Lægmandsbeskrivelse

Crohns sygdom er en kronisk inflammatorisk tarmsygdom (inflammatory bowel disease, IBD) som kendetegnes ved vedvarende inflammation i tarmen. Den er livslang og behandles med betændelsesdæmpende lægemidler. Formålet med forskningsprojektet er først at udvikle, og siden validere, strategier for individuelt tilpasset ophør af avanceret medicinsk behandling med infliximab (IFX) hos patienter med Crohns sygdom i langvarig sygdomsremission (klinisk, biokemisk og endoskopisk). Projektet tager udgangspunkt i et klinisk og patientnært behov: Hvilke patienter kan ophøre medicinske behandling efter at der er kommet fuldstændig ro i sygdommen med ingen eller meget lav risiko for at sygdommen blusser op igen. Behandling med biologiske lægemidler, f.eks. IFX, har revolutioneret behandlingen af IBD, men den livslange fortsættelse af disse behandlinger udgør både en medicinsk og samfundsøkonomisk udfordring. Langvarig behandling medfører øget risiko for bivirkninger, f.eks. alvorlige infektioner, hud- og led-problemer, og er forbundet med betydelige økonomiske og personlige omkostninger. Mange patienter ønsker at undgå livslang medicinering, men der er ikke data, der understøtter, hvem der med fordel kan ophøre behandlingen igen. Projektet kombinerer kliniske, molekylære, terapeutisk lægemiddelmonitoring (TDM) samt patientcentrerede perspektiver i fire delstudier, som adresserer denne problemstilling. Først undersøges patienternes holdninger, præferencer og bekymringer i relation til behandlingsophør i et nationalt spørgeskemastudie på de fem største danske IBD-centre. Dernæst evalueres molekylære biomarkører i blodet som potentielle prædiktorer for sygdomstilbagefald efter behandlingsophør. Disse biomarkører kan afspejle en såkaldt "molekylær remission", som rækker ud over de kliniske og endoskopiske kriterier, der anvendes i dag. I det tredje delstudie analyseres TDM – dvs. måling af IFX-koncentrationen og antistoffer mod IFX – som en mulig metode til at identificere patienter med lav risiko for tilbagefald i sygdommen. Studie 2 og 3 baseres på opbevarede blodprøver fra det prisvindende studie STOP IT[1,2]. Kombinationen af molekylære og klinisk farmakologiske markører forventes at muliggøre en præcis risikostratificering af patienter og kunne identificere hvem der har lav risiko for tilbagefald efter behandlingsophør. Dette undersøges i det fjerde studie, hvor patienter med den identificerede lavrisikoprofil tilbydes ophør af IFX-behandling under tæt klinisk opfølgning som led i et prospektiv studie på fem førende danske universitetshospitaler. Denne del skal validere, om strategien er sikker, gennemførlig og realistisk i klinisk praksis. Projektet forventes at skabe et evidensbaseret grundlag for personaliserede, sikre og patientcentrerede strategier til behandlingsophør ved Crohns sygdom. Den forventede gevinst er betydelig: Forbedret patientautonomi og livskvalitet, færre bivirkninger, reduktion af overbehandling og lavere udgifter både direkte til medicin men også afledte sundhedsudgifter forbundet med overvågning af patienter i avanceret medicinsk behandling. Derudover vil resultaterne bidrage til udviklingen af fremtidige kliniske behandlingsretningslinjer og understøtte overgangen til præcisionsmedicin. Projektet repræsenterer således både et klinisk relevant og innovativt bidrag til patientnær forskning, med potentiale til at ændre behandlingspraksis for en stor og voksende patientgruppe.

1. Buhl S, Steenholdt C, Brynskov J, et al. Discontinuation of Infliximab Therapy in Patients with Crohn's Disease. *NEJM Evidence*. 2022;1(8). doi:10.1056/EVIDoa2200061
2. Kliniske Forsøg [Internet]. København: Kliniske Forsøg; c2025 [cited 2025 dec 11]. Available from: https://www.kliniskeforsoeg.dk

PROJEKTBESKRIVELSE

1. BAGGRUND

Crohns sygdom (CD, Crohn's disease) er en kronisk tarmsygdom, hvor kroppens immunforsvar skaber vedvarende betændelse i tarmen. Sygdommen kan ramme hele mave-tarm-kanalen og give symptomer som diarré, mavesmerter, vægttab og træthed. Betændelsen kan føre til arvæv, forsnævringer og bylder, og mange patienter oplever betydelig påvirkning af livskvalitet, arbejdsevne og sociale relationer. Omkring 1% har kronisk inflammatorisk tarmsygdom (IBD, inflammatory bowel disease) i Danmark, og de samlede udgifter til behandling og sygefravær er store[1,2]. I mange år bestod behandlingen af binyrebarkhormon og immundæmpende medicin, som kun delvist holdt sygdommen i ro. Med biologisk medicin som infliximab (IFX) er mulighederne forbedret markant. Mange patienter opnår således i dag ro i sygdommen med opheling af tarmen[3]. Et vigtigt spørgsmål er derfor, hvor længe denne behandling skal fortsætte. I dag behandles mange patienter livslangt, selv når sygdommen har været i ro i mange år. Denne praksis er dyr, forbundet med risiko for bivirkninger og ofte i modstrid med patienternes ønske om at stoppe medicinen, hvis det er muligt[4,5]. Vores forskningsgruppe og andre har vist, at omkring halvdelen af disse patienter får tilbagefald, hvis behandlingen stoppes – mens den anden halvdel fortsat har ro i tarmen efter 1 år[4,6,7] . I dette projekt undersøges, om personlig medicin – dvs. specifikke biomarkører (proteiner) samt lægemiddelkoncentrationen (TDM: Therapeutic drug monitoring) i blodprøver - kan identificere de patienter, der kan stoppe behandlingen med IFX med meget lav risiko for sygdomstilbagefald efter ophør.

2. FORMÅL

Formålet er at udvikle, og siden validere, personaliserede strategier for ophør af behandling med IFX hos patienter med CD i langvarig klinisk–biokemisk–endoskopisk sygdomsremission. Projektet kombinerer patientpræferencer, biomarkører og TDM i fire delstudier med følgende delmål:1) At undersøge patienternes præferencer og bekymringer i relation til ophør af behandling. 2) At definere og evaluere molekylære biomarkører som prædiktor for risiko for sygdomstilbagefald efter ophør af IFX. 3) At undersøge TDM som prædiktiv markør for sygdomstilbagefald. 4) Anvende disse resultater til at udvælge patienter med meget lav risiko for tilbagefald efter behandlingsophør, og som derfor tilbydes at ophøre IFX og følges fremadrettet.

3. METODE

3.1 Spørgeskemaundersøgelse om ophør af avanceret medicinsk behandling

3.1.1 Baggrund

Dette delstudie er et nationalt multicenter spørgeskemaundersøgelse, der inkluderer patienter med CD ≥18 år, som aktuelt modtager eller for nylig har modtaget behandling med avancerede lægemidler. Rekruttering finder sted på fem universitetshospitaler, der repræsenterer hver af de danske regioner: Aalborg, Århus, Odense, Herlev og Køge. Det forventede antal deltagere er 200 personer, svarende til omkring 40 pr. center. Der er ikke udført en formel styrkeberegning, da formålet er deskriptivt og fokuserer på at belyse patienters holdninger til ophør af behandling med IFX. En population på 200 patienter vurderes at være tilstrækkelig og repræsentativ for danske patienter med Crohns sygdom i avanceret behandling og giver et robust grundlag for de planlagte analyser.

3.1.2 Formål

Projektets formål er: 1) Undersøge patienters bekymringer i relation til langvarig behandling med avanceret betændelsesdæmpende medicin. 2) Afdække under hvilke omstændigheder patienter kunne overveje at ophøre denne behandling samt bekymringer og risikotolerance i forhold til sygdomstilbagefald. 3) Belyse hvilken type og mængde information patienter ønsker at modtage forud for behandlingsophør. 4) Undersøge patienters præferencer for opfølgning og undersøgelser efter ophør af behandling.

3.1.3 Datahåndtering og analyse

Data indsamles og håndteres i REDCap-databasen. Analyserne vil primært være deskriptive med henblik på at beskrive fordeling af patientpræferencer og eventuelle sammenhænge med demografi og kliniske karakteristika. Forskelle mellem regioner og hospitaler vil blive analyseret ved hjælp af parametriske statistiske metoder.

3.2 Individuelt tilpasset ophør af IFX baseret på molekylær profilering

3.2.1 Baggrund og formål

Tidligere studier har ikke identificeret kliniske faktorer eller biokemiske målinger, der kan forudsige, hvilke CD patienter i sygdomsremission, der kan ophøre IFX uden væsentlig risiko for tilbage-

fald. Helt nye data tyder imidlertid på, at proteinbaserede biomarkører i blodet kan forudsige sygdomsforløbet efter ophør[8–10]. Formålet er at vurdere, om disse biomarkørkandidater kan identificere patienter med lav risiko for sygdomstilbagefald efter ophør med IFX.

3.2.2 Design og statistik

Observationelt studie baseret på blodprøver indsamlet i STOP-IT studiet, hvor vi i et randomiseret klinisk forsøg undersøgte ophør af IFX hos 115 patienter med CD [4]. Der analyseres blodprøver fra alle 56 patienter, som ophørte IFX. Analyserne udføres i samarbejde med internationale anerkendte eksperter og med udgangspunkt i nylige fund i to tilsvarende patientgruppe – og vores resultater sammenlignes med disse (Nicolas Pierre, GIGA Institute, University of Liège).[7–11] Langtidsopfølgning af vores patientgruppe indgår som del af undersøgelsen (ca. 5 års opfølgningstid). Biomarkørniveauer sammenlignes mellem patienter med og uden sygdomstilbagefald ved logistisk regression og signifikante fund testes med ROC-analyse for optimale tærskelværdier. Der er ikke udført formel styrkeberegning, idet vi anvender alt tilgængeligt materiale. Størrelsen af vores materiale er sammenlignelig med de tidligere studier[8–10].

3.3 Individuelt tilpasset ophør af IFX baseret på lægemiddelkoncentration i blodet

3.3.1 Baggrund og formål

TDM omfatter måling af lægemiddelkoncentration og antistoffer i blodprøver og anvendes rutinemæssigt til optimering af biologisk behandling i CD. Formålet er at undersøge, om IFX-niveauer og antistoffer udviklet mod IFX kan forudsige hvem der kan ophøre IFX-behandling med meget lav risiko for sygdomstilbagefald hos patienter med Crohns sygdom i langvarig remission.

3.3.2 Design og statistik

Observationelt studie baseret på blodprøver fra STOP-IT studiet (se ovenfor)[4]. Der analyseres prøver taget ved inklusion (dalværdi) samt supplerende prøver taget umiddelbart efter behandling (peak-niveauer) fra alle inkluderede patienter. Analyser for IFX og antistoffer mod IFX udføres af vores samarbejdspartner med validerede teknikker (Morten Beck Trelle, Klinisk Biokemisk Afdeling, OUH Svendborg). Langtidsopfølgning indgår i studiet som beskrevet i 3.2.2. Sammenhængen mellem TDM og sygdomstilbagefald vurderes ved logistisk regression, og ROC-analyse anvendes til at bestemme optimale tærskelværdier.

3.4 Prospektiv kohorteundersøgelse af personaliseret ophør af IFX hos lavrisikopatienter

3.4.1 Baggrund og formål

Delstudie 2-3 har til formål at identificere biomarkører og TDM-markører, der kan forudsige lav risiko for sygdomstilbagefald efter ophør af behandling med IFX. På baggrund af disse resultater er formålet med delstudie 4 at undersøge, om ophør af IFX kan gennemføres sikkert og effektivt hos patienter med CD, der netop opfylder den identificerede lavrisikoprofil for biomarkører og/eller TDM.

3.4.2 Design og analyse

Prospektivt, ublindet, kohortestudie, der inkluderer 33 patienter med CD i klinisk-biokemisk-endoskopisk remission i behandling med IFX fra fem danske universitetshospitaler (Aalborg, Århus, Odense, Herlev og Køge). Patienter med den identificerede lav-risiko profil defineret ud fra delstudie 2-3 tilbydes ophør af behandlingen. Deltagerne følges tæt gennem struktureret kontrolprogram i 12 måneder efter behandlingsophør med kliniske-, biokemiske-, ultralyd- og endoskopiske vurderinger. Det primære endepunkt er andelen af patienter, der får sygdomstilbagefald 12 måneder efter ophør af behandling med IFX. Det primære endepunkt sammenlignes med højkvalitets historiske data fra 3 randomiserede kliniske forsøg (170=patienter)[12]. Sekundære endepunkter omfatter tid til recidiv, bivirkninger og patientrapporterede outcomes. Patienterne sammenlignes desuden med patienter med højrisikoprofilen og som fortsætter IFX behandling. Sammenligninger mellem patienter, der ophører med IFX-behandling og historiske kohorter / fortsat IFX-behandling udføres ved Fischer's exact test for binære udfald og Kaplan-Meier og Cox-regressionsanalyse for tidsafhængige hændelser. Antallet af forsøgsdeltagere er beregnet med formel styrkeberegning: Forventet 1-års risiko for sygdomstilbagefald med 10% blandt lavrisikopatienter defineret ud fra vores kriterier (interventionskohorten) sammenlignet med 31% i historiske populationer (kontrolkohorten)[12]. Ved en styrke på 80%, signifikansniveau på 0,05 og forventet frafald på 10% er sample size 33 patienter.

3.5 Godkendelser

Alle delstudier gennemføres i overensstemmelse med gældende dansk lovgivning. Anvendelsen af TDM-analyser af blodprøver i delstudie 3 er dækket af en eksisterende godkendelse (EudraCT 2012-002702-51; Etisk Komite: H-4-2012-099; Datatilsynet: 2007-58-0015/HEH.750.89-27). Delstudie 2 og 4 vil blive anmeldt til alle relevante myndigheder. Delstudie 1 er fuldstændigt anonymiseret og kræver ikke myndighedsgodkendelse. PhD-projektet er godkendt ved Syddansk Universitet (SDU) per 7/10-2025.

3.6 Forskningsmiljø og samarbejdspartnere

Delstudie 2-3 udføres på Odense Universitetshospital (OUH) og anvender allerede indsamlede prøver fra STOP-IT-studiet[4]. Undersøgelser af biomarkerer i delstudie 2 udføres i samarbejde med Nicolas Pierre (GIGA Institute, Liège) og TDM i delstudie 3 af Morten Beck Trelle (Klinisk Biokemisk Afdeling, OUH Svendborg). Delstudie 1+4 er danske multicenterstudier, der efter aftale finder sted på minimum fem store danske IBD-centre: Aalborg (Lone Madsen), Aarhus (Mette Julsgaard), Køge (Nynne Nybo Andersen), Herlev (Mohamed Attauabi) og Odense (ansøger).

3.7. Relevans

Crohns sygdom er en kronisk, invaliderende tarmsygdom med betydelig indvirkning på sundhedsvæsenet, livskvalitet og samfundsøkonomi. IFX har revolutioneret behandlingen, men langvarig vedligeholdelsesbehandling fastholdes ofte, selv ved langvarig og stabil sygdomsremission med helet tarm og uden betændelsesaktivitet. Dette øger risikoen for bivirkninger, sundhedsudgifter og er i modsætning til mange patienters ønsker om at undgå livslang medicinering. Ph.d.-projektet undersøger, om personlig medicin – baseret på molekylær profilering og måling af lægemiddelkoncentrationen – kan identificere patienter, der kan ophøre IFX-behandling med meget lav risiko for sygdomstilbagefald. Studiet bygger på en unik patientkohorte fra vores prisvindende STOP-IT-studie og kombinerer langsigtet klinisk opfølgning med avancerede biomarkør- og TDM-analyser. Disse fund afprøves i et prospektivt studie, hvor patienter med lavrisikoprofil ophører IFX. Hvis hypotesen bekræftes, kan resultaterne danne grundlag for en paradigmeændring i behandlingen af Crohns sygdom. Vi belyser desuden patienternes indstilling og bekymringer i forbindelse med eventuelt behandlingsophør. Individualiseret ophør af biologisk behandling vil kunne reducere risikoen for bivirkninger, øge patienternes autonomi og livskvalitet samt medføre betydelige besparelser for sundhedsvæsenet. Disse besparelser relaterer både direkte til medicinudgifter, men også til udgifter forbundet med medicinindgift, sygeplejerske- og lægeressourcer forbundet med overvågning af sygdommen og bivirkninger til behandlingen, blodprøver og andre supplerende undersøgelser (kikkertundersøgelser, scanninger). Desuden vil andelen af patienter med opblussen efter ophør af behandlingen reduceres væsentligt, hvorved afledte udgifter forbundet hermed ligeledes reduceres (f.eks. hospitalsindlæggelse, behandling med anden dyr medicin, evt. kirurgi). Samtidig vil projektet bidrage til den generelle udvikling af præcisionsmedicin i kroniske inflammatoriske sygdomme og kunne få bred overførbarhed til andre patientgrupper behandlet med avancerede lægemidler samt andre avancerede lægemidler som bruges til behandling af IBD.

3.8. REFERENCER

1. Agrawal M, Christensen HS, Bøgsted M, Colombel JF, Jess T, Allin KH. The Rising Burden of Inflammatory Bowel Disease in Denmark Over Two Decades: A Nationwide Cohort Study. *Gastroenterology*. 2022;163(6):1547-1554.e5. doi:10.1053/j.gastro.2022.07.062

2. Lo B, Vind I, Vester-Andersen MK, Bendtsen F, Burisch J. Direct and Indirect Costs of Inflammatory Bowel Disease: Ten Years of Follow-up in a Danish Population-based Inception Cohort. *J Crohns Colitis*. 2020;14(1):53-63. doi:10.1093/ecco-jcc/jjz096

3. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. *Gastroenterology*. 2021;160(5):1570-1583. doi:10.1053/j.gastro.2020.12.031

4. Buhl S, Steenholdt C, Brynskov J, et al. Discontinuation of Infliximab Therapy in Patients with Crohn's Disease. *NEJM Evidence*. 2022;1(8). doi:10.1056/EVIDoa2200061

5. Kobayashi T, Motoya S, Nakamura S, et al. Discontinuation of infliximab in patients with ulcerative colitis in remission (HAYABUSA): a multicentre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2021;6(6):429-437. doi:10.1016/S2468-1253(21)00062-5

6. Gisbert JP, Donday MG, Riestra S, et al. Withdrawal of antitumour necrosis factor in inflammatory bowel disease patients in remission: a randomised placebo-controlled clinical trial of GETECCU. *Gut*. 2025;74(3):387-396. doi:10.1136/gutjnl-2024-333385

7. Louis E, Resche-Rigon M, Laharie D, et al. Withdrawal of infliximab or concomitant immunosuppressant therapy in patients with Crohn's disease on combination therapy (SPARE): a multicentre, open-label, randomised controlled trial. *Lancet Gastroenterol Hepatol*. 2023;8(3):215-227. doi:10.1016/S2468-1253(22)00385-5

8. Pierre N, Huynh-Thu VA, Marichal T, et al. Distinct blood protein profiles associated with the risk of short-term and mid/long-term clinical relapse in patients with Crohn's disease stopping infliximab: when the remission state hides different types of residual disease activity. *Gut*. 2023;72(3):443-450. doi:10.1136/gutjnl-2022-327321

9. Pierre N, Baiwir D, Huynh-Thu VA, et al. Discovery of biomarker candidates associated with the risk of short-term and mid/long-term relapse after infliximab withdrawal in Crohn's patients: a proteomics-based study. *Gut*. 2021;70(8):1450-1457. doi:10.1136/gutjnl-2020-322100

10. Pierre N, Huynh-Thu VA, Baiwir D, et al. External validation of serum biomarkers predicting short-term and mid/long-term relapse in patients with Crohn's disease stopping infliximab. *Gut*. Published online August 12, 2024:gutjnl-2024-332648. doi:10.1136/gutjnl-2024-332648

11. Louis E, Mary J, Vernier–Massouille G, et al. Maintenance of Remission Among Patients With Crohn's Disease on Antimetabolite Therapy After Infliximab Therapy Is Stopped. *Gastroenterology*. 2012;142(1):63-70.e5. doi:10.1053/j.gastro.2011.09.034

12. Katibian DJ, Solitano V, Polk DB, et al. Withdrawal of Immunomodulators or TNF Antagonists in Patients With Inflammatory Bowel Diseases in Remission on Combination Therapy: A Systematic Review and Meta-analysis. *Clinical Gastroenterology and Hepatology*. 2024;22(1):22-33.e6. doi:10.1016/j.cgh.2023.08.039

Budget

	År 1	År 2	År 3
Løn, Ph.d.-studerende	696.468 kr.	710.397 kr.	724.605 kr.
Indskrivningsafgift	62.500 kr.	62.500 kr.	62.500 kr.
Publikationsudgifter	20.000 kr	20.000 kr	20.000 kr
Kongresrejser	15.000 kr	15.000 kr	15.000 kr
OPENRedcap	15.000 kr. (Studie 1)	15.000 kr. (studie 4)	
Forsendelse af blodprøver (Belgien + Svendborg)	13.000 kr. (Studie 2+3)	13.000 kr. (Studie 4)	
Analyse af prøver (TDM)	300 blodprøver x 325 kr. = 97500 kr. (Studie 3)	60 x 325 kr. = 19500 kr. (studie 4)*	
Analyse af blodprøver (Molekylære biomarkører)	56 blodprøver x 423 euro = 176.937 kr. (Studie 2)	66 x 423 euro = 208.519 kr. (Studie 4)*	
Biobank (blodprøver, afføringsprøver og vævsprøver)		50.000 kr. (Studie 4)	50.000 kr (Studie 4)
Ophold ved samarbejdslaboratoriet i Belgien		50.000 kr.	
Overhead/Administrationsbidrag (5%)	54.820 kr	58.195 kr	43.605 kr
Beløb	1.151.225 kr.	1.163.916	915.710 kr

*Inkluderer 33 inkluderede i studiet og 33 screeningsfailures (Dvs. inkluderede patienter, som ikke vurderes som lav-risiko for sygdomstilbagefald). Disse patienter inkluderes som sammenligningsgruppe til opfølgning.

Ansøges om ved CCF:

100.000 kr til analyser + forsendelse (Studie 3) + 5000 (5% overhead)

Har modtaget:

Munksgaard Fond: 850.000 kr

Overlægerådets forskningsfond: 50.000 kr

SDU-stipendiat (1 års løn + indskrivningsafgift)

Har søgt hos/Søges snarest

Bønnelycke fonden, Louis Hansen-Fonden, Mærsk Fonden, Region Syd PhD-pulje, OUH PhD-pulje, DFF, Fonden af 17-12-1981

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FORSKNING

2022 - 2023: Forskningsprojekt og specialeskrivning ved infektionsmedicinsk afdeling Q, OUH. Dataindsamling blev lavet sideløbende med 10. semester, mens dataanalyse og udarbejdelse af artikel forløb sig hen over 11. semester (Specialesemester). Artiklen blev publiceret i et internationalt tidsskrift i 2024, hvor jeg er delt førsteforfatter.

2025- : Siden maj 2025 har jeg været forskningsaktiv ved Forskningsenheden for Medicinsk Gastroenterologi på Odense Universitetshospital. Jeg er førsteforfatter på et projekt, som forventes indsendt som originalartikel januar 2026. Projektets abstrakt blev ved DSGH's (Dansk selskab for gastroenterologi og hepatologi) årsmøde udvalgt til oral præsentation i september 2025. Abstraktet er desuden accepteret ved ECCO (European Cronh's and Colitis Organization) som poster (februar 2026) og indsendt til DDW (Digestive Disease Week) december 2025. Jeg er medforfatter på et andet projekt, som netop er godkendt til publikation. Abstract herfra er også indsendt til ECCO november 2025 og accepteret som poster samt indsendt til DDW december 2025. Slutteligt er jeg førsteforfatter på et tredje projekt, som ligeledes er indsendt til DDW november 2025 og accepteret som oral præsentation (DOP) ved ECCO, og som forventes indsendt som originalartikel primo 2026.

Publikationsliste Mathilde J. Nissen december 2025

Originale artikler (Peer reviewed)

1. Albulena Imishti*, **Mathilde Jepsen Nissen***, Anne Øvrehus, Lykke Larsen. Ability to return to work and persistent symptoms six months after viral meningitis – a retrospective single-centre cohort study. Infect Dis (Lond). 2025 Jun;57(6):551-560. doi:10.1080/23744235.2025.2463960. PMID: 39943919.
   *Contributed equally as first authors.
2. Ørtoft F, Steenholdt C, **Nissen MJ**, Kjeldsen J, Ainsworth M. Acute severe ulcerative colitis without systemic toxicity: a retrospective cohort study suggesting refining the definition of acute severe ulcerative colitis. Inflamm Bowel Dis. Accepted for publication 8/12-2025.

Artikler under forberedelse

1. **Nissen M**, Ovesen P, Ørtoft F, Ainsworth M, Kjeldsen J, Steenholdt C. High baseline infliximab clearance when starting rescue therapy for ASUC predicts need for dose intensification to achieve treatment outcomes comparable to patients with low drug clearance. *Manuscript in preparation*, jan 2026
2. **Nissen M**, Gill P, Buhl S, Brynskov J, Christensen KR, Dorn-Rasmussen M, Thomsen OØ, Klausen TW, Dahlerup JF, Sørensen HG, Jahnsen J, Molazahi A, Pedersen N, Kjeldsen J, Almer S, Dahl EE, Vind I, Cannon AG, Marsal J, Sipponen T, Agnholt JS, Kievit HAL, Aure SL, Martinsen L, Meisner S, Hansen JM, Ainsworth M, Steenholdt C. Health-related quality of life impairment precedes manifestation of clinical relapse by seven weeks in patients with Crohn's disease discontinuing infliximab. *Manuscript in preparation*, jan 2026

Abstrakts

1. **Nissen M**, Ovesen PD, Ørtoft F, Ainsworth M, Kjeldsen J, Steenholdt C. High baseline infliximab clearance when starting rescue therapy for ASUC predicts need for dose intensification to achieve treatment outcomes comparable to patients with low drug clearance. DSGH (Dansk selskab for Gastroenterologi og Hepatologi) Annual Meeting, 2025.
2. **Nissen M**, Gill P, Buhl S, Brynskov J, Christensen KR, Dorn-Rasmussen M, Thomsen OØ, Klausen TW, Dahlerup JF, Sørensen HG, Jahnsen J, Molazahi A, Pedersen N, Kjeldsen J, Almer S, Dahl EE, Vind I, Cannon AG, Marsal J, Sipponen T, Agnholt JS, Kievit HAL, Aure SL, Martinsen L, Meisner S, Hansen JM, Ainsworth M, Steenholdt C. Health-related quality of life impairment precedes manifestation of clinical relapse by seven weeks in patients with Crohn's disease discontinuing infliximab. *Manuscript in preparation*, 2025.

Orale præsentationer

1. **Nissen M**, Ovesen PD, Ørtoft F, Ainsworth M, Kjeldsen J, Steenholdt C. High baseline infliximab clearance when starting rescue therapy for ASUC predicts need for dose intensification to achieve treatment outcomes comparable to patients with low drug clearance. DSGH (Dansk selskab for Gastroenterologi og Hepatologi) Annual Meeting, 2025.

Title: Patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Chron's disease

Decision correspondence

Decision: **Accept**
Date of decision: 2025-10-07
Decision email title: Accept application
Decision email text: PhD project proposal: SDU-2025-152 - (3281) - Patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Chron's disease
Authors: Mathilde Jepsen Nissen (Applicant), Casper Steenholdt (Supervisor), Jens Kjeldsen (Cosupervisor), Mark Andrew Ainsworth (Cosupervisor), Nicolas Pierre (Cosupervisor)
Date submitted: 2025-09-23

Dear Ms Nissen

It is a pleasure to inform you that your project proposal is accepted as basis for enrollment in the PhD programme at the Graduate School of Health Sciences, SDU. The Graduate School has also approved you as a potential PhD student.

This approval is valid for 12 months from today.
If you are not able to meet the criteria for enrollment with in the 12 months, you can apply for an extension of the project approval.
Please see our website for more information.

You and your main supervisor are asked to fill in a form concerning your enrolment and your PhD Plan. Please click here to download form:
http://www.sdu.dk/~/media/Files/Forskning/PhD/Phd_sundhedvidenskab/skemavejl/Enrolment_form.doc

Do to the regulations regarding employment contracts, The Graduate School needs the enrollment form and documentation for financing at least 6 weeks before the desired start date (For non-EU citizens please add an extra 4 weeks).

For a guide to filling in the enrolment form, please see:
https://www.sdu.dk/en/forskning/phd/phd_skoler/phdskolensundhedsvidenskab/for_future_students/application_for_enrollment

Please be aware that in order to enroll you we must receive documentation that you are fully financed. This means that you need to have signed documents stating that three years of salary, three years of tuition fees, and at least 50 % of your working/running expenses are guaranteed. This information must be submitted alongside the enrolment form to phd@health.sdu.dk with all relevant signatures.

Please note that if you intend to apply for a Faculty Scholarship this must be done before submitting the Enrolment form to the PhD School.

Please be aware that you cannot be enroled until the Graduate School has approved your PhD plan (part of your enrolment form). The plan can however change during the course of your PhD programme.

When the Graduate School has approved both your financial plan and your PhD Plan the enrollment procedure will continue.

PhD students are encouraged to make use of the Faculty of Health Sciences' biostatistical consultancy service, when relevant. For more information, please see: https://www.sdu.dk/en/forskning/ebb/vejledning

Sincerely,

Mark Ainsworth

mark.ainsworth@rsyd.dk
SDU Graduate School of Health

Reviewer 1 report:
Comments to authors
Thank you for the opportunity to evaulate the PhD project proposal entitled "Patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Crohn’s disease". This study aims to determine patient preferences and concerns in relation to stopping treatment with infliximab, determine biomarkers to predict relapse of Crohn's disease and examine the discontinuation of infliximab based on a biomarker profile. This is done in two biobank studies and a subsequent prospective cohort study.

Approval of PhD Project

Title of PhD project:

Patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Crohn's disease.

We hereby confirm that the above-mentioned PhD project, conducted by PhD-student Mathilde Jepsen Nissen, can be carried out at:

Department of Medical Gastroenterology, Odense University Hospital

Research Unit of Medical Gastroenterology, Department of Clinical Research, University of Southern Denmark

The project is approved and supported by both the Head of Department and the Head of Research.

Head of Department

Department of Medical Gastroenterology

Odense University Hospital

Benedicte Vibjerg Wilson

benedicte.vibjerg.wilson@rsyd.dk

Benedicte Vibjerg Wilson

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Dato: 2025.10.06 07:51:58 +02'00'

Head of Research

Research Unit of Medical Gastroenterology

Department of Clinical Research

University of Southern Denmark

Aleksander Krag

Aleksander.Krag@rsyd.dk

Aleksander Krag

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Dato: 2025.10.06 08:03:43 +02'00'

Region Syddanmark

patienten først OUH

SDU University of Southern Denmark

Letter of Support

I hereby endorse Mathilde Nissen's application for OUH PhD Fund. The PhD protocol has been approved University of Southern Denmark (SDU) Graduate School of Health as of 7th of October, 2025. I also confirm support of the Department of Medical Gastroenterology, Odense University Hospital (OUH) as the hosting environment for her project.

Mathilde Nissen completed her medical university degree (MD) in 2024 at the Faculty of Health Sciences, University of Southern Denmark. She then completed 'Klinisk Basis Uddannelse' (KBU) at Hvidovre Hospital and will finalize an Introduction position at Department of Medical Gastroenterology at Herlev Hospital by February, 2026. Having decided to pursue a career in medical gastroenterology, she is now planning to move to Odense on a permanent basis to pursue her clinical and research ambitions including a PhD program which will start on 1st of March, 2026, provided sufficient funding is obtained. Of note, several funding applications to support her PhD has recently been submitted and others are planned in the near future.

Mathilde Nissen has previous co-first authored an original article in another field published in an international peer-reviewed journal. Despite a brief career in IBD research, she has already orally presented her first original study on drug clearance in patients with ulcerative colitis at the yearly conference in Danish Society of Gastroenterology and Hepatology. Furthermore, she is currently finalizing this article for submission to an international peer-reviewed gastroenterology journal (to be submitted within one month), and is co-author on another IBD publication currently under revision after a positive review in Inflammatory Bowel Diseases. In addition, she is involved in an ongoing study on quality of life during infliximab discontinuation which is directly relevant to her PhD program. Hence, Mathilde Nissen has proven highly effective, dedicated and focused in her research. The planned PhD program will combine real-world insights, translational and clinical pharmacology research, and a prospective cohort study to provide an outstanding platform for her scientific development and career as a physician-scientist.

I will serve as principal supervisor. As Professor and Chief Physician at the Department of Medical Gastroenterology, OUH, and SDU, I bring 20 years of experience in IBD research, investigator-initiated randomized clinical trials, and translational gastroenterology. To date, I have co-supervised 9 PhD students, 4 postdocs, and several resident-, master, and bachelor research projects. Co-supervisors are Professors Mark Ainsworth and Jens Kjeldsen (OUH/SDU), both highly experienced clinician-scientists. In addition, PhD Nicolas Pierre (GIGA-Institute, University of Liège, BE) will serve as co-supervisor contributing with expert knowledge on biomarker analyses. Together, we provide comprehensive expertise spanning translational science, clinical pharmacology, advanced trial design, and patient-centered outcomes. The PhD will involve collaborations with international partners (Nicolas Pierre), as well as Danish clinical partners (5 IBD centers will participate in the survey study and prospective cohort study) and therapeutic drug monitoring experts (Morten Beck Trelle, Department of Clinical Biochemistry, OUH Svendborg).

15/10/2025

The PhD will be based at Department of Medical Gastroenterology, OUH, in one of Denmark's leading centers for IBD. Here, we provide dedicated trial staff and advanced data management systems, biobanking facilities, access to intestinal ultrasound, endoscopy, and state-of-the-art laboratories, and a strong track record of successful investigator-initiated multicenter trials.

The proposed PhD project on patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Crohn's disease aligns closely with the research priorities of OUH and SDU. It also fits directly within my broader research strategy as recently appointed Clinical Professor, which emphasizes:

1. Development of innovative therapies to overcome the current therapeutic ceiling in IBD (stem cell therapy, regenerative medicine).
2. Smarter, better, safer use of existing treatments, including therapeutic drug monitoring and steroid-sparing approaches.
3. Patient-centered outcomes, quality of life, and disease monitoring.

Mathilde Nissen's PhD project will strengthen my effort to establish a dedicated IBD research center at OUH, fostering multidisciplinary collaboration, translational innovation, and international leadership in IBD research.

In conclusion, I strongly endorse Mathilde Nissen's application and confirm that she will be fully supported by the host institution. I am confident that her project will make a significant contribution to advancing care for patients with IBD while the PhD training will prepare her for a distinguished career in gastroenterology and IBD research.

15/10/2025

Casper Steenholdt, Professor, Chief Physician, PhD, DMSc

Department of Medical Gastroenterology, Odense University Hospital, Denmark

Department of Clinical Research, Research Unit of Medical Gastroenterology, University of Southern Denmark, Odense, Denmark

Statement of acceptance

We hereby confirm supervision of Dr. Mathilde Jepsen Nissen's PhD project at South Denmark University (SDU) and Odense University Hospital (OUH) entitled:

Patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Crohn's disease

20/9/25

Casper Steenholdt[1,2], Professor, Chief Physican, MD, PhD, DMSc
Main supervisor

20/9/2025

Mark Ainsworth[1,2], Professor, Chief Physican, MD, PhD, DMSc
Co-supervisor

20.9.2025

Jens Kjeldsen[1,2], Professor, Chief Physican, MD, PhD
Co-supervisor

[1] Department of Medical Gastroenterology, Odense University Hospital, Denmark

[2] Research Unit of Medical Gastroenterology, Department of Clinical Research, University of Southern Denmark, Odense, Denmark

Statement of acceptance

I hereby confirm supervision of Dr. Mathilde Jepsen Nissen's PhD project at South Denmark University (SDU) and Odense University Hospital (OUH) entitled:

Patient-centered and personalized medicine approaches to discontinuing advanced therapy with infliximab in Crohn's disease

Nicolas Pierre[1], postdoc, PhD, Co-supervisor

[1]Laboratory of Translational Gastroenterology, GIGA-institute, University of Liège, Liège, Belgium

23/09/2025

Curriculum Vitae Casper Steenholdt

Date of birth	June 4, 1980	(Denmark, Danish citizen)
Education	1999	Matematisk Studentereksamen, Birkerød Gymnasium
	2007	MD, University of Copenhagen (Aut.ID 06G1H)
	2013	PhD, Faculty of Health and Medical Sciences, University of Copenhagen
	2016	DMSc, Faculty of Health and Medical Sciences, University of Copenhagen
	2025	Specialist authorization in Medical Gastroenterology and Hepatology
Positions	2007-9	Medical and surgical internship (Vestsjællands Amt)
	2009-12	PhD student, Dept. of Gastroenterology, Herlev Hospital
	2011-16	Falck Healthcare
	2012	Dept. of Dermatology, Gentofte Hospital (Introduction position)
	2013	Dept. of Internal Medicine, Gentofte Hospital (Introduction position)
	2013	Postdoc, Dept. of Gastroenterology, Herlev Hospital
	2014	Dept. of Gastroenterology, Herlev Hospital (Introduction position)
	2014-25	Resident in Internal Medicine: Gastroenterology & Hepatology (Glostrup Hospital, Rigshospitalet, Herlev Hospital). - 1/4/2015-30/6/2015: Leave (postdoc) - 14/10/2016 – 1/9/2019: Leave (personal matters) - 25/5/2023-7/6/2023 and 13/3/2024-17/5/2024: Leave (maternity) - 1/9/2019-31/5/2024: 20% research time - 1/6/2024-28/2/2025: 40% research time
	2022-	Associate professor, Dept. of Clinical Medicine, University of Copenhagen: evaluation of foreign physicians applying for Danish medical authorization
	2023	External substitute, Medical Gastroenterology, Holbæk Hospital
	2024-5	Assistant prof., Dept. of Medical Gastroenterology, Odense University Hospital
	2024-5	Postdoc at reNEW stem cell center, University of Copenhagen
	1/5/2025-	Professor in Medical Gastroenterology and Chief Physician, Dept. of Medical Gastroenterology, Odense University Hospital (OUH)
Research	ORCID	0000-0003-3898-4212
	H index	27 (October 9, 2025) (Web of Science)
	Citations	2,757 total (average per publication 19)
	Publications	90 peer-reviewed publications - First author: 35 - Last author: 14 - Original articles: 56 - Review articles: 13 - Case reports: 9 - Comments/letters: 11 - Book chapters: 1
	Supervisor	Postdoc: 4 (2 ongoing) PhD co-supervisor: 9 (4 ongoing) Pre-PhD research: 7 (5 ongoing) Resident research training program: 6 (2 ongoing) Master thesis: 9 (2 ongoing) Bachelor thesis: 2 (0 ongoing)
	RCT/GCP	Experience from own investigator initiated RCT: - Steenholdt C et al. Gut 2014;63:919-927. - Steenholdt C et al. Clin Gastroenterol Hepatol. 2022;20:559-568.e5. - Buhl S et al. NEJM Evidence 2022;1:EVIDoa2200061. - Frimor C et al. BMJ Open Gastroenterol. In press. August, 2025. Course: GCP and investigator initiated clinical trials (ECTS 2 points) (2011) Course: GCP online course via GCP units in Denmark (2023)
	Awards	Best oral presentation, Herlev Hospital Research Conference (2009) Abstract award, ECCO (European Crohn's and Colitis Organisation) (2013) Poster of Distinction, Digestive Disease Week (2014) Poster of Distinction, Digestive Disease Week (2015) Poster of Distinction, Danish Society of Gastroenterology (2016) Best oral presentation, IBD Nordic Conference (2019) Oral presentation selected for 'Best of Digestive Disease Week' (2019) RCT selected 'Best clinical trial in Denmark' (www.kliniskeforsoeg.dk) (2022)

		Oral presentation selected for 'Best of ECCO' (2024)
		Oral presentation abstract award, PAGE conference (2025)
		Lewis Sheiner Student Award (Zrinka Duvnjak), PAGE 2025
	Peer reviewer	Peer reviewer >30 scientific articles submitted to international journals
		Abstracts for Herlev Hospital's Research Conference (2012)
		Programme De Recherche Translationnelle En Sante (FR) (2013)
		Abstracts ECCO conference (2013-23)
		Leading opponent PhD thesis (Silje Thorsvik, Trondheim University) (2019)
Dissemination		Invited speaker at conferences and society meetings.
		Teaching: university, postgraduate, resident courses (including course director).
		Target audiences: doctors, nurses, students, patient societies and patients etc.
		Complete list available upon request.
Admin.	2006	11th semester at Vanderbilt University, Nashville, TN, USA
	2009-11	Chairman for Society of Young Researchers, Herlev Hospital
	2010-11	Member of the Research Council, Herlev University
	2012	Representing Young Physicians in Patient Quality Council, Gentofte Hospital
	2012	Responsible for electronic patient files, Dept. of Dermatology, Gentofte Hosp.
	2013-4	Mentor for young physicians organized via Danish Medical Association
	2014-5	'Uddannelsesassisterende YL', Dept. of Internal Medicine, Glostrup Hospital
	2015	Ad-hoc member of 'Rådet for Anvendelse af Dyr Sygehusmedicin' (RADS)
	2016	Work schedule planner, Dept. of Medical Gastroenterology, Rigshospitalet
	2019-	Clinical supervisor (6 introduction positions)
	2020	Employment group (hiring 2 doctors), Dept. of Gastroenterology, Herlev Hosp.
	2020-5	'Uddannelseskoordinerende Yngre Læge', Dept. of Gastroenterology, Herlev
	2020-5	Responsible for transition of children to adult GI care, Herlev Hospital
	2021	Introduction to University Pedagogy. University of Copenhagen. ECTS 3
	2021-2	Danish group for advancing therapeutic drug monitoring in IBD
	2023-5	Clinical Tutor for medical students, Dept. of Gastroenterology, Herlev Hospital
	2023-5	DSGH guideline on use of conventional immunosuppression in IBD
	2024	Local guideline on CMV colitis, Dept. of Gastroenterology, Herlev Hospital
	2025	Local guideline on TDM in IBD, Dept of Medical Gastroenterology, OUH
	2025-	Scientific board member, Danish Society of Gastroenterology and Hepatology

Selected 10 publications

1. Steenholdt C et al. Clinical implications of variations in anti-infliximab antibody levels in patients with inflammatory bowel disease. Inflamm Bowel Dis 2012;18:2209-2217.
2. Frederiksen MT, Ainsworth MA, Brynskov J, Thomsen OØ, Bendtzen K, Steenholdt C. Antibodies against infliximab (IFX) are associated with de novo development of antibodies to adalimumab (ADL) and therapeutic failure in IFX-to-ADL switchers with inflammatory bowel disease. Inflamm Bowel Dis 2014;20:1714-1721.
3. Steenholdt C et al. Individualized therapy is more cost-effective than dose intensification in Crohn's disease patients who fail anti-TNF treatment: a randomized, controlled trial. Gut 2014;63:919-927.
4. Grišić AM, Dorn-Rasmussen M, Brynskov J, Ilvemark JFKF, Bolstad N, Warren DJ, Ainsworth MA, Huisinga W, Ben-Horin S, Kloft C, Steenholdt C. Infliximab clearance decreases in 2nd and 3rd trimesters of pregnancy in inflammatory bowel disease. United European Gastroenterol J. 2021;9:91-101.
5. Steenholdt C et al. Patient Satisfaction of Propofol versus Midazolam and Fentanyl Sedation during Colonoscopy in Inflammatory Bowel Disease. Clin Gastroenterol Hepatol. 2022;20:559-568.e5.
6. Buhl S, Steenholdt C, Brynskov J et al. Discontinuation of Infliximab Therapy in Patients with Crohn's Disease. NEJM Evidence 2022;1:EVIDoa2200061.
7. Steenholdt C et al. Tofacitinib for acute severe ulcerative colitis: a systematic review. J Crohns Colitis. 2023;17:1354-1363.
8. Post F, Hausmann A, Kabatnik S, Steigerwald S, Brand A, Clement DL, Skov J, Lõhmussaar K, Larsen HL, Maimets M, Boye TL, Jez G, Sato T, Steenholdt C, Rosenberger F, Mund A, Nielsen AH, Jensen KB, Mann M. Deep Visual Proteomics advances human colon organoid models by revealing a switch to an in vivo-like phenotype upon xenotransplantation. Cell Syst. 2025;16:101396.
9. Hammerhøj A, Boye TL, Yao J, Hausmann A, Kellermann L, Maciag GJ, Sandelin A, Steenholdt C, Jensen KB, Nielsen OH. Inflamed intestinal epithelial cells from patients with ulcerative colitis restore a noninflamed transcriptional profile upon in vitro expansion. Lab Invest. 2025;105:104172.
10. Larson C, Berinstein JA, Tedesco N, Seidelin JB, Ovesen PD, Uzzan M, Amiot A, Nuzzo A, Laharie D, Constant BD, Albenberg L, El-Hussuna A, Bishu S, Cohen-Mekelburg S, Higgins PDR, Steenholdt C. Postoperative Outcomes in Tofacitinib-Treated Patients With Acute Severe Ulcerative Colitis Undergoing Colectomy. Clin Gastroenterol Hepatol. 2025 Apr 14. Epub ahead of print.

Curriculum vitae for Jens Kjeldsen

Personal data and current position

Born April 22, 1962. Danish citizenship. Married, two children.
Lead Consultant, professor, Dept. of Medical Gastroenterology, Odense University Hospital.
Autorization ID: 00fn8

Education and academic degrees

1988	MD, Odense University, DK-5230 Odense M Denmark
1988	Authorization as a Physician and in 1994 Permission to Practice Indepently as a Physician
1996	Degree of PhD in Health Science, Medical Gastroenterology. "Biochemical parameters of disease activity in inflammatory bowel disease. Control and assessment of glucocorticoid therapy".
2000	Medical specialist in Medical Gastroenterology.
2002	Medical specialist in General Internal Medicine.

Professional Employments

From 1988 to 2001	Registrar, senior registrar, Depts of internal medicine, gastroenterology, orthopedics
01.12.01-31.01.02	Senior Registrar, Dept. of Medicine, Vejle sygehus.
01.02.02-31.03.03	Staff Specialist, Dept. of Medical Gastroenterology S, Odense University Hospital.
01.04.03-31.03.04	Staff Specialist, Dept. of Medicine V, Århus Kommunehospital.
01.04.04-31.8.05	Staff Specialist, Dept. of Medical Gastroenterology, S, Odense University Hospital.
01.09.05 – 31.05.22	Consultant, Dept. of Medical Gastroenterology S, Odense University Hospital
01.01.15 - ongoing	Professor, Dept. of Medical Gastroenterology S, Odense University Hospital
01.06.22 - ongoing	Lead Consultant, Dept. of Medical Gastroenterology S, Odense University Hospital

Memberships and administrative duties

- External examiner of 8 PhD at Universities in Denmark
- Co-Head, Graduate programme for Clinical Research at Faculty of Health Sciences, University of Southern Denmark (2012-2016).
- Reviewer for Ugeskrift for Læger, Scandinavian Journal of Gastroenterology, Italian Journal of Gastroenterology, Pathophysiology of Haemostasis and Thrombosis, Lancet, Clinical Journal of Gastroenterology and Hepatology. Reviewer for Broad Medical Research Program IBD Grants
- Chairman Danish Medicines Council, therapy area: biological treatment of chronic IBD.
- Chairman for BioIBD, national quality database for biological treatment of IBD. 2016-2019.

Major funding (projects and funding)

- *Best nutritional care in cancer patients. A comparative randomized study of supplemental parenteral nutrition to patients with GI cancer compared to best supportive nutritional care*. External funding around 4 mio DKR.
- *Effect of Remote Ischemic Conditioning (RIC) on inflammation and remodelling of extracellular matrix proteins in patients with inflammatory bowel diseases.* Funding around 2.5 mio DKR
- *Nordtreat project:* 2.1 mio DKR (in total 30 mio DKR for centers in Sweden, Norway, Iceland, Denmark).
- *Does Disease Activity after induction Treatment with Anti–Tumor Necrosis Factor, Predict Short-Term Outcomes in Crohn's Disease and Ulcerative Colitis?* 495.000 DKR from Janssen
- *COVID-19 infection, patients with autoimmune and chronic inflammatory diseases in medical treatments and clinical outcomes*," Pfizer DKK 578.000 DKR
- *COVID-19 infection, patients with autoimmune and chronic inflammatory diseases in medical treatment and clinical outomes, part II*", Pfizer 600.000 DKR.
- *Nationwide Danish cohort studies: Identification of populations at high risk for long-term. severe COVID-19 with a focus on the elderly, middle-aged, and those with comorbidity.* Pfizer 196.550 USD.
- *Consequences of biological therapy and disease activity in patients with chronic inflammatory bowel disease.* Janssen 932.000 DKR.

Previous experience with clinical trials:

Extensive experience with clinical trials currently and in the past. <u>At present, february 2025:</u> (1) primary investigator on investigator initiated clinical trial in treatment of IBD patients (the Nordtreat trial); (2) primary investigator on one phase II trial in the treatment of fibrostenosing Crohns disease; (3) primary investigator on three study sponsored by TAKEDA – on Crohns disease and ulcerative colitis, including an extension trial; (4) primary investigator on a

study sponsored by Abbvie for treatment of Crohns disease; (5) subinvestigator on ongoing study sponsored by MSD for the treatment of Crohns disease.

Past experience:
Primary investigator and subinvestigator on approximately 20 sponsor initiated clinical trials.

GCP-training
Has participated regularly in GCP-training - last training 17.10.24 – course developed by the GCP-unit in Denmark.

Teaching, university, and supervision of phd-students

- Main supervisor and supervisor for 17 previous and ongoing Ph.D.-projects.
- Supervisor for 20 medical candidate research projects at the Faculty of Health Science and 1 bachelor project at Biomedicine.
- Since 2003 employed as clinical lecturer (associate professor) at Institute of Clinical Research, University of Southern Denmark teaching in the following modules: (1) K5 Diseases of the gastrointestinal tract, (2) K14 Clinical Courses (gastrointestinal diseases). Responsible for the annual teaching in gastrointestinal diseases in module 3B Clinical Pharmacology and Therapy B.
- From 2017 responsible for the module K3 “The digestive tract, nutrition, and metabolism”.

Summary of publications:
Publication: 165. H-index: 43 Citations:4677. Orchid: https://orcid.org/0000-0001-8148-6572

Dynamics of inflammation-associated plasma proteins following faecal microbiota transplantation in patients with psoriatic arthritis and healthy controls: exploratory findings from the FLORA trial. Kragsnaes MS, Jensen JRB, Nilsson AC, Malik MI, Munk HL, Pedersen JK, Horn HC, Kruhøffer M, Kristiansen K, Mullish BH, Marchesi JR, Kjeldsen J, Röttger R, Ellingsen T. RMD Open. 2024 Jan 30;10(1):e003750.

Kousgaard, SJ, Cold, F, Halkjær, SI, Petersen, AM, Kjeldsen, J, Møller Hansen, J, Dall, SM, Albertsen, M, Nielsen, HL, Kirk, KF, Duch, K, Sønderkær, M & Thorlacius-Ussing, O 2024, 'The effect of non-pooled multi-donor faecal microbiota transplantation for inducing clinical remission in patients with chronic pouchitis: Results from a multicentre randomised double-blinded placebo-controlled trial (MicroPouch)', Journal of Crohn's and Colitis, vol. 18, no. 11, pp. 1753–1766

Jochumsen, EA, Kragsnaes, MS, Nilsson, AC, Rasmussen, KF, Ellingsen, T, Juul, MA, Kjeldsen, J & Holm, DK 2024, ‘‘Does this fecal microbiota transplant work?’ Quality assurance of capsule based fecal microbiota transplant production', Scandinavian Journal of Gastroenterology, vol. 59, no. 11, pp. 1234-1239.

Small Intestinal Permeability and Metabolomic Profiles in Feces and Plasma Associate With Clinical Response in Patients With Active Psoriatic Arthritis Participating in a Fecal Microbiota Transplantation Trial: Exploratory Findings From the FLORA Trial. Kragsnaes MS, Miguens Blanco J, Mullish BH, Serrano-Contreras JI, Kjeldsen J, Horn HC, Pedersen JK, Munk HL, Nilsson AC, Salam A, Lewis MR, Chekmeneva E, Kristiansen K, Marchesi JR, Ellingsen T. ACR Open Rheumatol. 2023 Nov;5(11):583-593.

Inflammatory Bowel Disease in Adults and Elderly: The Use of Selected Non-IBD Medication Examined in a Nationwide Cohort Study. Lund K, Zegers FD, Nielsen J, Brodersen JB, Knudsen T, Kjeldsen J, Larsen MD, Nørgård BM. Inflamm Bowel Dis. 2023 Oct 24:izad244. doi: 10.1093/ibd/izad244. Online ahead of print.

A population-based nationwide study on total colectomy for ulcerative colitis and risk of ten prevalent inflammatory or autoimmune diseases. Mark-Christensen A, Jølving LR, Anru PL, Murray JA, Nielsen RG, Qvist N, Laurberg S, Engberg H, Kjeldsen J, Nørgård BM. Scand J Gastroenterol. 2023 Jul-Dec;58(12):1398-1404. doi: 10.1080/00365521.2023.2231586. Epub 2023 Jul 6.

Diagnostic accuracy of pan-enteric capsule endoscopy and magnetic resonance enterocolonography in suspected Crohn's disease. Brodersen, J. B., Knudsen, T., Kjeldsen, J., Juel, M. A., Rafaelsen, S. R. & Jensen, M. D., 7. sep. 2022, (E-pub ahead of print) I: United European Gastroenterology Journal.

Kragsnaes, MS, Kjeldsen, J, Horn, HC, Munk, HL, Pedersen, JK, Just, SA, Ahlquist, P, Pedersen, FM, de Wit, M, Möller, S, Andersen, V, Kristiansen, K, Kinggaard Holm, D, Holt, HM, Christensen, R & Ellingsen, T 2021, 'Safety and efficacy of faecal microbiota transplantation for active peripheral psoriatic arthritis: an exploratory randomised placebo-controlled trial', Annals of the Rheumatic Diseases, vol. 80, no. 9, pp. 1158-1167.

Short

Curriculum Vitae

Mark Andrew Ainsworth

Personal information:

Name: Mark Andrew Ainsworth

Age: 63

Address: Kongensgade 69B, 5000 Odense C

Education and training

2007 Board certified specialist in medical gastroenterology and hepatology (Denmark)

2001 Board certified specialist internal medicine (Denmark)

1986 Medical doctor (cand. med.) Copenhagen University (Denmark)

Scientific degrees

2000 dr.med. (DMSc) University of Southern Denmark, Medical faculty.

1992 Ph.D. Odense University (now University of Southern Denmark), Medical Faculty.

Professional Experience

More than 20 years of clinical experience, 5 years full time research experience and more than 5 years regulatory experience (for most recent appointments, please see below)

Mar 2024-Present	Head of Graduate School at the faculty of Health at University of Southern Denmark
Jun 2021- Present	Professor, Odense University Hospital and University of Southern Denmark
Feb 2018- Present	Chief physician, Odense University Hospital (Denmark)
Feb 2018- May 2020	Chief Medical Officer, Danish Medicines Agency, Denmark
Jul 2014-Jan 2018	Head of Department, Associate professor, Copenhagen University Hospital at Herlev (Denmark)
Jan 2010-Jan 2018	Associate Clinical Professor, University of Copenhagen, Denmark

Publications:

Please see https://www.webofscience.com/wos/author/record/2375812

Web of Science ResearcherID CAA-2707-2022

https://orcid.org/0000-0002-4899-1048

Profile summary:

151 Total documents

136 Web of Science Core Collection publications

2 Dissertations or Theses

64 Verified peer reviews

Web of Science Core Collection metrics

H-Index 29

Sum of Times Cited 3,533

Chairman at several international scientific conferences in gastroenterology and regulatory science.

Invited speaker at several international and national conferences covering gastroenterological and regulatory issues.

Pre- and postgraduate supervision/mentor functions:

Supervisor for students writing bachelor thesis, master's thesis. Supervisor for PhD students.

Mentor for research fellows completing dr.med. thesis. Clinical supervisor for physicians completing post-graduate basic clinical training ("KBU"), introduction to specialty ("introduktionsstilling" and specialist training ("hoveduddannelse")

Research management and administrative experience

Supervision and organizing research projects carried out by master and PhD students. Head of research for large Danish multicentre study involving a large fraction of all the specialized gastroenterological centres I Denmark.

Head of research for large Nordic multicentre study involving specialised gastroenterological centres I Denmark, Norway, Sweden and Finland.

Administrative experience related to areas other than research included: 3 years as Head of section in the Danish Medicines Agency in charge of 24 employees, primarily academic. 2 years as Head of Section in Medical Section, Gastroenheden, Copenhagen University Hospital at Herlev in charge of 20 physicians. 4 years as Head of Department, Gastroenheden, Copenhagen University Hospital at Herlev in charge of more than 70 physicians.

As Head of Graduate School at the faculty of Health at University of Southern Denmark since overseen the evaluation of Ph.D. projects, enrolment of Ph.D. students, planning of Ph.D. courses, establishment of Ph.D. assessment committees, evaluation of Ph.D. theses and all administrative work related to Ph.D. students. There are currently more than 600 students enrolled at The Graduate School at the faculty of Health at University of Southern Denmark.

Clinical Research experience

Planned, organised, supervised and published two large scale, national/international investigator initiated randomised, controlled GCP compliant drug studies in the field of biologic treatment of patients with inflammatory bowel disease (principal investigator).

Participated in 4 commercial GCP compliant drug studies as sub-investigator

Nicolas Pierre
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@ResearchGate: https://www.researchgate.net/profile/Nicolas_Pierre2

EDUCATION

2014-PhD. Faculty of Motor Sciences/Institute of Neurosciences, Université catholique de Louvain (UCL), Belgium
2014-University certificate of formation in Molecular Genetics (the greatest distinction) UCL, Belgium
2012-Master in motors skills: general (the greatest distinction). Faculty of Motor Sciences, UCL, Belgium
2008-Master in physiotherapy (distinction). Faculty of Motor Sciences, UCL, Belgium

RESEARCH EXPERIENCE

2024-2025: Scientific collaborator fellowship from the Fonds de la Recherche Scientifique (FNRS), laboratory of Translational Gastroenterology (GIGA institute, University of Liege, Belgium)
2016-2024: post-doc in the laboratory of Translational Gastroenterology (GIGA institute, University of Liege, Belgium).
2015-2016: post-doc in the Movement, Sport and health Sciences laboratory (M2S) (University of Rennes, France).
2008-2014: Assistant at the Faculty of Motor Sciences (UCL, Belgium).

RECOGNITION

Reviewer for: Journal of Crohns and Colitis, Crohn's & Colitis 360, Inflammatory Bowel Diseases, Journal of Clinical Medicine Theurapeutics advances in Gastroenterology, Journal of Molecular Medicine, Gastroenterology Report, BMC gastroenterology, Frontiers in Medicine, Proteomics, Journal of Proteome Research, and the European Crohn's and Colitis Organisation (ECCO) grant program.

Editorial board: Journal of Crohns and Colitis

Prize of the best investigator-initiated study (ECCO congress 2021 and 2023)

ECCO grant 2023 (80 000€)

Selection for oral presentation: ECCO congress (2021 and 2023), Belgian Week of Gastroenterology (2021, 2023, 2024), conference of the Belgian Proteomics Association (2022).

MAIN PUBLICATIONS

1-Pierre, N., Huynh-Thu, V. A., Baiwir, D., Mazzucchelli, G., Fleron, M., Trzpiot, L., Eppe, G., De Pauw, E., Laharie, D., Satsangi, J., Bossuyt, P., Vuitton, L., Vieujean, S., Colombel, J.-F., Meuwis, M.-A., Louis, E., & GETAID and the SPARE-Biocycle research group. (2024). External validation of serum biomarkers predicting short-term and mid/long-term relapse in patients with Crohn's disease stopping infliximab. Gut.

2-Pierre, N., Huynh-Thu, V. A., Baiwir, D., VIEUJEAN, S., Bequet, E., Reenaers, C., Van Kemseke, C., Salée, C., Massot, C., Fleron, M., Mazzucchelli, G., Trzpiot, L., Eppe, G., De Pauw, E., Louis, E., & Meuwis, M.-A. (2024). Serum proteome signatures associated with ileal and colonic ulcers in Crohn's disease. Journal of Proteomics.

3-Pierre, N., Vieujean, S., Peyrin-Biroulet, L., Meuwis, M.-A., & Louis, E. (2023). Defining biological remission in Crohn's disease: interest, challenges and future directions. Journal of Crohn's and Colitis.

4-Pierre, N., Huynh-Thu, V. A., Marichal, T., Allez, M., Bouhnik, Y., Laharie, D., Bourreille, A., Colombel, J.-F., Meuwis, M.-A., Louis, E., & GETAID (Groupe d'Etude Thérapeutique des Affections Inflammatoires du tube Digestif). (2022). Distinct blood protein profiles associated with the risk of short-term and mid/long-term clinical relapse in patients with Crohn's disease stopping infliximab: when the remission state hides different types of residual disease activity. Gut

5-Pierre, N., Baiwir, D., Huynh-Thu, V. A., Mazzucchelli, G., Smargiasso, N., De Pauw, E., Bouhnik, Y., Laharie, D., Colombel, J.-F., Meuwis, M.-A., & Louis, E. (2021). Discovery of biomarker candidates associated with the risk of short-term and mid/long-term relapse after infliximab withdrawal in Crohn's patients: a proteomics based study. Gut.

6-Pierre, N., Salée, C., Vieujean, S., Bequet, E., Merli, A.-M., Siegmund, B., Meuwis, M.-A., & Louis, E. (2021). Review article: distinctions between ileal and colonic Crohn's disease: from physiology to pathology. Alimentary Pharmacology and Therapeutics.

7-Pierre, N., Salée, C., MASSOT, C., BLETARD, N., Mazzucchelli, G., Smargiasso, N., Morsa, D., Baiwir, D., DePauw, E., REENAERS, C., VAN KEMSEKE, C., LOLY, J.-P., Delvenne, P., Meuwis, M.-A., & Louis, E. (2019). Proteomics highlights common and distinct pathophysiological processes associated with ileal and colonic ulcers in Crohn's disease. Journal of Crohn's and Colitis.

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Subjet: Invitation

My collaborators and myself will be pleased to welcome Mathilde Jepsen Nissen at the GIGA proteomic platform (University of Liège, Belgium) during its PhD. The aim of the visit will be to gain hands-on insight into the laboratory methods (mass spectrometry-based proteomics), strengthen collaboration, and facilitate joint interpretation of data.

Best regards.

Nicolas Pierre