	Percentage of Participants with Achievement of BICLA response at Week 12

End point description:

Study participants were considered to be a BICLA responder if all of the following were fulfilled:

• BILAG 2004 improvement without worsening (A scores at Baseline improved to B, C or D; B scores improved to C or D; no new A scores and less than or equal to [≤] 1 new B.); Here, score A (“Active”): Severely active disease; score B (“Beware”): Moderately active disease; score C (“Contentment”): Mild stable disease; score D (“Discount”): Inactive now but previously active and
• No worsening in the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) total score compared to Baseline Visit (defined as no increase in SLEDAI-2K total score); and
• No worsening in the PGA compared to Baseline Visit defined as ≤ 10 mm increase on a 100 mm VAS.

The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

Week 12

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	29.0	39.9		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in proportion responding between SOC+DZP 24mg/kg and SOC+PBO was estimated and tested using the CMH risk difference estimate controlling for the randomization stratification factors, Pooled Region (North America vs Western Europe/Asia-Pacific vs Latin America/Eastern Europe), Screening disease activity (chronic active vs acute flaring) and Screening SLEDAI score (<10 vs >=10).

Comparison groups	PBO+SOC v DZP+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0518
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportions (%)
Point estimate	10.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	21.7

Secondary: Percentage of Participants with Achievement of prevention of severe British Isles Lupus Assessment Group (BILAG) flares (severe BILAG flare-free) through Week 48

End point title	Percentage of Participants with Achievement of prevention of severe British Isles Lupus Assessment Group (BILAG) flares (severe BILAG flare-free) through Week 48

End point description:

A severe BILAG flare was defined as a british isles lupus assessment group disease activity index 2004 (BILAG 2004) Grade A in any system due to individual items that were new or worse qualifying for the Grade A. Determination of items that were new or worse and were qualifying for the Grade A were according to the supplementary information for the numerical scoring of the BILAG-2004 index. Here, Grade A ("Active"): Severely active disease (sufficient to require systemic immunosuppressant or anticoagulant therapy. The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

During Treatment Period up to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	76.6	88.4		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in proportion responding between SOC+DZP 24mg/kg and SOC+PBO was estimated and tested using the CMH risk difference estimate controlling for the randomization stratification factors, Pooled Region (North America vs Western Europe/Asia-Pacific vs Latin America/Eastern Europe), Screening disease activity (chronic active vs acute flaring) and Screening SLEDAI score (<10 vs >=10).

Comparison groups	PBO+SOC v DZP+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0257
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportions (%)
Point estimate	11.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.4
upper limit	21.6

Secondary: Percentage of Participants with Achievement of Lupus Low Disease Activity State (LLDAS) in ≥50% of post-Baseline visits through Week 48

End point title	Percentage of Participants with Achievement of Lupus Low Disease Activity State (LLDAS) in ≥50% of post-Baseline visits through Week 48

End point description:

The LLDAS includes domains that capture the absence of organ-threatening disease activity and harmful treatment burden. The LLDAS is defined as:

- SLEDAI-2K score was ≤4 with no activity in major organ systems.
- No new and/or worsening disease activity defined as no SLEDAI-2K component documented as present that was not documented present at the previous visit.
- PGA ≤ 33 mm.
- Prednisone equivalent systemic dose for systemic lupus erythematosus (SLE) indication ≤ 7.5 mg per day.
- Stable standard maintenance doses of immunosuppressive drugs as allowed by protocol, defined as no increase in dose in the past 12 weeks and no dose higher than allowed as per protocol.

The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

During Treatment Period up to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	15.9	23.6		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The difference in proportion responding between SOC+DZP 24mg/kg and SOC+PBO was estimated and tested using the Cochran-Mantel-Haenszel (CMH) risk difference estimate controlling for the randomization stratification factors, Pooled Region (North America vs Western Europe/Asia-Pacific vs Latin America/Eastern Europe), Screening disease activity (chronic active vs acute flaring) and Screening SLEDAI score (<10 vs >=10).

Comparison groups	PBO+SOC v DZP+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1042
Method	Cochran-Mantel-Haenszel
Parameter estimate	Difference in Proportions (%)
Point estimate	7.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.5
upper limit	16

Secondary: Percentage of Participants with Achievement of BILAG improvement without worsening at Week 48

End point title	Percentage of Participants with Achievement of BILAG improvement without worsening at Week 48

End point description:

The BILAG improvement without worsening defined as A scores at Baseline improved to B, C or D; B scores improved to C or D; no new A scores and ≤1 new B Score. Here, score A (“Active”): Severely active disease (sufficient to require systemic immunosuppressant or anticoagulant therapy; score B (“Beware”): Moderately active disease (requires low dose or local immunosuppressant therapy or symptomatic therapy; score C (“Contentment”): Mild stable disease (no indication for changes in treatment); score D (“Discount”): Inactive now but previously active. The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	34.6	49.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at Week 48

End point title	Change from Baseline in Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) at Week 48

End point description:

The SLEDAI-2K is a global index which includes 24 clinical and laboratory variables such as antibodies, renal, and hematological components measured 30 days before, and at the timepoint of assessment. The variables were weighted by the type of manifestation, but not by severity or dynamic of the individual item. The SLEDAI-2K includes scoring for antibodies (anti-dsDNA positive or negative) and low complement, as well as some renal and hematologic parameters. The total score falls between 0 and 105, with higher scores representing increased disease activity. Mixed effects models for repeated measurements (MMRM). The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: score on a scale				
least squares mean (standard error)	-4.2 (± 0.39)	-6.1 (± 0.26)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

The Least Squares (LS) Mean, the difference (DZP+SOC versus PBO+SOC), and the 95% CIs was computed from the MMRM.

Comparison groups	PBO+SOC v DZP+SOC

Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0001
Method	MMRM
Parameter estimate	Difference of Change(DZP+SOC vs PBO+SOC)
Point estimate	-1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	-0.9

Secondary: Percentage of Participants with Achievement of prevention of moderate/severe BILAG flares (moderate/severe BILAG flare-free) through Week 48

End point title	Percentage of Participants with Achievement of prevention of moderate/severe BILAG flares (moderate/severe BILAG flare-free) through Week 48

End point description:

Achievement of prevention of moderate/severe BILAG flares through Week 48 was defined as % of participants with no moderate or severe flare through Week 48. Severe BILAG flare: BILAG 2004 Grade A in any system due to individual items that were new or worse qualifying for Grade A. Determination of items that were new or worse and were qualifying for Grade A, according to supplementary information for numerical scoring of BILAG-2004 index. A moderate BILAG flare: 2 or more BILAG 2004 Grade B due to individual items that were new or worse and were qualifying for Grade B in any system. Determination of items that were new or worse qualifying for Grade B, according to supplementary information for numerical scoring of BILAG- 2004 index. Here, Grade A (Active): Severely active disease; Grade B (Beware):Moderately active disease. FAS consisted of all study participants randomized into study except 6 participants excluded from FAS due to persistent GCP non-compliance at site enrolling them.

End point type	Secondary

End point timeframe:

During Treatment Period up to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	63.0	78.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Achievement of Systemic Lupus Erythematosus Responder Index response - 4 (SRI-4) response at Week 48

End point title	Percentage of Participants with Achievement of Systemic Lupus Erythematosus Responder Index response - 4 (SRI-4) response at Week 48

End point description:

The SRI-4 define responders as meeting all of the following criteria:

- Reduction in SLEDAI-2K score of ≥ 4.
- No shift from BILAG 2004 Grade B, C, D, or E to A post-Baseline. Here, Grade A ("Active"): Severely active disease; Grade B ("Beware"): Moderately active disease; Grade C ("Contentment"): Mild stable disease; Grade D ("Discount"): Inactive now but previously active; Grade E ("Excluded"): Never affected.
- No more than 1 shift from BILAG 2004 Grade C, D, or E to B post-Baseline.
- No worsening in the PGA compared to study entry defined as ≤ 10 mm increase on a 100 mm visual analog scale, equivalent to less than a 10 mm increase in the PGA compared to study entry score.

The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: percentage of participants				
number (not applicable)	41.1	60.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to severe BILAG Flare through Week 48

End point title	Time to severe BILAG Flare through Week 48

End point description:

Time to severe BILAG flare (the event) through Week 48 was defined as the time from randomization until the start of the event. A severe BILAG flare was defined as a BILAG 2004 Grade A in any system due to individual items that were new or worse qualifying for the Grade A. Determination of items that were new or worse and were qualifying for the Grade A, according to the supplementary information for the numerical scoring of the BILAG-2004 index. Here, Grade A ("Active"): Severely active disease. The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them. Here, 99999 indicates the time to flare estimate of the 25 percentile, median, 75 percentile time could not be calculated and presented due to the low number of events (less than 25%, 50%, 75% participants respectively had flare events in both arms).

End point type	Secondary

End point timeframe:

During Treatment Period up to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: weeks				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	PBO+SOC v DZP+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0111
Method	Logrank

Secondary: Change from Baseline in Physician’s Global Assessment (PGA) at Week 48

End point title	Change from Baseline in Physician’s Global Assessment (PGA) at Week 48

End point description:

The PGA is a measure of systemic lupus erythematosus (SLE) signs and symptoms by the physician using a visual analog scale of 0 to 100mm, Where 0 indicate “very good”, asymptomatic, and no limitation of normal activity and 100 indicate “severe disease”. The FAS consisted of all study participants randomized into the study except 6 participants excluded from FAS due to persistent GCP non-compliance at the site enrolling them.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: score on a scale				
least squares mean (standard error)	-33.4 (± 1.99)	-39.6 (± 1.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with treatment-emergent adverse events (TEAEs) during the study

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs) during the study

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of investigational medicinal product (IMP), whether or not considered related to the IMP. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of IMP. Treatment-emergent AEs were those with onset date on or after the first administration of study drug, and up to 60 days after last dose. The SS consisted of all study participants who were randomized and had received at least 1 dose (any amount) of study medication.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 54)

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	213		
Units: percentage of participants				
number (not applicable)	75.0	82.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with serious treatment-emergent adverse events during the study

End point title	Percentage of participants with serious treatment-emergent adverse events during the study

End point description:

A serious adverse event (SAE) is defined as any untoward medical occurrence that, at any dose: Results in death; Is life-threatening, Requires in patient hospitalization or prolongation of existing hospitalization; Results in persistent disability/incapacity; Is a congenital anomaly/birth defect; and Other important medical events which based on medical or scientific judgement may jeopardize the patients, or may require medical or surgical intervention to prevent any of the above. Treatment-emergent AEs were those with onset date on or after the first administration of study drug, and up to 60 days after last dose. The SS consisted of all study participants who were randomized and had received at least 1 dose (any amount) of study medication.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 54)

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	213		
Units: percentage of participants				
number (not applicable)	14.8	9.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with treatment-emergent adverse events of special interest during the study

End point title	Percentage of participants with treatment-emergent adverse events of special interest during the study

End point description:

An adverse event of special interest (AESIs) is any AE that a regulatory authority has mandated be reported on an expedited basis, regardless of the seriousness, expectedness, or relatedness of the AE to the administration of a product/compound. The SS consisted of all study participants who were randomized and had received at least 1 dose (any amount) of study medication.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 54)

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	213		
Units: percentage of participants				
number (not applicable)	0.9	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to moderate/severe BILAG flare through Week 48

End point title	Time to moderate/severe BILAG flare through Week 48

End point description:

Time to moderate/severe BILAG flare (event): time from randomization until start of event. Moderate BILAG flare: as 2 or more BILAG 2004 Grade B due to individual items that were new or worse and were qualifying for Grade B in any system. Determination of items that were new or worse qualifying for Grade B, as per supplementary information for numerical score of BILAG-2004. Severe BILAG flare: as BILAG 2004 Grade A in any system due to individual items that were new/worse qualifying for Grade A. Determination of items that were new/worse and are qualifying for Grade A, as per supplementary information for numerical score of BILAG-2004. Here, Grade A (Active): Severely active disease; Grade B (Beware): Moderately active disease. FAS was used. 99999: indicates that time to flare estimate of 25 percentile, median, 75 percentile time could not be calculated and presented in case of low number of events (less than 25%, 50%, 75% participants respectively had flare events).

End point type	Secondary

End point timeframe:

During Treatment Period up to Week 48

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	107	208		
Units: weeks				
median (inter-quartile range (Q1-Q3))	99999 (36.1 to 99999)	99999 (99999 to 99999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	PBO+SOC v DZP+SOC
Number of subjects included in analysis	315
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0228
Method	Logrank

Secondary: Percentage of participants with treatment-emergent adverse events of special monitoring during the study

End point title	Percentage of participants with treatment-emergent adverse events of special monitoring during the study

End point description:

An AE of special monitoring is a product-specific AEs, adverse reactions, or safety topics considered as requiring special monitoring by UCB. The SS consisted of all study participants who were randomized and had received at least 1 dose (any amount) of study medication.

End point type	Secondary

End point timeframe:

From Baseline (Day 1) until Safety Follow-Up (up to Week 54)

End point values	PBO+SOC	DZP+SOC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	213		
Units: percentage of participants				
number (not applicable)	24.1	36.6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline (Day 1) until Safety Follow-Up (up to Week 54)

Adverse event reporting additional description:

Treatment-emergent AEs were those with onset date on or after the first administration of study drug, and up to 60 days after last dose. The SS consisted of all study participants who were randomized and had received at least 1 dose (any amount) of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	PBO+SOC

Reporting group description:

Participants received placebo (PBO) as an intravenous (iv) infusion every 4 weeks (Q4W) in combination with Standard of Care (SOC) during 48 weeks Treatment Period.

Reporting group title	DZP+SOC

Reporting group description:

Participants received Dapirolizumab pegol (DZP) 24 milligrams/kilogram (mg/kg) as an iv infusion Q4W in combination with SOC during 48 weeks Treatment Period.

Serious adverse events	PBO+SOC	DZP+SOC	
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 108 (14.81%)	21 / 213 (9.86%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to central nervous system			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shrinking lung syndrome			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Suicidal ideation	Additional description: The AE of suicidal ideation occurred before administration of the first dose of study treatment. Only for technical reasons it was listed in the analysis as "treatment emergent" as the onset date was the day of first study treatment.		
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Limb injury			

subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 108 (0.00%)	2 / 213 (0.94%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lupus myocarditis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Lupus enteritis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cutaneous vasculitis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	1 / 108 (0.93%)	3 / 213 (1.41%)	
occurrences causally related to treatment / all	0 / 1	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			

subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial colitis			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			

subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal perforated			
subjects affected / exposed	1 / 108 (0.93%)	0 / 213 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint tuberculosis			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 108 (0.00%)	1 / 213 (0.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster	Additional description: The two events were reported as "herpes zoster over left eyelid and forehead, V1" and "left herpes zoster ophthlamicus (dermatome V1/V2)".		
subjects affected / exposed	0 / 108 (0.00%)	2 / 213 (0.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PBO+SOC	DZP+SOC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 108 (43.52%)	109 / 213 (51.17%)	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 108 (6.48%)	15 / 213 (7.04%)	
occurrences (all)	8	24	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	10 / 108 (9.26%)	15 / 213 (7.04%)	
occurrences (all)	12	15	
Nausea			
subjects affected / exposed	6 / 108 (5.56%)	9 / 213 (4.23%)	
occurrences (all)	9	9	
Infections and infestations			
COVID-19			
subjects affected / exposed	17 / 108 (15.74%)	44 / 213 (20.66%)	
occurrences (all)	18	44	
Herpes zoster			
subjects affected / exposed	6 / 108 (5.56%)	4 / 213 (1.88%)	
occurrences (all)	7	4	
Bronchitis			
subjects affected / exposed	5 / 108 (4.63%)	11 / 213 (5.16%)	
occurrences (all)	6	13	
Upper respiratory tract infection			
subjects affected / exposed	8 / 108 (7.41%)	20 / 213 (9.39%)	
occurrences (all)	9	23	
Nasopharyngitis			
subjects affected / exposed	13 / 108 (12.04%)	18 / 213 (8.45%)	
occurrences (all)	19	23	
Urinary tract infection			
subjects affected / exposed	9 / 108 (8.33%)	28 / 213 (13.15%)	
occurrences (all)	10	36	
Oral herpes			
subjects affected / exposed	6 / 108 (5.56%)	4 / 213 (1.88%)	
occurrences (all)	8	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 October 2020	Protocol Amendment 1 was dated 14 Oct 2020: • Updated the planned analysis. • Added exploratory biomarker analysis on the immune response to infectious antigens (eg, severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]). • Clarified the handling of protocol-defined criteria and actions related to the SARS-CoV-2 pandemic. • Clarified unclear or misinterpretable text and inconsistencies between different sections.
14 January 2022	Protocol Amendment 3 was dated 14 Jan 2022: • Provided recommendations for contraception during mycophenolate treatment. • Added additional guidance on COVID-19 vaccinations in immunosuppressed participants.
16 March 2023	Protocol Amendment 4 was dated 16 Mar 2023: • Reduced the sample size and consequently removed the interim analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported