



Kirurgisk behandling af komplekse perianale Crohn fistler

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Andreas Nordholm-Carstensen, ovl., ph.d., klin. lektor
Abdominalcenter K og K-forskning, BBH

DSAK - perianale Crohn fistler





Disclosures

- Grant/research support: No disclosure
- Speaker's bureau: No disclosure
- Consultant: Takeda Pharma A/S, Sacomed A/S, BK Medical Aps
- Major shareholder: None
- Other: No disclosure



Epidemiologi

- Perianal involvering hos 3,8% - 80% af patienter med Crohn's sygdom (CD) (afh. af definition)
- 10% af patienter med CD vil debutere med en perianal fistel, og CD diagnosen stilles siden indenfor 1 år (ca. 2/3), 1-5 år (ca. 1/3), efter 5 år (meget få procent)
- ~5% udelukkende perianal CD
- Forekomst stiger desto mere analt i mavetarmkanalen CD er lokaliseret:
 - Perianale fistler:
 - 12% ved ileal CD
 - 15% ileokolisk CD
 - 41% kolon CD (uden rektal involvering)
 - 92% rektal CD

Sangwan YP et al. *Dis Colon Rectum.* 1996
Lockhart-Mummery HE. *Dis Colon Rectum.* 1975
Singh B et al. *Br J Surg.* 2004
Alabaz O., *Fundamentals of Anorectal Surgery.* 2nd ed. Philadelphia, PA: WB Saunders; 1999. Anorectal Crohn's disease
Hellers G et al. *Gut.* 1980



Kompleks perianal Crohn - definition

- Simple
 - Intersphincteric
 - Low transsphincteric
- Complex
 - High transsphincteric
 - Suprasphincteric
 - Anterior transsphincteric in women
 - Horse-shoe fistula, blind tracks
 - Crohn's

Classification of perianal fistulas

American Gastroenterological Association

Simple	Complex
<ul style="list-style-type: none">• Low originsuperficial, low transphincteric• Single external orifice• No pain or fluctuationsuggesting perianal abscess• No rectovaginal fistula oranorectal stenosis	<ul style="list-style-type: none">• High origin• Multiple external orifices• Pain or fluctuationsuggesting perianal abscess• +/- recto-vaginal fistulas,stenosis, active rectal disease

AGA technical review on perianal Crohn's disease. Gastroenterology 2003;125:1508–1530.



Kompleks perianal Crohn - afgrænsning

- Anatomisk udbredelse?
- Tilgængelighed for kirurgi?
- Respons på medicinsk terapi?
- Komorbiditet?
- Livskvalitet?
- Andet?

Internationale data:

- 78% af pt. med kompleks pCD udvikler kompleks fistel
- 1/3 med kompleks pCD opnår vedvarende remission
- Gns > 2,5 år for at opnå heling
- >80% af fistler recidiverer ved ophørt terapi
- Hyppigere stomi (64% vs. 27%) og extirpation (25% vs. 7%) end ved simpel pCF

Bell SJ, et al. Aliment Pharmacol Ther 2003;17:1145-1151
Molendijk et al. Inflamm Bowel Dis 2014;20:2022-2028



Perianal CD

- Skin tags
- Lymfødem
- Fissurer
- Ragader
- Analstenose
- Abscesser og fistler



Komorbiditet

- HS
- Pilonidalcystesygdom
- Crohn betingede hudforandr.
- Inkontinens



Perianal Crohn – sygdomsforløb (DK tal)

- CD patienter i DK 1997-2005: 9739 patienter
- 1812 (19%) med perianal CD (pCD), hyppigst fistelsygdom
- Incidens af pCD uændret over tid
- Risiko for større abdominalkirurgi associeret med pCD (HR 1.51; 95%CI: 1.40-1.64)
- 84% af patienter med pCD krævede operation (mediant 2 procedurer)

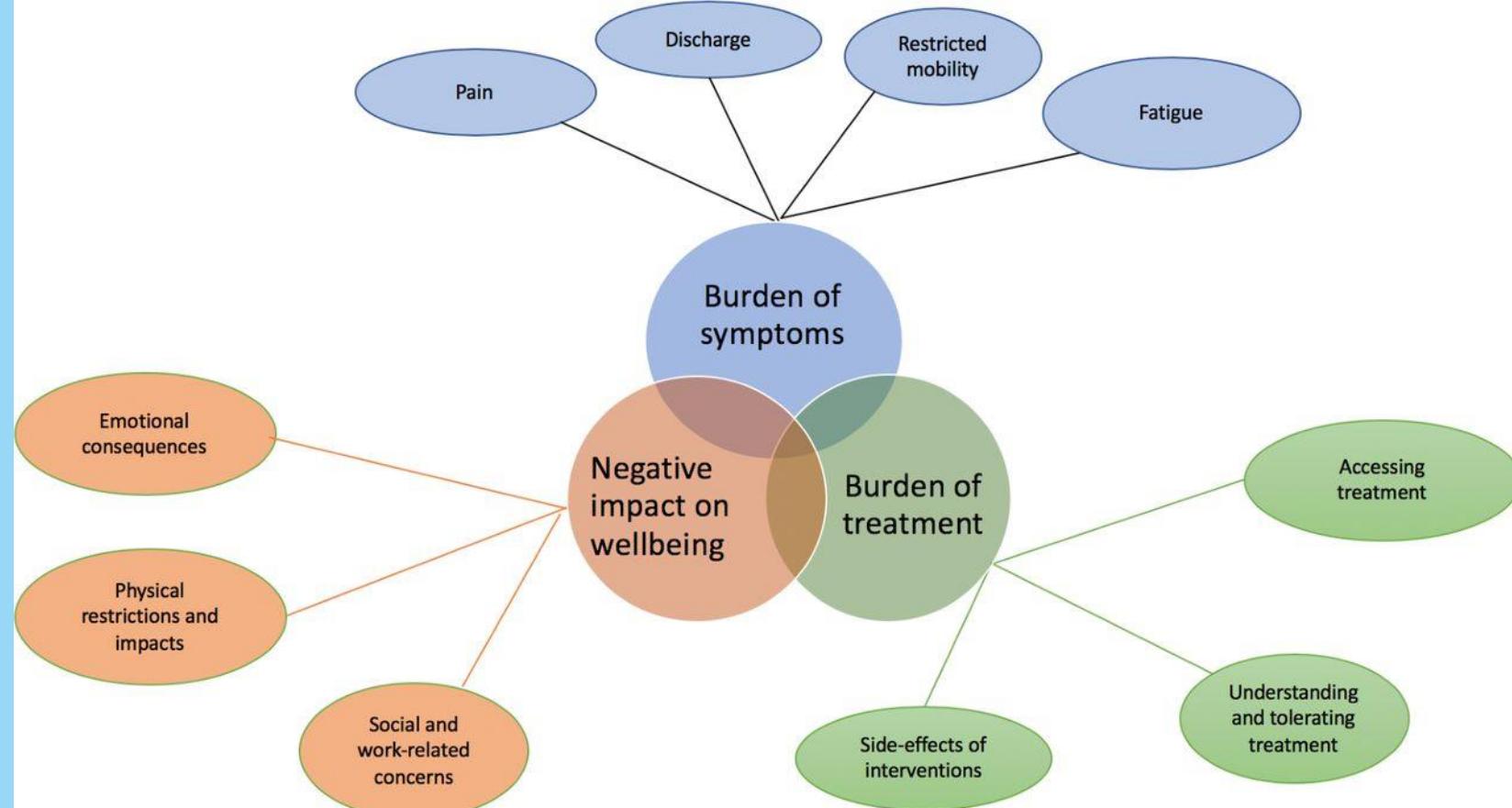


Behandlingsmål ved komplekse perianale Crohn fistler

- Kort sigt
 - Abscesdrænage (behandling eller forebyggelse af sepsis, klargøring til medicinsk behandling)
 - Symptomlindring
- Lang sigt
 - Nedbringe fistelsekretion
 - Øge livskvalitet
 - Bevare kontinensfunktion
 - Fistelheling
 - Undgå stomi
 - Undgå proktktomi
 - **Forhindre recidiv**



Kompleks perianal Crohn



Adegbola SO, et al. Gut 2021;70:1649–1656.

Livskvalitet

- Fistelsymptomer
- Beh. gener
- Livskvalitet
- Korrelerer til
 - HADS
 - IBD-Q score

Crohn's Anal Fistula Quality of Life Scale (CAFQoL)
 Please consider how your anal fistula has affected your life over the last **6-8 weeks**.
 If you are unsure how to answer any question, please just give the best answer you can. Do not spend too much time thinking about your answer as your first thoughts are likely to be most accurate.

Domain A		Never Occasionally One/twice a week Daily Several times a day					
<i>This section is about symptoms from your fistula</i>							
PLEASE CIRCLE ONE NUMBER FOR EACH QUESTION THAT COMES CLOSEST TO REFLECTING YOUR OPINION. IF YOU HAVE MORE THAN ONE FISTULA, TELL US ABOUT YOUR WORST CURRENT FISTULA							
1	Do you get sharp, intense pain around the anus because of your fistula(s)?	0	1	2	3	4	
2	Do you get a dull / background discomfort around the anus because of your fistula(s)?	0	1	2	3	4	
3	Do you get any type of discharge from your fistula(s)?	0	1	2	3	4	
4	Do you get sore skin around your fistula(s) because of discharge?	0	1	2	3	4	
5	Is sitting, standing or walking restricted by your fistula(s)?	0	1	2	3	4	

Domain B		Strongly Disagree Disagree Unsure Agree Strongly Agree					
<i>This section is about the effects of your current fistula treatment (medication, operations, seton)</i>							
PLEASE CIRCLE ONE NUMBER FOR EACH QUESTION THAT COMES CLOSEST TO REFLECTING YOUR OPINION							
6	I am bothered by the side effects from the medication I take for my fistula	0	1	2	3	4	no meds
7	I am bothered by the side effects of surgery I had for my fistula (e.g. scarring, appearance, wound problems)	0	1	2	3	4	no surgery
8	My seton (stitch/string/loop) causes me pain/discomfort/irritation	0	1	2	3	4	no seton
9	Anything else about your symptoms or the effects of your current treatment you want to say:						

		Domain C: This section is about how your fistula impacts upon your quality of life over the last 6-8 weeks . PLEASE CIRCLE ONE NUMBER FOR EACH QUESTION THAT COMES CLOSEST TO REFLECTING YOUR OPINION					Strongly Disagree Disagree Unsure Agree Strongly agree
10	My sleep is disturbed because of my fistula	0	1	2	3	4	
11	I avoid getting physically close to another person (hugging, sitting next to each other etc.) because of my fistula	0	1	2	3	4	
12	My sexual activity is (or would be) restricted because of my fistula	0	1	2	3	4	
13	My socialising (meeting friends-going to parties, other social events) is restricted because of my fistula	0	1	2	3	4	
14	My exercise / activities (e.g. swimming, cycling, running) that I would like to do are restricted because of my fistula	0	1	2	3	4	
15	My travelling (driving, taking the train/plane etc.) is restricted because of my fistula	0	1	2	3	4	
16	Having a fistula causes me embarrassment / shame	0	1	2	3	4	
17	I am concerned that others may find out that I have a fistula	0	1	2	3	4	
18	My ability to work or study is restricted because of my fistula	0	1	2	3	4	
19	I have lost out financially because of my fistula	0	1	2	3	4	
20	Because of my fistula, I worry about finding or needing the toilet ('toilet mapping') when I am away from home	0	1	2	3	4	
21	Because of my fistula, I only go to places where I know there's a clean toilet and washing facilities	0	1	2	3	4	
22	Because of my fistula, I have to take spare underwear and wipes with me when I go out	0	1	2	3	4	
23	It is hard for me to keep myself feeling clean because of my fistula	0	1	2	3	4	
24	I am concerned that other people may be able to smell the discharge from my fistula	0	1	2	3	4	
25	I feel anxious or depressed, down or hopeless because of my fistula	0	1	2	3	4	
26	I worry that my fistula will never be cured	0	1	2	3	4	
27	I worry I might one day need to have a stoma because of my fistula	0	1	2	3	4	Tick if you have a stoma <input type="checkbox"/>
28	I worry about my temporary stoma becoming permanent because of my fistula	0	1	2	3	4	Tick if any below apply: <input type="checkbox"/> I don't have a temporary stoma <input type="checkbox"/> I have a permanent stoma

Adegbola SO, et al. Gut 2021;70:1649–1656.



Symptomscore – Perianal Disease Activity Index

Item	Points	Type of perianal disease	Points
Discharge		No perianal disease	0
No discharge	0	Anal fissure or mucosal tear	1
Minimal mucous discharge	1	<3 perianal fistulas	2
Moderate mucous or purulent discharge	2	>3 perianal fistulas	3
Substantial discharge	3	Anal sphincter ulceration or fistulas with significant undermining skin	4
Gross fecal soiling	4		
Pain/restriction of activities		Degree of induration	
No activity restriction	0	No induration	0
Mild discomfort, no restriction	1	Minimal induration	1
Moderate discomfort, some limitation	2	Moderate induration	2
Marked discomfort, marked limitation	3	Substantial induration	3
Severe pain, severe limitation	4	Gross fluctuance/abscess	4
Restriction of sexual activity			
No restriction of sexual activity	0		
Slight restriction of sexual activity	1		
Moderate limitation of sexual activity	2		
Marked limitation of sexual activity	3		
Unable to engage in sexual activity	4		

Irvine E.J. Clin Gastroenterol 1995;20:27-32.



Symptomscore – afføringsinkontinens

Incontinent	Never	Rarely	Sometimes	Weekly	Daily
Solid stool ^a	0	1	2	3	4
Liquid stool ^a	0	1	2	3	4
Gas ^a	0	1	2	3	4
Alteration in lifestyle ^a	0	1	2	3	4
Wears pad ^b	0	1	2	3	4
			No	Yes	
Need to wear a pad or plug ^c			0	2	
Taking constipating medication ^c			0	2	
Lack of ability to defer defecation for 15 min ^c			0	4	

Never: no episodes in the past 4 weeks; rarely: 1 episode in the past 4 weeks; sometimes: >1 episode in the past 4 weeks, but <1 a week; weekly: 1 or more episodes a week but <1 a day; daily: 1 or more episodes a day

^a Vaizey and Wexner items

^b Only Wexner item

^c Only Vaizey item

Bols et al. Int Urogynecol J. 2013 Mar;24(3):469-78



Klassifikationsskemaerne / udfordringen

- Baserer sig på fistelmorfologi, anatomi, aktivitet og/eller symptomer
- Giver ikke klare rekommendationer for den kliniske håndtering
- Giver anledning til stor heterogenitet i studiedesigns/outcomes



Morfologi, anatomi, symptomer, aktivitet...? Ny klassifikation

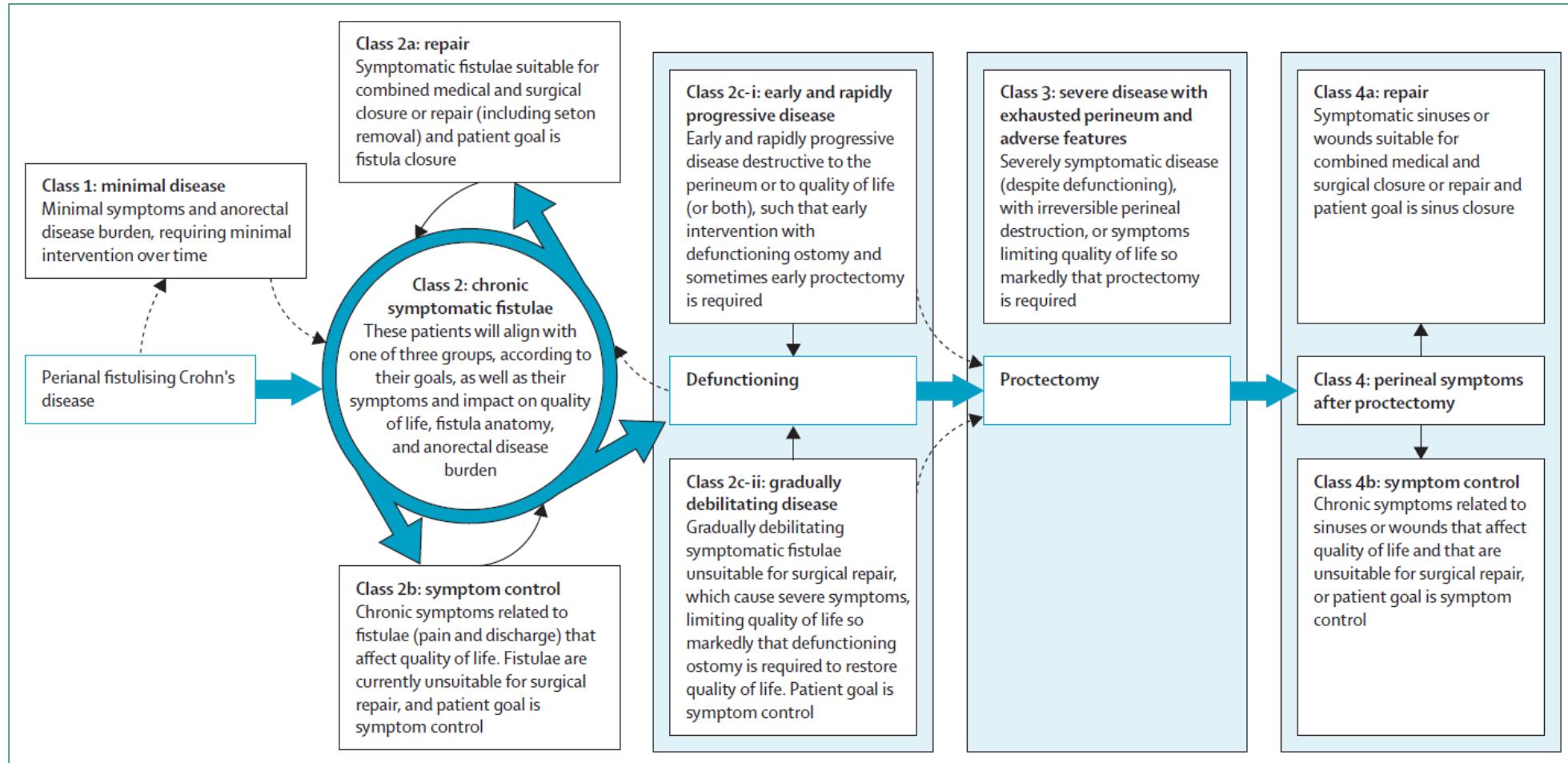


Figure: Classification of perianal fistulising Crohn's disease

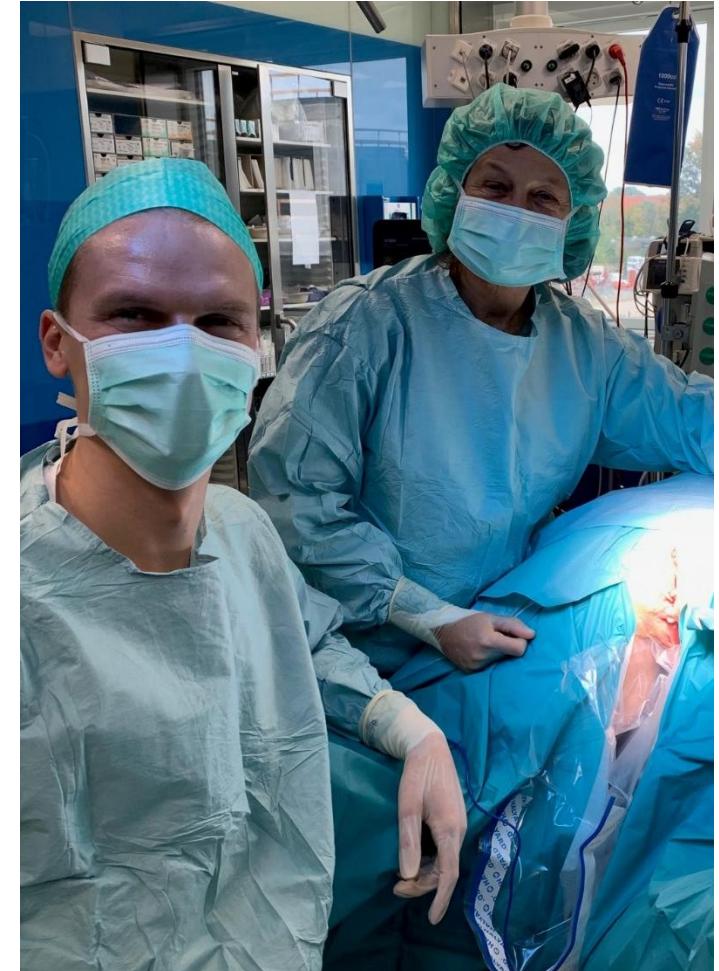
At any moment throughout its disease course, perianal fistulising Crohn's disease can be classified into one of four classes. The diagram illustrates the flexibility of these classes through which patients can cycle over time. Each specific class comes with a paired treatment strategy suggestion and description of trial suitability (see tables 1-3).

Geldof et al.
Lancet Gastroenterol Hepatol 2022

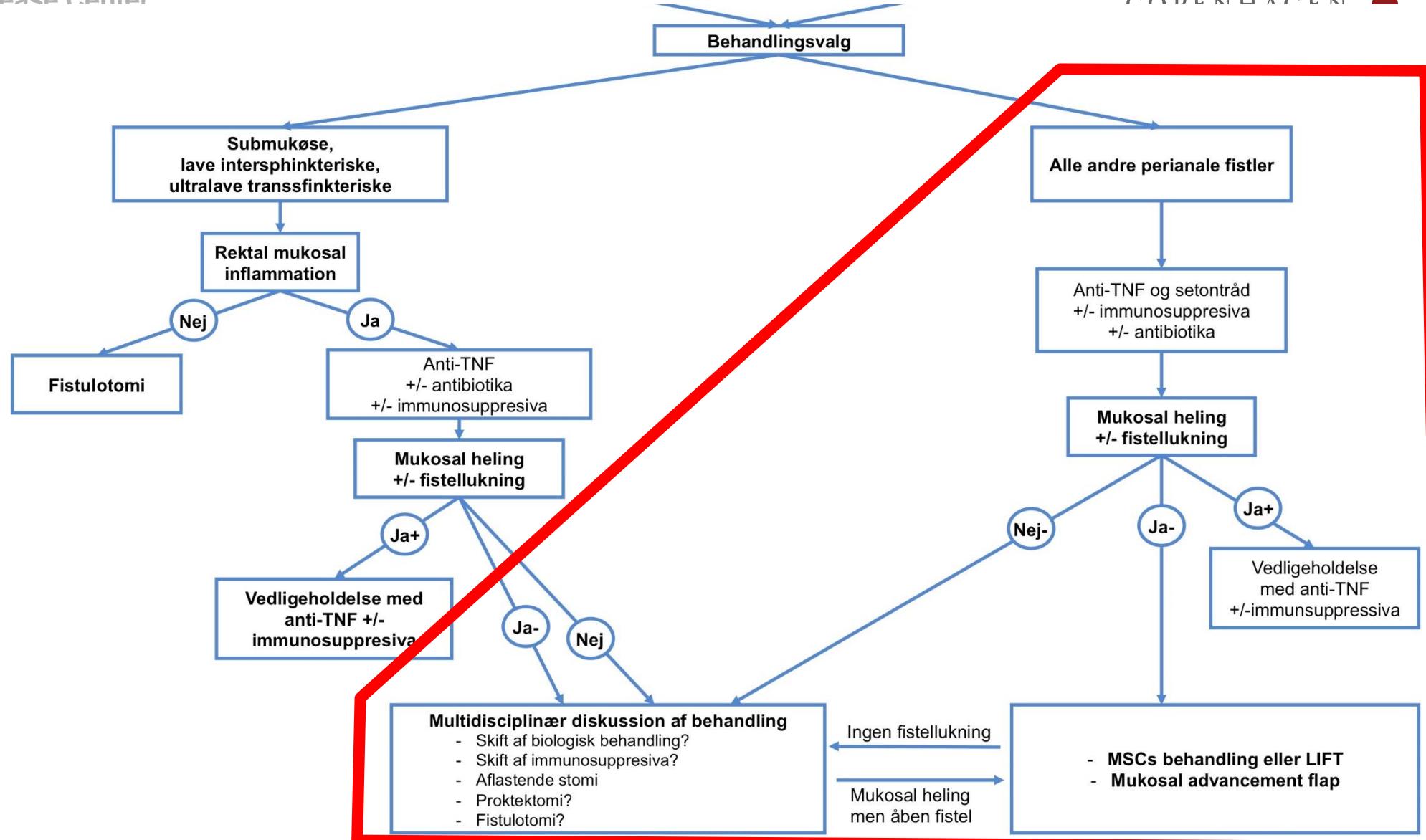


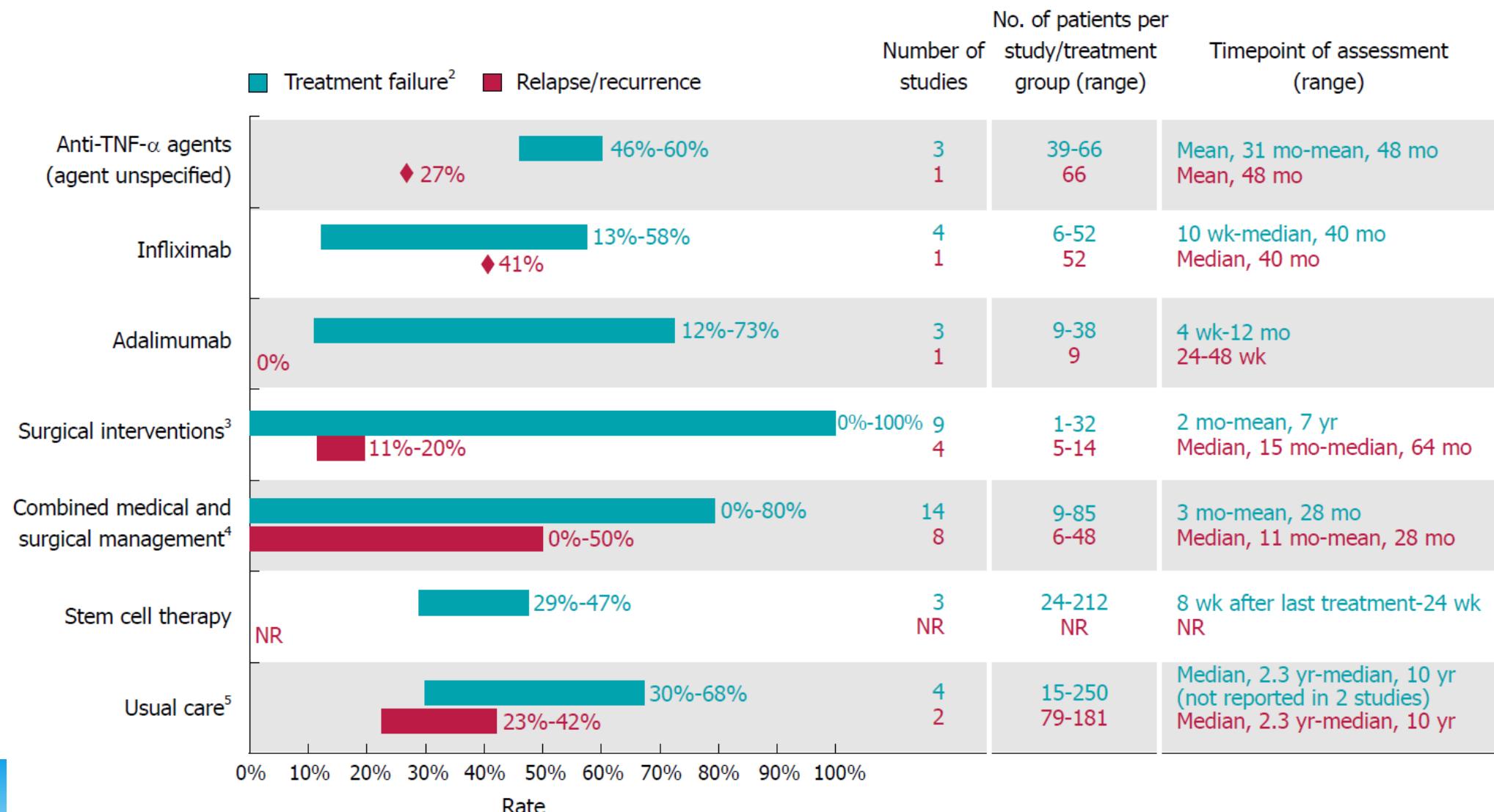
Team'et – multidisciplinær indsats

- Fistelsygeplejerske
- IBD sygeplejerske
- Fistelkirurg
- Gastromediciner
- Kolorektalkirurg
- Gynækolog
- Dermatolog
- Socialrådgiver
- Fysioterapeut
- Psykolog
- Diætist
- (Dedikeret) radiolog
- Plastikkirurg
- Forskningssygeplejersker



DSGH







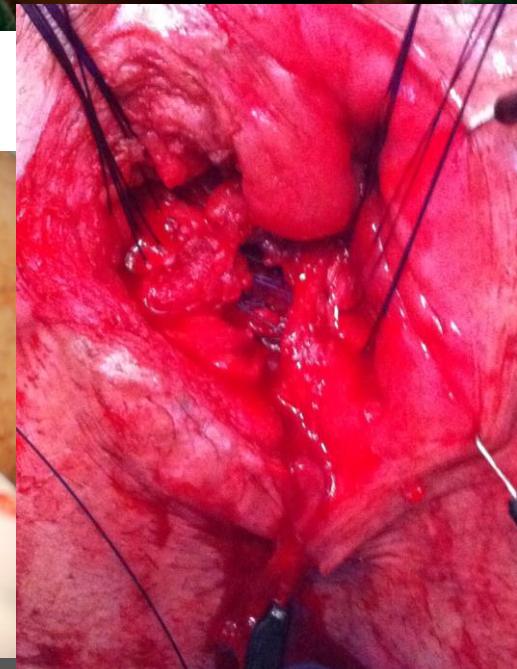
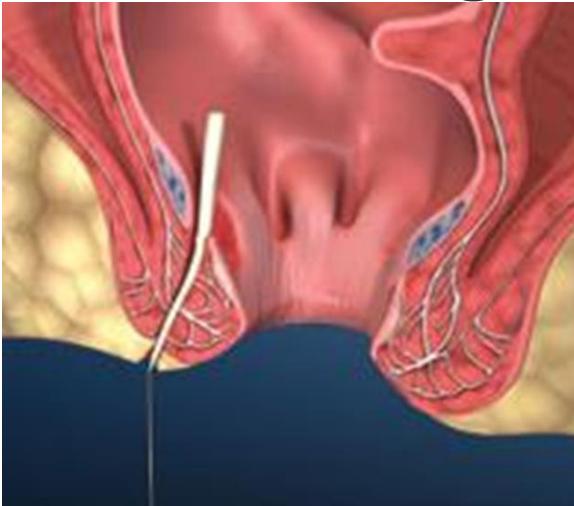
ECCO statement:

- Statement 1.1.
- *No prospective study directly compares medical or surgical treatment of complex perianal Crohn's disease fistulae, either in isolation or in combination with both modalities. Observational studies support a combined medical/surgical approach to control sepsis and luminal activity [EL5].*

Adamina M et al. Journal of Crohn's and Colitis, 2020, 155–168

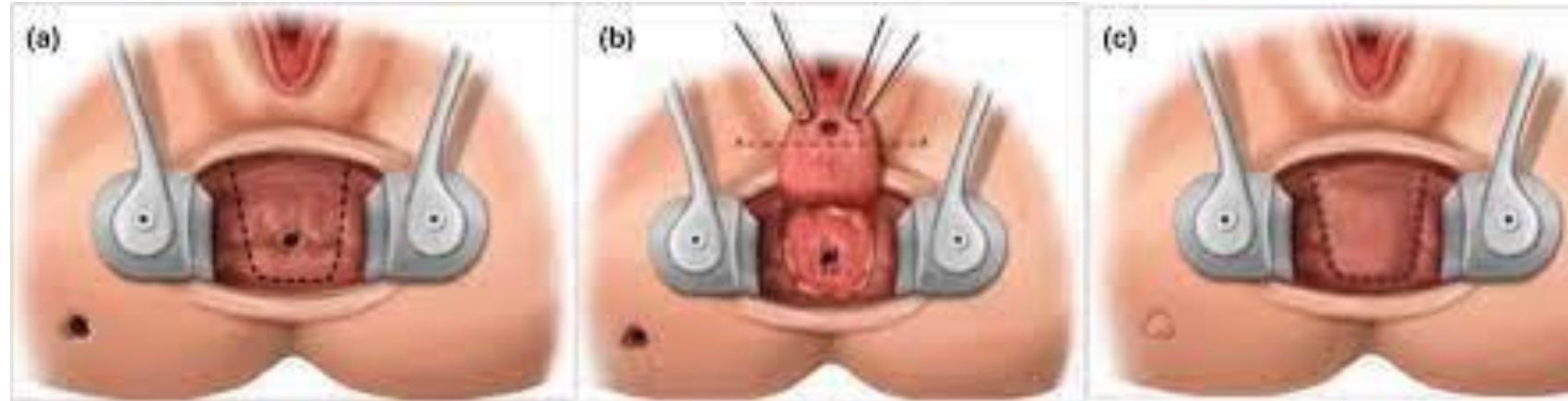


Kirurgiske behandlinger – "traditionelle"





Kirurgi – Endorectal advancement flap



- Succesrate 64% (81% hos non-Crohn patienter)
- 10% risiko for soiling
- Ikke egnet ved proktitis eller stenose
- Ingen effekt af aflastende stomi

Soltani A et al. Dis Colon Rectum. 2010;53:486-495.

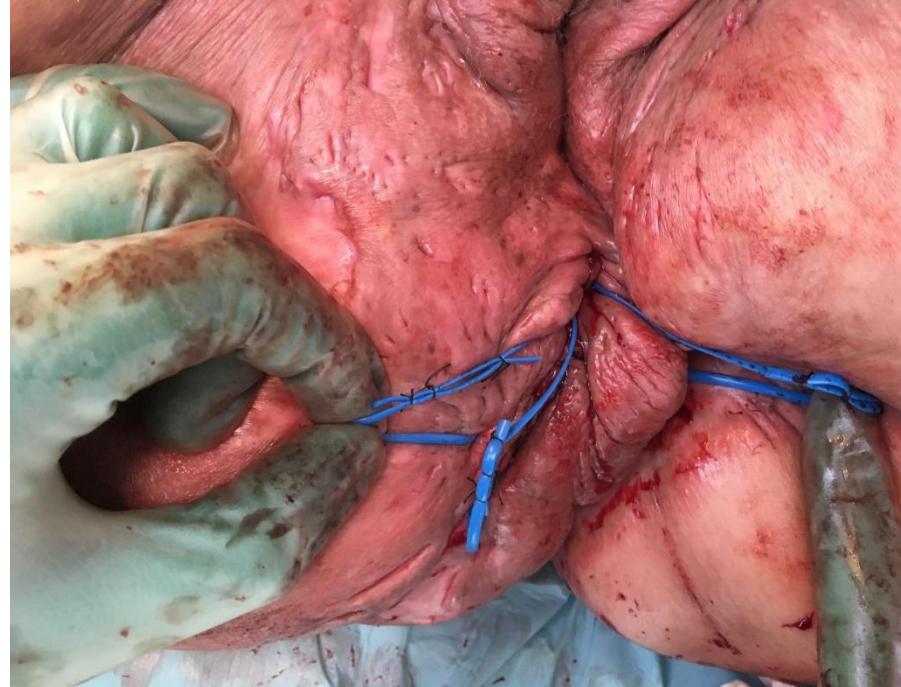


Kirurgi – Ligation of Intersphincteric Fistula Tract (LIFT)

- Succesrate 67% (15 patienter!)
- Længere fistler, væk fra midtlinjen ass. med succes
- Sphinkterbevarende tilgang attraktiv
- Recidiv oftest intersphinkterisk



Seton





Kirurgisk behandling – *new kids on the block*

Int J Colorectal Dis (2003) 18:451–454
DOI 10.1007/s00384-003-0490-3

CASE REPORT

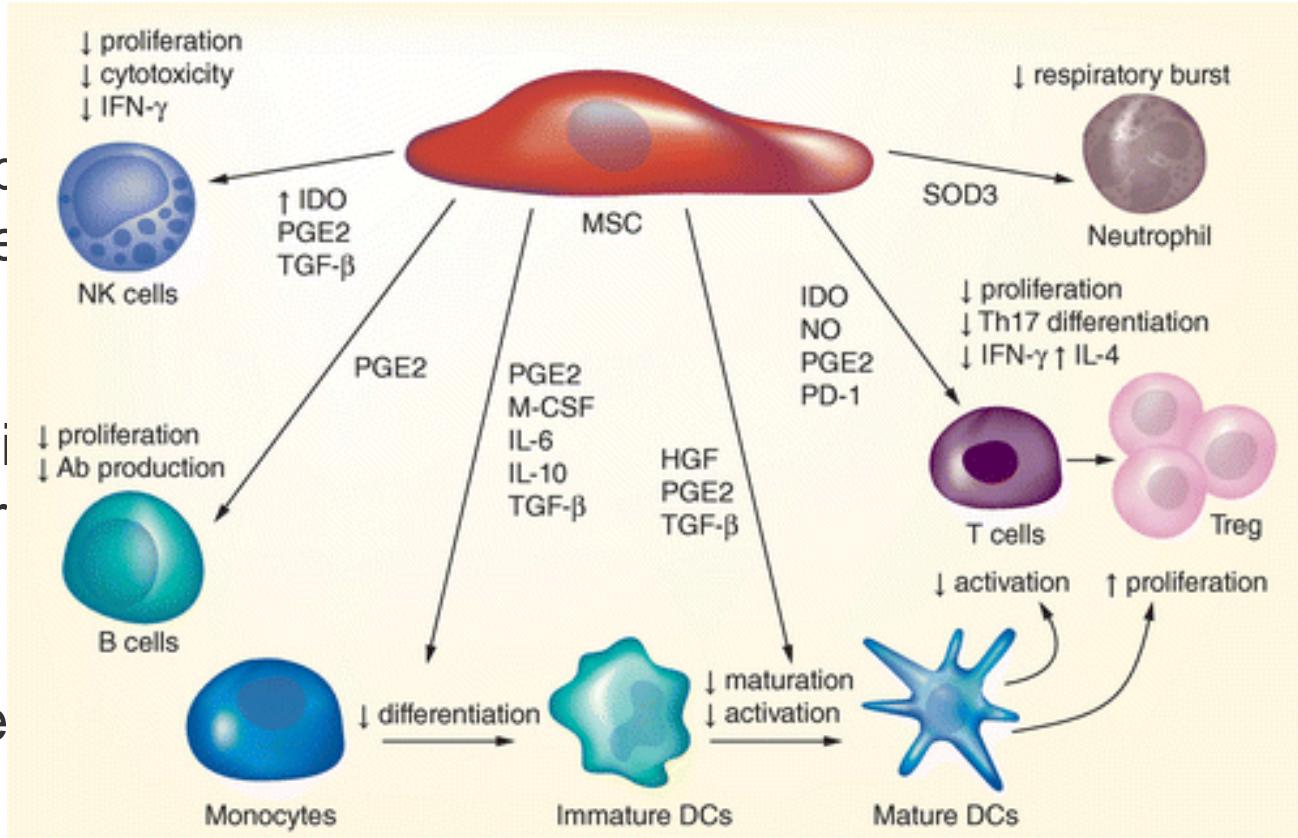
Damian García-Olmo
Mariano García-Arranz
Lourdes Gómez García
Eduardo Serna Cuellar
Ignacio Fernández Blanco
Luis Asensio Prianes
José Antonio Rodríguez Montes
Francisca Lima Pinto
Dolores Herreros Marcos
Luis García-Sancho

**Autologous stem cell transplantation
for treatment of rectovaginal fistula
in perianal Crohn's disease:
a new cell-based therapy**



Stamcellen

- Ny lovende, eksperimentel terapi indenfor mange sygdomsgrupper
- Multipotent og kan differentiere i mange forskellige celleretninger
- Immunmodulerende og secerne mange cytokiner, som påvirker inflammations- og degenerative processer i ødelagt væv



Study; location	Type of study	N (total)	Cell type and source	Outcome	Results (healed)	Results (respond)
García-Olmo et al. [15] (2005); Spain	Phase I trial	5	Autologous, adipose tissue	Reepithelialization of external opening	3/4 healed at 8 weeks	1/4 incomplete closure at 8 weeks
Garcia-Olmo et al. [16] (2009); Spain	Phase II, trial; RCT	14	Autologous, adipose tissue	Reepithelialization of external opening	5/7 in MSCs at 8 weeks; 1/7 in fibrin glue alone at 8 weeks	2/7 incomplete closure at 8 weeks
Ciccocioppo et al. [17] (2011); Italy	Phase I trial	10	Autologous, bone marrow	Reepithelialization plus absence of collections measured by MRI	6/9 healed at 8 weeks	3/9 incomplete closure at 8 weeks
Guadalajara et al. [18] (2012); Spain	Phase II, trial RCT	8	Autologous, adipose tissue	Reepithelialization plus absence of collections measured by MRI	2/4 in MSCs at 40 months; 1/2 in fibrin glue alone at 40 months	Unknown
De la Portilla et al. [19] (2013); Spain	Phase I/Ia trial	24	Allogeneic, adipose tissue	Reepithelialization plus absence of collections measured by MRI	5/18 healed at 12 weeks	12/19 incomplete closure at 12 weeks
Cho et al. [20] (2013); Korea	Phase I trial	10	Autologous, adipose tissue	Reepithelialization of external opening	3/9 healed at 8 weeks	5/9 incomplete closure at 8 weeks
Lee et al. [21] (2013); Korea	Phase II trial	43	Autologous, adipose tissue	Reepithelialization of external opening	27/33 healed at 8 weeks	5/33 closure by more than 50% of fistula tract with a decrease in drainage of more than 50%
Cho et al. [22] (2015); Korea	Phase II trial	41	Autologous, adipose tissue	Reepithelialization of external opening	21/26 healed at 24 weeks	5/26 incomplete closure
Molendijk et al. [23] (2015); Netherlands	Phase II trial RCT	21	Allogeneic, bone marrow	Reepithelialization plus absence of collections measured by MRI	7/15 in MSCs at 12 weeks; 2/6 in saline at 12 weeks	5/15 incomplete closure in MSCs at 12 weeks; 1/6 in saline at 12 weeks
Panés et al. [24] (2016); Israel	Phase III trial RCT	212	Allogeneic, adipose tissue	Absence of drainage and < 2 cm fluid collection on MRI	53/103 in MSCs vs 36/101 in placebo at 24 weeks	18/103 in MSCs vs 20/101 in placebo at 24 weeks
Park et al. [25] (2016); Korea	Phase I trial	6	Allogeneic, adipose tissue	Reepithelialization plus absence of collections measured by MRI	1/5 healed in 8 weeks	4/5 incomplete closure in 8 weeks
Dietz et al. [26] (2017); USA	Phase I trial	12	Autologous, adipose tissue	Absence of drainage and < 2 cm fluid collection on MRI	10/12 healed in 6 months	Unknown
Panés et al. [27] (2018)	Phase III trial RCT	212	Allogeneic, adipose tissue	Absence of drainage and < 2 cm fluid collection on MRI	58/103 in MSCs vs 39/101 in placebo in 52 weeks	10/103 in MSCs vs 17/101 in placebo in 52 weeks

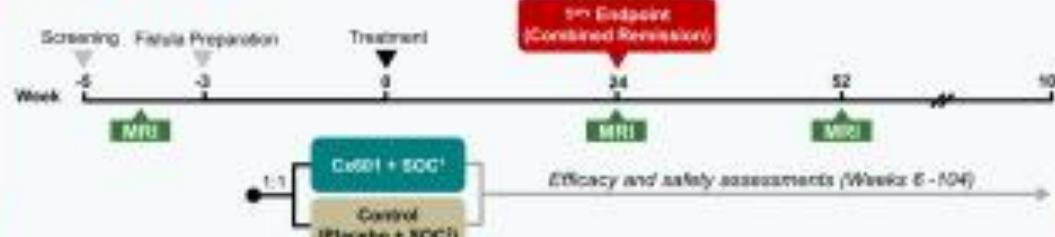
Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial

ADMIRE CD Study: Cx601 for Complex Perianal Fistulas in Crohn's disease

Treatment

Cx601 is a suspension of allogeneic expanded adipose-derived stem cells (eASC) injected locally, and has been shown to be efficacious and well tolerated in Crohn's disease patients with treatment-refractory complex perianal fistulas.

Study design



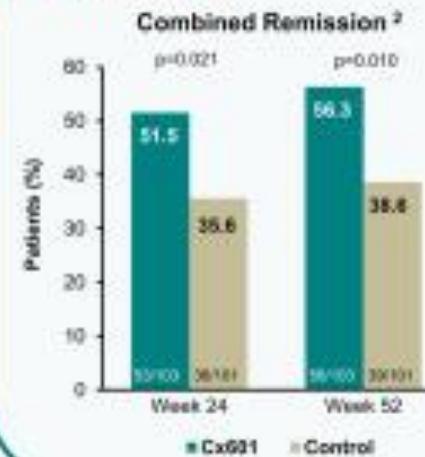
1. Standard of care; 2. mITT population (modified intention to treat)

Tilskud	Udlevering	Disp.form og styrke	Vnr.	Pakning	Pris i kr.	Pris DDD
	(BEGR)	Injektionsvæske, susp. 5,000,000 cells/ml	480329	4 x 6 ml	571.546,85	

REGION

DSAK - perianale Crohn fistler

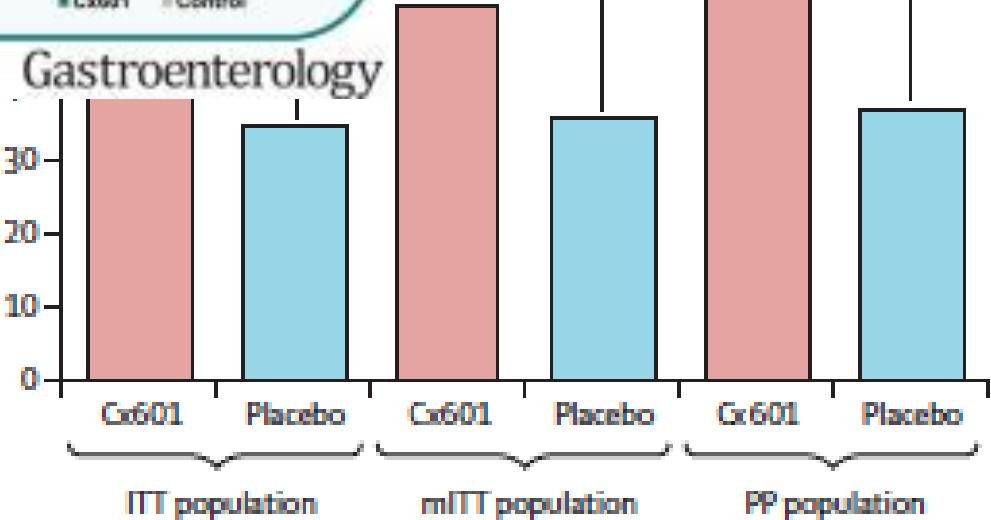
Efficacy



Difference
15.8%
(97.5% CI 0.5-31.2)
p=0.021

Difference
20.1%
(97.5% CI 3.3-36.9)
p=0.010

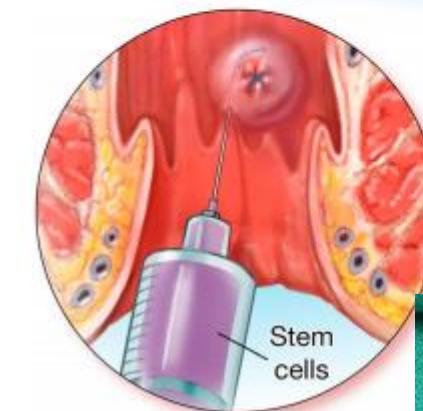
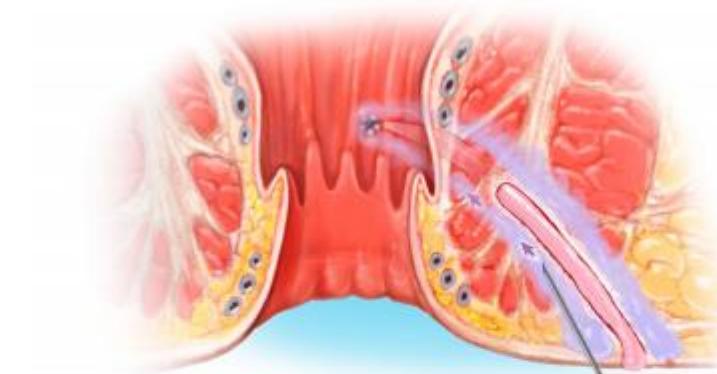
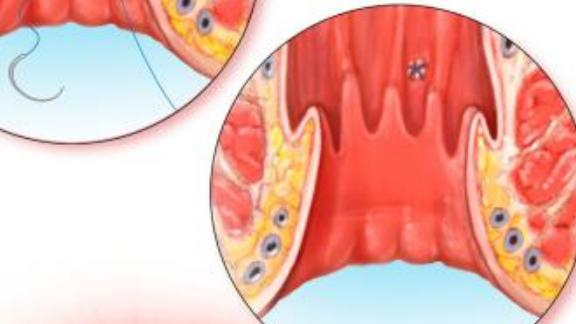
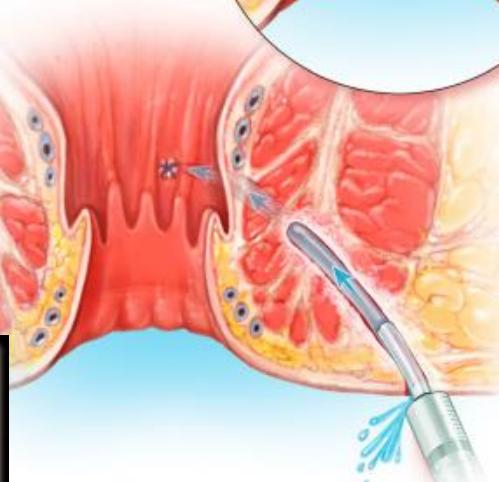
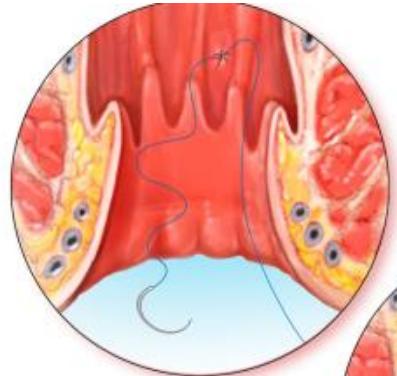
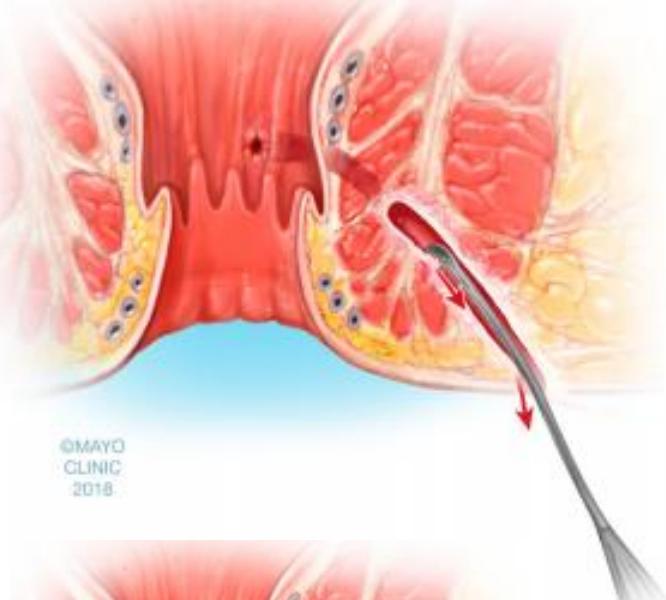
Gastroenterology



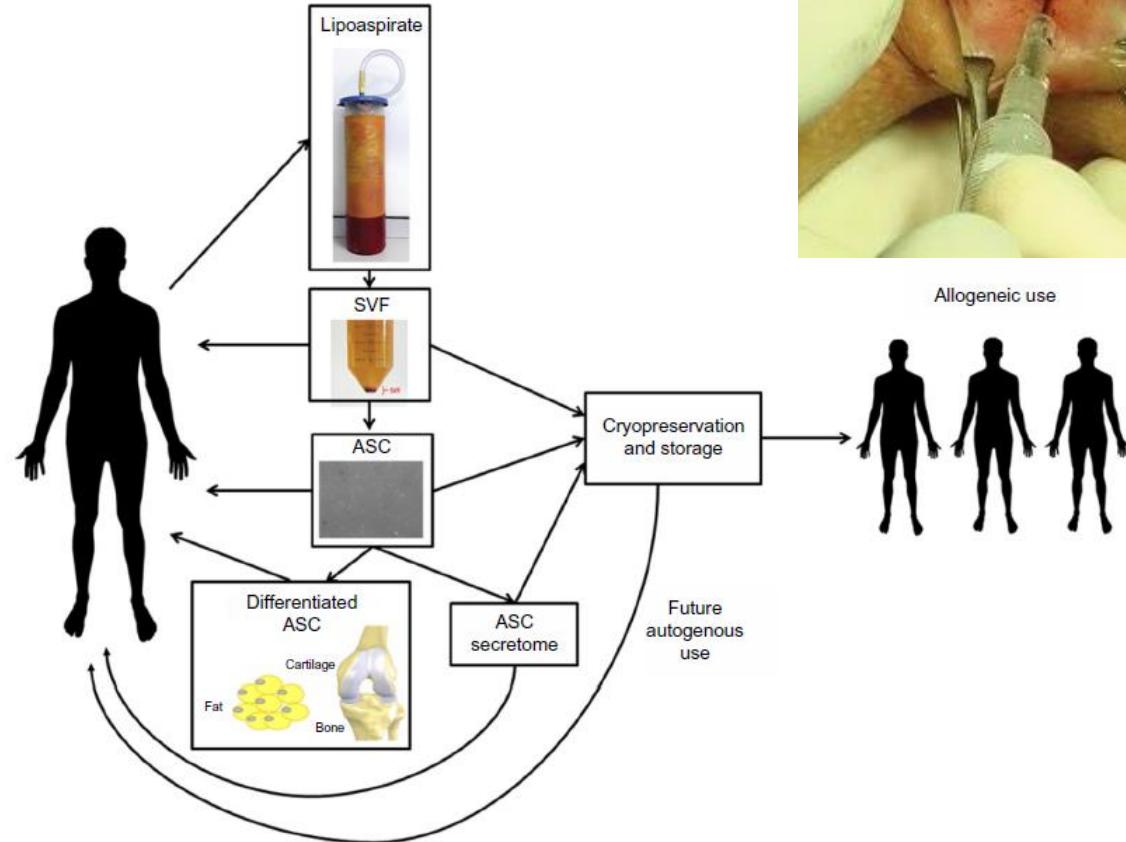
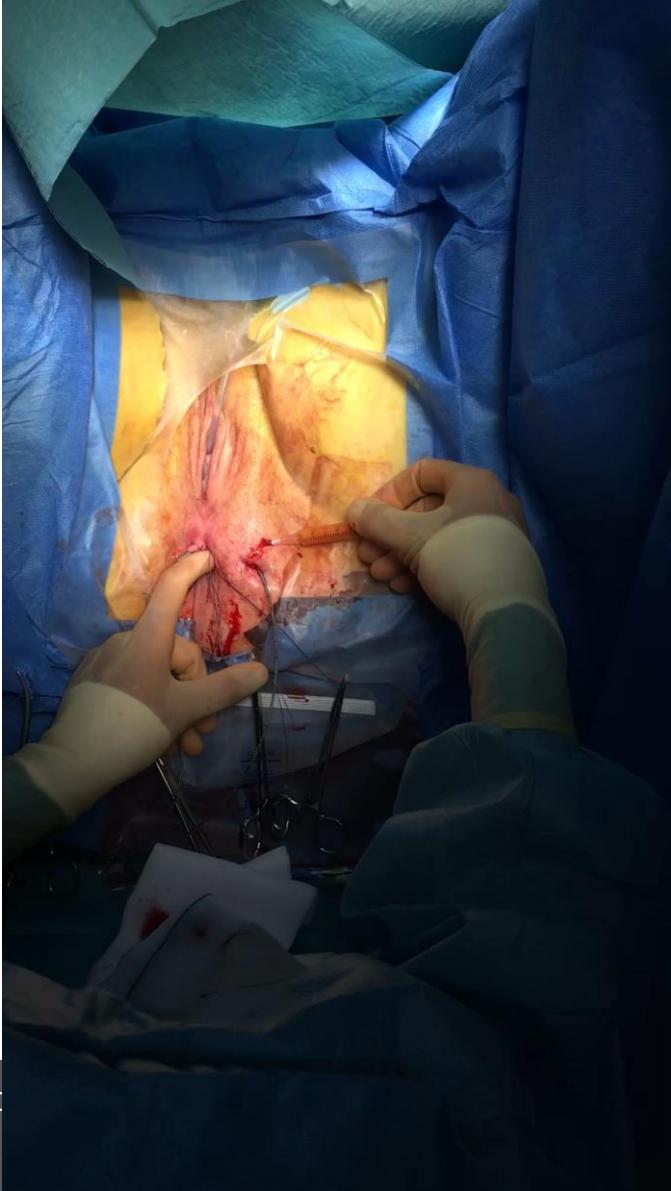


Admire-CD-II studiet

- This study is to assess the efficacy and safety of Cx601, eASC, for the treatment of complex perianal fistulas in participants with Crohn's disease.
- The study will randomize approximately 554 participants.
- Cx601 eASCs intralesional injection
- Placebo - Cx601 placebo-matching eASCs intralesional injection
- Study treatments will be allocated, on a 1:1 ratio, by central randomization through interactive web response system (IWRS). The study will follow an add-on design, participants receiving any ongoing concomitant medical treatment, at stable doses at the time of screening, for the CD will be allowed to continue it throughout the study.
- The primary efficacy analysis, will be conducted at Week 24 timepoint. The double blind design will be maintained up to Week 52 (both participant and investigator) by a specific blinding for study treatment administration and for evaluating its efficacy.
- This multicenter trial will be conducted globally across 150 centers. The overall time to participate in this study is approximately 5 years.



Stamcellen – i kirurgisk perspektiv





Erfaringerne fra Aarhus

Efficacy of Injection of Freshly Collected Autologous Adipose Tissue Into Perianal Fistulas in Patients With Crohn's Disease



Anders Dige,¹ Helene Tarri Hougaard,² Jørgen Agnholt,¹ Bodil Ginnerup Pedersen,³ Michaela Tencerova,⁴ Moustapha Kassem,⁴ Klaus Krogh,¹ and Lilli Lundby²

¹Department of Hepatology and Gastroenterology, Aarhus University Hospital, Aarhus, Denmark; ²Department of Surgery, Pelvic Floor Unit, Aarhus University Hospital, Aarhus, Denmark; ³Department of Radiology, Aarhus University Hospital, Aarhus, Denmark; and ⁴Molecular Endocrinology and Stem Cell Research Unit, Department of Endocrinology and Metabolism, Odense University Hospital and Institute of Clinical Research, University of Southern Denmark, Denmark

Efficacy of Injection of Freshly Collected Autologous Adipose Tissue Into Perianal Fistulas (PF) in Patients With Crohn's Disease(CD)

21 CD Patients w/ PF

- 13 transsphincteric
- 7 anovaginal
- 1 intersphincteric

Repeated injections
Two injections: 9 pt.
Three injections: 4 pt.

Injection(s) with autologous adipose tissue



Results 6 months after

- Overall response in 76%
- Fistula healing in 57%
- Ceased secretion in 14%
- Reduced secretion in 5%

Complications

Abscess ($n=2$), postoperative urinary retention ($n=1$), proctalgia ($n=4$), bleeding ($n=1$)



Mekanismen bag fædtinjektion?

*The non-adipocyte fraction of freshly collected adipose tissue, termed stromal vascular fraction (SVF), contains numerous living stromal (mesenchymal) stem cells. Thus, stromal (mesenchymal) stem cells constitute 10%–50% of the cells in SVF. Therefore, freshly collected adipose tissue may represent an easily accessible alternative to *in vitro* expanded autologous or allogeneic adipose-derived stem cells.*



Det Nationale Fedtprojekt

Primært endepunkt

- Antal patienter der har opnået fuldstændig heling af behandlede fistler 6 måneder efter behandling med frisk høstet autolog fedtvæv. Fuldstændig opheling defineres som a) ingen synlig ydre fistelåbning og b) ingen palpabel indre fistelåbning ved klinisk undersøgelse samt c) ingen symptomer i form af fistelsekretion foruden d) ingen synlige væskespor ved MR-scanning af bækkenet.
- Nationalt multicenter (6 centre), dobbeltblindet randomiseret og placebokontrolleret studie. 140 patienter vil blive inkluderet
- Skejby, Bispebjerg, Herlev, Odense, Aalborg, (Køge)



Rektovaginale fistler

- 10% af patienter med Crohn
- 1/3 har få/ingen symptomer, resten:
 - Luft og afføring per vaginam
 - Dyspareuni
 - Vaginalt udflåd
 - Smerter i perineum
 - Recidiverende UVI
- Behandlingen kompleks, traditionelt stomi/proktektomi,
- I dag mere minimalt invasiv



Sidste udvej...stomi og rectumextirpation



Sidste udvej...stomi og rectumextirpation

- ved ukontrollabel eller svær recidiverende perianal sepsis, inkontinens og udtalt sekretion fra fistlerne (2/3 af disse patienter har behov for yderligere kirurgi, herunder proktektomi)
- kan få en øget livskvalitet ved behandling med stomi
- kan resultere i remission hos 83% af patienterne med svær perianal Crohn
- Ved svær perianal Crohn er risikoen for permanent stomi 49% syv år efter sygdomsdebut



Mennigen et al. Gastroenterol Res Pract. 2015;2015:286315



Sidste udvej...DK tal

- 337/1812 (19%) med perianal Crohn fik stomi (8% blandt CD pt. uden pCD)
- Median 2,6 år (IQR: 0,7-6,5år) efter CD diagnose (hos pCD patienter)
- Tilbagelægningsrater: 51% (CD); 39% (pCD); 37% (pCAF)
- Proktekтомi: 5% ved pCD; 7% ved pCAF



Sidste udvej...proktektoni

- Varierer i litteraturen fra 8%-40%
- Risikofaktorer: antal tidligere kirurgiske indgreb, midlertidig stomi, kolorektal Crohn
- Høj risiko for komplikationer, om muligt anbefales intersphinkterisk dissektion, alternativt ved udbredt perianal Crohn myokutan lap



Malign transformation



Malign transformation

- Fistel-associeret anal carcinom (FAAC), hyppigst mucinproducerende AC
- Frygtet, men sjælden (est. prævalens 0,004-0,7%)
- Usikker patogenese, men langvarig inflammation (>15 år), immunosuppression, HPV infektion, rygning antages at være risikofaktorer
- *Dårlig prognose (ofte avanceret stadium ved diagnose), hyppigere recidiv*
- Årlig surveillance? Biopsier?

Thomas M et al. *J Gastrointest Surg.* 2010;14:66–73.

Baars JE et al. *J Gastroenterol.* 2011;46:319–325.

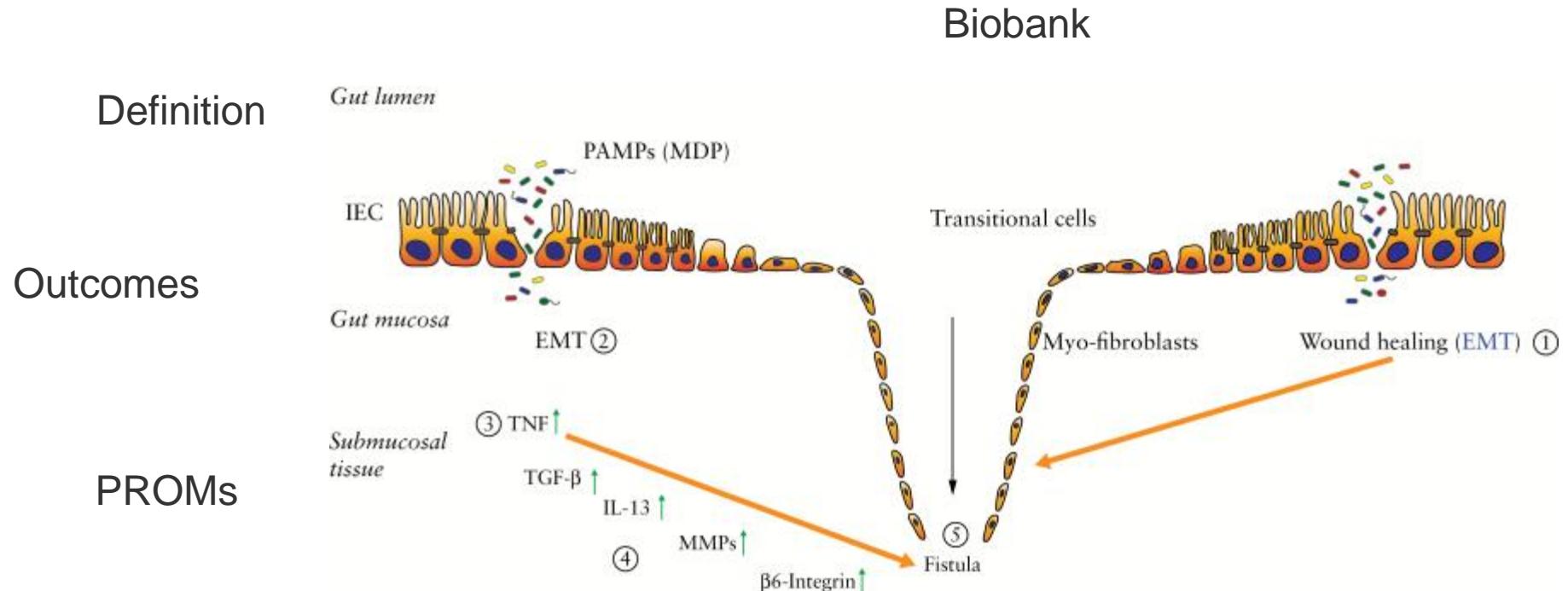
Alcalde-Vargas A, Trigo-Salado C, Leo-Carnerero E et al. *Rev Esp Enferm Dig.* 2013;105:115–116.



Cancer (DK tal)

- Cancer ani:
 - Risiko for analkræft højere hos CD patienter ($aHR = 4.17$ [95% CI: 2.51 to 6.94, $p <0.001$]) vs. Non-IBD matchede kontroller
 - Ved pCD: $aHR = 12.09$, 95% CI: 5.00 to 29.47, $p <0.001$
- Cancer recti:
 - CD vs. Non-IBD kontroller: $aHR = 1.24$, 95% CI: 0.92 to 1.68, $p = 0.16$
 - pCD vs. Non-IBD kontroller: $aHR = 2.42$, 95% CI: 1.32 to 4.43, $p = 0.004$

Perspektivering





Spørgsmål?

- andreas.nordholm-carstensen@regionh.dk

