Clinical trial results:
A Phase IV Multicenter, Open-Label Study Evaluating B Cell Levels in Infants of Lactating Women With CIS or MS Receiving Ocrelizumab

Summary

EudraCT number	2021-000063-79
Trial protocol	ES DE
Global end of trial date	

Results information

Result version number	v1
This version publication date	12 April 2025
First version publication date	12 April 2025

Trial information

Trial identification

Sponsor protocol code	MN42989

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04998851
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, +41 616878333, global.trial_information@roche.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	Interim
Date of interim/final analysis	29 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 March 2024
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the pharmacokinetics of ocrelizumab in the breastmilk of lactating women with clinically isolated syndrome (CIS) or multiple sclerosis (MS) (in line with the locally approved indications) treated with ocrelizumab, by assessing the concentration of ocrelizumab in mature breastmilk, as well as the corresponding exposure and pharmacodynamic effects (blood B-cell levels) in the infants.

Protection of trial subjects:

All study participants were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 4
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	26
EEA total number of subjects	2

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	8
Infants and toddlers (28 days-23 months)	5
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	13
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 13 mother-infant pairs took part in the study across 7 sites in United States, Spain and United Kingdom. Data up to primary cut-off date is reported here. Final data will be reported 1 year after study completion date.

Pre-assignment

Screening details:

Lactating mothers with clinically isolated syndrome (CIS) or multiple sclerosis (MS), who, in consultation with their treating physician chose to continue or start postpartum treatment with commercial ocrelizumab were enrolled in this study.

Period 1

Period 1 title	Treatment and Sampling Period (60 days)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Mothers

Arm description:

Lactating mothers initiating ocrelizumab received two doses of 300 milligrams (mg), as an intravenous (IV) infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1 at the discretion of the physicians, in accordance with local prescribing information.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Mothers initiating, administered ocrelizumab 300 mg, as an IV infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1.

Arm title	Infants

Arm description:

Infants of mothers who received commercial IV ocrelizumab at the discretion of the physicians, in accordance with local prescribing information were observed until 1 month (+30 days) after the first dose of measles, mumps, and rubella (MMR) vaccine (if first dose is administered at 11 months of age or later) or 1 month (+ 30 days) after second dose of MMR vaccine (if first dose is administered before 11 months of age), or at Month 13 of chronological age (+30 days) if MMR vaccine is not planned to be administered.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Mothers	Infants
Started	13	13
Completed	12	12
Not completed	1	1
Consent withdrawn by subject	1	1

Period 2

Period 2 title	Vaccination Period (11 Months)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Mothers

Arm description:

Lactating mothers initiating ocrelizumab received two doses of 300 milligrams (mg), as an intravenous (IV) infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1 at the discretion of the physicians, in accordance with local prescribing information.

Arm type	Experimental
Investigational medicinal product name	Ocrelizumab
Investigational medicinal product code	RO4964913
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Mothers initiating, administered ocrelizumab, 300 mg, as an IV infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1.

Arm title	Infants

Arm description:

Infants of mothers who received commercial IV ocrelizumab at the discretion of the physicians, in accordance with local prescribing information were observed until 1 month (+30 days) after the first dose of MMR vaccine (if first dose is administered at 11 months of age or later) or 1 month (+ 30 days) after second dose of MMR vaccine (if first dose is administered before 11 months of age), or at Month 13 of chronological age (+30 days) if MMR vaccine is not planned to be administered.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Mothers	Infants
Started	12	12
Completed	6	6
Not completed	6	6
Consent withdrawn by subject	2	1
Reason Not Specified	-	1
Ongoing in the study	4	4

Baseline characteristics

Reporting groups	
Reporting group title	Mothers
Reporting group description:	
Lactating mothers initiating ocrelizumab received two doses of 300 milligrams (mg), as an intravenous (IV) infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1 at the discretion of the physicians, in accordance with local prescribing information.	
Reporting group title	Infants
Reporting group description:	
Infants of mothers who received commercial IV ocrelizumab at the discretion of the physicians, in accordance with local prescribing information were observed until 1 month (+30 days) after the first dose of measles, mumps, and rubella (MMR) vaccine (if first dose is administered at 11 months of age or later) or 1 month (+ 30 days) after second dose of MMR vaccine (if first dose is administered before 11 months of age), or at Month 13 of chronological age (+30 days) if MMR vaccine is not planned to be administered.	

Reporting group values	Mothers	Infants	Total
Number of subjects	13	13	26
Age categorical Units: Subjects			
Pre-term newborn - gestational age < 37 wk	0	0	0
Newborns (0-27 days)	0	8	8
Infants and toddlers (28 days-23 months)	0	5	5
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	13	0	13
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
median	35.0	0.02	
full range (min-max)	30 to 40	0.00 to 0.33	-
Sex: Female, Male Units: participants			
Female	13	6	19
Male	0	7	7

End points

End points reporting groups

Reporting group title	Mothers

Reporting group description:

Lactating mothers initiating ocrelizumab received two doses of 300 milligrams (mg), as an intravenous (IV) infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1 at the discretion of the physicians, in accordance with local prescribing information.

Reporting group title	Infants

Reporting group description:

Infants of mothers who received commercial IV ocrelizumab at the discretion of the physicians, in accordance with local prescribing information were observed until 1 month (+30 days) after the first dose of measles, mumps, and rubella (MMR) vaccine (if first dose is administered at 11 months of age or later) or 1 month (+ 30 days) after second dose of MMR vaccine (if first dose is administered before 11 months of age), or at Month 13 of chronological age (+30 days) if MMR vaccine is not planned to be administered.

Reporting group title	Mothers

Reporting group description:

Lactating mothers initiating ocrelizumab received two doses of 300 milligrams (mg), as an intravenous (IV) infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1 at the discretion of the physicians, in accordance with local prescribing information.

Reporting group title	Infants

Reporting group description:

Infants of mothers who received commercial IV ocrelizumab at the discretion of the physicians, in accordance with local prescribing information were observed until 1 month (+30 days) after the first dose of MMR vaccine (if first dose is administered at 11 months of age or later) or 1 month (+ 30 days) after second dose of MMR vaccine (if first dose is administered before 11 months of age), or at Month 13 of chronological age (+30 days) if MMR vaccine is not planned to be administered.

Primary: Percentage of Infants with B Cell Levels (Cluster of Differentiation 19 [CD19+] Cells) Below the Lower Limit of Normal (LLN) Measured at Day 30 After the Mother's First Ocrelizumab Postpartum Infusion

End point title	Percentage of Infants with B Cell Levels (Cluster of Differentiation 19 [CD19+] Cells) Below the Lower Limit of Normal (LLN) Measured at Day 30 After the Mother's First Ocrelizumab Postpartum Infusion[1][2]

End point description:

Infant blood samples were collected at Day 30 after the mothers received their first postpartum ocrelizumab infusion (regardless of whether women receive a 600 mg or a 2x300 mg dose). The percentage of infants with B cell levels below LLN are reported with the two-sided Clopper Pearson 95% confidence interval (CI). B-cell reference ranges by week of life (absolute and percentage counts) are defined by Borriello et al. 2022. Full Analysis Set Infants (FASI) included all the infants of women in the Full Analysis Set Mothers (FASM) population. Number analyzed is the number of participants with data available for analyses.

End point type	Primary

End point timeframe:

At Day 30

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical analysis was planned for this endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 30.85)			

Statistical analyses

No statistical analyses for this end point

Primary: Estimated Average Oral Daily Infant Dosage (ADID)

End point title	Estimated Average Oral Daily Infant Dosage (ADID)[3][4]

End point description:

ADID was calculated as the arithmetic mean of the mother's daily ocrelizumab milk concentration (micrograms/milliliters [µg/mL]) over 60 days post-ocrelizumab infusion 1 multiplied by an estimated infant milk intake of 150 milliliters/kilograms/day (mL/kg/day) and based on the weight [kilograms (kg)] recorded at the Day 30 visit. Ocrelizumab concentrations reported as below the lower limit of quantification [LLQ=160 nanograms/millilitres (ng/mL)] are imputed to zero for the calculation ADID. Pharmacokinetic Analysis Set Mothers (PASM) included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Primary

End point timeframe:

Up to Day 60

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: No formal statistical analysis was planned for this endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: micrograms (µg)				
arithmetic mean (confidence interval 95%)	64.50 (21.415 to 107.587)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of CD19+ B Cell in the Infant

End point title	Percentage of CD19+ B Cell in the Infant[5]

End point description:

Infant blood samples were collected at Day 30 after the mothers received their first postpartum ocrelizumab infusion (regardless of whether women receive a 600 mg or a 2x300 mg dose). FASI included all the infants of women in the FASM population. Number analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

At Day 30

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: percentage of cells				
median (full range (min-max))	21.80 (10.0 to 31.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute CD19+ B Cell Count in the Infant

End point title	Absolute CD19+ B Cell Count in the Infant[6]

End point description:

Infant blood samples were collected at Day 30 after the mothers received their first postpartum ocrelizumab infusion (regardless of whether women receive a 600 mg or a 2x300 mg dose). FASI included all the infants of women in the FASM population. Number analyzed is the number of participants with data available for analyses.

End point type	Secondary

End point timeframe:

At Day 30

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: cells per microliter (cells/µL)				
median (full range (min-max))	1431.50 (869.0 to 2241.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Concentration (Cmax) of Ocrelizumab in Breastmilk

End point title	Maximum Concentration (Cmax) of Ocrelizumab in Breastmilk[7]

End point description:

PASM included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Secondary

End point timeframe:

One 600 mg infusion: before infusion and at 24 hours (Day 1), Days 7, 30 and 60 post-infusion; Two 300 mg infusions: before infusion 1 and at 24 hours (Day 1), Days 7, 14, 15 (24 hours after infusion 2), 21, 30 and 60 post-infusion 1

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: µg/mL				
arithmetic mean (standard deviation)	0.18 (± 0.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Concentration of Ocrelizumab in Breastmilk (Cmean)

End point title	Average Concentration of Ocrelizumab in Breastmilk (Cmean)[8]

End point description:

PASM included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Secondary

End point timeframe:

One 600 mg infusion: before infusion and at 24 hours (Day 1), Days 7, 30 and 60 post-infusion; Two 300 mg infusions: before infusion 1 and at 24 hours (Day 1), Days 7, 14, 15 (24 hours after infusion 2), 21, 30 and 60 post-infusion 1

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: µg/mL				
arithmetic mean (standard deviation)	0.074 (± 0.077)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Milk Concentration-Time Curve (AUC) of Ocrelizumab in Mature Breastmilk

End point title	Area Under the Milk Concentration-Time Curve (AUC) of Ocrelizumab in Mature Breastmilk[9]

End point description:

PASM included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Secondary

End point timeframe:

One 600 mg infusion: before infusion and at 24 hours (Day 1), Days 7, 30 and 60 post-infusion; Two 300 mg infusions: before infusion 1 and at 24 hours (Day 1), Days 7, 14, 15 (24 hours after infusion 2), 21, 30 and 60 post-infusion 1

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: micrograms/millilitres*day (µg/mL*day)				
arithmetic mean (standard deviation)	3.98 (± 4.93)			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of Ocrelizumab in the Infant at Day 30

End point title	Serum Concentration of Ocrelizumab in the Infant at Day 30[10]

End point description:

Serum concentration of ocrelizumab in the infant measured at Day 30 after the mother's first ocrelizumab postpartum infusion. Concentrations reported as below the lower limit of quantification (LLQ=156 ng/mL) are set to zero for calculation of summary statistics. Pharmacokinetic Analysis Set Infants (PASI) included all infants in the FASI with a serum sample to allow measurement of ocrelizumab concentration. 9999 indicates that the mean and SD were not evaluable as samples were below the limit of quantification (BLQ).

End point type	Secondary

End point timeframe:

At Day 30

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	9			
Units: µg/mL				
arithmetic mean (standard deviation)	9999 (± 9999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time of Maximum Concentration (Tmax) of Ocrelizumab in Breastmilk

End point title	Time of Maximum Concentration (Tmax) of Ocrelizumab in Breastmilk[11]

End point description:

PASM included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Secondary

End point timeframe:

One 600 mg infusion: before infusion and at 24 hours (Day 1), Days 7, 30 and 60 post-infusion; Two 300 mg infusions: before infusion 1 and at 24 hours (Day 1), Days 7, 14, 15 (24 hours after infusion 2), 21, 30 and 60 post-infusion 1

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: days				
median (full range (min-max))	3.97 (0.00 to 59.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Average Relative Infant Dose (RID)

End point title	Average Relative Infant Dose (RID)[12]

End point description:

Average RID over 60 days was calculated as the ADID (mg/kg/day) divided by the maternal dosage (mg/kg/day) over 60 days multiplied by 100. PASM included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: percentage				
arithmetic mean (standard deviation)	0.50 (± 0.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated Maximum Oral Daily Infant Dosage (MDID)

End point title	Estimated Maximum Oral Daily Infant Dosage (MDID)[13]

End point description:

MDID was calculated at the subject level as the peak ocrelizumab milk concentration (µg/mL) multiplied by an estimated infant milk intake of 150 mL/kg/day measured over 60 days after the mother's first postpartum ocrelizumab infusion. PASM included all mothers in the FASM with a breastmilk sample to allow measurement of ocrelizumab concentration.

End point type	Secondary

End point timeframe:

Up to Day 60

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: µg				
arithmetic mean (standard deviation)	153.20 (± 137.15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Titers of Antibody Immune Responses to Measles, Mumps, and Rubella (MMR) Vaccination

End point title	Mean Titers of Antibody Immune Responses to Measles, Mumps, and Rubella (MMR) Vaccination[14]

End point description:

The immune response to MMR vaccine will be assessed 1 month after the first dose of MMR vaccine (if the first dose is administered at 11 months of age or later) or 1 month after the second dose of MMR vaccine (if the first dose is administered before 11 months of age), or at Month 13 of chronological age if MMR vaccine is not planned to be administered. This is to evaluate whether infants can mount humoral immune responses to clinically relevant vaccines. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[15]			
Units: titers				
arithmetic mean (standard deviation)	()			

Notes:

[15] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Mothers With of Adverse Events (AEs)

End point title	Percentage of Mothers With of Adverse Events (AEs)[16]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and regardless of causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. The data collection is ongoing, and results will be disclosed within 1 year from the study completion date (SCD).

End point type	Secondary

End point timeframe:

Up to 16 months

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the mothers only.

End point values	Mothers			
Subject group type	Reporting group			
Number of subjects analysed	0[17]			
Units: percentage of mothers				

Notes:

[17] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infants With Positive Humoral Response to MMR Vaccination

End point title	Percentage of Infants With Positive Humoral Response to MMR Vaccination[18]

End point description:

Percentage of infants with positive humoral response (seroprotective titers as defined for the individual vaccine) will be presented for each immunoglobulin G (IgG) antibody titer. Seroprotective titer based on vaccine tests for MMR vaccine are as follows: Anti-Measles Vir IgG(-70)CL: ≥ 120 milli-international units/milliliter (mIU/mL); Anti-MumpsAT Vir iGG(-70)CL: ≥ 17 units per milliliters (U/mL); Anti-Rub Vir IgG(-70)RUOCL: ≥ 10 international units/milliliters (IU/mL). The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[19]			
Units: titers				
arithmetic mean (standard deviation)	()			

Notes:

[19] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Titers of Antibody Immune Responses to Diphtheria-Tetanus-Pertussis (DTP) Vaccine

End point title	Mean Titers of Antibody Immune Responses to Diphtheria-Tetanus-Pertussis (DTP) Vaccine[20]

End point description:

The immune response to DTP vaccine will be assessed 1 month after the first dose of MMR vaccine (if the first dose is administered at 11 months of age or later) or 1 month after the second dose of MMR vaccine (if the first dose is administered before 11 months of age), or at Month 13 of chronological age if MMR vaccine is not planned to be administered. This is to evaluate whether infants can mount humoral immune responses to clinically relevant vaccines. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[21]			
Units: titers				
arithmetic mean (standard deviation)	()			

Notes:

[21] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infants With of Adverse Events (AEs)

End point title	Percentage of Infants With of Adverse Events (AEs)[22]

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and regardless of causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 16 months

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[23]			
Units: percentage of infants				

Notes:

[23] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infants With Positive Humoral Response to DTP Vaccine

End point title	Percentage of Infants With Positive Humoral Response to DTP Vaccine[24]

End point description:

Percentage of infants with positive humoral response (seroprotective titers as defined for the individual vaccine) will be presented for each IgG antibody titer. Seroprotective titer based on vaccine tests for DTP vaccine are as follows: Anti-Diphtheria IgG(-70)CL and Anti-Tetanus Toxoid IgG(-70)RUO: ≥ 0.01 IU/mL; Bordetella pertussis antibodies, IgG: > 1.04 cut-off index (COI). The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[25]			
Units: percentage of participants				
number (not applicable)				

Notes:

[25] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infants With Positive Humoral Response to Hib Vaccine

End point title	Percentage of Infants With Positive Humoral Response to Hib Vaccine[26]

End point description:

Percentage of infants with positive humoral response (seroprotective titers as defined for the individual vaccine) will be presented for each IgG antibody titer. Seroprotective titer based on vaccine tests for Hib vaccine are as follows: Hib, IgG: ≥ 0.15 µg/mL. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[27]			
Units: percentage of participants				
number (not applicable)				

Notes:

[27] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Titers of Antibody Immune Responses to Haemophilus Influenzae Type B (Hib) Vaccine

End point title	Mean Titers of Antibody Immune Responses to Haemophilus Influenzae Type B (Hib) Vaccine[28]

End point description:

The immune response to Hib vaccine will be assessed 1 month after the first dose of MMR vaccine (if the

first dose is administered at 11 months of age or later) or 1 month after the second dose of MMR vaccine (if the first dose is administered before 11 months of age), or at Month 13 of chronological age if MMR vaccine is not planned to be administered. This is to evaluate whether infants can mount humoral immune responses to clinically relevant vaccines. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[29]			
Units: titers				
arithmetic mean (standard deviation)	()			

Notes:

[29] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Titers of Antibody Immune Responses to Hepatitis B Vaccine (HBV)

End point title	Mean Titers of Antibody Immune Responses to Hepatitis B Vaccine (HBV)[30]

End point description:

The immune response to HBV vaccine will be assessed 1 month after the first dose of MMR vaccine (if the first dose is administered at 11 months of age or later) or 1 month after the second dose of MMR vaccine (if the first dose is administered before 11 months of age), or at Month 13 of chronological age if MMR vaccine is not planned to be administered. This is to evaluate whether infants can mount humoral immune responses to clinically relevant vaccines. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[31]			
Units: titers				
arithmetic mean (standard deviation)	()			

Notes:

[31] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infants With Positive Humoral Response to PCV-13

End point title	Percentage of Infants With Positive Humoral Response to PCV-13[32]

End point description:

Percentage of infants with positive humoral response (seroprotective titers as defined for the individual vaccine) will be presented for each IgG antibody titer. Seroprotective titer based on vaccine tests for PCV-13 vaccine are as follows: 13 Valent anti-pneumococcal antibody panel: ≥ 0.35 µg/ml. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[33]			
Units: percentage of participants				
number (not applicable)				

Notes:

[33] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Infants With Positive Humoral Response to HBV

End point title	Percentage of Infants With Positive Humoral Response to

End point description:

Percentage of infants with positive humoral response (seroprotective titers as defined for the individual vaccine) will be presented for each IgG antibody titer. Seroprotective titer based on vaccine tests for HBV vaccine are as follows: Anti-HBs: ≥ 10 mIU/mL. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[35]			
Units: percentage of participants				
number (not applicable)				

Notes:

[35] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Titers of Antibody Immune Responses to 13-valent Pneumococcal Conjugate Vaccine (PCV-13)

End point title	Mean Titers of Antibody Immune Responses to 13-valent Pneumococcal Conjugate Vaccine (PCV-13)[36]

End point description:

The immune response to PCV-13 vaccine will be assessed 1 month after the first dose of MMR vaccine (if the first dose is administered at 11 months of age or later) or 1 month after the second dose of MMR vaccine (if the first dose is administered before 11 months of age), or at Month 13 of chronological age if MMR vaccine is not planned to be administered. This is to evaluate whether infants can mount humoral immune responses to clinically relevant vaccines. The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

End point type	Secondary

End point timeframe:

Up to 1 month after the first or second dose of MMR vaccine (at approximately Month 13)

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint reports data for the infants only.

End point values	Infants			
Subject group type	Reporting group			
Number of subjects analysed	0[37]			
Units: titers				
arithmetic mean (standard deviation)	()			

Notes:

[37] - The data collection is ongoing, and results will be disclosed within 1 year from the SCD.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Mothers: Up to approximately 73.3 weeks
Infants: Up to approximately 62.7 weeks

Adverse event reporting additional description:

SAFM included all mothers who met the eligibility criteria and received any post-partum dose of ocrelizumab. SAFI included all infants of women in FASM population. Data up to primary cut-off date is reported here. Final data will be reported 1 year after study completion date.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Infants

Reporting group description:

Infants of mothers who received commercial IV ocrelizumab at the discretion of the physicians, in accordance with prescribing information were observed until the last visit which was at 1 month (+ 30 days) after the first dose of MMR vaccine (if first dose is administered at 11 months of age or later) or 1 month (+ 30 days) after second dose of MMR vaccine (if first dose is administered before 11 months of age), or at Month 13 of chronological age (+ 30 days) if MMR vaccine is not planned to be administered.

Reporting group title	Mothers

Reporting group description:

Lactating mothers initiating ocrelizumab received two doses of 300 mg, as an IV infusion on Day 1 and Day 14, and mothers resuming ocrelizumab received a single dose of 600 mg, as an IV infusion on Day 1 at the discretion of the physicians, in accordance with local prescribing information.

Serious adverse events	Infants	Mothers	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 13 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	Infants	Mothers	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 13 (84.62%)	10 / 13 (76.92%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	

Haemangioma			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 13 (23.08%)	1 / 13 (7.69%)	
occurrences (all)	3	1	
Pain			
subjects affected / exposed	1 / 13 (7.69%)	2 / 13 (15.38%)	
occurrences (all)	1	2	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	2	1	
Throat irritation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Upper respiratory tract congestion			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 13 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Multiple sclerosis pseudo relapse			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Paraesthesia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Eye disorders			
Strabismus			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	1	1	
Teething			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Oral pruritus			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Skin fissures			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Rash			

subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	2 / 13 (15.38%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Dermatitis diaper			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Dermatitis atopic			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Infections and infestations			
Infected cyst			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Mastitis			
subjects affected / exposed	0 / 13 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	2	
Nasopharyngitis			

subjects affected / exposed	2 / 13 (15.38%)	2 / 13 (15.38%)	
occurrences (all)	3	3	
Oral herpes			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Otitis media			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Parainfluenzae virus infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Fungal infection			
subjects affected / exposed	0 / 13 (0.00%)	2 / 13 (15.38%)	
occurrences (all)	0	3	
Ear infection			
subjects affected / exposed	3 / 13 (23.08%)	0 / 13 (0.00%)	
occurrences (all)	3	0	
Conjunctivitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
COVID-19			
subjects affected / exposed	4 / 13 (30.77%)	6 / 13 (46.15%)	
occurrences (all)	5	6	
Bronchiolitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 13 (0.00%)	
occurrences (all)	2	0	
Rhinovirus infection			

subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Varicella			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 13 (7.69%)	
occurrences (all)	0	1	
Upper respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	1 / 13 (7.69%)	
occurrences (all)	1	2	
Suspected COVID-19			
subjects affected / exposed	1 / 13 (7.69%)	0 / 13 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 April 2022	1. A note on referral to sites was added, to allow referral of potentially eligible women to study sites. Women could be referred to study sites; and the possibility of home-based study visits was extended to all visits (conducted by a mobile nurse, and by the investigator using telemedicine [i.e., remotely]). 2. Woman agreed to use acceptable contraceptive methods or alternative methods during the study as described below and, if applicable, upon study treatment discontinuation, as defined by the local prescribing information.
05 June 2023	1. The secondary objectives were amended to include the evaluation of the relative exposure as measured by the RID to ocrelizumab in infants of lactating women with CIS or MS receiving ocrelizumab postpartum. 2. The sample size was reduced from at least 20 to at least 10 women with CIS or MS. 3. The total length of the study was increased from approximately 2 years to approximately 3 years, due to the extension of the enrolment period from approximately 8 months to approximately 21 months. 4. The list of antibody (Ab) titers of responses to vaccines administered as per local practice, had been updated to detail that the following were included: antimeasles Ab IgG, anti-rubella Ab IgG, anti-mumps Ab IgG, PCV-13 Ab (all serotypes), anti-tetanus toxoid IgG, anti-diphtheria IgG, Bordetella pertussis Ab IgG, hepatitis B surface Ab, Hemophilus influenza B IgG.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported