



Ranibizumab

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CASRN: 347396-82-1

Drug Levels and Effects

Summary of Use during Lactation

Preliminary evidence indicates that milk levels of ranibizumab are very low. It is also likely to be partially destroyed in the infant's gastrointestinal tract and absorption by the infant is probably minimal.[1] Premature infants who have been administered ranibizumab intravitreally in both eyes for retinopathy of prematurity have had no apparent adverse effects up to the second year of life.[2] There appears to be no reason to withhold breastfeeding after intravitreal ranibizumab.

Ranibizumab inhibits vascular endothelial growth factor (VEGF). Since VEGF is present in human milk and is thought to help in maturation of the infant's gastrointestinal tract, concern has been raised about the maternal use of VEGF inhibitors during breastfeeding. Two infants were breastfed, apparently without noticeable harm, following maternal intravitreal ranibizumab injections. VEGF levels in breastmilk fell only slightly following the injection in two mothers, but another woman who did not breastfeed had decreasing VEGF levels in milk over a 28-day period. The role that breastfeeding has in maintaining VEGF levels is not clear. Ranibizumab has the shortest half-life of the VEGF inhibitors used in the eye, and thus might be the preferred agent.[3] Note that the typical alternative to breastmilk is infant formula, which contains no VEGF.

Drug Levels

Maternal Levels. One mother who was nursing a 16-month-old infant received an unspecified dose of ranibizumab intraocular injection for myopic choroidal neovascularization. At the time of her first dose, breastfeeding was stopped and milk samples were obtained 1 hour before the injection and on days 1 through 7, 14, 21, and 28 after injection. Ranibizumab was undetectable (<1.6 mcg/L) for the first 2 days after injection and then was 34.7 mcg/L on day 3. On day 6, the concentration was about 55 mcg/L, then it drifted slowly up to a concentration of about 130 mcg/L on day 28 after the injection.[4]

Another mother studied at the same center was given ranibizumab 0.5 mg intravitreal injections for myopic choroidal neovascularization and continued to breastfeed her 1 month-old infant. A trough milk sample was taken 4 weeks after a dose and then on days 1 through 7, 14, 21, and 28 after injection. All milk samples had

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ranibizumab concentrations below the lower limit of quantification of 1.6 mcg/L. The investigators hypothesized that continuous nursing resulted in the low levels of ranibizumab in milk.[4]

A woman received an injection of ranibizumab 0.5 mg in each eye with a 1-week interval between eyes. Milk samples were obtained at baseline and then daily for 14 days after the first injection. Ranibizumab levels in the mother's breast milk remained below the lower limit of quantitation of the assay at all time points.[5]

Infant Levels. A woman received an injection of ranibizumab 0.5 mg in each eye with a 1-week interval between eyes. Her infant was breastfed exclusively, except for the 3 days after each injection during which formula was given exclusively. Infant blood samples were obtained daily for 11 days starting on the day before breastfeeding was resumed. Ranibizumab levels remained below the lower limit of quantitation of the assay at all time points in the infant's serum. Plasma VEGF-A levels in the infant remained undetectable at all time points, except for days 9 and 11 when slightly low levels were found.[5]

Effects in Breastfed Infants

Relevant published information was not found as of the revision date.

Effects on Lactation and Breastmilk

A woman was given 3 intravitreal injections of bevacizumab for scar-associated choroidal neovascularization in her left eye. Vascular endothelial growth factor (VEGF) was measured in serum and breastmilk. After the intravitreal injection of bevacizumab, the VEGF level in breastmilk decreased from 13.3 to 8.6 mcg/L over a 2-week period. After changing therapy to ranibizumab therapy, no decrement in breastmilk VEGF was seen during the 42 days following injection.[6] It is not clear from the article if the mother continued breastfeeding after the injection.

Two women received ranibizumab intraocular injections for myopic choroidal neovascularization. In one who did not breastfeed, VEGF decreased from 22.8 mcg/L at baseline to 12.3 mcg/L on day 1 and to 4.9 mcg/L on day 28 after her dose. The second woman who did breastfeed her infant, had VEGF levels that were largely unchanged, varying between about 8 and 12 mcg/L over the 28-day follow up. The investigators hypothesized that continuous nursing resulted in the lower levels in the relative lack of VEGF reduction in milk.[4]

A woman received an injection of ranibizumab 0.5 mg in each eye with a 1-week interval between eyes. Milk samples were obtained at baseline and then daily for 14 days after the first injection. VEGF-A levels in the breast milk gradually decreased from 5266 ng/L at baseline to 1537 ng/L on day 11, and then increased to 3438 ng/L on day 14.[5]

The mother of a breastfed 6-month-old infant was given 4 intravitreal injections of ranibizumab 0.5 mg for choroidal neovascularization. VEGF was measured in breastmilk before the first two injections and at 1 to 3, 6, 12, 24, 48 and 72 hours after all of the injections. The greatest decrease in milk VEGF levels occurred 6 to 12 hours after each dose and was about a 40% decrease. Milk VEGF levels returned to pretreatment levels by 24 hours.[7]

A mother with macular edema and decreased visual acuity was breastfeeding a 3-week-old infant. She received intravitreal injections of ranibizumab (dose not stated) every 4 weeks for 2 doses and then every 6 weeks for 2 doses. She then received injections at intervals of 12 weeks. By 9 months postpartum she had discontinued breastfeeding. There was no indications of a developmental disorder of children up to the 2nd year of age.[8]

Alternate Drugs to Consider

(Intravitreal) [Aflibercept](#), [Bevacizumab](#)

References

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Substance Identification

Substance Name

Ranibizumab

CAS Registry Number

347396-82-1

Drug Class

Breast Feeding

Lactation

Milk, Human

Antibodies, Monoclonal

Angiogenesis Inhibitors