

Evaluating the Presence and Concentration of BRIUMVI® (ublituximab-xiyy) in Breastmilk (PROVIDE): An Interim Report

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OBJECTIVE

- To present initial results from a post-marketing study characterizing the transfer of ublituximab in breastmilk of lactating women with RMS.

OVERVIEW IN BRIEF

- The study aims to enroll up to 16 breastfeeding women to obtain at least 10 completed mother-infant dyads.
- 10 participants are currently enrolled and actively participating in the study.
- Demographics, baseline characteristics, and AEs from the first 6 mothers and infants, and milk PK parameters from the first 5 participants, are presented herein.

CONCLUSIONS

- Milk PK parameters from 5 mothers and their healthy full-term infants demonstrate negligible amounts of ublituximab in breastmilk which is undetectable by Day 60 post infusion for all participants.
- Relative infant dose was calculated to be 0.2% which is well within the minimal range, and IgG1 consumed orally has near-zero bioavailability, posing low exposure risk for breastfed infants.
- Adverse event profiles for infants and mothers are consistent with common childhood illnesses occurring during the first year of life and with the established safety profile of ublituximab.
- Results are consistent with what has been reported for physiological IgG1 as well as for other anti-CD20 mAbs.
- These data and those from additional participants will support evidence-based clinical decision-making for lactating women with RMS who are treated with ublituximab.



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- REFERENCES**
- Krysko KM, Bove R, Dobson R, Jukabaitis V, Hellwig K. Treatment of Women with Multiple Sclerosis Planning Pregnancy. *Curr Treat Options Neurol*. 2021;23(4):11. doi:10.1007/s11940-021-00666-4
 - Habes S, Ciplea AI, Tokic M, Timmesfeld N, Thiel S, Gold R, Langer-Gould AM, Hellwig K. Early postpartum treatment strategies and early postpartum relapses in women with active multiple sclerosis. *J Neurol Neurosurg Psychiatry*. 2024. Jan 11;95(2):151-157. doi:10.1136/npp-2023-031520. PMID: 37636926. PMCID: PMC10980706
 - Krysko KM, Rulatangwa A, Graves J, Lazar A, Wazabari E. Association Between Breastfeeding and Postpartum Multiple Sclerosis Relapses: A Systematic Review and Meta-analysis. *JAMA Neurol*. 2020;77(3):327-338. doi:10.1001/jamaneurol.2019.4172
 - Srinivas R, Tortorella C, Ghiselli A. Influence of Pregnancy in Multiple Sclerosis and Impact of Disease-Modifying Therapies. *Front Neurol*. 2021;12:697974. Published 2021 Jul 1. doi:10.3389/fneur.2021.697974
 - European Medicines Agency. Committee for Medicinal Products for Human Use. Guideline on clinical investigation of medicinal products for the treatment of multiple sclerosis. EMA/CHMP/717/18/2011 Rev. 2, 2015.
 - Centers for Disease Control and Prevention (CDC). Breastfeeding. Breastfeeding Report Card. Published August 31st 2022. <https://www.cdc.gov/nchs/data/infantandchild/breastfeeding/recommendations/breastfeedr.html>. Accessed June 29 2023
 - Coltrone S, Kodali S, Toossi AT. The protective role of breastfeeding in multiple sclerosis: Latest evidence and practical considerations. *Front Neurol*. 2023;13:1090133. Published 2023 Jan 24. doi:10.3389/fneur.2022.1090133
 - Food and Drug Administration (FDA). Clinical lactation studies. Considerations for study design. 2019. <https://www.fda.gov/media/124749/download>. Accessed April 30, 2023
 - Anderson A, Rowles W, Poole S, Balan A, Bevan C, Brandtstadter R, Ciplea A, Cooper J, Fabian M, Hale T, W. Jacobs D, Kakara M, Krysko K, Longbrake E, E. Marcus J, Repovic P, Riley C, S. Romeo A, R. Rulatangwa A, West T, Hellwig K, LaHue S, C. and Bove, R. (2023). Anti-CD20 monoclonal antibody therapy in postpartum women with neurological conditions. *Ann Clin Transl Neurol*. 10: 2063-2064. <https://doi.org/10.1002/actn.11883>
 - Witt L, Dost-Kováčková K, Friedmann N, et al. Olanzapine-exposed breastfeeding in multiple sclerosis patients. *Multiple Sclerosis Journal*. 2025;31(3):338-351. doi:10.1177/13524585241307165
 - Witt L, Friedmann N, Habes S, et al. Safety of breastfeeding under monoclonal antibodies in the offspring of mothers with multiple sclerosis or neuromyotonia: optic spectrum disorder. *Journal of Neurology, Neurosurgery & Psychiatry* Published Online First: 27 February 2026. doi:10.1136/npp-2025-338062
 - Kwan KC. Oral bioavailability and first-pass effect published correction appears in *Drug Metab Dispos*. 1997;25(12):1329-1336.
 - Rei BE, Tonksden B, Mayhew M, Be L, Wengler S. Safety of breastfeeding during rituximab treatment in multiple sclerosis [published online ahead of print 2022 Jul 25]. *J Neurol Neurosurg Psychiatry*. 2022;94(1):38-41. doi:10.1136/npp-2022-329545
 - Sun W, Ferrimore B, Bealieu CB, Avanesou R, Stein AC, Chen J, et al. Vedolizumab Concentrations in Breast Milk: Results from a Prospective, Postmarketing, Milk-Only Lactation Study in Nursing Mothers with Inflammatory Bowel Disease. *Clin Pharmacol Ther*. 2021;90(5):811-818.
 - BRIUMVI Prescribing Information. 2026; https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761238a0001_b1.pdf

BACKGROUND

- Increased inflammatory activity (clinical and radiologic) has been demonstrated in women with multiple sclerosis (MS) during the first post-partum trimester.¹⁻⁴
- Exclusive breastfeeding post-delivery is often recommended for its general benefits and may reduce relapse risk in people with mild to moderate MS but not in people with highly active disease.^{3,6-7}
- The use of effective disease-modifying therapies (DMTs) in combination with breastfeeding may further minimize risk of post-partum inflammatory activity.²⁻⁸
- Understanding the capacity for DMT transfer into breastmilk may have important clinical implications for both mothers and infants.
- Studies of IgG1 antibodies have demonstrated very low transfer into breastmilk, with concentrations unlikely to be orally bioavailable or pharmacologically relevant.⁹⁻¹⁴
- BRIUMVI® (ublituximab-xiyy) is a glycoengineered monoclonal IgG1 antibody targeting CD20 and approved for treatment of adults with relapsing MS (RMS). No data are currently available to describe the concentration of ublituximab in human milk.¹⁵

METHODS

- This multicenter, prospective, post-marketing study is designed to assess the presence and concentration of ublituximab in breastmilk of lactating women with RMS.
- The study includes both breastfeeding adults (18 years or older) with RMS receiving ublituximab who provide consent to participate and meet the criteria for inclusion, as well as their infants.
- Milk collection occurred at a series of 14 timepoints over 90 days: 1 pre-infusion (spot) and 13 post-infusion: Day 1 (0-4 hrs, 4-8 hrs, 8-12 hrs, 12-18 hrs, 18-24 hrs), and spot collection on Days 2, 3, 7, 10, 14, 28, 60, and 90.
- Estimates of exposure for breastfed infants were calculated based on the concentration of ublituximab in milk.
- Adverse events (AEs) in mothers and infants were collected.

KEY INCLUSION CRITERIA

Maternal	Infant
Independently decided to be treated with ublituximab prior to consent	Gestational age at delivery ≥35 weeks
Diagnosis of RMS to include CIS, RRMS, and active SPMS	Birthweight >10 th percentile
Established lactation in the index post-partum period (breastfeeding or pumping for at least 2 weeks at time of Day 1 to ensure mature milk production)	Weight >10 th percentile as reported by the mother at the time of enrollment
Willing to breastfeed or pump during the study period and exclusively pump for 24-hour period of breastmilk collection Day 1 post IV dose	
Plans to give infant breastmilk for at least duration of study	

KEY EXCLUSION CRITERIA

Maternal	Infant
Received any investigational compound or approved biologic within 30 days or 5 half-lives (whichever is longer) other than ublituximab	Any abnormality noted or clinically significant medical condition at the time of screening that may make implementation of the protocol or interpretation of the trial difficult or would put the trial at risk
Any active infection or other condition that would prevent breastfeeding	Infant has any abnormality that may interfere with breastfeeding or milk absorption
History of breast implants, breast augmentation, or breast reduction surgery, or mastectomy that significantly impacts breastfeeding	
Current use of drugs known to transfer to the breastmilk and with established or potential deleterious effects for the infant, including but not limited to aspirin, tetracyclines, or fluoroquinolones	

STUDY DESIGN AND ENDPOINTS

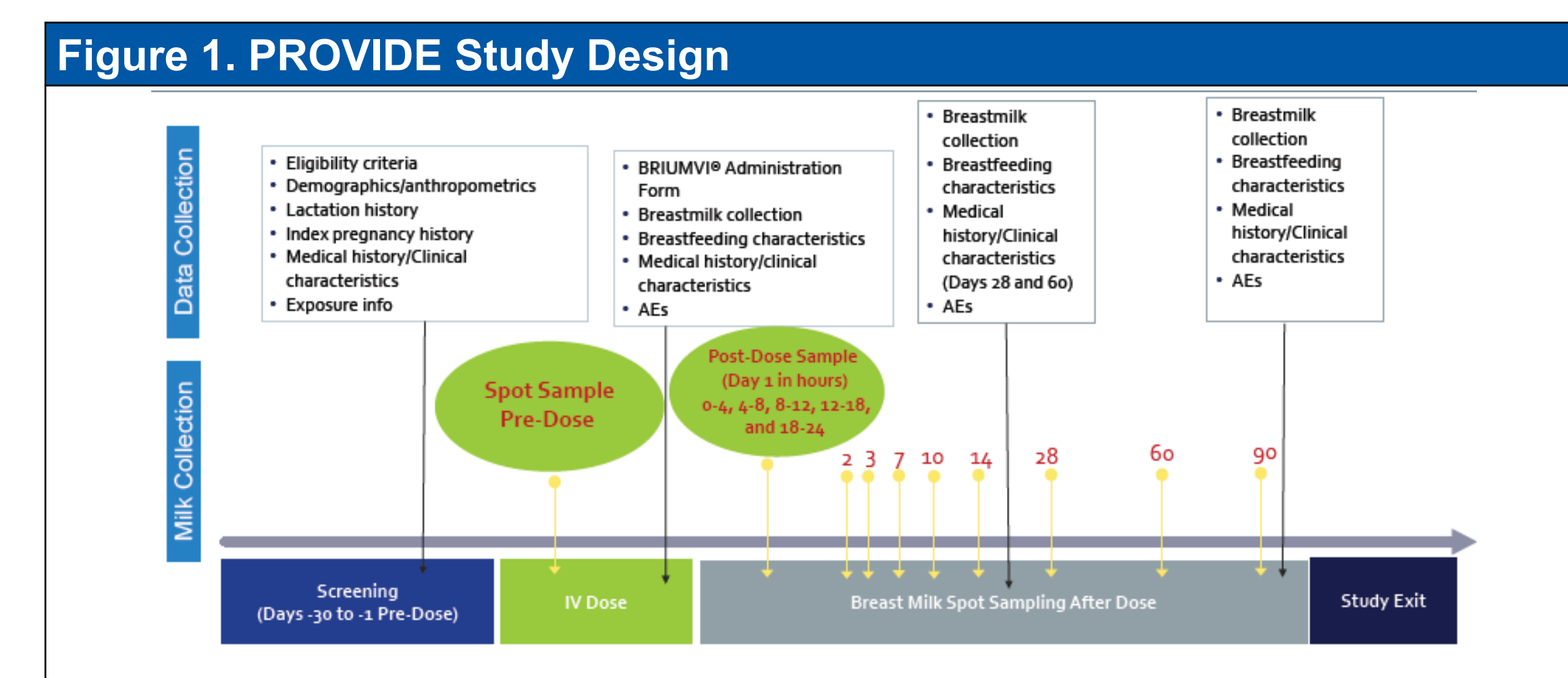


Figure 2. Primary and Secondary Endpoints

Primary	Secondary
Milk PK Parameters: <ul style="list-style-type: none">Area under the concentration-time curveConcentration at the end of dosing intervalMaximum observed concentrationTime of first occurrence of maximum concentration	Amount of ublituximab excreted in milk <ul style="list-style-type: none">Fraction of dose excreted in milkEstimates of infant exposure (infant dosage and relative infant dosage)
	Infant AEs

RESULTS

Table 3. Demographics and Baseline Characteristics of Mothers	
At screening	Mothers (N = 6)
Age, years	30.3 (25-37)
Race, n (%)	
White	6 (100)
Ethnicity, n (%)	
Hispanic or Latino	1 (16.7)
Not Hispanic or Latino	5 (83.3)
RRMS, n (%)	6 (100)
Ublituximab prior to pregnancy, n (%)	4 (66.7)
Pregnancy history, n (%) > 1 previous pregnancy	4 (66.7)

- PROVIDE has enrolled 10 women with relapsing MS with 5 completed to date.

Table 4. Demographics and Baseline Characteristics of Infants	
At birth	Infants (N = 6)
Delivery, n (%)	
Vaginal	6 (100)
Caesarean	0 (0)
Gestational age at delivery, weeks	38.5 (37-39)
Sex, n (%)	
Male	4 (66.7)
Female	2 (33.3)
Race, n (%)	
White	6 (100)
Ethnicity, n (%)	
Hispanic or Latino	1 (16.7)
Not Hispanic or Latino	5 (83.3)
Length, cm	51.3 (48.3-53.3)*
Weight, kg	3.4 (3.0-3.6)*
Congenital abnormalities, n (%)	0 (0)

- PROVIDE has enrolled 10 healthy full-term infants with 5 completed to date.

RESULTS (cont.)

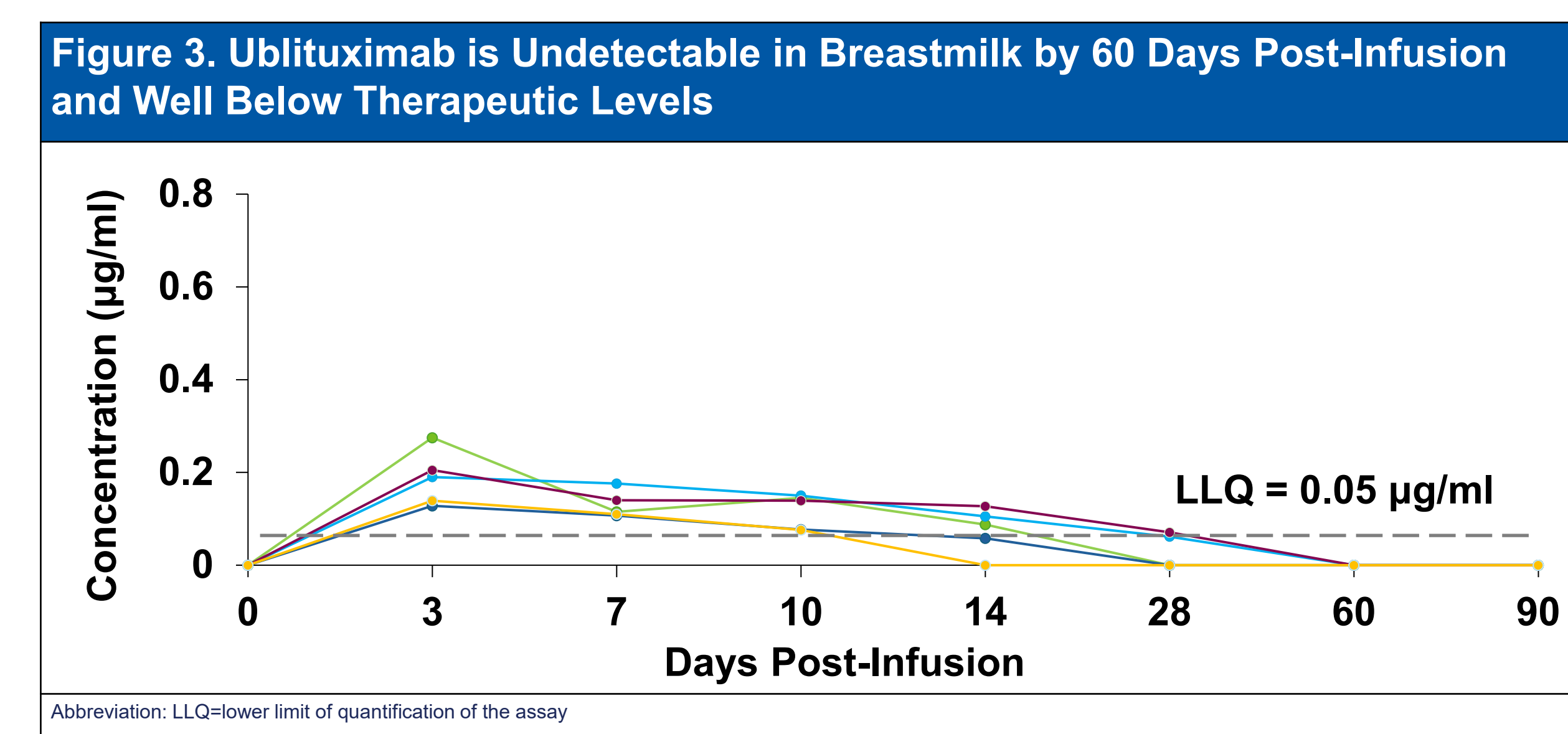


Table 5. Milk PK Parameters

PK parameters measured over 90 days post-infusion	Mothers (N = 5)
ADID, mean (range), µg	47.4 (25.1-64.0)
MDID, mean (range), µg	123.7 (84.5-181.5)
Average RID, mean (range), %	0.2 (0.1-0.3)
Maximum RID, mean (range), %	0.5 (0.3-0.7)
Average ublituximab milk concentration over 90 days, mean (range), µg/mL	0.07 (0.04-0.10)
Maximum ublituximab milk concentration over 90 days, mean (range), µg/mL	0.19 (0.13-0.28)

ADID calculated as the arithmetic mean of the mother's daily UBLI milk concentration (µg/mL) over 90 days post 450mg UBLI infusion multiplied by an estimated infant milk intake of 150 mL/kg/day and based on the current weight (kg). MDID is calculated as the subject level as the peak UBLI milk concentration (µg/mL), measured over 90 days after the mother's first 450mg postpartum UBLI infusion multiplied by an estimated infant milk intake of 150 mL/kg/day and based on the current weight (kg). The average RID over 90 days is calculated as the ADID divided by the average maternal dosage over 90 days multiplied by 100. The maximum RID is calculated as the MDID divided by the average maternal dosage over 90 days multiplied by 100. Infant weight used: 4.4kg; Maternal weight used 78.8kg; ADID, average daily infant dose; MDID, maximal daily infant dosage; PK, pharmacokinetic; UBLI, ublituximab; RID, relative infant dose.

- Average ublituximab concentration, maximum ublituximab concentration, ADID, MDID, and RID all demonstrate transfer of ublituximab into breastmilk was negligible and infant exposure was minimal.

Table 6. Maternal Safety	
Number of mothers with ≥1, n (%)	Mothers (N = 6)
Adverse Event	4 (66.7)
AE leading to infusion modification/interruption	0 (0.0)
Related AE*	1 (16.7)
Infusion-related reaction	1 (16.7)
Infection: Viral gastroenteritis (n=1) and common cold (n = 1)	2 (33.3)
Serious Adverse Event	0 (0.0)

TEAEs defined as AEs occurring after 1st dose of drug on study. Percentages are based on N in column heading. *Related AEs were oral pruritus and throat irritation. All AEs were mild and resolved.

- Maternal health outcomes were consistent with the established safety profile of ublituximab.

Table 7. Infant Safety	
Infants with ≥1 Event, n (%)	Infants (N = 6)
Adverse Event	2 (33.3)
Infections, n (%)	
Conjunctivitis	1 (16.7)
Nasopharyngitis/Pharyngitis	1 (16.7)
Streptococcal	
Serious Adverse Event	0 (0.0)

TEAEs defined as AEs occurring after 1st dose of drug on study. Percentages are based on N in column heading. AEs were typical childhood infections, mild to moderate, and all resolved.

- Infant health outcomes were consistent with common childhood illness in the first year of life.