



**REFERRAL TO CARE NELLE MALATTIE
INFIAMMATORIE
CRONICHE INTESTINALI**
IL PATIENT JOURNEY del paziente con IBD

MILANO
STARHOTELS ANDERSON
Piazza Luigi di Savoia, 20, Milano

**26 Marzo
2024**

IL TRATTAMENTO PRECOCE DELLE MICI

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Ambulatorio IBD
SC Gastroenterologia



Fondazione IRCCS
San Gerardo dei Tintori

Sistema Socio Sanitario



Regione
Lombardia

Disclosures

CV has served as consultant for Abbvie, AlfaSigma, Celltrion, Janssen-Cilag, Galapagos;

has received lecture fee from Abbvie, Alfasigma, Janssen-Cilag, Pfizer;

has received research grant from Celltrion and Pfizer.

Agenda

. Why is early treatment important in IBD?

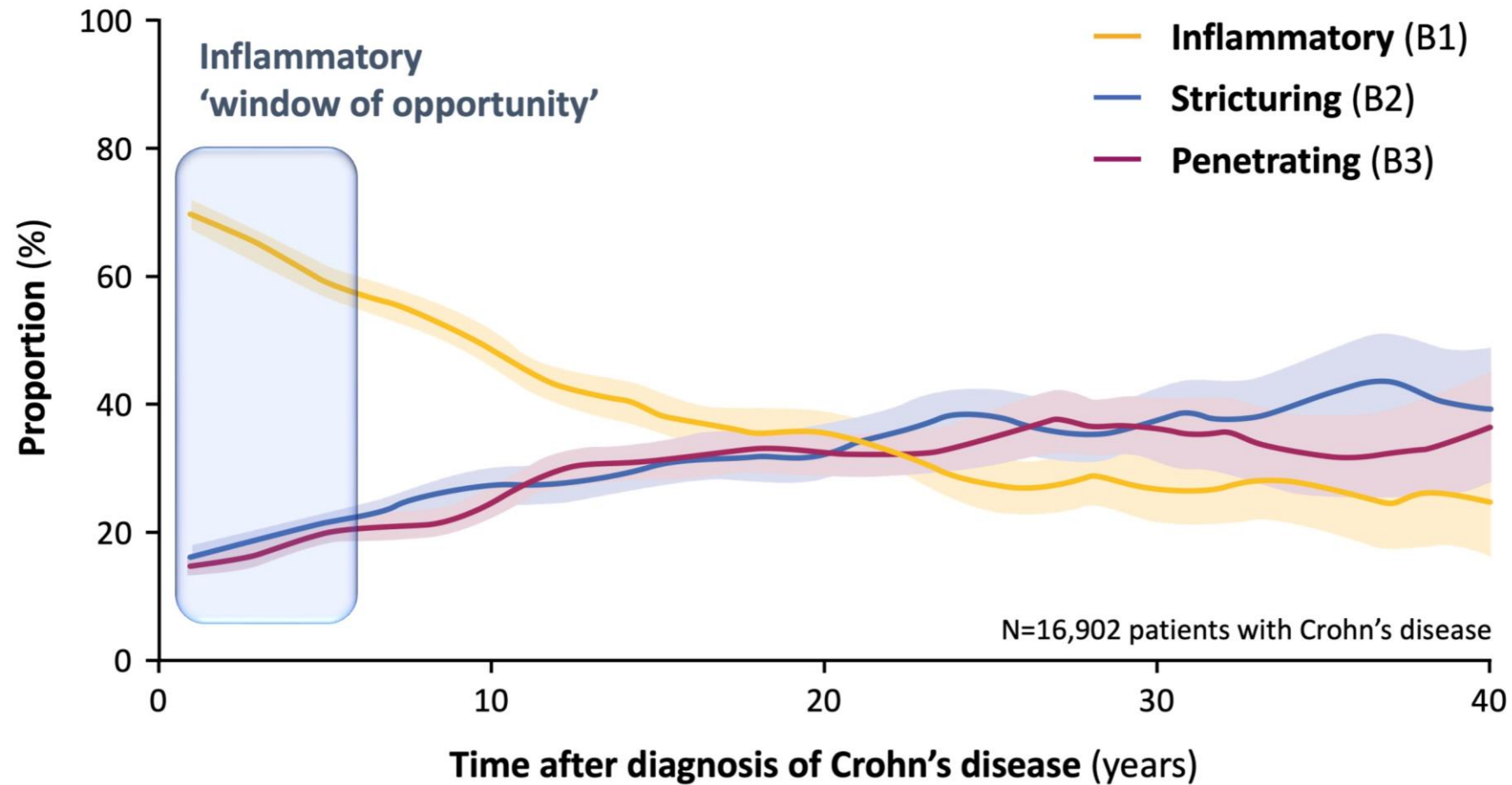
Prevention of bowel damage

Improved response to treatment

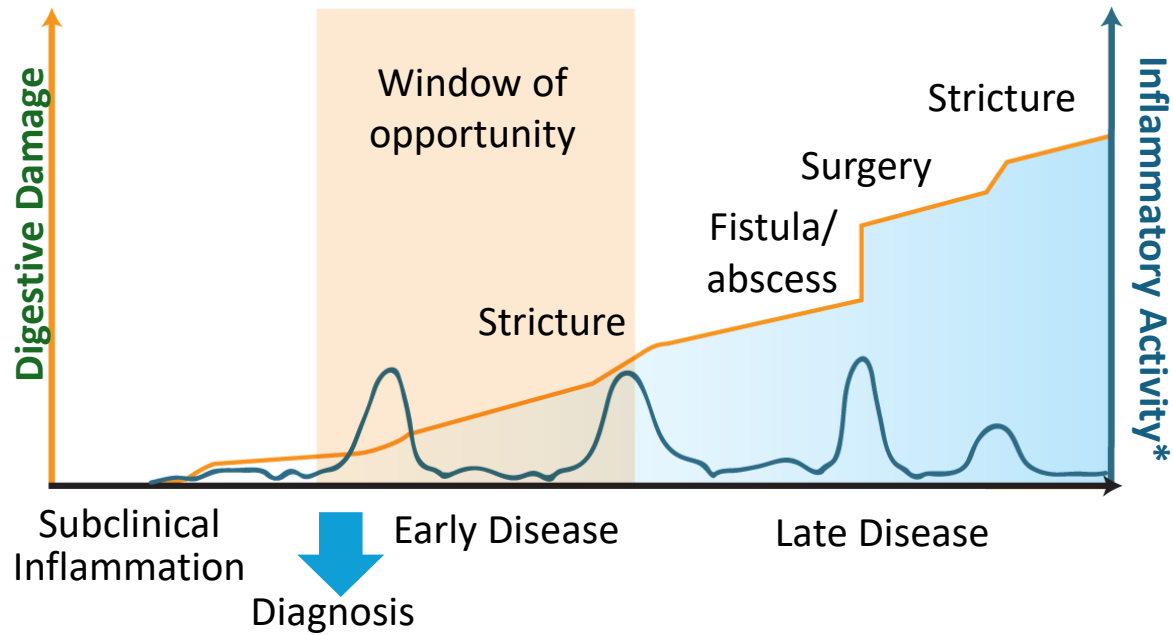
. What is “early” treatment? Do we treat early enough?

- Data are mainly available for **CD**
- Similar principles hypothesized in **UC** but not as clear

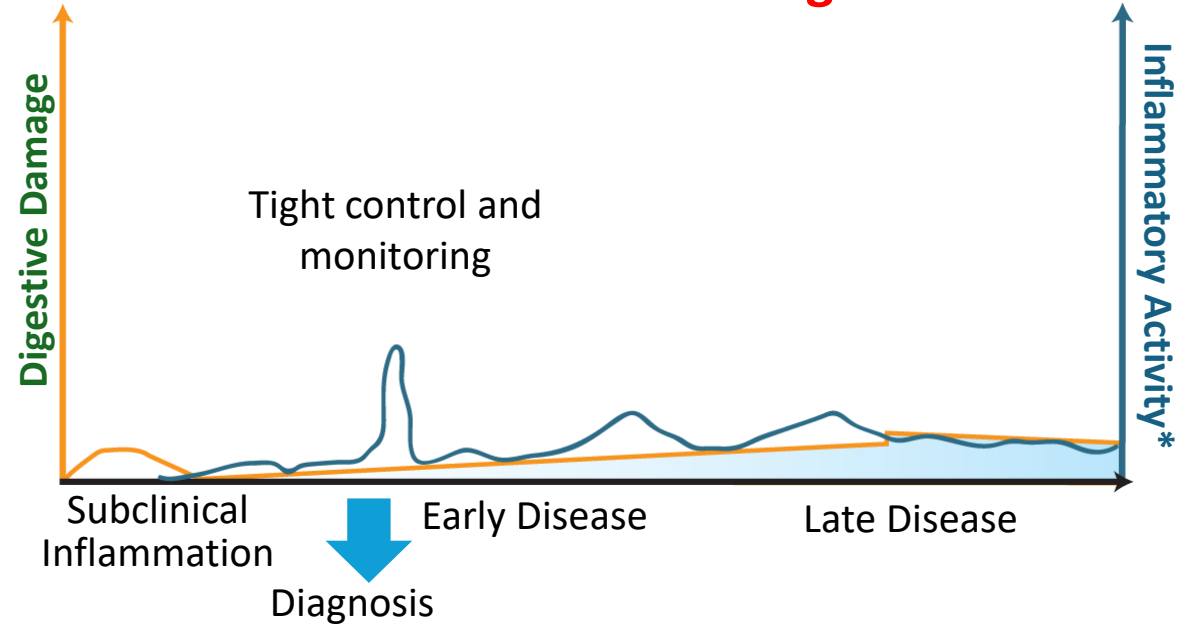
Crohn's disease is progressive



Natural Course of CD



Theoretical Impact of Early Effective Treatment on Disease Progression



*Assessed by CDAI, CDEIS, and/or CRP.

Early effective treatment can prevent bowel damage and improve outcome?

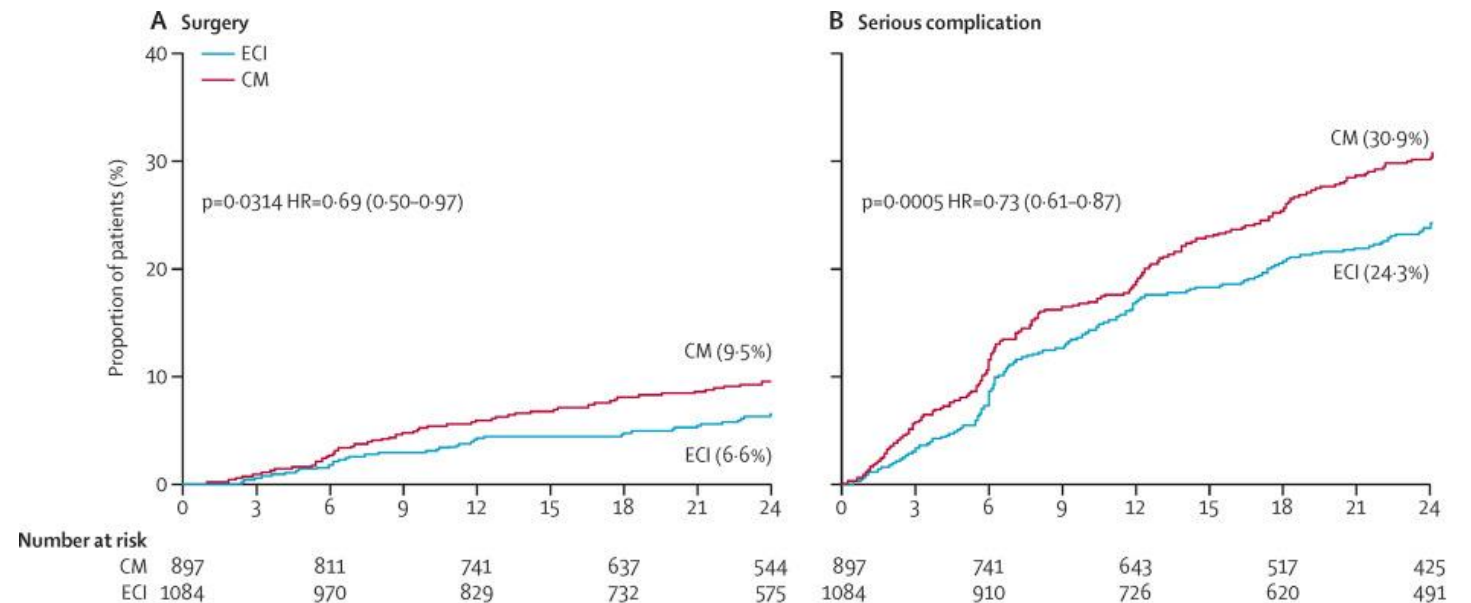
- In CD there is a consistent body of evidence demonstrating that earlier treatment results in better outcomes (from RCT post-hoc and long term extensions)
- Data from observational studies have been conflicting
- The majority of evidence has been generated for antiTNFs



The Randomised Evaluation of an Algorithm for Crohn's Treatment (REACT-1)

Open-label cluster RCT of 41 community centers caring for 1982 patients with CD comparing early combined immunosuppression vs conventional treatment

- No improvement in the primary outcome of clinical remission
- Advantage in many major secondary outcome measures at 24 months, including need for surgery and any serious CD-related complications



Deep Remission at 1 Year Prevents Progression of Early CD

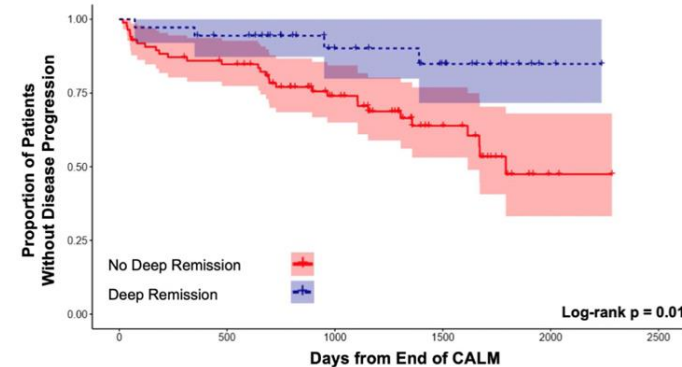
Early Crohn's Disease (CD) patients from the CALM study (n=122)
Bionative, recently diagnosed, treated with anti-TNF biologic



Deep Remission at 1 year
(Endoscopic remission AND clinical remission AND no steroids)



Decreased Risk of Disease Progression
aHR (0.19, 95% CI 0.07-0.31)



Gastroenterology

Early CD (median 0.2 yrs, IQR 0.1 – 0.5)

Ungaro R, Gastroenterology 2020



Data from Real world observational cohort in CD yielded conflicting results



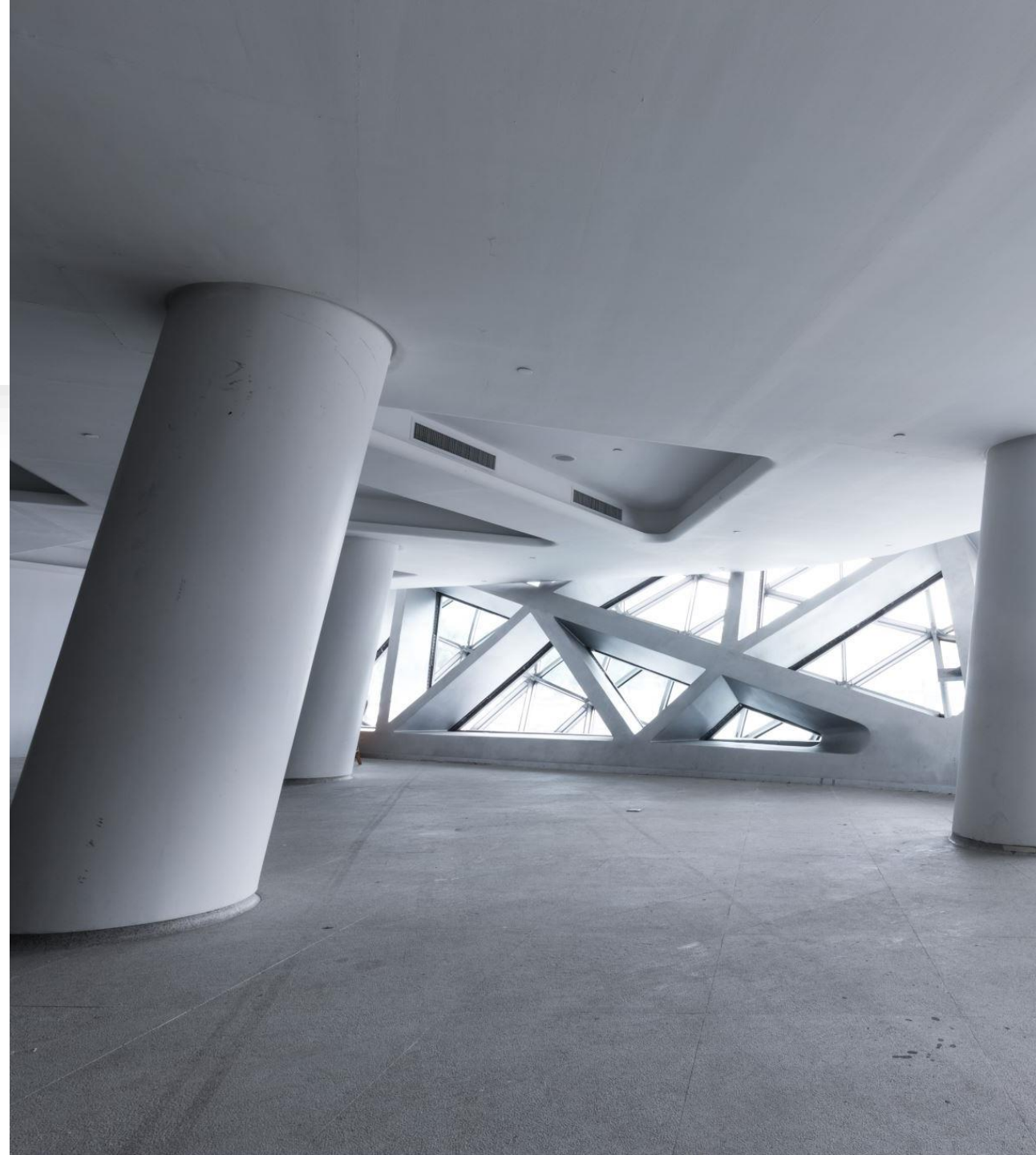
Perhaps many of these treatments may not have been used early enough in the disease course?



.....The initial suggestion of 2-year window might not be early enough

The therapeutic ceiling

- There is a therapeutic ceiling, with only around 30% of patients achieving noticeable improvements.
- Perhaps treatment are being initiated too late?
- An earlier introduction of treatments could achieve higher treatment response?



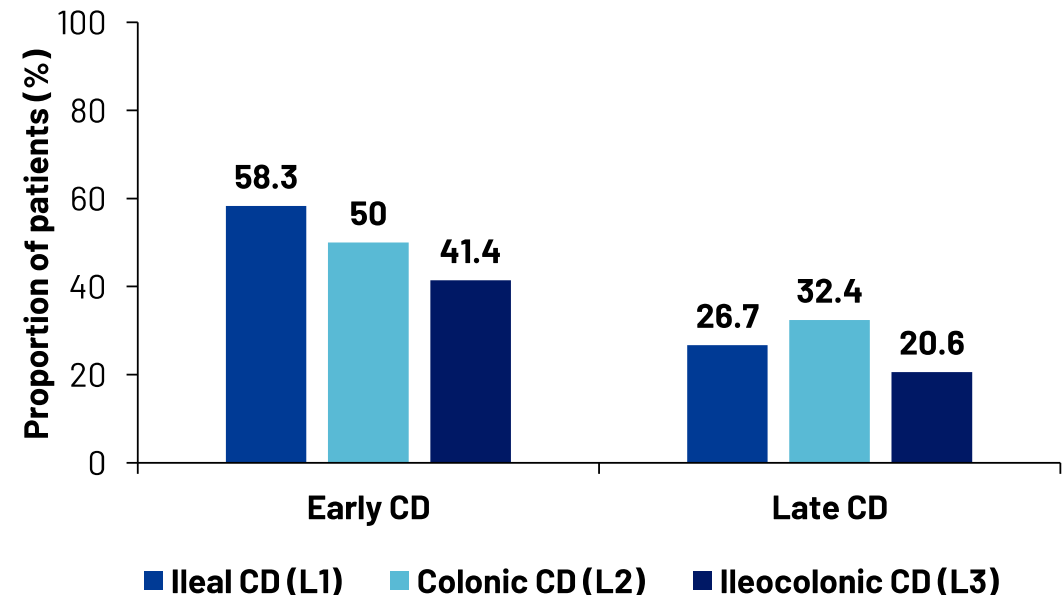
Early CD is associated with higher endoscopic healing rate

LOVE-CD
ITT analysis
(N=186)

Ulcer-free endoscopy achieved
at Week 52 (ITT population)

Disease location	Proportion of patients (%)	p-value
L1	35.7	0.327
L2	38.5	
L3	27.2	

Absence of ulcers at Week 52
(SES-CD ulcer score 0)



N numbers were not reported for the graph.

CD, Crohn's disease; ITT, intent-to-treat; L, location; SES, Simple Endoscopic Score; VDZ, vedolizumab.

Hens B, et al. Presented at European Crohn's Colitis Organisation. Stockholm, Sweden. February 21-24, 2024. P845.

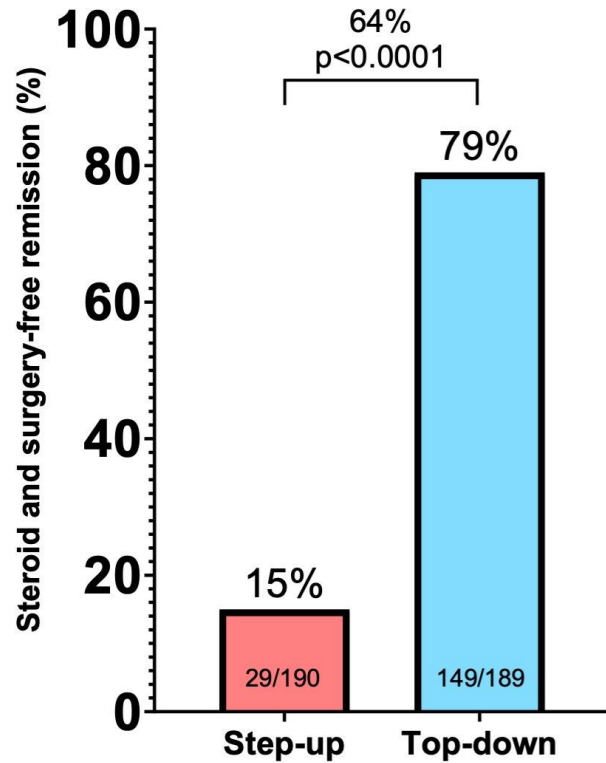
Figure adapted from Hens B, et al. Presented at
European Crohn's Colitis Organisation.
Stockholm, Sweden. February 21-24, 2024. P845.

Primary endpoint - sustained steroid-free and surgery-free remission through to week 48



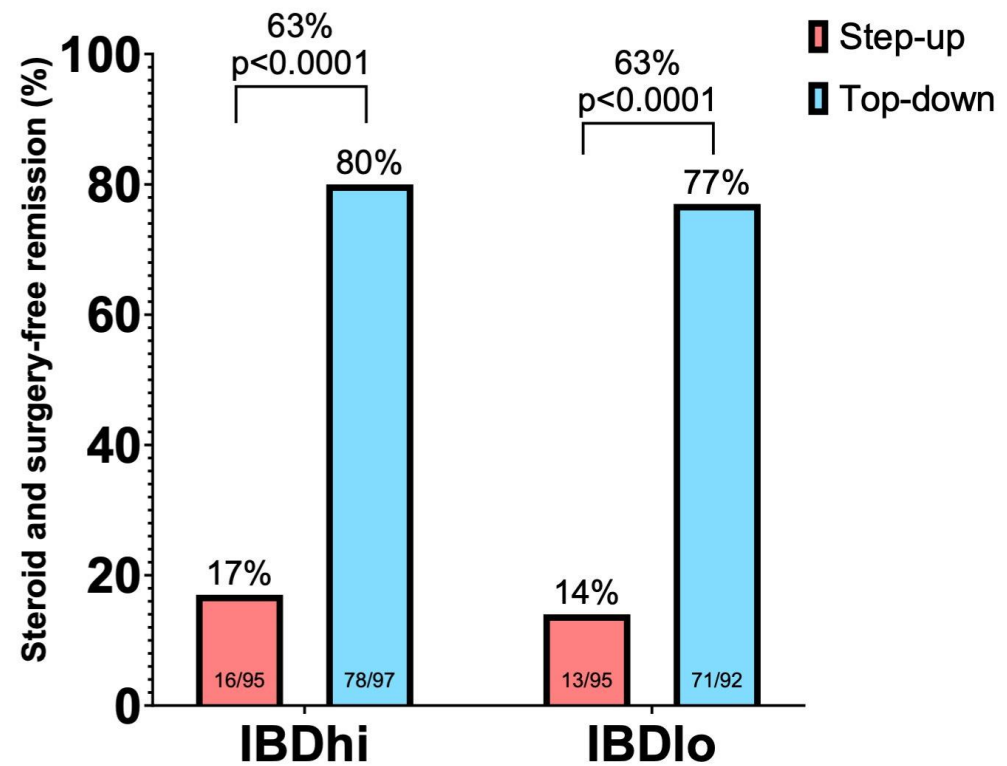
Treatment effect

64% (95% CI=57 to 72%, p<0.0001)



Biomarker effect

1% (95% CI=-15% to +15%, p<0.944)



©Speaker:

Dr Nuru Noor at ECCO'24 Congress

In CD treat effectively early, very early.....at least in high risk patients

Disease Risk in IBD

Crohn Disease
High risk for poor prognosis
<ul style="list-style-type: none">▪ Age at diagnosis <30 yr▪ Extensive anatomic involvement▪ Perianal and/or severe rectal disease▪ Deep ulcers▪ Prior surgical resection▪ Stricturing and/or penetrating disease▪ Elevated CRP and low albumin▪ >10 loose stools/wk and/or anorectal symptoms

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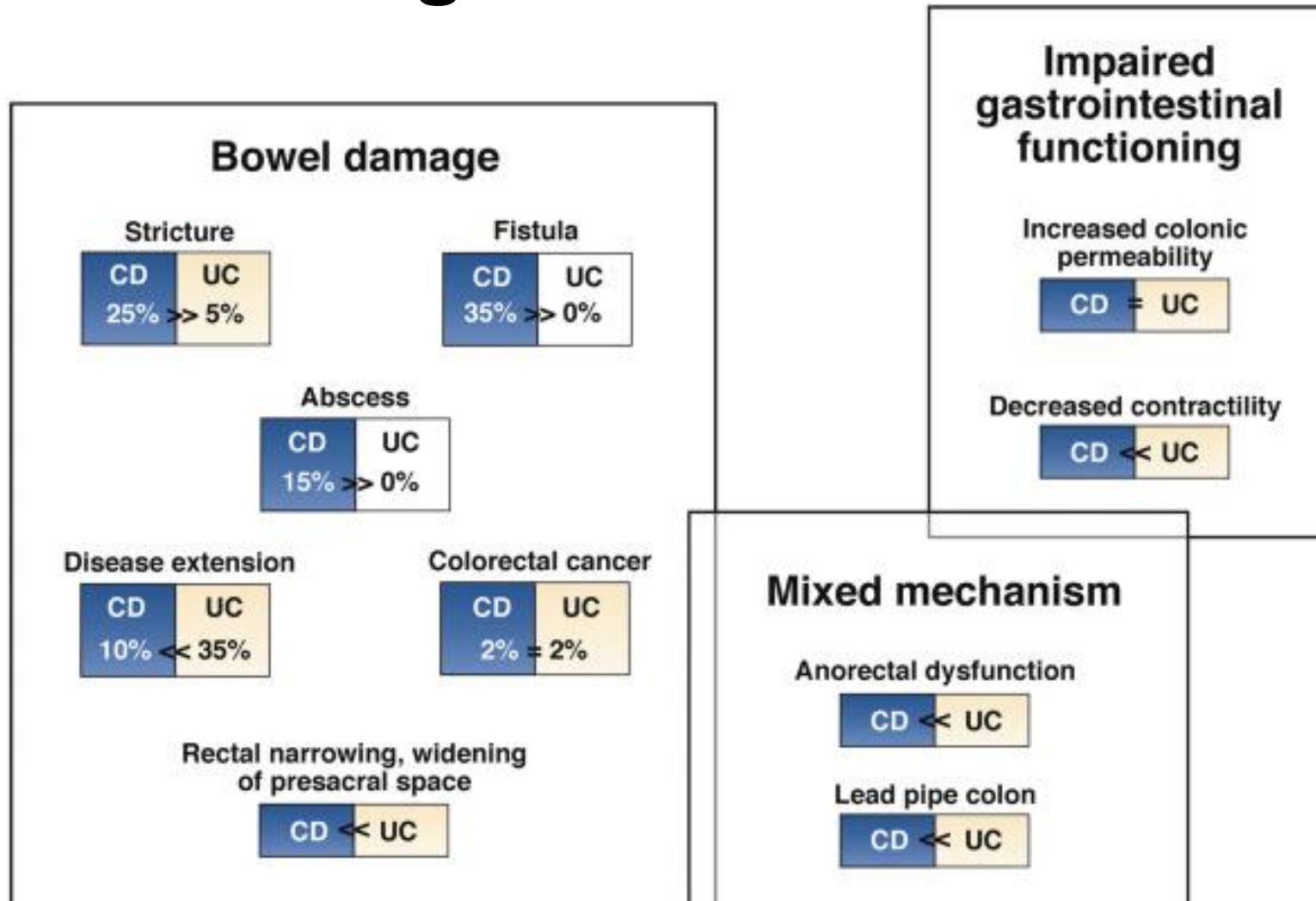
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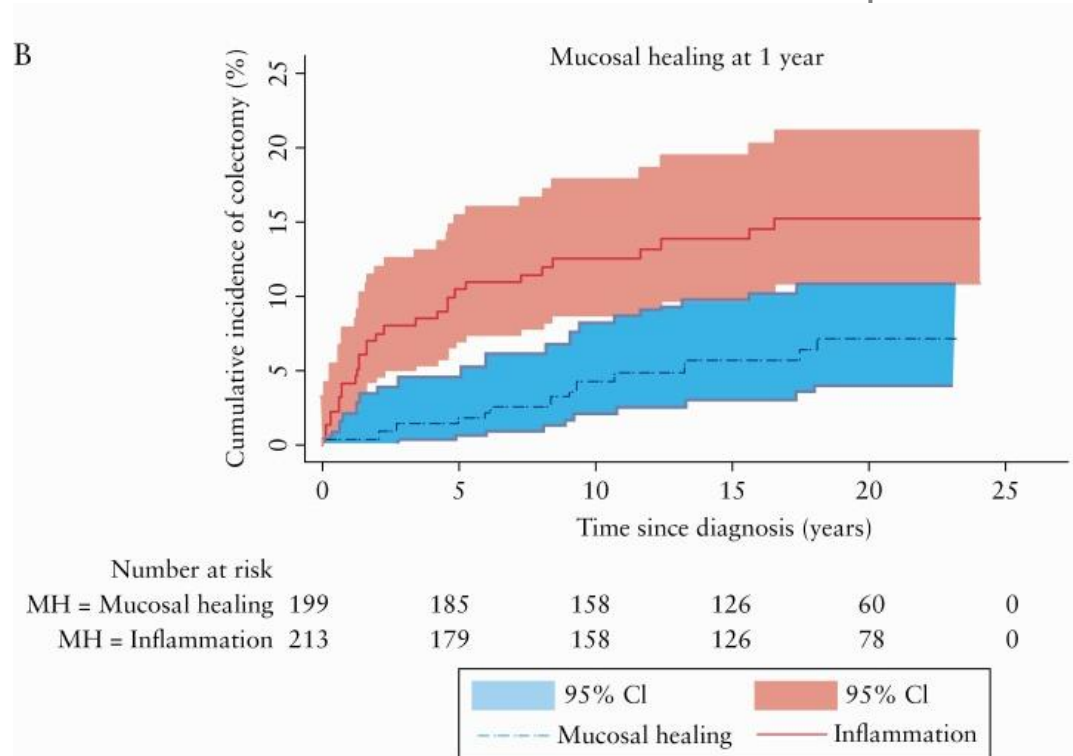
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Digestive damage in UC



Mucosal Healing reduces the risk of colectomy in UC in a Prospective Population-based Inception Cohort from South-Eastern Norway, the IBSEN Study



Mostad IL, JCC 2021

Lack of benefit for early escalation to advanced therapies in UC

Table 2. Real-world evidence on utility of early vs late escalation to advanced therapies.

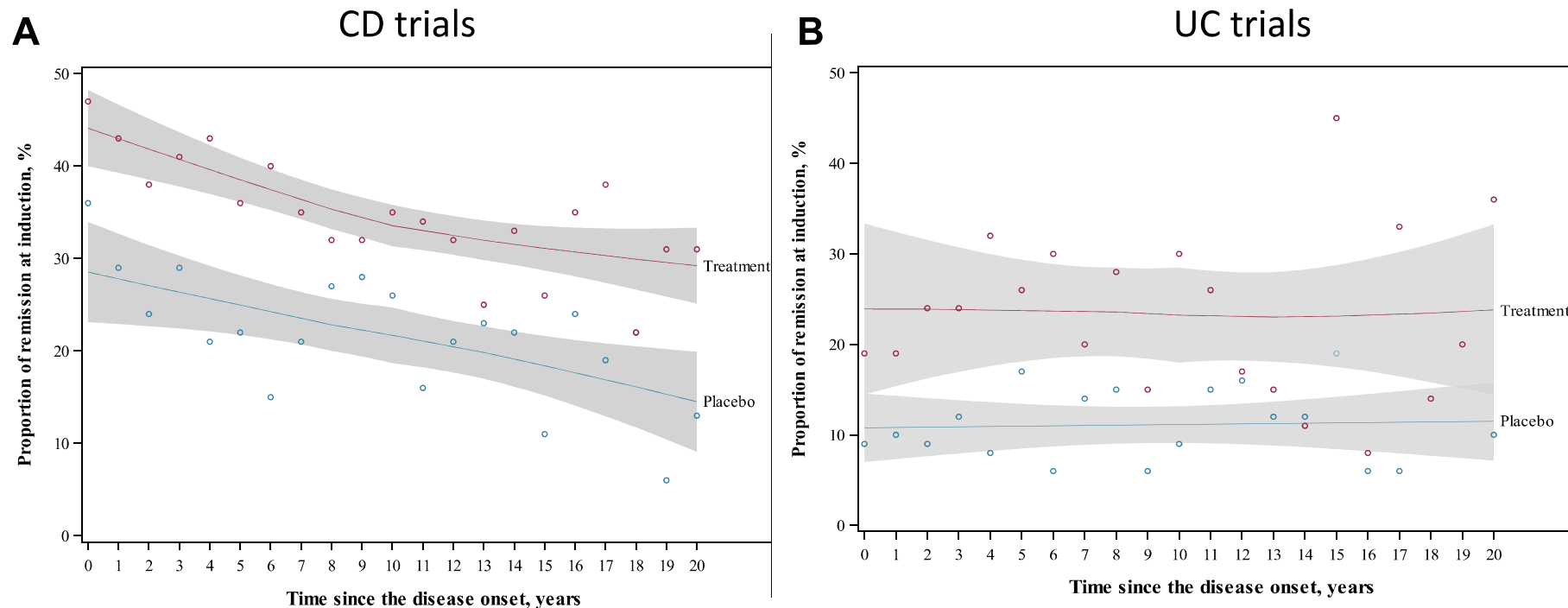
Study	No benefit for the outcomes	Definition of early disease	Follow-up duration	Patient numbers
Mandel <i>et al.</i> 2014	Hospitalization rates	≤3 years		<i>n</i> = 42
Nuij <i>et al.</i> 2013	Abscess formation, fistula formation, extraintestinal manifestations, mucosal healing, or surgery over a median	≤16 months	Median of 39 months	<i>n</i> = 27
Ma <i>et al.</i> 2016	Colectomy, UC-related hospitalization, clinical secondary loss of response	≤3 years	Median of 175.6 weeks	<i>n</i> = 115
Faleck <i>et al.</i> 2019	Clinical remission, corticosteroid-free remission, endoscopic remission	≤2 years	6 months	<i>n</i> = 437
Han <i>et al.</i> 2020	Need for colectomy, UC-related emergency room visits, UC-related hospitalization or new corticosteroid use	≤2 years	1.7 years	<i>n</i> = 698
Targownik <i>et al.</i> 2022	Hospitalization rates, adjusted cumulative rate of IBD hospitalizations, or all-cause hospitalizations, or surgery	≤2 years	Up to 5 years	<i>n</i> = 318

Burish J, JCC 2023

Efficacy of Biologic Drugs in Short-Duration Versus Long-Duration Inflammatory Bowel Disease: A Systematic Review and an Individual-Patient Data Meta-Analysis of Randomized Controlled Trials



Shomron Ben-Horin,^{1,2} Lena Novack,^{3,4} Ren Mao,¹ Jing Guo,¹ Yue Zhao,¹ Ruslan Sergienko,⁴ Jian Zhang,² Taku Kobayashi,⁵ Toshifumi Hibi,⁵ Yehuda Chowers,⁶ Laurent Peyrin-Biroulet,⁷ Jean Frederic Colombel,⁸ Gilaad G. Kaplan,⁹ and Min-hu Chen¹



Rate of remission induction by duration of disease at initiation of treatment for (A) CD and (B) UC trials. The dots denote proportion of an outcome averaged per the respective year

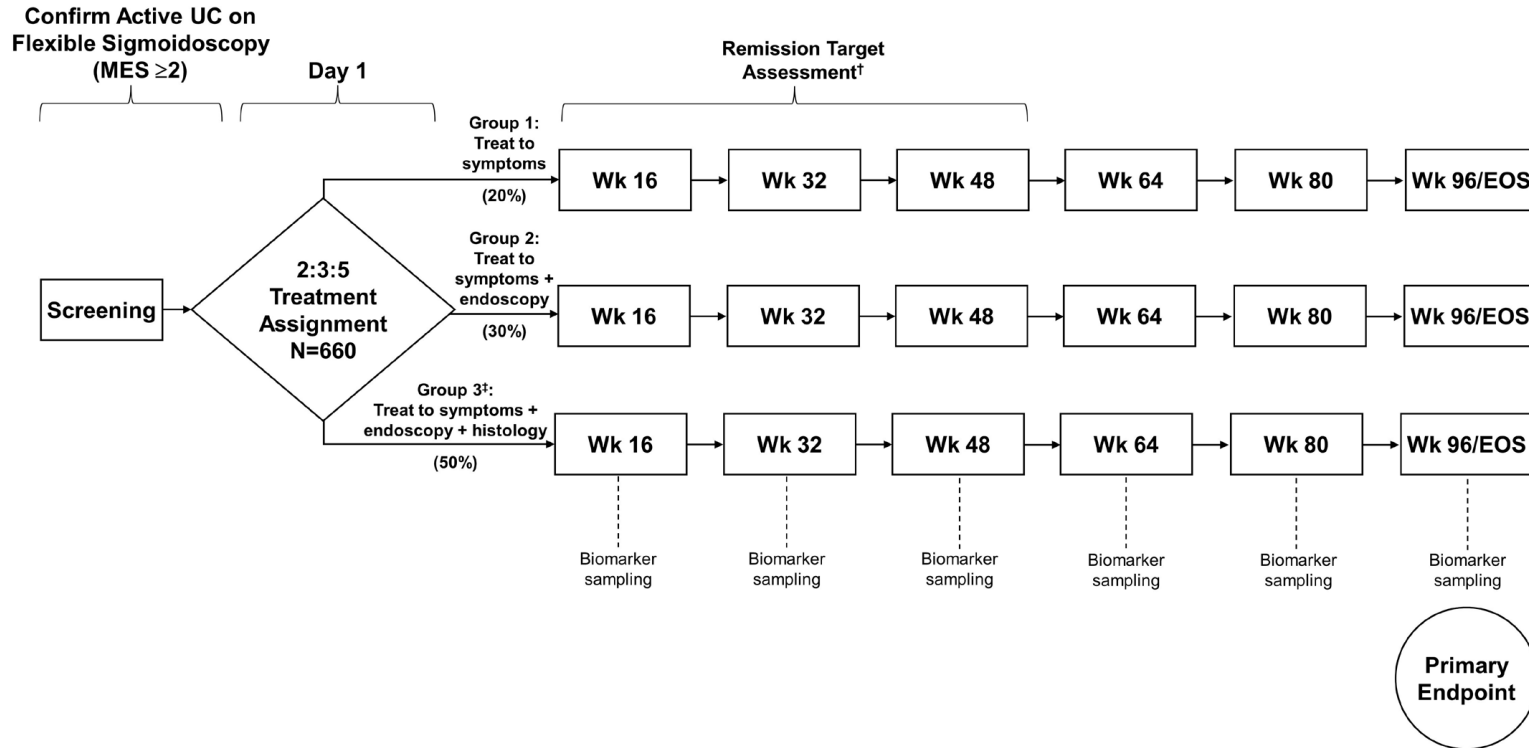
Determination of the Optimal Treatment Target in Ulcerative Colitis (VERDICT)

ClinicalTrials.gov ID ⓘ NCT04259138

Sponsor ⓘ Alimentiv Inc.

Information provided by ⓘ Alimentiv Inc. (Responsible Party)

Last Update Posted ⓘ 2024-02-22



Difference in Time to UC-related Complication Between Treatment Target Groups 1 and 3 [Time Frame: From date of treatment target achievement until date of first UC-related complication until end of study (Week 96)]

Conclusions

In CD early treatment with effective drugs reduces long term complication and may enhance treatment response

CD patients with high risk characteristics should be treated early

In UC there is currently no evidence that early escalation to advanced treatment is of benefit

Still achievement of stringent treatment goal is mandatory

