

Colitis-Crohn Foreningen
Kongensgade 66-68, 2. th
5000 Odense

Ansøgning om støtte til forskningsprojekt

Herved ansøger undertegnede læge, Ph.d-studerende Christina Lykke Balmer om støtte fra Colitis-Crohn Foreningen til det lægevidenskabelige forskningsprojekt **"Overførsel af det biologiske lægemiddel risankizumab fra mor til barn under graviditeten"**

Projektet udføres ved medicinsk Lever-, Mave- & Tarmsygdomme på Aarhus Universitetshospital i samarbejde med 11 danske hospitaler.

Der ansøges om i alt DKK 300.000

Midlernes anvendelse

Der er ansøges om økonomiske midler til delvis dækning af driftsudgifter i form af blodprøvetagning, forsendelse af prøvemateriale fra danske hospitaler, indkøb af Elisa kit mhp. bestemmelse af risankizumab koncentrationerne, og utensilier til brug ved ELISA analyserne

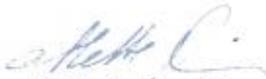
Ingen af forskerne i projektgruppen har økonomiske interesser i projektet. Projektet vil blive finansieret af offentlige og private fondsmidler. ***En delvis imødekomelse af ansøgningen vil således også være til stor gavn for projektet.***

Ansøgningen fremsendes med håb om velvillig behandling. Vi står gerne til rådighed for yderligere oplysning om projektet

Med venlig hilsen


Christina Lykke Balmer
Projektkoordinator
Læge, Ph.d-studerende
chbalm@rm.dk


Jens Kelsen
Cheflæge, overlæge, Ph.d
jenskels@rm.dk


Mette Julsgaard
Forskningsleder for IBD og graviditet, projektansvarlig
Afdelingslæge, Ph.d
metjulni@rm.dk


Henning Grønbaek
Lærestolsprofessor, overlæge Ph.d.
henning.gronbaek@aarhus.rm.dk

Vedlagt:

1. Lægmandsrapport
2. Protokol
3. Budget
4. CV for ansøger
5. Anbefaling fra afdelingslæge Mette Julsgaard

midt
regionmidtjylland

16.12.2025
Christina Lykke Balmer
MD, Ph.d-studerende
Mobil: +45 2030 1693
chbalm@rm.dk

Overførsel af det biologiske lægemiddel risankizumab fra mor til barn under graviditeten

Projektet skal belyse brugen af det biologiske lægemiddel risankizumab under graviditet. Vi undersøger, hvor meget af medicinen der overføres fra mor til barn, medicinniveauer hos mor under graviditeten og hvor hurtigt barnet udskiller lægemidlet efter fødslen. Derudover undersøger vi barnets udvikling og risiko for infektioner i det første leveår.

Omkring 60.000 danskere og næsten 7 millioner mennesker på verdensplan lever med kronisk inflammatorisk tarmsygdom (IBD). Sygdommen rammer ofte i en alder, hvor mange ønsker at stifte familie. Det kan give bekymringer om fertilitet, graviditetsforløb, medicinsk behandling og barnets sundhed.

Kvinder med kronisk tarmsygdom fravælger hyppigere at stifte familie end raske mennesker, ofte pga. frygten for at sygdommen forringer muligheden for at opnå og gennemføre graviditet, og få et raskt barn. En del af bekymringerne er desværre velbegrundede; vi ved for eksempel, at der er øget risiko for spontan abort, for tidlig fødsel og lav fødselsvægt, særligt hvis sygdommen er aktiv, hvilket ofte betyder, at behandling med biologiske lægemidler fortsætter under graviditeten. Vi ved også, at der kan være en øget risiko for ubehagelige bivirkninger ved at vaccinere børn af mødre, der fik biologisk medicin under graviditeten. Flere af bekymringerne kan vi imødekomme ved grundig rådgivning og planlægning af familieførelsen - men det kræver, at vi ved, hvad vi taler om, og at vores råd hviler på erfaring og evidens.

Vi har tidligere vist, at andre biologiske lægemidler kan overføres til barnet i forskellig grad, og at tiden til lægemidlet er helt udskilt fra barnet, varierer lægemidlerne imellem. For TNF- α -hæmmere og ustekinumab er koncentrationen i navlesnorsblod højere end i moderens serum, mens koncentrationen af vedolizumab er lavere. Udskillelsen hos børn varierer og tager gennemsnitligt 4 måneder for adalimumab, 7 måneder for infliximab (op til 12 måneder), 6 måneder for ustekinumab og 3,8 måneder for vedolizumab. Kendskab til udskillestiderne er vigtig i planlægningen af vaccination med levende vacciner, som først kan gives, når lægemidlet ikke længere kan måles i barnet.

Viden om risankizumab under graviditet og amning er meget begrænset. En artikel med 3 mor/barn par tyder på lavere koncentrationer i navlesnorsblod end i moderens serum. Der findes ingen data på, hvor længe man kan måle lægemidlet i barnet efter fødslen. Det vides heller ikke om medicinen påvirker barnets udvikling og infektionsrisiko, eller om graviditet ændrer moderens omsætning af risankizumab. Projektet skal belyse disse forhold.

Studiet udføres i et nationalt samarbejde mellem mave-tarm medicinske-, klinisk biokemiske-, og fødselsafdelinger på 11 danske hospitaler. Vi indsamler blodprøver fra 50 mor-barn-par ved fødslen og fra barnet hver tredje måned, indtil risankizumab ikke længere kan måles. Infektionsrisiko vurderes via spørgeskemaer og journaloplysninger, og barnets udvikling vurderes med det internationalt validerede ASQ-3[®]-skema.

Kronisk inflammatorisk sygdom i forbindelse med graviditet og familieliv kræver øget opmærksomhed. Bedre viden kan styrke rådgivningen, øge trygheden under graviditet og sikre mere hensigtsmæssig behandling for de mange kvinder, der ønsker børn. Projektets resultater vil danne grundlag for klare, klinisk relevante anbefalinger om behandling og vaccinationsstrategi for børn eksponeret under graviditeten og dermed bidrage til bedre sundhed for både mor og barn.

Projektet er godkendt af Videnskabsetisk Komite (j.nr. 1-10-72-123-25).

Protocol Intra-uterine exposure to risankizumab

(Overførsel af det biologiske lægemiddel risankizumab fra mor til barn under graviditeten)

Principal investigator: Medical doctor, Ph.D. Mette Julsgaard, department of Hepatology & Gastroenterology, Aarhus University Hospital. Email: mjn@clin.au.dk

Project coordinator: Medical doctor, Christina Lykke Balmer, department of Hepatology & Gastroenterology, Aarhus University Hospital. Email: chbalm@rm.dk

Background:

Inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) are chronic immune-mediated diseases of the gastrointestinal tract. The global incidence of IBD is rising(1, 2), affecting equal numbers of men and women with disease manifestation during their reproductive years(3, 4). Active disease during conception and pregnancy is associated with adverse pregnancy outcomes such as miscarriage, preterm birth, low birth weight and stillbirth(3, 5, 6). Thus, achieving clinical remission is essential, often requiring medical treatment to induce and maintain remission during pregnancy to prevent adverse outcomes(6).

Although improved therapies allow more women with IBD to consider pregnancy, concerns about the safety of medications, particularly biologics that cross the placenta, are common. Interleukin (IL)-23 inhibitors, such as risankizumab are used for aggressive IBD when conventional treatments fail.

IL-23 inhibitors are humanized monoclonal antibodies targeting the p19 subunit of IL-23. The blocking of the IL-23-mediated cytokine cascade inhibits the inflammation process that drives IBD. Is an immunoglobulin G1 (IgG1) antibody.

Pregnancy can alter pharmacokinetics of biologics. Pharmacokinetic studies on biologics in pregnancy reveal differences. The concentration of the anti-TNF-agent infliximab increased in the second and third trimester due to reduced clearance, while concentrations of the anti-TNF-agent adalimumab remain stable during pregnancy(7-9). Concentrations of vedolizumab, an IgG1 that blocks $\alpha 4\beta 7$ - integrin decrease during pregnancy (9). Concentrations of ustekinumab, an IgG1 targeting the p40 subunit shared by IL-12 and IL-23 remain stable throughout pregnancy (10).

The pharmacokinetics of risankizumab during pregnancy remain unexplored.

Placental transfer of infliximab, adalimumab, and ustekinumab is substantial. Cord blood levels at birth exceed those in maternal circulation(10-14), whereas less vedolizumab transfers through placenta with cord blood levels of vedolizumab approximately half of the maternal concentration(12, 14, 15).

A case-report of three mother-child-pairs found cord blood levels of risankizumab one-third of maternal concentrations(17), potentially due to reduced binding affinity to the placental Fc-receptor, because of a point-mutation made during the engineering of the drug to reduce binding to the Fc-receptor(18)

The mean time to infant clearance after *in utero* exposure for biologics vary: adalimumab clears in 4 months, infliximab in 7 months, although detectable infliximab levels has been found up until 12 months of life (11, 20). ustekinumab and vedolizumab clear in 6 and 3,8 months, respectively (13, 15). The clearance times for risankizumab requires further investigation. The timing of biologic clearance is crucial when planning live vaccinations (e.g., measles-mumps-rubella, varicella, Bacille Calmette-Guerin) during the first year of life. It is recommended that live vaccines should be withheld during the first 6-12 months or until biologics are no longer detectable in the infant's blood (6), as five fatal cases have been reported following BCG vaccination in infants exposed to TNF inhibitors in utero.

Overall, biologics show no significant increase in adverse pregnancy outcomes or infection risk, and all evaluated agents are considered low risk in pregnancy(6, 19, 21). However, no pharmacokinetic data exist for risankizumab in pregnancy, and outcome data after in utero exposure are limited(22, 23).

Due to ethical constraints, conducting randomized clinical trials to assess the safety of risankizumab during pregnancy is not feasible. However, given the known risks of active disease during pregnancy, Risankizumab is used for managing severe IBD who have failed other types of standard treatments. Understanding pharmacokinetics and establishing clearance times will guide dosing in pregnancy and infant vaccine timing. Larger cohort studies are required to assess maternal-fetal transport, clearance and verify low risk of adverse pregnancy outcomes, ensuring better counselling for women of reproductive age with IBD with potential

applications for other immune-mediated diseases.

Hypotheses:

1. The pharmacokinetic profile of risankizumab is affected by pregnancy
2. Concentrations of serum risankizumab at time of delivery are lower in cord blood from the offsprings compared with the mothers.
3. Concentrations of serum risankizumab are detectable during the first 6-12 months of life in infants exposed to the drug during the late second and third trimesters of pregnancy.
4. There is no association between birth outcome, child development or risk of infections following *in utero* exposure to risankizumab.

Aims:

1. To determine overall trough concentrations of risankizumab throughout pregnancy to assess whether pregnancy influences the pharmacokinetics of the drug and if dose adjustments are required.
2. To determine overall serum concentrations of risankizumab in cord blood and compare these levels to maternal concentrations, as well as to the duration of maternal medical treatment during pregnancy
3. To establish overall time to clearance of risankizumab in infants exposed to any of the drugs in utero
4. To investigate child development and infant risk of infections during the first year of life in infants exposed *in utero* to risankizumab

Methods:

1. Pregnant women with IBD, aged 18 to 50 years, who are receiving treatment with risankizumab, during pregnancy are referred to Aarhus University Hospital for joint care during pregnancy with the internationally recognized expert in IBD and pregnancy, Dr. Mette Julsgaard. Patients will be referred from the eleven major Danish IBD sites. The pregnant women will be informed that blood collection for the measurement of the concentration of the risankizumab is a part of standard care. As with all standard blood collections in clinics, the patient can decline testing if one wishes to do so. Participation in the present research project involves storage of the excess serum from the routine blood collection, to be able to reanalyse serum as batch analysis at the end of the study period. Further, as a part of the research project all participants will be asked to fill in an electronic and a postage pre-paid paper questionnaire regarding the infants' first year of life (see below). A total of 50 mother-child pairs will be enrolled for each drug. The participation sites include:
 - a. Aarhus University Hospital: Principal investigator: Ass. Prof. Mette Julsgaard, MD, PhD, Ph.d.-fellow Christina Balmer, MD & Consultant Anne-Mette Haase, MD, PhD.
 - b. Herlev University Hospital: Ass. Prof. Jacob Wium Bjerrum, MD, PhD
 - c. Hvidovre University Hospital: Ass. Prof. Ida Vind, MD, PhD.
 - d. Køge University Hospital: Ass. Prof. Signe Wiese, MD, PhD
 - e. Nordsjællands University Hospital: Professor Pia Munkholm, MD, DMSc.
 - f. Aalborg University Hospital: Ass. Prof. Lone Larsen, MD, PhD.
 - g. Odense University Hospital: Professor Jens Kjeldsen, MD, PhD
 - h. Rigshospitalet: Ass. Prof. Anja Poulsen, MD, PhD
 - i. Esbjerg Hospital: Ass. Prof. Jacob B Brodersen, MD, PhD
 - j. Lille Baelt Hospital, Vejle: Consultant Lars Koch Hansen, MD, PhD
 - k. Bispebjerg Hospital: Consultant Ida Benedikte Gottschalck, MD

Other collaborating partners: Consultant Casper Steenholdt, expert in pharmacokinetics, department of medical Gastrointestinal Diseases, Odense University Hospital, Odense, Denmark. Ass. Professor Jens Fuglsang, department of obstetrics and gynaecology, Aarhus, Aarhus University Hospital: Statistician Bo Martin Bibby, Department of Biostatistics, University of Aarhus. Paediatrician prof. Tine Brink Henriksen, Department of Paediatrics, Aarhus University Hospital, Aarhus, Denmark

2. Participant data will be collected from medical records and passed on to the project. The data of interest includes:
 - i. Diagnosis: Crohn's disease or ulcerative colitis
 - ii. Demographics: height and weight prior to pregnancy, weight gain during pregnancy, previous abdominal or perianal surgeries in relation to IBD.
 - iii. Disease activity around conception, during each trimester in pregnancy and postpartum.
 - iv. Concomitant medications
 - v. Duration, dosage and concentrations of routine measurements of risankizumab, during pregnancy, in the umbilical cord and the infant blood samples.
 - vi. Single/multiple pregnancy
 - vii. Abortion (induced or spontaneous), and if so in which gestational week.
 - viii. Pregnancy outcome (intrauterine death after 12 weeks of gestation, live birth, neonatal death)
 - ix. Premature delivery (<36 weeks), small for gestational age
 - x. APGAR score, Birth weight and length
 - xi. Congenital anomalies
 - xii. Breast feeding practices and duration. In an online survey the women will also be asked to state breastfeeding practice and duration because such data might be missing in the medical file.

Once participants consent to the project and only hereafter, the project group will have access to the included participants' medical files. The Danish authorities ("kontrolmyndigheder") will also get access to all data in case of inspection of the project.

3. Women with IBD aged 18 to 50 years, who have recently experienced a spontaneous or induced abortion while being treated with risankizumab will be included in the study based on data from medical records only.
4. Results from standard measurement of maternal trough concentration of risankizumab will be incorporated into the present study. However, for the present study, excess serum from the standard blood samples will be stored in a research biobank with the option to reanalyse all samples as batch analysis at the end of the study.
5. Results from standard testing of cord blood and routine infant blood samples will be incorporated into the present study. In addition, excess serum from the standard blood samples will be stored in a research biobank with the option to reanalyse all samples as batch analysis at the end of the study.
6. Analyses of blood samples for concentration of risankizumab:

Enzyme immunoassay for the quantitative determination of free risankizumab in serum is currently only available in Denmark at Aarhus University Hospital, dept. of Hepatology and Gastroenterology. Blood samples will be sent by courier to Aarhus University Hospital for analysis. In accordance with the standard procedure for blood collection and handling, blood samples will be spun within an hour of collection and frozen at -20 degrees Celsius. If the samples are stored more than a week prior to shipment to Aarhus University Hospital samples will be stored at - 80 degrees.
7. Surveys

An electronic survey will be sent to the women 12 months after delivery to obtain specific information regarding

 - a. Breastfeeding practice, and if so duration of breastfeeding
 - b. Child participation in the National Immunization Program
 - c. Child infections

Twelve months after delivery, a questionnaire will be sent by regular mail to the mother to collect information about the child's development during the first year of life. Development will be assessed using the internationally validated ASQ-3 Ages & Stages Questionnaires®. The letter will include a prepaid return envelope.

Statistical analysis:

Statistical analyses will be performed in R version 4.5.0, a P-value of less than 0.05 will be considered statistically significant.

Frequency tables of key study variables will be created, and biochemical data will be normalized through log transformation. Relative risk (RR) with corresponding 95% confidence intervals (CI) will be used to assess relapse in the third trimester based on the timing of risankizumab discontinuation, infections in the offspring based on the continuation of maternal risankizumab treatment after GW 29, as well as infections in the offspring associated with maternal combination therapy involving thiopurine and risankizumab.

The Wilcoxon rank-sum test will be applied to compare risankizumab concentrations and infections in infants during the first year of life. Simple linear regression analysis will be employed to identify factors influencing drug concentration at birth. The following variables will be assessed: weeks since the last risankizumab dose, duration of risankizumab use, 5-aminosalicylic acid use, thiopurine use, maternal weight prior to pregnancy, infant weight, gestational age at birth, and type of IBD. Maternal trough concentrations will be analysed using a nonlinear mixed-effects pharmacokinetic modelling approach. As a starting point for pregnancy model development, a pharmacokinetic model of risankizumab, from the drug development program will be used, respectively. Employing the final model for each drug, different dosing scenarios will be simulated. Underexposure to each of the three drugs will be defined as concentrations below the lower level of therapeutic level from the drug development programs in adult non-pregnant patients. A non-linear mixed effects regression model will be used to analyse the infant clearance data. More specifically, for each of the two parameters describing the exponentially decreasing drug concentration, i.e. the concentration at birth and the elimination rate constant, and a random infant effect will be included. Model validation will be performed by comparing individual observed and fitted values and examining residuals. The time to complete drug clearance will be estimated directly from the non-linear mixed effects regression.

Perspectives:

In the past decade, the treatment of IBD has advanced considerably, with the development of more targeted immunomodulating drugs, many of which are also used during pregnancy and lactation. Understanding placental transfer is crucial for counselling and treating women of reproductive age with severe IBD. This research project aims to provide evidence-based guidance to ensure the health and well-being of both mothers and infants. Additionally, these immunomodulatory drugs are also used to treat other immune-mediated diseases, such as severe psoriasis and rheumatoid arthritis, so the findings of this project may be applicable to women in these patient groups who are planning a pregnancy

Publications policy:

Authorships are defined according to the Vancouver guidelines for each publication before drafting. On all original articles the first author will be MD, Christina Lykke Balmer (dept. of Hepatology & Gastroenterology, Aarhus University Hospital) and Ass. Prof. MD, Mette Julsgaard (dept. of Hepatology & Gastroenterology, Aarhus University Hospital) will be the senior author. All sites enrolling a minimum of one patient with a full dataset will be granted one co-authorship. All data, inconclusive, positive and negative results will be published in peer reviewed medical/scientific publications and presented at appropriate scientific meetings. No individual participants will be identified in any published data – as only group data will be published.

Time frame:

Application for funding: Summer 2025

Inclusion of participants - start: September 1st, 2025

Inclusion of participants – will be finalized no later than: August 31st, 2030

Analyses and presentation of data: No later than two years after patient inclusion has been closed. Patient inclusion will be closed once the target of 50 mother-child pairs for each drug has been reached.

Reference list:

1. Jairath V, Feagan BG. Global burden of inflammatory bowel disease. *The Lancet Gastroenterology & Hepatology*. 2020;5(1):2-3.
2. Li CJ, Wang YK, Zhang SM, Ren MD, He SX. Global burden of inflammatory bowel disease 1990-2019: A systematic examination of the disease burden and twenty-year forecast. *World J Gastroenterol*. 2023;29(42):5751-67.
3. Torres J, Mehandru S, Colombel JF, Peyrin-Biroulet L. Crohn's disease. *Lancet*. 2017;389(10080):1741-55.
4. Le Berre C, Honap S, Peyrin-Biroulet L. Ulcerative colitis. *Lancet*. 2023;402(10401):571-84.

5. Fonager K, Sørensen HT, Olsen J, Dahlerup JF, Rasmussen SN. Pregnancy outcome for women with Crohn's disease: a follow-up study based on linkage between national registries. *Am J Gastroenterol*. 1998;93(12):2426-30.
6. Torres J, Chaparro M, Julsgaard M, Katsanos K, Zelinkova Z, Agrawal M, et al. European Crohn's and Colitis Guidelines on Sexuality, Fertility, Pregnancy, and Lactation. *J Crohns Colitis*. 2023;17(1):1-27.
7. Seow CH, Leung Y, Vande Casteele N, Ehteshami Afshar E, Tanyingoh D, Bindra G, et al. The effects of pregnancy on the pharmacokinetics of infliximab and adalimumab in inflammatory bowel disease. *Aliment Pharmacol Ther*. 2017;45(10):1329-38.
8. Grišić AM, Dorn-Rasmussen M, Ungar B, Brynskov J, Ilvemark J, Bolstad N, et al. Infliximab clearance decreases in the second and third trimesters of pregnancy in inflammatory bowel disease. *United European Gastroenterol J*. 2021;9(1):91-101.
9. Flanagan E, Gibson PR, Wright EK, Moore GT, Sparrow MP, Connell W, et al. Infliximab, adalimumab and vedolizumab concentrations across pregnancy and vedolizumab concentrations in infants following intrauterine exposure. *Aliment Pharmacol Ther*. 2020;52(10):1551-62.
10. Flanagan E, Prentice R, Wright EK, Gibson PR, Ross AL, Begun J, et al. Ustekinumab levels in pregnant women with inflammatory bowel disease and infants exposed in utero. *Aliment Pharmacol Ther*. 2022;55(6):700-4.
11. Julsgaard M, Christensen LA, Gibson PR, Garry RB, Fallingborg J, Hvas CL, et al. Concentrations of Adalimumab and Infliximab in Mothers and Newborns, and Effects on Infection. *Gastroenterology*. 2016;151(1):110-9.
12. Mahadevan U, Long MD, Kane SV, Roy A, Dubinsky MC, Sands BE, et al. Pregnancy and Neonatal Outcomes After Fetal Exposure to Biologics and Thiopurines Among Women With Inflammatory Bowel Disease. *Gastroenterology*. 2021;160(4):1131-9.
13. Julsgaard M, Wieringa JW, Baunwall SMD, Bibby BM, Driessen GJA, Kievit L, et al. Infant Ustekinumab Clearance, Risk of Infection, and Development After Exposure During Pregnancy. *Clin Gastroenterol Hepatol*. 2025;23(1):134-43.
14. Mitrova K, Pipek B, Bortlik M, Bouchner L, Brezina J, Douada T, et al. Safety of Ustekinumab and Vedolizumab During Pregnancy-Pregnancy, Neonatal, and Infant Outcome: A Prospective Multicentre Study. *J Crohns Colitis*. 2022;16(12):1808-15.
15. Julsgaard M, Baumgart DC, Baunwall SMD, Hansen MM, Grosen A, Bibby BM, et al. Vedolizumab clearance in neonates, susceptibility to infections and developmental milestones: a prospective multicentre population-based cohort study. *Aliment Pharmacol Ther*. 2021;54(10):1320-9.
16. Kane SV, Acquah LA. Placental transport of immunoglobulins: a clinical review for gastroenterologists who prescribe therapeutic monoclonal antibodies to women during conception and pregnancy. *Am J Gastroenterol*. 2009;104(1):228-33.
17. Mahadevan U, Long M. Low Placental Transfer Rates of Risankizumab Among Pregnant Women With Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2024;30(11):2240-1.
18. Singh S, Kroe-Barrett RR, Canada KA, Zhu X, Sepulveda E, Wu H, et al. Selective targeting of the IL23 pathway: Generation and characterization of a novel high-affinity humanized anti-IL23A antibody. *MAbs*. 2015;7(4):778-91.
19. Sousa P, Gisbert JP, Julsgaard M, Selinger CP, Chaparro M. Navigating Reproductive Care in Patients With Inflammatory Bowel Disease: A Comprehensive Review. *J Crohns Colitis*. 2024;18(Supplement_2):ii16-ii30.
20. Mahadevan U, Wolf DC, Dubinsky M, Cortot A, Lee SD, Siegel CA, et al. Placental transfer of anti-tumor necrosis factor agents in pregnant patients with inflammatory bowel disease. *Clin Gastroenterol Hepatol*. 2013;11(3):286-92; quiz e24.
21. Brondfield MN, Mahadevan U. Inflammatory bowel disease in pregnancy and breastfeeding. *Nature Reviews Gastroenterology & Hepatology*. 2023;20(8):504-23.
22. Dernoncourt A, Liabeuf S, Bennis Y, Masmoudi K, Bodeau S, Laville S, et al. Fetal and Neonatal Adverse Drug Reactions Associated with Biologics Taken During Pregnancy by Women with Autoimmune Diseases: Insights from an Analysis of the World Health Organization Pharmacovigilance Database (VigiBase®). *BioDrugs*. 2023;37(1):73-87.
23. Jeong YD, Jo H, Cho H, Jang W, Park J, Lee S, et al. Biologics Use for Psoriasis during Pregnancy and Its Related Adverse Outcomes in Pregnant Women and Newborns: Findings from WHO Pharmacovigilance Study. *Int Arch Allergy Immunol*. 2024:1-15.

Overførsel af risankizumab fra mor til barn under graviditeten

Totalbudget

Totalbudget	
Udgiftspost	DKK
Løn (1)	
Bioanalytiker (ELISA forsøg), 1,5 mdr	110.000
Bioanalytiker (Prøvehåndtering), 1,5 mdr	110.000
Postdoc Christina Balmer, 12 mdr	582.087
PI Mette Julsgaard, 3 mdr	263.002
Total	1.065.090
Drift og analyser	
Ekstern prøvetagning (2)	240.000
Transport og forsendelse af prøvemateriale (3)	43.000
Kontraktgebyr vedr prøvetagning og opbevaring, 15 stk (4)	22.500
KBA AUH prøvetagning og utensilier (5)	5000
Risankizumab analyser i blod (ELISA kits) (6)	360.000
Basisutensiler (7)	69.000
Fryserdrift, 3 år (8)	35.700
Total	775.200
Formidling af aktiviteter	
Publikationer (9)	25.000
Konference deltagelse (10)	50.000
Total	75.000
Direkte omkostninger i alt	1.915.290
Overhead/administrationsgebyr (11)	59.374
I alt, DKK	1.974.664

Budgetforklaringer

- (1) Løn inkluderer nettoløn, tillæg, pension, feriepenge, jobbidrag og 2% lønfremskrivning over 3 år
- (2) blodprøvetagning, processering og opbevaring af indsamlede prøver indtil de sendes til AUH
- (3) Estimat ud fra antagelse om at der sendes prøver hvert kvartal til 1000 kr pr forsendelse, fra 5 sites, i to år, + 2 % årlig inflation over 3 år
- (4) Gebyr for indgåelse af kontrakt med klinisk biokemiske afdelinger i Danmark, stykpris 1500 DKK
- (5) Inkluderer blodprøvetagning på AUH
- (6) Listepriis pr. 2025 inkl. Fragt (37 kits) + 2 % årlig inflation over 3 år
- (7) Inkluderer alle nødvendige utensilier til brug af håndtering af blodprøver, nedfrysning og ELISA assays + 2 % årlig inflation over 3 år
- (8) Fryserdrift efter endt forsøg, pris 2025 11900 + 2% årlig inflation over 6 år
- (9) Pris for publikationer inkluderer estimerede omkostninger til sproglig korrektur samt gebyr til tidsskrift
- (10) Prisen er estimeret i henhold til "tjenesterejsecirkulæret" og inkluderer flyrejse, ophold og deltagergebyr
- (11) Overhead sat til 3,1% iht regler om beregning af administrationsomkostninger ved Aarhus Universitetshospital

Christina Lykke Balmer

ORCID ID: orcid.org/0009-0005-8018-5096



+45 20 30 16 93



chbalm@rm.dk



Education

2017 - 2020	Master of Science in Medicine GPA Unweighted: 10,2. Weighted: 10,4	Copenhagen University
2014 - 2017	Bachelor of Science in Medicine GPA Unweighted: 8,7. Weighted: 9,1	Copenhagen University

Current position

2025 –	PhD-fellow PhD fellow in Inflammatory Bowel Disease (IBD) with a focus on early-life risk factors for IBD. Research areas include IBD and early life, early risk factors, fertility, pregnancy, lactation, and health outcomes in infants born to parents with IBD. Conducting a national multicenter study of pregnant women with IBD treated with IL-23 inhibitors	Faculty of Health, Aarhus University
--------	--	---

Previous clinical positions

2024 – 2025	Medical Doctor, Junior Resident First year of residency of Hepatology and Gastroenterology	Dept. Hepatology/Gastroenterology, AUH
2023 - 2023	Medical Doctor, Junior Resident First year of residency of Intern Medicine	Dept. of Medicine, Regional Hospital Horsens
2022 - 2023	Medical doctor, Intern 6 months employment as part of the basic clinical training of young doctors.	GP, Lægerne ved Volden Fredericia
2020 - 2022	Medical doctor, Intern 6 months employment as part of the basic clinical training of young doctors.	Dept of Surgery, Kolding Hospital

Previous research positions

2025 (3 months)	Scientific ass., Gastroenterology	Dept. of Clinical Medicine, Aarhus University
2019 (6 months)	Pregraduate research student	Dept of Pediatrics and Adolescent Medicine, Herlev Hospital.
2014 - 2016	Research assistant	Herlev/Østerbro Undersøgelsen, Herlev Hospital

Teaching activities

- | | |
|--------|---|
| 2020 - | <ul style="list-style-type: none">• Postgraduate teaching of junior doctors in topics within gastroenterology at Aarhus University hospital• Undergraduate teaching of medical student in gastroenterology at Aarhus University Hospital• Undergraduate teaching of medical students in clinical examination skills at Aarhus University• Undergraduate teaching of medical and nursing students in interprofessional communication at Aarhus University• Post- and undergraduate teaching of junior doctors and medical students including bedside teaching, clinical supervision at Aarhus University hospital, Regional Hospital Horsens, Kolding Hospital• Clinical supervisor for two junior doctors, Aarhus University Hospital, Regional Hospital Horsens |
|--------|---|

Presentations and conferences

- 2026 • Poster presentation of original research: *Early-life animal exposure does not influence the risk of inflammatory bowel disease* at the 21st Congress of ECCO, 2026
- 2025 • Oral presentation of original research on early-life factors and inflammatory bowel disease (IBD) at the Regional Gastroenterology and Hepatology Consultants' Meeting.
- 2019 • Oral presentation of original research in pediatrics and asthma at the annual research meeting and at the Education Day for the Asthma and Allergy Team, Department of Pediatrics and Adolescent Medicine, Herlev Hospital.

Organizational work

2023 **Educational Coordinator for Junior Doctors** Dept. of Medicine, Regional Hospital Horsens

Publications

- 2025 **Balmer CL**, Anderson PO, Korgaard J, Kjelsen J, Wildt S, Julsgaard M. Ustekinumab Use in Lactation: Drug Pharmacokinetics and Normal Development in Exposed Infants. *Resubmitted to Inflamm Bowel Dis. Dec 2 2025.*
- 2025 Julsgaard M, Wieringa JW, Baunwall SMD, Bibby BM, Driessen GJA, Kievit L, Brodersen JB, Poulsen A, Kjeldsen J, Hansen MM, Tang HQ, **Balmer CL**, Glerup H, Seidelin JB, Haderslev KV, Svenningsen L, Wildt S, Juel MA, Neumann A, Fuglsang J, Jess T, Haase AM, Hvas CL, Kelsen J, Janneke van der Woude C. Infant Ustekinumab Clearance, Risk of Infection, and Development After Exposure During Pregnancy. *Clin Gastroenterol Hepatol.* 2025;23(1):134–43.
- 2020 **Jacobsen CL**, Dagnegård J, Hermansen MN, Larsen S, Hansen KS, Chawes BL. Predictors of completion and outcome of exercise challenge tests in childhood asthma. *Pediatr Allergy Immunol.* 2020 Jul;31(5):574-578.

Aarhus, 15. december 2025

Udtalelse vedrørende Christina Balmer,

Jeg udtaler mig i egenskab af ansvarlig for behandling af og forskning i gravide patienter med kronisk inflammatorisk tarmsygdom (IBD) ved afdelingen for Lever-, Mave- & Tarmsygdomme, Aarhus Universitetshospital.

Christina Balmer besidder et markant forskertalent. Hun har en stærk analytisk sans, arbejder metodisk og systematisk, og har en udpræget faglig drivkraft, der gør hende i stand til at løfte selv komplekse forskningsopgaver med stor kvalitet. Hun kombinerer overblik med effektivitet og udviser allerede et fagligt niveau, der ligger langt over, hvad man normalt ser i hendes karrierestadie.

Hun formidler sine forskningsresultater klart og overbevisende og har allerede vist potentiale for publikationer på højt internationalt niveau. Hendes evne til at planlægge, koordinere og gennemføre forskningsaktiviteter skaber stor tillid hos samarbejdspartnere.

Fra hendes tidligere kliniske ansættelser ved jeg, at hun var særdeles vellidt blandt patienter og kolleger. Hun har en behagelig og respektfuld tilgang, som gør samarbejdet gnidningsfrit, og hendes positive væsen bidrager til et konstruktivt og trygt arbejdsmiljø.

Jeg er overbevist om, at Christina Balmer har både det faglige potentiale og den personlige integritet, der skal til for at gennemføre projektet **"Overførsel af det biologiske lægemiddel risankizumab fra mor til barn under graviditeten"** med stor succes under min vejledning. Jeg giver Christina Balmer min bedste anbefaling.

Jeg håber, at Colitis Crohn Foreningen – foreningen for tarmsyge, ser sig i stand til at støtte projektet. Opbakning fra CCF vil have en særdeles positiv effekt på fremtidige fondsansøgninger og styrke projektets gennemslagskraft.

Med venlig hilsen,



Mette Julsgaard
Klinisk Lektor, Afdelingslæge, PhD
Ansvarlig for gravide med kronisk inflammatorisk tarmsygdom, AUH