Clinical trial results:
A Phase 2, Randomized, Double-blind, Placebo-controlled Evaluation of the Safety and Efficacy of BMS-986165 with Background Treatment in Subjects with Lupus Nephritis

Summary

EudraCT number	2018-004142-42
Trial protocol	DE BE NL CZ ES GB IT
Global end of trial date	17 September 2021

Results information

Result version number	v1 (current)
This version publication date	04 October 2022
First version publication date	04 October 2022

Trial information

Trial identification

Sponsor protocol code	IM011-073

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03943147
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussée de la Hulpe 185, Brussels, Belgium, 1170
Public contact	EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.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	29 October 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 September 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objectives are to assess the safety and tolerability of BMS-986165 in participants with lupus nephritis and to evaluate the efficacy of BMS-986165 compared with placebo with regard to proteinuria.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 July 2019
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	China: 1
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	16
EEA total number of subjects	1

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)	16
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with an inadequate renal response to MMF may be randomized to blinded study treatment BMS-986165 3 mg BID, BMS-986165 6 mg BID, or placebo BID, as add-on therapy to MMF in Part B. No participants were randomized to receive BMS-986165 3 mg BID or placebo BID due to low enrollment.

Period 1

Period 1 title	Open-Label MMF Run-in (Part A)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Open Label MMF

Arm description:

All study participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks.

The following suggested target doses of MMF should be reached by the time of randomization:
- 1.5 to 2.0 g/day for participants self-described as Asian or of Asian descent
- 3.0 g/day for participants self-described as Black, African American, or of African descent
- 2.0 g/day for all others

Arm type	Experimental
Investigational medicinal product name	Mycophenolate Mofetil (MMF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose of 1.5 to 3.0 g/day

Number of subjects in period 1	Open Label MMF
Started	16
Completed	6
Not completed	10
Adverse event, non-fatal	1
Protocol-specified withdrawal criterion met	1
Non-compliance with study drug	1
Study terminated by sponsor	3
Other reasons	4

Period 2

Period 2 title	Blinded Treatment (Part B)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Open Label MMF

Arm description:

After participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks in Part A, Participants who meet the criteria to continue in Part B but do not meet the randomization criteria may continue on open-label MMF with or without corticosteroids.

Arm type	Experimental
Investigational medicinal product name	Mycophenolate Mofetil (MMF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose of 1.5 to 3.0 g/day

Arm title	Open Label MMF + BMS-986165

Arm description:

After participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks in Part A, participants meeting randomization criteria for Part B receive BMS-986165 6 mg BID + continued open-label MMF with or without corticosteroids through 52 weeks. Randomized participants may continue to receive blinded study treatment for 52 additional weeks.

Arm type	Experimental
Investigational medicinal product name	BMS-986165
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

6 mg twice daily (BID)

Investigational medicinal product name	Mycophenolate Mofetil (MMF)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dose of 1.5 to 3.0 g/day

Number of subjects in period 2	Open Label MMF	Open Label MMF + BMS-986165
Started	5	1
Completed	2	1
Not completed	3	0
Study terminated by sponsor	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Open Label MMF

Reporting group description:

All study participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks.

The following suggested target doses of MMF should be reached by the time of randomization:
- 1.5 to 2.0 g/day for participants self-described as Asian or of Asian descent
- 3.0 g/day for participants self-described as Black, African American, or of African descent
- 2.0 g/day for all others

Reporting group values	Open Label MMF	Total	
Number of subjects	16	16	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	16	16	
>=65 years	0	0	
Sex: Female, Male Units: Participants			
Female	10	10	
Male	6	6	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	5	5	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	3	3	
White	6	6	
More than one race	0	0	
Unknown or Not Reported	2	2	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	6	6	
Not Hispanic or Latino	9	9	
Unknown or Not Reported	1	1	

End points

End points reporting groups

Reporting group title	Open Label MMF

Reporting group description:

All study participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks.

The following suggested target doses of MMF should be reached by the time of randomization:
- 1.5 to 2.0 g/day for participants self-described as Asian or of Asian descent
- 3.0 g/day for participants self-described as Black, African American, or of African descent
- 2.0 g/day for all others

Reporting group title	Open Label MMF

Reporting group description:

After participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks in Part A, Participants who meet the criteria to continue in Part B but do not meet the randomization criteria may continue on open-label MMF with or without corticosteroids.

Reporting group title	Open Label MMF + BMS-986165

Reporting group description:

After participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks in Part A, participants meeting randomization criteria for Part B receive BMS-986165 6 mg BID + continued open-label MMF with or without corticosteroids through 52 weeks. Randomized participants may continue to receive blinded study treatment for 52 additional weeks.

Primary: The Number of Participants Experiencing Averse Events in the Blinded Treatment Period (Part B)

End point title	The Number of Participants Experiencing Averse Events in the Blinded Treatment Period (Part B)[1]

End point description:

An adverse event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study drug and that does not necessarily have a causal relationship with this treatment. Data collected from the week 12 visit in Part A will be used for baseline values in Part B.

End point type	Primary

End point timeframe:

From baseline up to 52 weeks after first dose in Part B

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: Only summary statistics planned for this endpoint

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: The Number of Participants with Clinically Significant ECG Abnormalities in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Clinically Significant ECG Abnormalities in the Blinded Treatment Period (Part B)[2]

End point description:

The number of participants with clinically significant abnormalities in electrocardiograms (ECGs) parameters. The following ECG parameters will be measured: HR, PR-interval, QRS-duration, QT-interval, QTc-interval. A single 12-lead ECG will be recorded after the participant has been supine for at least 5 minutes. Data collected from the week 12 visit in Part A will be used for baseline values in Part B.

End point type	Primary

End point timeframe:

From baseline up to 52 weeks after first dose in Part B

Notes:

[2] - 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: Only summary statistics planned for this endpoint

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: The Percent Change in Vital Sign Measurements in the Blinded Treatment Period (Part B)

End point title	The Percent Change in Vital Sign Measurements in the Blinded Treatment Period (Part B)[3]

End point description:

The percent change from baseline in Vital sign measurements including: blood pressure, heart rate, respiratory rate, and temperature. Blood pressure and heart rate are measured after the participant has been resting quietly for at least 5 minutes. Data collected from the week 12 visit in Part A will be used for baseline values in Part B.

End point type	Primary

End point timeframe:

From baseline up to 52 weeks after first dose in Part B

Notes:

[3] - 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: Only summary statistics planned for this endpoint

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Percent change from baseline				
number (not applicable)				
Diastolic Blood Pressure(mmHg)	-3.45			

Systolic Blood Pressure(mmHg	5.22			
Heart Rate(beats/min)	16.87			
Respiratory Rate(breaths/min)	6.25			
Temperature(C)	-1.35			

Statistical analyses

No statistical analyses for this end point

Primary: Percent Change from Baseline in 24-hour Urine Protein:Creatinine Ratio (UPCR) at Week 24 in the Blinded Treatment Period (Part B)

End point title	Percent Change from Baseline in 24-hour Urine Protein:Creatinine Ratio (UPCR) at Week 24 in the Blinded Treatment Period (Part B)[4]

End point description:

The percent change from baseline in UPCR based on 24-hour urine collections. 24-hour urine specimens measure the levels of proteins and creatinine in urine and will be used for the UPCR at baseline (week 12) and week 24.

End point type	Primary

End point timeframe:

Week 24

Notes:

[4] - 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: Only summary statistics planned for this endpoint

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Percent change from baseline				
number (not applicable)	-34.86			

Statistical analyses

No statistical analyses for this end point

Primary: The Number of Participants with Abnormal Laboratory Parameters of Clinical Significance in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Abnormal Laboratory Parameters of Clinical Significance in the Blinded Treatment Period (Part B)[5]

End point description:

The number of participants with abnormal laboratory parameters (Chemistry, hematology, coagulation, immunohematology) that have been considered clinically significant. Clinically relevant laboratory results are determined by the investigator. Data collected from the week 12 visit in Part A will be used for baseline values in Part B.

End point type	Primary

End point timeframe:

From baseline up to 52 weeks after first dose in Part B

Notes:

[5] - 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: Only summary statistics planned for this endpoint

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Partial Renal Response (PRR) at Week 24 in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Partial Renal Response (PRR) at Week 24 in the Blinded Treatment Period (Part B)

End point description:

The number of participants with partial renal response (PRR) defined as ≥ 50% reduction from baseline in 24-hour Urine Protein:Creatinine Ratio (UPCR). 24-hour urine specimens measure the levels of proteins and creatinine in urine and will be used for the UPCR at baseline (week 12) and week 24.

End point type	Secondary

End point timeframe:

Week 24

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Complete Renal Response (CRR) at Week 24 in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Complete Renal Response (CRR) at Week 24 in the Blinded Treatment Period (Part B)

End point description:

The number of participants with complete renal response (CRR) defined as a 24-hour Urine Protein:Creatinine Ratio (UPCR) ≤ 0.5 mg/mg and an estimated glomerular filtration rate (eGFR) (using the MDRD equation) ≥ 60 mL/min or ≤ 20% decrease from baseline.

End point type	Secondary

End point timeframe:

Week 24

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Partial Renal Response (PRR) at Week 52 in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Partial Renal Response (PRR) at Week 52 in the Blinded Treatment Period (Part B)

End point description:

The number of participants with partial renal response (PRR) defined as ≥ 50% reduction from baseline in 24-hour Urine Protein:Creatinine Ratio (UPCR). 24-hour urine specimens measure the levels of proteins and creatinine in urine and will be used for the UPCR at baseline (week 12) and week 52.

End point type	Secondary

End point timeframe:

Week 52

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Complete Renal Response (CRR) Plus Successful Corticosteroid Taper to ≤ 7.5 mg/day at Week 24 in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Complete Renal Response (CRR) Plus Successful Corticosteroid Taper to ≤ 7.5 mg/day at Week 24 in the Blinded Treatment Period (Part B)

End point description:

The number of participants with complete renal response (CRR) defined as a 24-hour Urine Protein:Creatinine Ratio (UPCR) ≤ 0.5 mg/mg and an estimated glomerular filtration rate (eGFR) (using the MDRD equation) ≥ 60 mL/min or ≤ 20% decrease from baseline who was also able to successfully taper corticosteroid use to ≤ 7.5 mg/day.

End point type	Secondary

End point timeframe:

Week 24

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Complete Renal Response (CRR) at Week 52 in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Complete Renal Response (CRR) at Week 52 in the Blinded Treatment Period (Part B)

End point description:

The number of participants with complete renal response (CRR) defined as a 24-hour Urine Protein:Creatinine Ratio (UPCR) ≤ 0.5 mg/mg and an estimated glomerular filtration rate (eGFR) (using the MDRD equation) ≥ 60 mL/min or ≤ 20% decrease from baseline.

End point type	Secondary

End point timeframe:

Week 52

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: The Number of Participants with Complete Renal Response (CRR) Plus

Successful Corticosteroid Taper to ≤ 7.5 mg/day at Week 52 in the Blinded Treatment Period (Part B)

End point title	The Number of Participants with Complete Renal Response (CRR) Plus Successful Corticosteroid Taper to ≤ 7.5 mg/day at Week 52 in the Blinded Treatment Period (Part B)

End point description:

The number of participants with complete renal response (CRR) defined as a 24-hour Urine Protein:Creatinine Ratio (UPCR) ≤ 0.5 mg/mg and an estimated glomerular filtration rate (eGFR) (using the MDRD equation) ≥ 60 mL/min or ≤ 20% decrease from baseline who was also able to successfully taper corticosteroid use to ≤ 7.5 mg/day.

End point type	Secondary

End point timeframe:

Week 52

End point values	Open Label MMF + BMS-986165			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was assessed from first dose to study completion (up to approximately 26 months). SAEs and Other AEs were assessed from first dose to 30 days following last dose (up to approximately 16 months)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Open Label MMF

Reporting group description:

All study participants receive Mycophenolate Mofetil (MMF) at a dose of 1.5 to 3.0 g/day for 12 weeks in Part A.

Participants who meet the criteria to continue in Part B but do not meet the randomization criteria may continue on open-label MMF with or without corticosteroids.

The following suggested target doses of MMF should be reached by the time of randomization:
- 1.5 to 2.0 g/day for participants self-described as Asian or of Asian descent
- 3.0 g/day for participants self-described as Black, African American, or of African descent
- 2.0 g/day for all others

Reporting group title	Open Label MMF + BMS-986165

Reporting group description:

All participants that met randomization criteria for Part B. Participants received BMS-986165 6 mg BID + continued open-label MMF with or without corticosteroids through 52 weeks. Randomized participants may continue to receive blinded study treatment for 52 additional weeks.

Serious adverse events	Open Label MMF	Open Label MMF + BMS-986165	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	1 / 1 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 16 (6.25%)	1 / 1 (100.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Open Label MMF	Open Label MMF + BMS-986165	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 16 (43.75%)	1 / 1 (100.00%)	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
International normalised ratio increased			
subjects affected / exposed	0 / 16 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Prothrombin time prolonged			
subjects affected / exposed	0 / 16 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Weight increased			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			

subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 1 (100.00%)	
occurrences (all)	0	1	
Arthralgia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	2	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	1 / 16 (6.25%)	0 / 1 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2019	Modified several inclusion and exclusion criteria. Clarified that subjects may begin treatment with non-study-supplied MMF during the screening period.
06 August 2020	Added a 52-week Long-term Extension (LTE) period. Modified study objectives and endpoints, including new primary and secondary efficacy endpoints. Updated statistical considerations based on updated endpoints and addition of LTE period. Modified inclusion/exclusion criteria details and previous and concomitant therapy allowed and prohibited.

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 low enrollment, the Sponsor chose to terminate the study on 01-Jul-2021. There is limited data available therefore no formal statistical analyses of endpoints were conducted.

Notes: