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Ustekinumab

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CASRN: 815610-63-0

Drug Levels and Effects

Summary of Use during Lactation

Ustekinumab is usually either not detectable in breastmilk or detectable at very low levels in breastmilk. It is also likely to be partially destroyed in the infant's gastrointestinal tract and absorption by the infant is probably minimal.[1] Many infants have been safely breastfed during maternal treatment with ustekinumab. If ustekinumab is required by the mother, it is not a reason to discontinue breastfeeding and some experts and professional organizations consider it acceptable during breastfeeding.[2-8] Waiting for at least 2 weeks postpartum to resume therapy may minimize transfer to the infant.[9]

Drug Levels

Maternal Levels. In a multi-center study of women with inflammatory bowel disease in pregnancy (the PIANO registry), 6 women receiving ustekinumab provided milk samples at 1, 12, 24, and 48 hours after drug administration. Some also provided samples at 72, 96, 120, and 168 hours after drug administration. Four of the women had detectable (>0.01 mg/L) ustekinumab levels in milk. Peak concentrations in breastmilk ranged from 0.72 to 1.57 mg/L and occurred at 12 to 72 hours after the dose. Only 3 of the women had a detectable concentration in milk beyond 48 hours.[10]

A woman with treatment-refractory Crohn's disease was treated during pregnancy with ustekinumab until the third trimester. It was reinitiated 7 weeks postpartum with a loading dose of 390 mg intravenously, then 90 mg every 8 weeks. A breastmilk sample taken 16 weeks after the dose was 3.2 mg/L. After the third dose, breastmilk levels of ustekinumab were 0.82 mg/L within the first day after the dose, 0.18 mg/L at 3 weeks after the third dose and 0.16 mg/L at 4 weeks after the third dose.[11]

Three mothers taking ustekinumab for Crohn's disease had breastmilk levels of ustekinumab measured 1 hour after a dose and sequentially for up to 2 weeks after the dose. In one patient who was receiving a dose of 90 mg every 4 weeks, the trough milk sample contained 43 mcg/L of ustekinumab and attained a peak level of 43.1 mcg/L two days after the dose. The milk level dropped to 16.7 mcg/L at 4 days after the dose, then rose again to 26.3 mcg/L at 5 days after the dose. The other two women were receiving a dosage of 90 mg every 8 weeks. One

had a trough ustekinumab milk level of 40 mcg/L. After the dose, the milk level gradually rose to a level of 45.1 mcg/L at 6 days after the dose. The third woman, who had not had any doses during pregnancy, had a trough milk value of 3 mcg/L. It rose to a peak of 7.4 mcg/L on day 3 and then plateaued between 5.4 and 6.6 mcg/L on days 4 to 6 after the dose.[12]

A pregnant woman with ulcerative colitis received ustekinumab 90 mg 4 times during pregnancy with the last dose at 29 weeks gestation She was also treated with mesalamine 4.8 grams daily during pregnancy and lactation. Postpartum, amlodipine 10 mg daily was begun for hypertension and at 5 days postpartum ampicillin-sulbactam was begun intravenously for suspected endometritis. Subcutaneous ustekinumab was restarted at 48 days postpartum and first detected in milk on day 49 at 1.5 mcg/L. On day 57, the milk concentration was 13.6 mcg/L. Milk concentrations then declined to 10.8, 7.9 and 3.4 mcg/L on days 64, 71 and 78 postpartum, respectively.[13]

Infant Levels. Sixty-nine breastfed infants were born to mothers who received ustekinumab during pregnancy and postpartum. The estimated mean half-life of ustekinumab in infants was 23.2 days (95% CI 21.5 to 24.9 days).[14]

Effects in Breastfed Infants

One woman receiving ustekinumab for severe psoriasis breastfed her infant. No adverse effects were reported in the infant, although the dosage of ustekinumab and the extent of breastfeeding were not reported.[15]

In a multi-center study of women with inflammatory bowel disease in pregnancy (the PIANO registry), 6 women received a ustekinumab while breastfeeding their infants. Among those who received ustekinumab or another biologic agent while breastfeeding, infant growth, development or infection rate was no different from infants whose mothers received no treatment. An additional 68 women received a biologic agent plus a thiopurine. Infant outcomes were similar in this group.[10]

A woman with treatment-refractory Crohn's disease was treated during pregnancy with ustekinumab until the third trimester. It was reinitiated 7 weeks postpartum with a loading dose of 390 mg intravenously, then 90 mg every 8 weeks. She breastfed her infant (extent and duration not reported). Follow-up of the infant at 12 months of age was normal.[11]

A woman with severe psoriasis was treated with ustekinumab 45 mg subcutaneously every 12 weeks until pregnancy was confirmed. After delivery ustekinumab was restarted while she was breastfeeding (extent and duration not stated). The infant reportedly had no complications and a normal growth curve.[16]

Three mothers taking ustekinumab for Crohn's disease breastfed (extent not stated) their infants. Their dosages were 90 mg every 4 weeks in one and 90 mg every 8 weeks in the other two. Infants were followed for 3 to 6 months and no developmental delays or excess infections of hospital admissions were noted.[12]

A pregnant woman with ulcerative colitis received ustekinumab 90 mg 4 times during pregnancy with the last dose at 29 weeks gestation. She was also treated with mesalamine 4.8 grams daily during pregnancy and lactation. Postpartum, amlodipine 10 mg daily was begun for hypertension and at 5 days postpartum ampicillin-sulbactam was begun intravenously for suspected endometritis. Subcutaneous ustekinumab was restarted at 7 weeks postpartum. The infant was partially (>50%) breastfed for 3 months. The infant had no adverse drug events at the 1 and 3-month checkups and received routine infant vaccinations with no adverse events.[13]

The DUMBO registry in Spain followed 526 newborns whose mothers had inflammatory bowel disease. During breastfeeding 4% of the mothers were receiving ustekinumab. Of children breastfed at least until month 6 and whose mothers were taking a biologic, 60% received the 1st and 2nd dose of rotavirus vaccine, and 17% the 3rd dose. Of children breastfed at least until month 12 and whose mothers were taking a biologic, 97% received the 1st dose of MMR vaccine; and from children breastfed at least until month 15 and whose mothers were under

biologics, 84% received the 1st dose of varicella vaccine. No serious adverse events related to live vaccines were reported.[17]

In a prospective, multicenter study, 20 infants were born to mothers taking ustekinumab during pregnancy. Of these, 18 were breastfed for a median of 7 months (range 0.5 to 27 months). Infants were followed for at least 6 months and a median of 18 months. All children had normal growth and normal psychomotor development. All but one child exposed to ustekinumab receive mandatory vaccinations with non-live vaccines without any serious or unexpected adverse events.[18]

Effects on Lactation and Breastmilk

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

Alternate Drugs to Consider

(Psoriasis) Adalimumab, Certolizumab Pegol, Etanercept, Infliximab, Phototherapy, Tretinoin

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Substance Identification

Substance Name

Ustekinumab

CAS Registry Number

815610-63-0

Drug Class

Breast Feeding

Lactation

Milk, Human

Antibodies, Monoclonal

Dermatologic Agents