Pregnancy and Infant Outcomes in Women Receiving Ocrelizumab for the Treatment of Multiple Sclerosis

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L Craveiro is an employee of and shareholder in F. Hoffmann-La Roche Ltd.

D Zecevic is an employee of and shareholder in F. Hoffmann-La Roche Ltd.

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Background

As of March 2022, more than 250,000 people with MS had initiated ocrelizumab globally[1]

Women with MS of childbearing potential represent a significant number of people with MS

The number of women with MS exposed to ocrelizumab before, during and after pregnancy is increasing[2]

MS, multiple sclerosis.

1. F. Hoffmann La-Roche Ltd. https://www.ocrelizumabinfo.global/. Accessed; 2. Dobson R, Hellwig K. *Curr Opin Neurol* 2021;34:303–311.

Objectives

To report on pregnancy outcomes among women with MS exposed to ocrelizumab before or during pregnancy
up to **31 March 2022**

To report on outcomes of infants ≤1 year of age exposed to ocrelizumab *in utero* and/or through breastfeeding
up to **31 March 2022**

MS, multiple sclerosis.

Methods
Sources, reporting period and type, and definition of *in utero* exposure

Sources

- Reports from the Roche Global Safety Database:
  (1) interventional or non-interventional clinical studies, (2) spontaneous reports, (3) non-interventional programme, (4) published literature

Reporting period

- Cumulative pregnancies reported from

November 2008 to **31 March 2022**

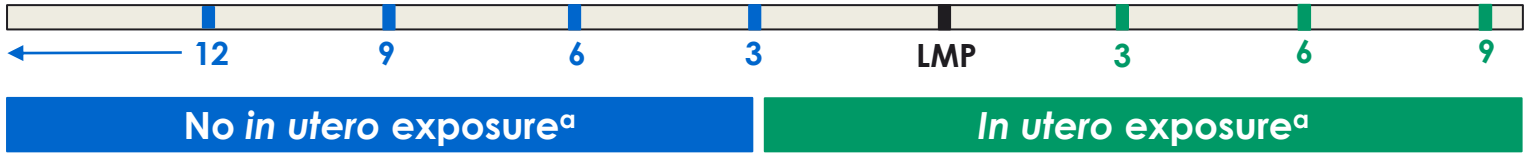
Reporting type

- **Prospective**: final outcomes were unknown at initial notification
- **Retrospective**: final outcomes were known at initial notification

← **This presentation focuses on pregnancy cases reported prospectively**

Exposure

Timing of last OCR dose in relation to date of LMP (months)



[a]Exposure classification is based on OCR $t_{1/2}$=26 days (full elimination from the body is expected by approximately 4.5 months) and assuming no relevant placental transfer of IgG1 antibodies occurs prior to 12 weeks of gestation[1,2]

IgG1, immunoglobulin G1; LMP, last menstrual period; OCR, ocrelizumab; $t_{1/2}$, half-life.

1. Palmeira P, *et al*. *Clin Dev Immunol* 2012;2012:985646; 2. Simister NE. *Vaccine* 2003;21:3365–3369.

Methods
Definitions of pregnancy and infant outcomes

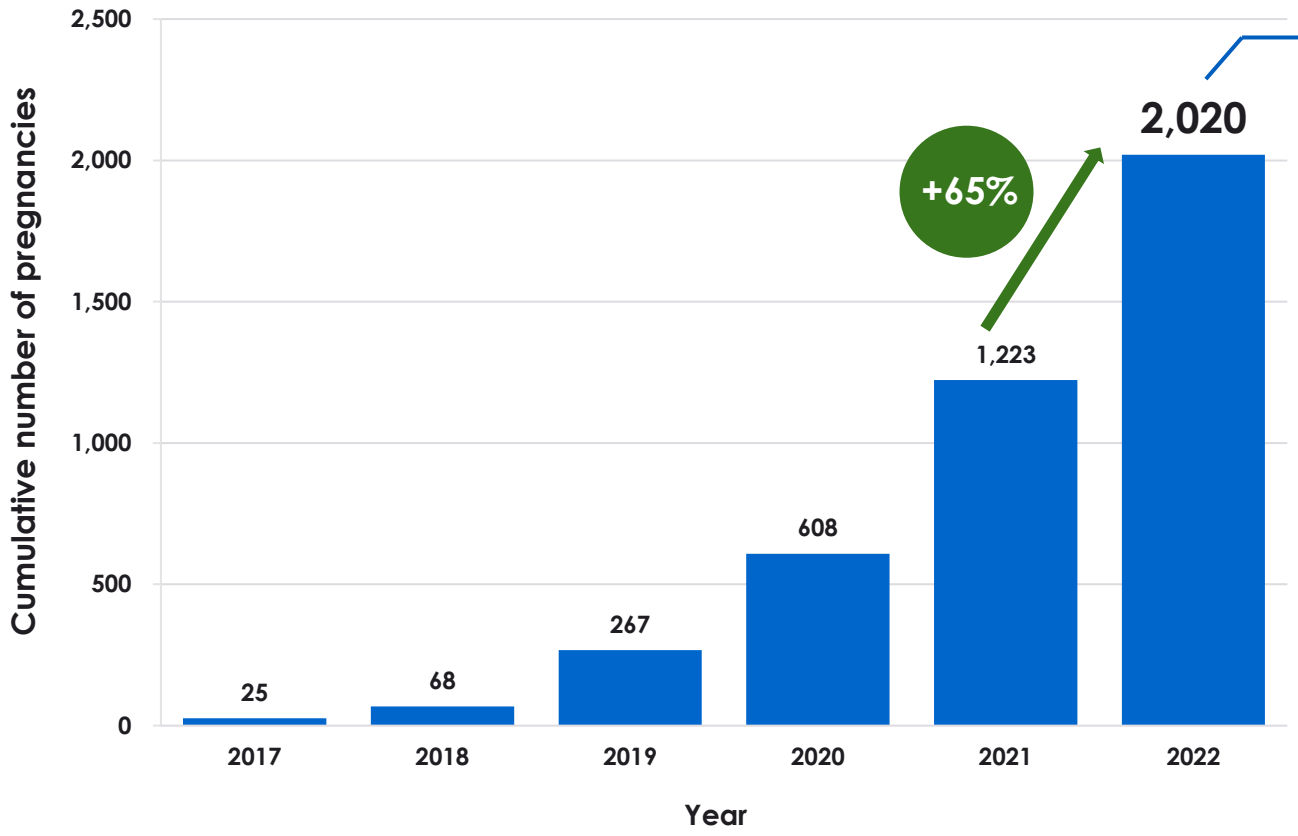
Please scan for detailed definitions
https://bit.ly/3V2QrRy

	Pregnancy	First year of life[b]
Pregnancy outcomes	**Ectopic pregnancy**	
	Elective termination	
	Intrauterine foetal death — 22 gestational weeks[a]	
	Spontaneous abortion ⟷ Still birth[1]	
	Live births — 37 gestational weeks	
	Preterm ⟷ Full term	
Infant outcomes	**Major congenital anomalies** Classified based on EUROCAT Guide 1.4[2]	• Infections and hospitalisations • Breastfeeding status • Adverse laboratory outcomes (e.g. decreased B-cell counts) • Vaccinations

[a]According to EMA definition[3] (other definitions use different thresholds, e.g. 20 or 24 completed weeks);
[b]Collected via guided questionnaires provided at birth and at 3, 6 and 12 months of age for follow-up.
EMA, European Medicines Agency; EUROCAT, European Registration of Congenital Anomalies and Twins.

1. Tavares Da Silva F, *et al*. *Vaccine* 2016;34:6057–6068; 2. European Surveillance of Congenital Anomalies (EUROCAT) Guide 1.4. https://eu-rdplatform.jrc.ec.europa.eu/sites/default/files/Full_Guide_1_4_version_28_DEC2018.pdf. Accessed October 2022; 3. Guideline on the exposure to Medicinal Products during pregnancy. https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-exposure-medicinal-products-during-pregnancy-need-post-authorisation-data_en.pdf. Accessed October 2022.

The cumulative number of pregnancies reported among women with MS treated with OCR continues to grow



As of March 2022, **2,020 pregnancies** had been reported among women with MS treated with OCR, an increase of approximately 65% relative to the previous data cut

- Most cases were reported prospectively, and outcomes were known for over half of the pregnancies
- Median **age at LMP** (range) was **32.0 (16–55) years**[a]

[a]Cases with known age: n=1,493 (73.9%).
LMP, last menstrual period; MS, multiple sclerosis; OCR, ocrelizumab.
Dobson R, *et al*. *ECTRIMS* 2021; Poster P641.

Pregnancy outcomes by exposure[a]

Prospective cases

- **Most pregnancies resulted in live births** (79.0%), and proportions were similar in the exposed and non-exposed groups

	Non-exposed (N=314)	Exposed (N=532)	Unknown (N=652)	Total (N=1,498)
Known outcomes	n=163	n=286	n=147	n=596
Live births[b]	84.0%	78.7%	74.1%	79.0%
Full term (≥37 weeks)[c]	63.0%	60.9%	41.3%	57.1%
Preterm (<37 weeks)[c]	10.9%	9.3%	10.1%	10.0%
Unknown gestational age[c]	25.5%	29.8%	48.6%	32.9%
Ectopic pregnancy[b]	1.8%	1.4%	2.7%	1.8%
Elective termination[b]	3.7%	11.5%	4.8%	7.7%
Intrauterine foetal death[b]				
Spontaneous abortion, ≤22 weeks	10.4%	8.0%	18.4%	11.2%
Stillbirth, >22 weeks	–	0.3%	–	0.2%

Please see supplementary materials for details on **all** cases.
[a]*In utero* exposure based on timing of last OCR dose relative to LMP; [b]Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total); [c]Percentages represent fractions of the total live births for the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total).
LMP, last menstrual cycle; OCR, ocrelizumab.

Pregnancy outcomes by exposure[a]

Prospective cases

- **Most live births were full term** (57.1%), a smaller proportion were preterm (10.0%) and the rest were unknown (32.9%)
- Proportions were similar in the exposed and non-exposed groups

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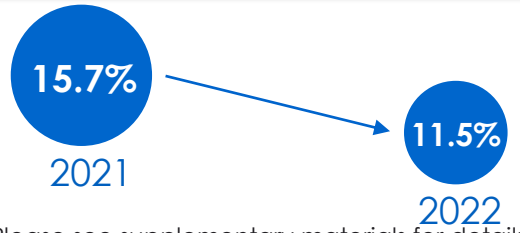
A higher proportion of elective terminations occurred in the exposed group, but the overall cumulative proportion of elective abortions is decreasing



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LMP, last menstrual cycle; OCR, ocrelizumab.

Pregnancy outcomes by exposure[a]

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- **A smaller proportion of spontaneous abortions** occurred in the exposed group (**8.0%**) compared with the non-exposed group (**10.4%**)

Please see supplementary materials for details on **all** cases.
[a]*In utero* exposure based on timing of last OCR dose relative to LMP; [b]Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total); [c]Percentages represent fractions of the total live births for the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total).
LMP, last menstrual cycle; OCR, ocrelizumab.

Major Congenital Anomalies in pregnancies with known outcomes

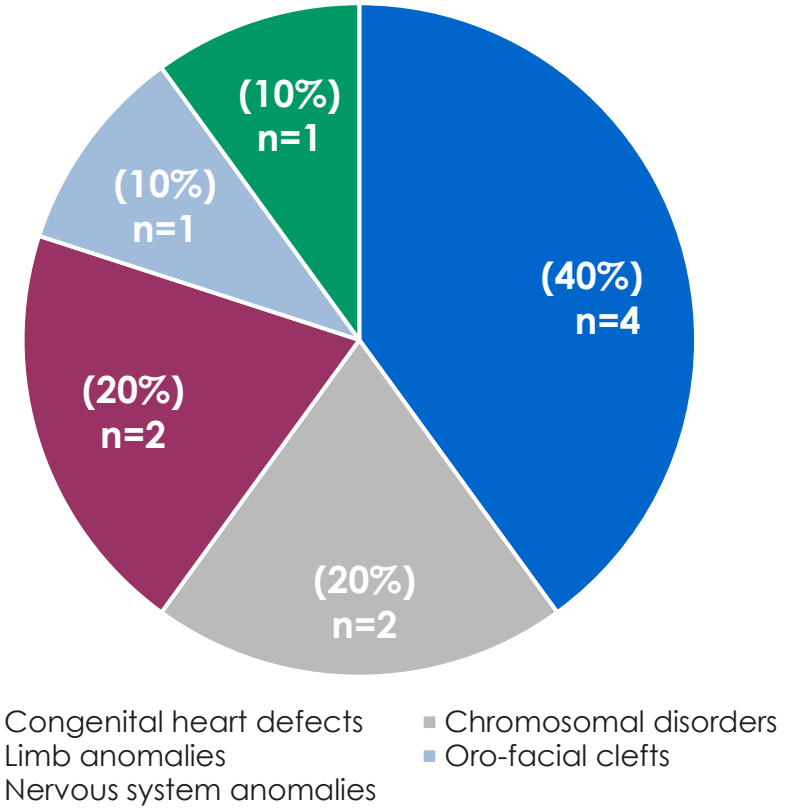
Proportions and types are consistent with epidemiological background[1,2]

Prospective and retrospective cases

Pregnancy outcome category	Non-exposed (N=278)	Exposed (N=443)	Unknown exposure (N=343)	All (N=1,064)
Live birth[a,b]	**N=222**	**N=349**	**N=238**	**N=809**
Full term with MCA, n (%)	–	4 (1.1%)	–	4 (0.5%)
Preterm with MCA, n (%)	–	4 (1.1%)	–	4 (0.5%)
Unknown gestational age with MCA, n (%)	–	–	–	–
Intrauterine foetal death[a,c], n (%)	**–**	**–**	**2 (2.5%)**	**2 (1.2%)**
Any live birth or intrauterine foetal death with MCA[a], n (%)	**–**	**8 (2.2%)**	**2 (0.8%)**	**10 (0.9%)**

Around 2–3% of all children born in Europe every year will have a MCA[1]

EUROCAT category, n (%)



[a]The dash indicates that no cases were reported; [b]Percentages represent fractions of total live births for the respective exposure category; [c]Percentages represent fractions of the total intrauterine foetal deaths for the respective exposure category.
EUROCAT, European Surveillance of Congenital Anomalies; MCA, major congenital anomaly.
1. Loane M, *et al*. *PLoS One* 2021;16:e0256535; 2. Lopez-Leon S, *et al*. *J Neurol* 2020;267:2721–2731.

Please scan QR code for further details on MCAs in the supplementary materials

https://bit.ly/3V2QrRy

Reports of infant outcomes throughout the first year of life *are very limited*

1,064 known pregnancy outcomes[a]

61 Infants with 1-year follow-up data

35 infants were exposed *in utero*

13 infants were not exposed *in utero*

13 infants had unknown exposure

Seven infants also exposed *in utero*

33 infants exposed via breastfeeding only

Infants with exposure via breastfeeding **40**

Data on reported infections, B-cell levels and vaccinations administered are very limited

For further details, see the supplementary materials

https://bit.ly/3V2QrRy

[a]Includes all known outcomes, either prospectively or retrospectively reported.

Conclusions

Largest dataset of pregnancy outcomes for an anti-CD20 therapy in MS, and continues to grow, reflecting the increasing real-world use of OCR among women with MS of childbearing potential

Updated data, with increased number of cases prospectively reported

1 **Data do not suggest an increased risk of adverse pregnancy or infant outcomes** with OCR use with or without *in utero* exposure. Data remain in line with previous reports and expected epidemiological ranges[1,2]

2 Proportion of **patients undergoing elective terminations has decreased** over the past year, which may suggest a change in pregnancy care practices among neurologists and women with MS

3 Reports of **infant outcomes throughout the first year of life are very limited;** continuous improvement of reporting by healthcare professionals is critical

Data continue to be collected through post-authorization commitments (Ocrevus pregnancy registry[3]) and two prospective phase IV studies examining infant B-cell levels and OCR pharmacokinetics across the placenta (MINORE, NCT04998812) and breast milk (SOPRANINO, NCT04998851)[4]

OCREVUS® Pregnancy Registry
MINORE MN42988
SOPRANINO MN42989

CD20, cluster of differentiate 20; MS, multiple sclerosis; OCR, ocrelizumab.

1. Lopez-Leon S, *et al*. *J Neurol* 2020;267:2721–2731; 2. Centers for Disease Control and Prevention (CDC). *MMWR Morb Mortal Wkly Rep* 2008;57:1–5;
3. OCREVUS® Pregnancy Registry. Available at: https://www.ocrevuspregnancyregistry.com/. Accessed October 2022. 4. Bove R, *et al*. Mult Scler Relat Disord. 2022;64:103963.

Supplementary materials/data tables

Methods

Definitions of pregnancy and infant outcomes[1,2]

Pregnancy outcome[1]	Definition
Ectopic pregnancies	Extrauterine pregnancy, most often in the fallopian tube.
Elective or therapeutic terminations	Induced or voluntary foetal loss during pregnancy due to medical or any other reasons.
Intrauterine foetal death[a]	Death prior to complete expulsion or extraction from the mother of a foetus, irrespective of the duration of pregnancy: **Spontaneous abortion*** Loss of a foetus before 22 completed weeks of gestation. **Stillbirth*** Loss of a foetus after 22 completed weeks of gestation and prior to birth. **Intrauterine foetal death** If gestational age unknown, not reported or could not be determined. *For cases of spontaneous abortion or stillbirth where the exact gestational age was not reported or could not be calculated, a definition of gestational age ≤22 or >22 completed weeks was assumed if there was reliable and objective documentation that confirmed the spontaneous abortion or stillbirth, respectively (this includes an autopsy report, results of prenatal tests [e.g. ultrasound] or a well-document clinical diagnosis recorded in the healthcare records).
Live birth	Complete expulsion or extraction from the mother of a foetus, irrespective of the duration of the pregnancy, that, after such separation, breathes or shows any evidence of life. **Pre-term live birth** Birth at less than 37 completed weeks (less than 259 days) of gestation. **Full-term birth** Birth at any time from 37 completed weeks (more than 259 days) of gestation. **Unknown** Gestational age at birth unknown or not reported.
Infant outcome[2]	**Definition**
Major congenital anomaly	Congenital anomalies (birth defects) are defined as any morphological, functional and/or biochemical developmental disturbance in the embryo or foetus whether detected at birth or not. The term congenital anomaly is broad and includes congenital abnormalities (structural birth defect, sometimes congenital malformation, foetal defect), foetopathies, genetic diseases with early onset or developmental delay. Congenital anomalies are classified as major according to the EUROCAT Classification System Version 1.4.

[a]Threshold of 22 weeks according to the EMA definition; global variations in the definition of spontaneous abortion versus stillbirths exist (FDA 20 weeks, UK 24 weeks, WHO 28 weeks).[3]

[1]European Medical Agency. Guideline on good pharmacovigilance practices. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-good-pharmacovigilance-practices-product-population-specific-considerations-iii_en.pdf. Accessed October 2022;
[2]European Surveillance of Congenital Anomalies (EUROCAT) Guide 1.4. Available from: https://eu-rd-platform.jrc.ec.europa.eu/sites/default/files/Full_Guide_1_4_version_28_DEC2018.pdf. Accessed Oct 2022; [3]Tavares Da Silva F, *et al. Vaccine* 2016:34:6057–6068.

EMA, European Medicines Agency; EUROCAT, European Surveillance of Congenital Anomalies; FDA, Food and Drug Administration; WHO, World Health Organization.

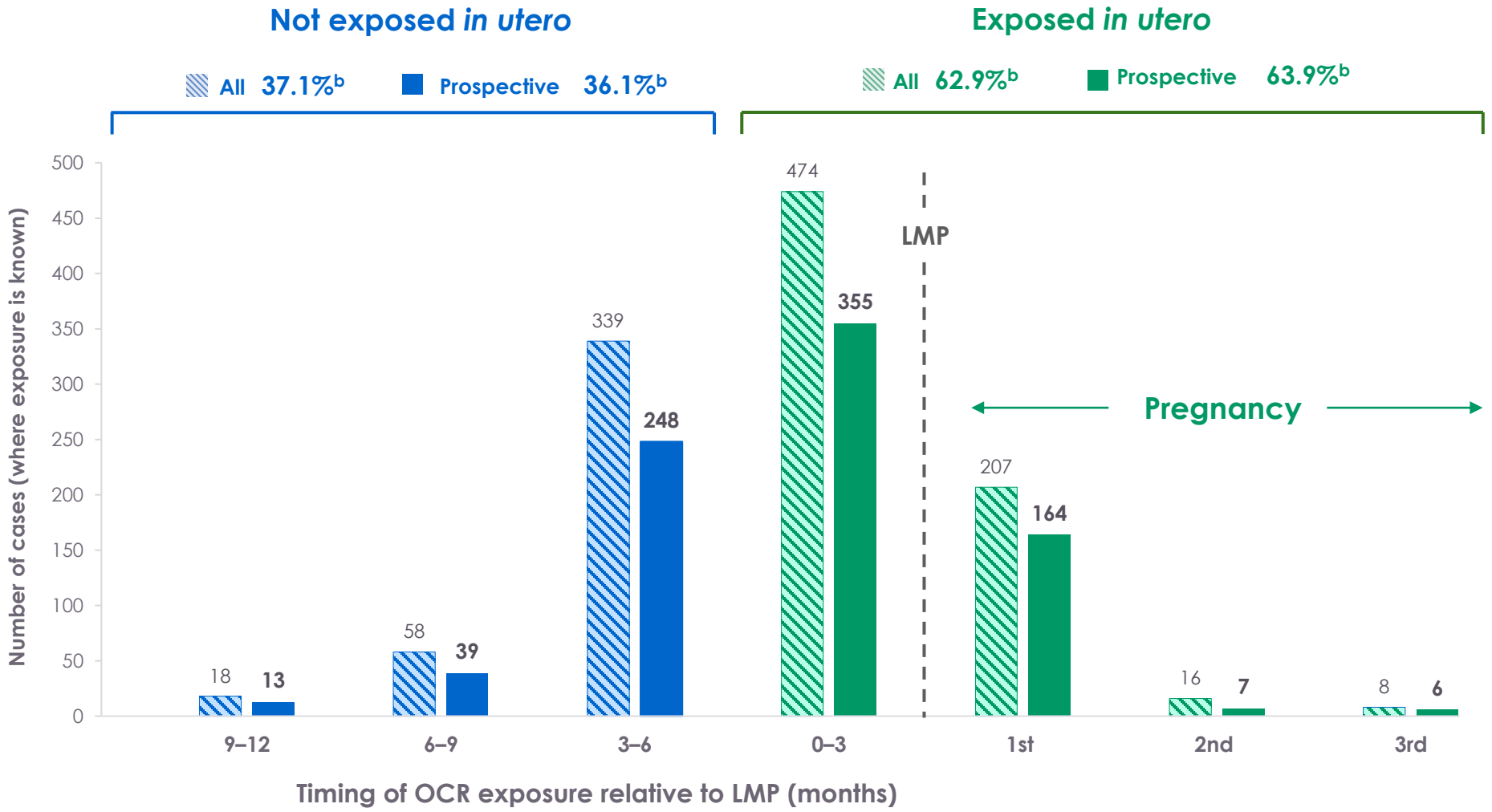
MS pregnancies by outcome status, data source, and reporting type

Distribution of cases, n (%)[a]	N=2020
By outcome status	
Known outcome	**1064 (52.7)**
Unknown, not reported or lost to follow-up	690 (34.2)
Pregnancy ongoing	266 (13.2)
By data source	
Non-interventional study/program	**1537 (76.1)**
Spontaneous report	277 (13.7)
Ocrevus pregnancy registry	181 (9.0)
Clinical studies	170 (8.4)
Literature review (case reports, case series)	36 (1.8)
By reporting type	
Prospective	**1498 (74.2)**
Retrospective	513 (25.4)
Unknown	9 (0.4)

[a]Percentages represent proportions of pregnancies in women with MS.
MS, multiple sclerosis.

MS pregnancies according to *in utero* exposure[a]

Timing of last OCR dose in relation to LMP was known for 56% of all or prospective cases



[a]Determined according to timing of last OCR dose in relation to date of LMP (months); exposure classification is based on OCR $t_{1/2}$=26 days (full elimination from the body is expected by approximately 4.5 months) and assuming no relevant placental transfer of IgG1 antibodies occurs prior to 12 weeks of gestation; [b]Percentage of cases with known exposure.
IgG1, immunoglobulin G1, LMP, last menstrual period; MS, multiple sclerosis OCR, ocrelizumab, $t_{1/2}$, half-life.

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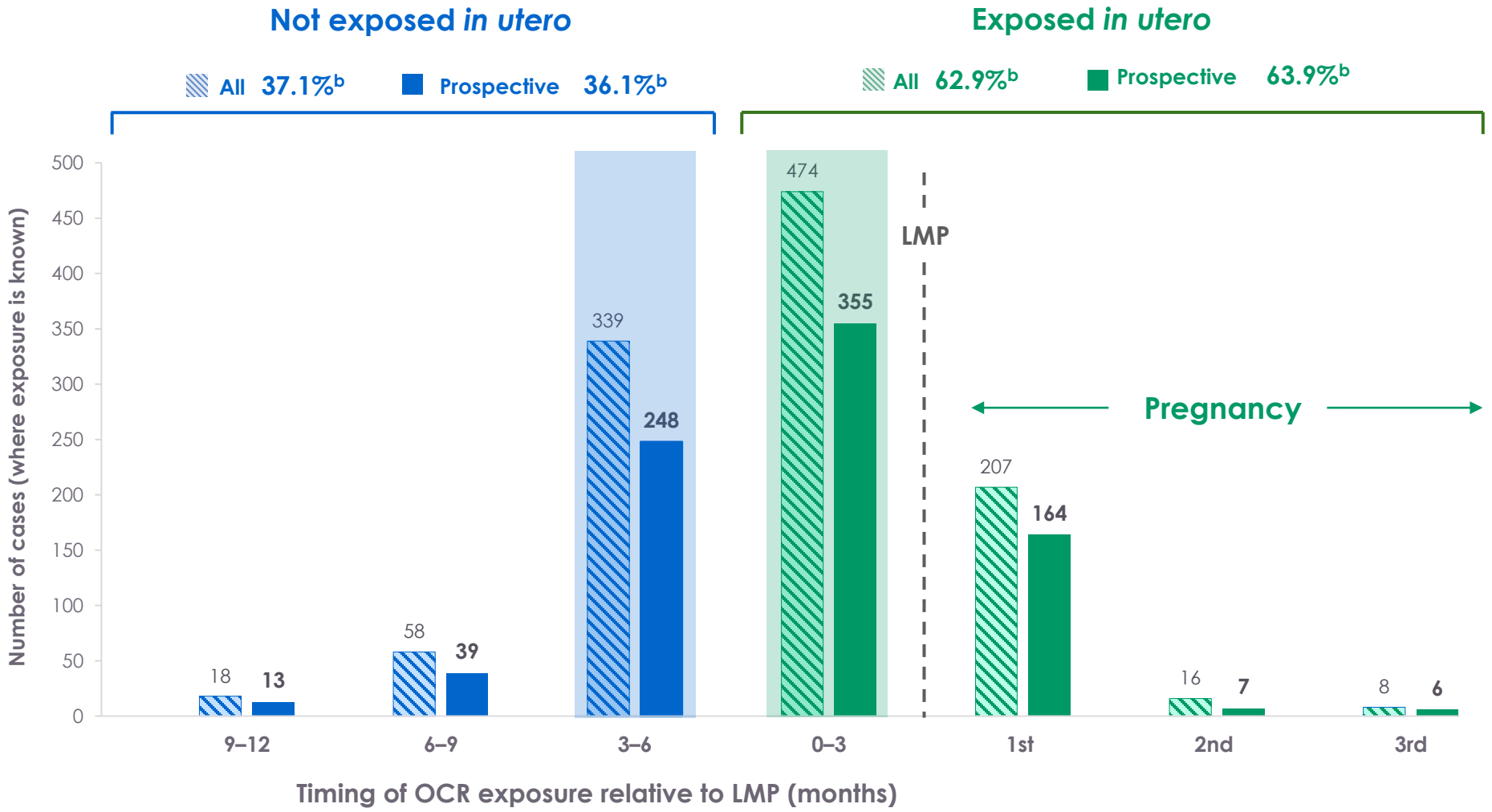

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IgG1, immunoglobulin G1, LMP, last menstrual period; MS, multiple sclerosis OCR, ocrelizumab, $t_{1/2}$, half-life.

Pregnancy outcomes by exposure[a]: prospective cases and all cases

	Prospective cases				All cases			
	Non-exposed, % (N=314)	Exposed, % (N=532)	Unknown, % (N=652)	Total, % (N=1498)	Non-exposed, %(N=433)	Exposed, % (N=705)	Unknown, % (N=882)	Total, % (N=2020)
Known outcomes	n=163	n=286	n=147	n=596	n=278	n=443	n=343	n=1064
Live births[b]	84.0 (n=137)	78.7 (n=225)	74.1 (n=109)	79.0 (n=471)	79.9 (n=222)	78.8 (n=349)	69.4 (n=238)	76.0 (n=809)
Full term (≥37 weeks)[c]	63.0 (n=87)	60.9 (n=137)	41.3 n=45)	57.1 (n=269)	**63.2** (n=140)	**54.2** (n=189)	**31.3** (n=74)	**49.8** (n=403)
Pre-term (<37 weeks)[c]	**10.9** (n=15)	**9.3** (n=21)	**10.1** (n=11)	**10.0** (n=47)	**8.2** (n=18)	**11.5** (n=40)	**7.6** (n=18)	**9.4** (n=76)
Unknown gestational age[c]	**25.5** (n=35)	**29.8** (n=67)	**48.6** (n= 53)	**32.9** (n=155)	**28.8** (n=64)	**34.4** (n=120)	**61.3** (n=146)	**40.8** (n=330)
Ectopic pregnancy[b]	**1.8** (n=3)	**1.4** (n=4)	**2.7** (n=4)	**1.8** (n=11)	**1.4** (n=4)	**0.9** (n=4)	**2.6** (n=9)	**1.7** (n=17)
Elective/therapeutic termination[b]	**3.7** (n=6)	**11.5** (n=33)	**4.8** (n=7)	**7.7** (n=46)	**4.7** (n=13)	**9.9** (n=44)	**4.4** (n=15)	**6.8** (n=72)
Intrauterine foetal death[b]								
Spontaneous abortion, ≤22 weeks	**10.4** (n=17)	**8.0** (n=23)	**18.4** (n=27)	**11.2** (n=67)	**13.7** (n=38)	**9.3** (n=41)	**23.0** (n=79)	**14.8** (n=158)
Stillbirth, >22 weeks	-	**0.3** (n=1)	-	**0.2** (n=1)	-	**1.1** (n=5)	**0.3** (n=1)	**0.6** (n=6)
Unknown gestational age	-	-	-	-	**0.4** (n=1)	-	**0.3** (n=1)	**0.2** (n=2)

[a]*In utero* exposure based on timing of last OCR dose relative to the last menstrual period; [b]Percentages represent fractions of the total known outcomes of the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total); [c]Percentages represent fractions of the total live births for the respective exposure categories (not exposed *in utero*, exposed *in utero*, unknown exposure, total).
OCR, ocrelizumab

Stillbirths/Intrauterine foetal deaths: case characteristics (n=8)

Type[1]	Case description	Maternal age, years	Gestational age, weeks	Time of last OCR infusion	Medical history including medication	Reporting
Stillbirth	First trimester screening, non-invasive prenatal testing **9/10 estimated risk of trisomy 21** (amniocentesis declined)	35	30	0-3 months before LMP	History of miscarriage and premature birth, family history of diabetes C: docosahexaenoic acid, eicosapentanoic acid, bupropion, gabapentin, calcium, macrogol, baclofen, vitamin D, cannabis oil	**Prospective**
Stillbirth	NR	25	Unknown	0-3 months before LMP	Blood clots in legs, stroke and unable to walk P: warfarin; C: enoxaparin and apixaban for thrombosis	Retrospective
Stillbirth	Mother hospitalized for mild **COVID-19 pneumonia** during pregnancy (recovered)	24	27	0-3 months before LMP	D: enoxaparin and corticosteroids for COVID-19 pneumonia	Retrospective
Stillbirth	Short-term inhalation of fluid, retroplacental hematoma and multiple infarctions with the placenta (autopsy confirmed). No infections.	28	Unknown	1st trimester	No previous history of spontaneous or therapeutic abortions P: interferon-beta-1a/1b; C: fexofenadine, paracetamol, sertraline, bromazepam, etilefrine, ascorbic acid, quetiapine fumarate	Retrospective
Stillbirth	**True knot in umbilical cord** confirmed upon autopsy	Unknown	39	1st trimester	Obesity, wheelchair-bound and venous stasis in lower extremities	Retrospective
Stillbirth	**Umbilical cord abnormality**, unknown if autopsy performed	32	Unknown	Unknown	NR	Retrospective
Intrauterine foetal death	**Foetal encephalocele** and retrognathia. Unknown if autopsy performed	Unknown	Unknown	Unknown	NR	Retrospective
Intrauterine foetal death **(maternal death)**	**Maternal death** due to acute bacterial pneumonia (autopsy confirmed, 11 weeks post-mortem)	36 (at time of death)	21-24 weeks (reported as 6 months)	3-6 months before LMP	Mother was healthy with no clinical symptoms (e.g. cough, trouble breathing, problem exercising)	Retrospective

[1]**Stillbirth** refers to the death of a foetus after 22 completed weeks of gestation and prior to birth. For cases of stillbirth where the exact gestational age is not reported or cannot be calculated, a definition of gestational age >22 completed weeks was assumed if there was reliable and objective documentation that confirms the stillbirth (this includes an autopsy report, results of prenatal tests [e.g., ultrasound], or a well-document clinical diagnosis recorded in the healthcare records. If gestational age unknown, not reported or could not be determined case was simply defined as intrauterine foetal death.

C, concurrent medication; D, disease treatment; P, previous medication; LMP, last menstrual period; NR, not reported; OCR, ocrelizumab.

Major congenital anomalies: case characteristics (n=10)

EUROCAT v1.4 Anomaly class	Anomaly type	Maternal age, years	Outcome	GA, weeks	Time of last OCR infusion	Pregnancy history	Medical history including current and past medication	Reporting
Congenital heart defects	Unclear if ASD, VSD or PFO	35	Live birth Full-term	38	2nd trimester	Gravida: unknown Para: 3 (full-term)	Current Grave's disease C: Carbimazole; P: Alemtuzumab, Dimethyl Fumarate, Fingolimod	Retrospective
Congenital heart defects	Aortic valve dysfunction, "two holes in the heart"	32	Live birth	Unknown	Unknown	Gravida: unknown Para: unknown	NR	Retrospective
Congenital heart defects	Ventricular septal defect	31	Live birth Full-term	Term	2nd trimester	Gravida: unknown Para: unknown	Diabetes type I P: alemtuzumab C: insulin	Retrospective
Congenital heart defects	Atrial septal defect with pulmonary stenosis	27	Live birth Pre-term	35	1st trimester	Gravida: unknown Para: unknown	Allergic asthma C: smoking, cetirizine and salbutamol	Retrospective
Chromosomal	Down Syndrome	36	Live birth Pre-term	34	0-3 months prior to LMP	Gravida: unknown Para: 1 (full-term)	NR	Prospective
Chromosomal	Down Syndrome	35	Stillbirth	30	0-3 months prior to LMP	Gravida: 1 (SA) Para: 1 (pre-term)	Family history of diabetes C: DHA, EPA, bupropion, gabapentin, calcium. macrogol, baclofen for neuralgia, vitamin D, cannabis oil	Prospective
Limb	Polydactyly	35	Live birth Full-term	37	1st trimester	Gravida: unknown Para: 1 (living child)	Father had polydactyly C: Paclitaxel, cannabidiol	Prospective
Limb	Polydactyly	18	Live birth Pre-term	35	2nd trimester	Gravida: unknown Para: unknown	Smoking, diplopia, dysarthria, ataxia C/P: Natalizumab; unknown if C: marijuana (THC) [started at 16.5 years]	Prospective
Oro-facial clefts	Cleft lip and palate	22	Live birth Full-term	38	0-3 months prior to LMP	NR	Concurrent depression, anxiety C: clonazepam, escitalopram, bupropion	Prospective
Nervous system	Encephalocele	Unknown	Intrauterine foetal death	Unknown	Unknown	Unknown	NR	Retrospective

ASD, atrial septal defect; C, concurrent; D, disease treatment; DHA, docosahexaenoic acid; DMF, dimethyl fumarate; EDSS, Expanded Disability Status Scale; EPA: eicosapentanoic acid; GA, gestational age; IU, intrauterine; LMP, last menstrual period; MCA, major congenital anomaly; NIPT, non-invasive prenatal testing; NR, not reported; OCR, ocrelizumab; P, previous; PFO, patent foramen ovale; RMS, relapsing multiple sclerosis; SA, spontaneous abortion; THC, tetrahydrocannabinol; Unk, unknown; VSD, ventricular septal defect.

Infants with follow-up in the first year of life (n=61)

Vaccinations, infections and B-cell levels

		Exposed *in utero* (N=35)	Not exposed *in utero* (N=13)	Unknown exposure (N=13)	Total (N=61)	Additional information reported
Vaccinations administered, n	**Yes**	26 (74.3%)	8 (61.5%)	8 (61.5%)	42 (68.6%)	
	No	–	–	–	–	
	NR/Unk/NA	9 (25.7%)	5 (38.5%)	5 (38.5%)	19 (31.1%)	
Infections reported, n	**Yes**	2 (5.7%)[b]	1 (7.7%)[c]	2 (15.4%)[d]	5 (8.2%)	[b]Mild common cold (n=1), mild infection (n=1) [c]Cold (at 20 weeks of age; resolved in 10 days) [d]Hospitalised with UTI at the age of 12 weeks, resolved without anti-infective treatment (n=1); Group B streptococcus infection requiring NICU at 37 weeks of birth (n=1)
	No	21 (60.0%)	7 (53.8%)	9 (69.2%)	37 (60.7%)	
	NR/Unk	12 (34.3%)	5 (38.5%)	2 (15.4%)	19 (31.1%)	
B-cell levels, n[a]	**Normal**	9 (25.7%)	–	3 (23.1%)	12 (19.7%)	
	Abnormal	3 (8.6%)[e]	–	–	3 (4.9%)	[e]n=1, at 17 days of age (85/µl); n=1, lower B-cell levels (not specified); n=1, at 2 weeks, CD19 was zero
	NR/Unk	23 (65.7%)	13 (100%)	10 (76.9%)	46 (75.4%)	

CD19, cluster of differentiation 19; NA, not applicable; NICU, neonatal intensive care unit; NR, not reported; Unk, unknown; UTI, urinary tract infection.
[a]Where actual B-cell levels were reported, adjudication on whether results were below the lower limit of normal was made according to Borriello *et al.*, 2022[1].

1. Borriello F, *et al*. *J Allergy Clin Immunol* 2022;18:S0091-6749(22)00835-1.

Infants with exposure to OCR through breastfeeding (n=40)

Vaccinations, infections and B-cell levels

	Vaccinations, n	**Infections**, n	**B-cell levels**, n[a]	**Exposure *in utero***, n	**Additional information reported**
Yes	6 (15%)	3 (7.5%)[b]	Normal 5 (12.5%)	7 (17.5%)	[b]Conjunctivitis and otitis media, treated with unspecific antibiotics, no hospitalisation required (**n=1**); eye infection resolved with intraocular erythromycin (**n=1**); pelvic inflammation/nephritis, hospitalised, resolved after 5 days (**n=1**)
No	34 (85.0%)	37 (92.5%)	Abnormal –	33 (82.5%)	
NR/Unk/NA			35 (87.5%)	–	

CD19, cluster of differentiation 19; NA, not applicable; NICU, neonatal intensive care unit; NR, not reported; Unk, unknown; UTI, urinary tract infection.
[a]Where actual B-cell levels were reported, adjudication on whether results were below the lower limit of normal was made according to Borriello *et al*., 2022[1].

1. Borriello F, *et al*. *J Allergy Clin Immunol* 2022;18:S0091-6749(22)00835-1.