Poster Presented at the 9th Joint ECTRIMS-ACTRIMS Meeting, 11–13 October 2023, Milan, Italy

P1648

Evaluating Ofatumumab Excretion in Breastmilk of Women With RMS: Phase 4 Study Design

Kerstin Hellwig[1], Xiaofang Shi[2], Igor Vostiar[3], Xixi Hu[4], Riley Bove[5]

[1]Department of Neurology, St. Josef Hospital, Ruhr University Bochum, Bochum, Germany; [2]China Novartis Institutes for BioMedical Research Co., Ltd, Shanghai, China; [3]Novartis Pharma AG, Basel, Switzerland; [4]Novartis Pharmaceutical Corporation, East Hanover, NJ, USA; [5]UCSF Weill Institute for Neuroscience, University of California San Francisco, San Francisco, CA, USA

SUMMARY

1. KATHAROS is a multicentre, prospective, open-label, single-arm, minimally interventional Phase 4 study to evaluate ofatumumab excretion in mature breastmilk
2. The study is planned to be initiated in early 2024 and will enroll about 20 lactating mothers with relapsing multiple sclerosis (RMS) who initiate/reinitiate treatment with ofatumumab between 2 to 24 weeks post-partum
3. This study will generate data to help inform treatment decision-making for women with RMS who wish to breastfeed and their treating physicians

INTRODUCTION

- Women with RMS are at an increased risk of relapses after giving birth.[1] Therefore, disease control with an effective multiple sclerosis (MS) disease-modifying therapy (DMT) in post-partum women is important[1]
- For women who wish to initiate/resume treatment with DMT and breastfeed at the same time, understanding the extent of drug excretion in milk is important[2]
- Currently, no data are available on whether ofatumumab is excreted in human milk[3,4]
- Excretion of antibodies (immunoglobulin G) after the first few days post-partum is low and, given the low systemic exposure to ofatumumab, the concentration in breastmilk is estimated to be very low (0.5–1 ng/mL) and not pharmacologically relevant[3–5]
- However, generation of data on the excretion of ofatumumab (KESIMPTA® is approved worldwide for the treatment of people with relapsing MS)[6] in the breastmilk of lactating women with RMS is still important to confirm these assumptions

OBJECTIVE

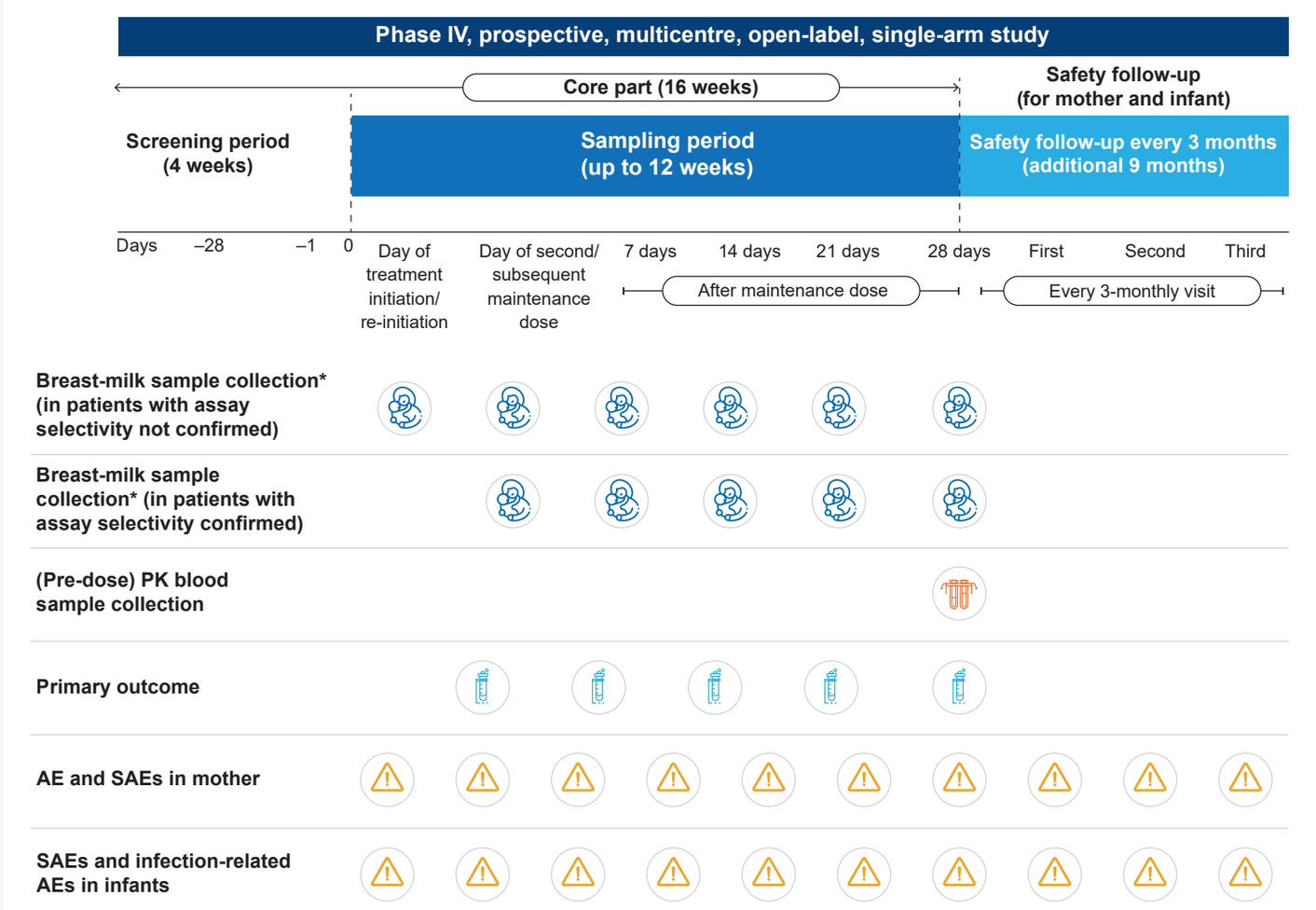
- To present the study design of a Phase 4 study (KATHAROS) to evaluate ofatumumab excretion in mature breastmilk of lactating women with RMS who initiate/reinitiate treatment with ofatumumab post-partum

METHODS

STUDY DESIGN

- KATHAROS is a multicentre, prospective, open-label, single-arm, minimally interventional, Phase 4 study consisting of two parts (**Figure 1**)
- **Core part:**
  - **Screening period (up to 4 weeks):** Physical examination and vital signs will be collected
  - **Sampling period (up to 12 weeks):**
    - First sampling time: 2 to 24 weeks post-partum (in mature breast milk)
    - On-treatment milk samples will be collected on the day of the second (or later) maintenance dose and then on days 7,14, 21 and (pre-dose) 28 after the maintenance dose
    - For at least the first 10 participants enrolled, a pre treatment milk sample will additionally be collected before initiation of ofatumumab post-partum to confirm the selectivity of the assay used for determination of ofatumumab in breastmilk
- **Safety follow-up:** Additional 9 months, with a visit every 3-months
- A hybrid study model combining onsite and offsite (remote) visits will be followed as per protocol to reduce patient burden

Figure 1. Study Design



AE, adverse event; PK, pharmacokinetic; SAE, serious adverse event. *Breastmilk sample collection on day of drug administration to be collected pre-dose

STUDY ENDPOINTS

Primary endpoint:

- Concentration of ofatumumab in breast milk at different time points

Secondary endpoints:

- Proportion of mothers with at least 1 sample with quantifiable ofatumumab concentration in breast milk
- Maximum concentration (C_{max}) and area under the curve of ofatumumab in breast milk over 28 days
- Milk/plasma ratio of ofatumumab
- Adverse events (AEs) / serious adverse events (SAEs) in mothers, and SAEs and infections in infants up to 12 months after ofatumumab initiation/reinitiation

Exploratory endpoint:

- Estimated average oral daily infant dose and maximum oral daily infant dose over 28 days

STATISTICAL ANALYSIS

- Primary endpoint will be analysed through descriptive summary statistics by sampling timepoint, and no hypothesis testing will be performed

STUDY POPULATION

Key Inclusion Criteria

- Female RMS participants aged ≥18 years
- Must be post-partum, plan to be exclusively breastfeeding, and willing to provide breastmilk samples
- Has delivered term infant (at least 37 weeks gestation)
- Who have or plan to initiate or reinitiate treatment with ofatumumab between 2 to 24 weeks post-partum
- Decision to be treated with ofatumumab and to breastfeed must be completely independent of the decision to participate in this study
- Written informed consent

Key Exclusion Criteria

- Received anti-CD20 agents during second or third trimester of pregnancy
- Females of childbearing potential should use effective contraception as per local label
- Any medical, obstetrical, psychiatric/other medical condition, in the opinion of Investigator, can jeopardise the subject's ability to participate study assessment
- Prior or current history of primary or secondary immunodeficiency/severely immune compromised state or history of malignancy of any organ system, treated or untreated (<5 years) or history of breast implants, breast augmentation or breast reduction surgery and any contradictions as per local label
- With active hepatitis B disease prior to the initiation or reinitiation of ofatumumab or active infections including mastitis

RESULTS

- About 20 adult lactating women with RMS initiating/reinitiating ofatumumab post-partum will be enrolled in this study
- Data from the study analyses will assess PK profile of ofatumumab in breastmilk over 28 days
- The planned start of enrolment is early 2024

CONCLUSIONS

- This minimally interventional study will generate information about the excretion of ofatumumab in mature breastmilk, and these data will help inform treatment decision-making for women with RMS who wish to breastfeed and their treating physicians

References: 1. Confavreux C et al. *N Engl J Med*. 1998;339 (5):285–91; **2.** Dobson R et al. *Neurol*. 2020; 94 (18):769–770; **3.** Kesimpta Prescribing information. https://www.novartis.us/sites/www.novartis.us/files/kesimpta.pdf. Accessed July 31, 2023; **4.** Kesimpta Summary of product characteristics. https://www.ema.europa.eu/en/documents/product-information/kesimpta-epar-product-information_en.pdf. Accessed July 31, 2023; **5.** Krysko KM et al. *Neurol Neuroimmunol Neuroinflamm*. 2020. 7(1):1–10; **6.** Kang C and Blair HA; *Drugs*; 2022:82(1): 55–62.

Abbreviations: AE, adverse event; **CD,** cluster of differentiation; **DMT,** disease-modifying therapy; **PK,** pharmacokinetic; **RMS,** relapsing multiple sclerosis; **SAEs,** serious adverse events.

Disclosures: Kerstin Hellwig has received compensation for serving as a consultant or speaker, or the institution she works for has received research support from Bayer, Roche, Schering Healthcare, Teva, Sanofi Aventis, Biogen Idec, Merck, Serono, and Novartis. **Riley Bove** has received consulting fees from Alexion, EMD Serono, Horizon, Janssen, and TG Therapeutics. **Igor Vostiar** was an employee of Novartis during the analysis and submission of the abstract. **Xiaofang Shi** and **Xixi Hu** are employees of Novartis.

Acknowledgements: This study was funded by Novartis Pharma AG, Basel, Switzerland. Medical writing support was provided by Amitha Thakur and Saimithra Thammera and design support by Vajhula Sarma, both of Novartis Healthcare Pvt. Ltd., Hyderabad, India. The final responsibility for the content lies with the authors.

Scan this QR code to download a copy of the Poster

Visit the web at: https://bit.ly/ectrims2023

Presenter email address:
kerstin.hellwig@ruhr-uni-bochum.de