



FIRST-IN-HUMAN DETECTION OF ROMIPLOSTIM DRUG LEVELS IN CORD BLOOD, BREASTMILK AND BLOOD IN A WOMAN WITH ITP AND HER NEWBORN INFANT

S. ROY¹, A.A. LABRECQUE², A. DUFOUR³, L. BRECHENMACHER⁴, D. YOUNG³, S.A. CHEN³, D. LE⁵, S. COOPER⁶, P. GIBSON⁷, A.E. CLARKE⁷, L. SKEITH⁷

1. Department of Critical Care Medicine, University of Calgary, Calgary, Alberta, Canada; 2. Department of Obstetrics and Gynecology, CHU Ste-Justine, Montreal, Quebec; 3. Department of Physiology and Pharmacology, Biochemistry and Molecular Biology, University of Calgary; 4. Southern Alberta Mass Spectrometry Core Facility, University of Calgary; 5. Department of Pediatrics, University of Calgary; 6. Department of Obstetrics and Gynecology, University of Calgary; 7. Department of Medicine, University of Calgary, Calgary, Alberta, Canada.



INTRODUCTION

Romiplostim is a thrombopoietin receptor agonist (TPO-RA) used to treat immune thrombocytopenia (ITP).

While small retrospective studies suggest that romiplostim use in pregnancy and the postpartum period may be safe, there is no published data about TPO-RA pharmacokinetics in pregnancy or lactation.

Romiplostim has a unique peptide sequence that we can measure using mass spectrometry.

We followed a pregnant patient with refractory ITP who was on romiplostim during pregnancy and the postpartum period, and we tested maternal and infant blood, cord blood and breastmilk samples for the presence of romiplostim (REB21-0401).

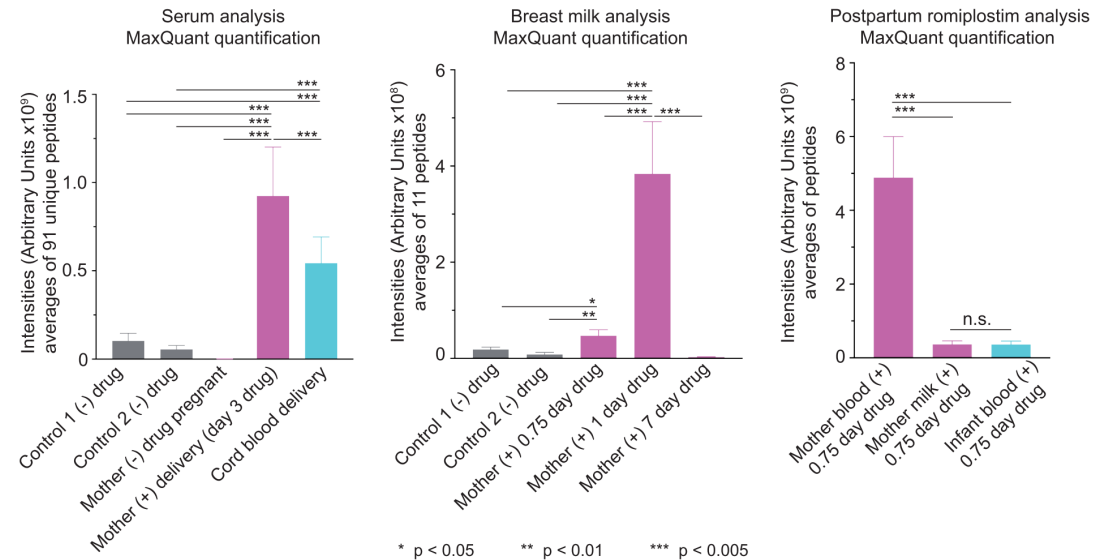
AIMS

To determine whether romiplostim crosses the placenta in a pregnant patient with chronic refractory ITP.

To determine whether romiplostim is detectable in breastmilk of a postpartum patient receiving romiplostim, compared to controls.

RESULTS

- Romiplostim was detected in the cord blood drawn at the time of delivery.** The neonatal platelet count measured on the same day was $288 \times 10^9/L$.
- Romiplostim was detected in the breastmilk sample** and the measurement was higher on day 1 post-dose, compared to day 7 post-dose ($p=0.006$).
- Romiplostim was detected in the breastfeeding infant's blood in small but identifiable quantities.**
- On postpartum day 56 (0.75 days post-dose), the participant mother's blood had 13 times more drug detected, compared to the infant's blood taken at the same time ($p=0.0002$).
- Breastfeeding was initiated immediately after birth and thrombocytosis was noted in the infant on day 9 of life. The infant's peak platelet count was $799 \times 10^9/L$ on day 22.
- On the infant's peripheral blood smear, there were rare immature cells suggestive of blasts.
- Two weeks after stopping breastfeeding, the thrombocytosis improved and no further immature cells were identified on the infant's peripheral blood smear. One year later, there have been no complications in the infant.

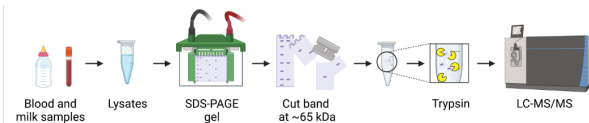


METHODS

A 34 year old G1P0 with refractory ITP received romiplostim 120 mcg (~2 mcg/kg) subcutaneously weekly starting in second trimester of pregnancy, which continued into the postpartum period.

Samples tested included the cord blood (at delivery), breastmilk (mother and 2 controls), and blood (mother, infant, and 2 controls). Serial platelet counts in the infant were recorded.

Semi-quantitative romiplostim drug levels were measured by mass spectrometry in blood, cord blood and breastmilk, after samples were separated using a SDS-PAGE electrophoresis system.



CONCLUSIONS

Romiplostim crosses the blood-placental barrier and is excreted into the breastmilk in measurable amounts.

Thrombocytosis and immature blast-like cells were identified in the blood of the breastfed infant. No serious clinical outcomes were observed after breastfeeding cessation.

These results will help to better inform physicians and patients when faced with a rare clinical scenario on the role of romiplostim use in pregnancy and breastfeeding.

REFERENCES

Michel M, Ruggeri M, Gonzalez-Lopez TJ, et al. Use of thrombopoietin receptor agonists for immune thrombocytopenia in pregnancy: results from a multicenter study. *Blood*. 2020;136:3056-3061.

Rosa María RN, Laura RL, Angeles PB, Laura LB. Use of Romiplostim during pregnancy as a rescue therapy in primary immune thrombocytopenia: Literature review and case description. *Platelets*. 2020;31:403-6.

Samuelson B, Baumann Kreuziger L, Gernsheimer T. Use of romiplostim for refractory primary immune thrombocytopenia during pregnancy. *Clin Obstet Gynecol Reprod Med* 2017;3:1-3.

ACKNOWLEDGEMENTS

CanVECTOR, the Canadian Venous Thromboembolism Research Network, has provided a Research Start-up Award to Dr. Steven Roy.

Thank you to our participant, as well as Alexandra Garven, Dr. Belal Alshaikh, Dr. Megan Drew-McKinstry, and Dr. Shannon Ruzycycki for their contributions to this project.

CONTACT INFORMATION

Dr. Leslie Skeith: laskeith@ucalgary.ca

Dr. Antoine Dufour: antoine.dufour@ucalgary.ca