# POST-DDW
# MALADIES INFLAMMATOIRES INTESTINALES

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Professeure agrégée
CIUSSS de l'Estrie-CHUS

# Conflits d’intérêts potentiels

| Nature des relations | Nom de l’organisation à but lucratif ou sans but lucratif |
|---|---|
| Les paiements directs incluant les honoraires | Abbvie, Janssen, Takeda, Eli Lilly, Sandoz, Amgen, Pfizer, Pendopharm, Celltrion |
| La participation à des comités consultatifs ou des bureaux de conférenciers | Abbvie, Janssen, Takeda, Eli Lilly, Sandoz, Amgen, Pfizer, Pendopharm, Celltrion |
| Le financement de subventions ou d’essais cliniques | |
| Les brevets sur un médicament, un produit ou un appareil | |
| Tout autre investissement ou toute autre relation qu’un participant raisonnable et bien informé pourrait considérer comme un facteur d’influence sur le contenu de l’activité éducative | |

# COMPÉTENCES CANMEDS


| | |
|---|---|
| X | **Expert médical** (En tant qu'experts médicaux, les médecins assument tous les rôles CanMEDS et s'appuient sur leur savoir médical, leurs compétences cliniques et leurs attitudes professionnelles pour dispenser des soins de grande qualité et sécuritaires centrés sur les besoins du patient. Pivot du référentiel CanMEDS, le rôle d'expert médical définit le champ de pratique clinique des médecins .) |
| | **Communicateur** (En tant que communicateurs, les médecins développent des relations professionnelles avec le patient et ses proches ce qui permet l'échange d'informations essentielles à la prestation de soins de qualité.) |
| | **Collaborateur** (En tant que collaborateurs, les médecins travaillent efficacement avec d'autres professionnels de la santé pour prodiguer des soins sécuritaires et de grande qualité centrés sur les besoins du patient.) |
| X | **Leader** (En tant que leaders, les médecins veillent à assurer l'excellence des soins, à titre de cliniciens, d'administrateurs, d'érudits ou d'enseignants et contribuent ainsi, avec d'autres intervenants, à l'évolution d'un système de santé de grande qualité.) |
| X | **Promoteur de santé** (En tant que promoteurs de la santé, les médecins mettent à profit leur expertise et leur influence en oeuvrant avec des collectivités ou des populations de patients en vue d'améliorer la santé. Ils collaborent avec ceux qu'ils servent afin d'établir et de comprendre leurs besoins, d'être si nécessaire leur porte-parole, et de soutenir l'allocation des ressources<br>permettant de procéder à un changement.) |
| X | **Érudit** (En tant qu'érudits, les médecins font preuve d'un engagement constant envers l'excellence dans la pratique médicale par un processus de formation continue, en enseignant à des tiers, en évaluant les données probantes et en contribuant à l'avancement de la science.) |
| X | **Professionnel** (En tant que professionnels, les médecins ont le devoir de promouvoir et de protéger la santé et le bien-être d'autrui, tant sur le plan individuel que collectif. Ils doivent exercer leur profession selon les normes médicales actuelles, en respectant les codes de conduite quant aux comportements qui sont exigés d'eux, tout en étant responsables envers la profession et la société. De plus, les médecins contribuent à l'autoréglementation de la profession et voient au maintien de leur santé.) |

# SCÉNARIOS SPÉCIFIQUES

Grossesse

Maladie fistulisante périanale

Utilisation concomitante de GLP-1

# 96 - PREGNANCY AND EARLY CHILDHOOD OUTCOMES AFTER IN UTERO EXPOSURE TO JAK INHIBITORS IN WOMEN WITH IBD: A GLOBAL MULTICENTER COHORT STUDY

11:30 a.m. - 11:45 a.m. HAE

samedi, mai 2, 2026

# 96 - PREGNANCY AND EARLY CHILDHOOD OUTCOMES AFTER IN UTERO EXPOSURE TO JAK INHIBITORS IN WOMEN WITH IBD: A GLOBAL MULTICENTER COHORT STUDY

11:30 a.m. - 11:45 a.m. HAE

samedi, mai 2, 2026

## Contexte

- Données humaines limitées sans clair signal en faveur d'anomalies congénitales ni de fausses couches.
- Majorité des données en provenance de mères qui ont arrêté l'inhibiteur de JAK en T1
- L'impact d'une exposition in utero continue sur les différentes issues (grossesse, enfant à naître, réponse à la vaccination, etc…) demeure incertain

## Méthode

- Étude observationnelle multicentrique rétrospective internationale (25 centres, 17 pays)
- Appel ouvert (ECCO Newsletter), endossé par ECCO Confer
- RedCap:
  - Activité de la maladie
  - Issues enfant-mère
  - Anomalies congénitales
  - Réponse vaccinale
  - Développement de l'enfant

# 96 - PREGNANCY AND EARLY CHILDHOOD OUTCOMES AFTER IN UTERO EXPOSURE TO JAK INHIBITORS IN WOMEN WITH IBD: A GLOBAL MULTICENTER COHORT STUDY

11:30 a.m. - 11:45 a.m. HAE

samedi, mai 2, 2026

## Baseline Characteristics

*58 JAKi exposed pregnancies*

| | | |
|---|---|---|
| **Type of IBD** | | |
| • Crohn's disease, n (%) | 5 | (8.6) |
| • Ulcerative colitis/U-IBD, n (%) | 53 | (91.4) |
| Maternal age, median (range) | 32 | (22-43) |
| Previous number of biologics prior to initiation of a JAKi, median (range) | 2 | (0-5) |
| Unplanned pregnancy, n (%) | 23 | (39.7) |
| Maternal BMI prior to pregnancy, median (range) | 22.7 | (17.5-53.1) |
| **Type of JAKi** | | |
| • Tofacitinib (5 mg or 10 mg BID), n (%) | 38 | (65.5) |
| • Upadacitinib (30 or 45 mg daily), n (%) | 18 | (31.0) |
| • Filgotinib, (200 mg daily) n (%) | 2 | (3.5) |
| **Concomitant steroids** | | |
| • Systemic prednisolone, n (%) | 18 | (31.0) |
| • Budesonide MMX, n (%) | 4 | (6.9) |
| Smoking, n (%) | 1 | (1.7) |
| Folic acid in pregnancy, n (%) | 39 | (67.3) |

**Tofacitinib, n=38**
- *5 mg BID or 10 mg BID*
- 26 (**68%**) received treatment **throughout pregnancy**
- 12 discontinued in pregnancy at median GW 7 (Range 5-31)

**Upadaticinib, n=18**
- *30 mg daily or 45 mg daily*
- 12 (**80%**) received treatment **throughout pregnancy**
- 3 discontinued in pregnancy at median GW 6 (Range 3-6)

**Filgotinib, n=2**
- *200 mg daily*
- 1 received treatment throughout pregnancy
- 1 discontinued in pregnancy at GW 11

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11:30 a.m. - 11:45 a.m. HAE

samedi, mai 2, 2026

## Issues maternelles

- 32 (55.2%) had active disease in pregnancy
- 10 (17.3%) initiated JAKi in pregnancy (Tofa n=3 & UPA n=7)
  - Trimester: 1st (n=1, GW 9); 2nd (n=5, GW 13-28); 3rd (n=4, GW 30-35)
- 39 (67.2%) received treatment with the JAKi through all 3 trimesters
- Of 19 (32.8%) that discontinued JAKi, 11 (57.9%) had a disease flare

**Overall, low risk of maternal complications**

- No DVT, no pre-eclampsia
- 4 (6.9%) with gestational diabetes
- 4 (6.9%) PROM (gestational age 34-37)
- 5 (8.6%) hospitalization due to infection
- 1 (1.7%) colectomy with ileostomy at GW 28

## Issues de grossesse et de l'enfant à naître

| | | |
|---|---|---|
| Spontaneous abortions, *n (%)* | 5 | (8.6) |
| Induced abortions, *n (%)* | 6 | (10.3) |
| Live born infants, *n (%)* | 47 | (81.1) |
| Median (IQR) gestational week for delivery | 40 | (38-41) |
| Cesarean section | 24 | (41.4) |
| • Elective CS | 16 | (66.6) |
| • Emergency CS | 8 | (33.3) |
| Median (IQR) birth weight | 3050 | (2870-3410) |
| Congenital abnormalities | 0 | - |
| Preterm | 2 | (3.4) |
| APGAR < 7 at 5 minutes, *n (%)* | 2 | (3.4) |
| Small for Gestational Age (SGA) | 4 | (6.9) |
| Low Birth Weight (≤ 2500 gram) | 6 | (10.3) |

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45 infants, median follow-up 15 months (range 1–92)

Of those women that breastfed (34; 75.6%), **10/34 (29.4%)** continued JAKi

2 infants (3.9%) hospitalized for infection; IV antibiotics, no sequelae

- Omphilitis (newborn) Term GW 41
  - UPA 30 mg (GW8 ->15 mg)
  - Flare week 30: steroids GW 30-37.
- Suspected sepsis due to neutropenia (birth & day 13). Term GW39
  - UPA 45 GW28 until birth GW 39
  - Flare GW 29. Steroids GW 29-37

Normal development in all infants

**No adverse effect with inactive and live vaccines**, including

- 8 (17.7%) who received the **BCG vaccine ~ 1 month of age**
- 14 (31.1%) who received the Rotavirus vaccine ~ 1.5-6 months of age
- 17 (37.8%) who received the MMR vaccine ~ ≥ 12 months of age

No malignancies observed

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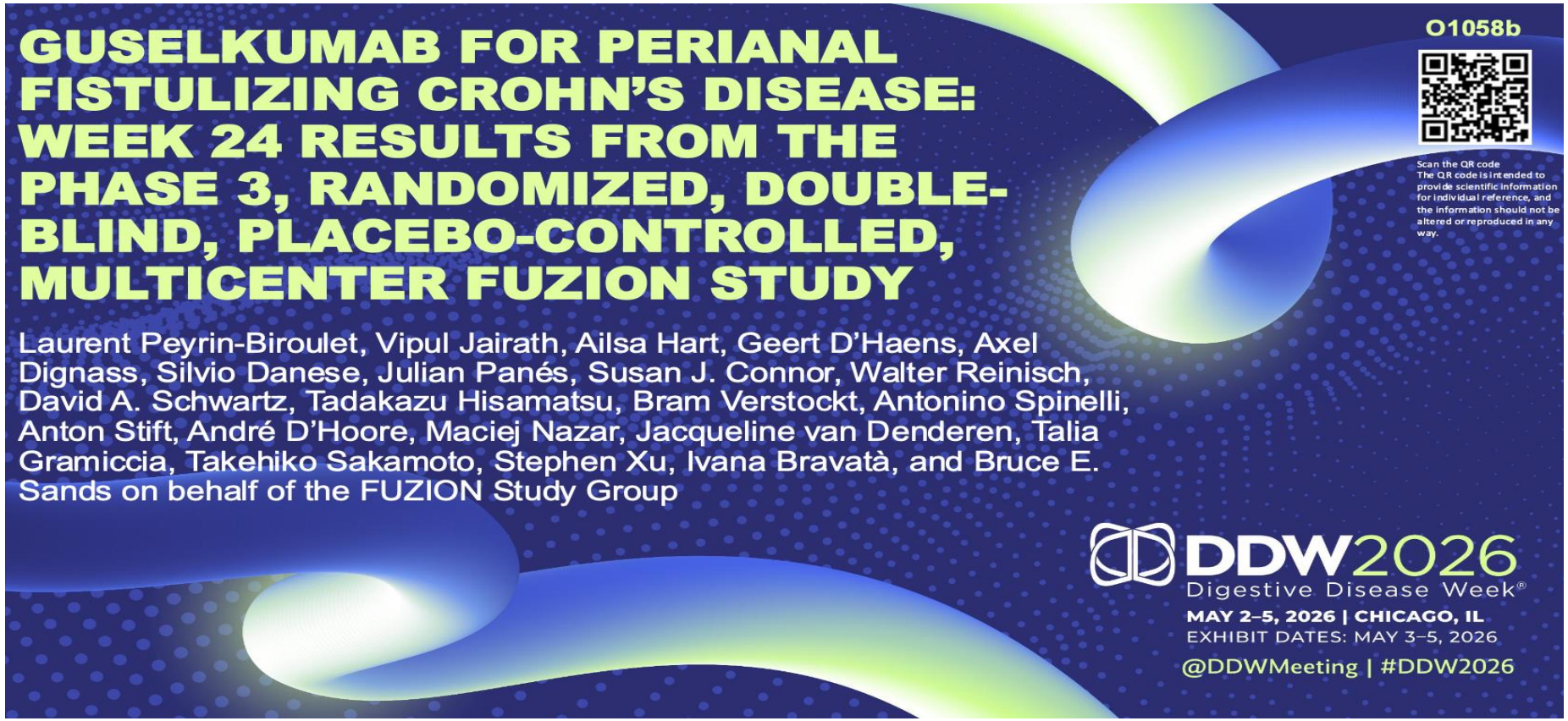
Conclusions

- Le maintien de la rémission en grossesse est le meilleur gage d'issues favorables en grossesse
- L'utilisation d'un JAKi peut être considérée si et seulement si aucune autre option viable est disponible pour la santé de la mère
- Importance d'une décision éclairée et partagée
- Aucun signal adverse de complications maternelles, d'issues défavorables de grossesse, de risque d'infection, de développement ou de réponse vaccinale défavorable mais peu de recul
- Si vous avez des cas : mjn@clin.au.dk

# GUSELKUMAB FOR PERIANAL FISTULIZING CROHN'S DISEASE: WEEK 24 RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER FUZION STUDY

11:45 a.m. - 12:00 p.m. HAE

mardi, mai 5, 2026



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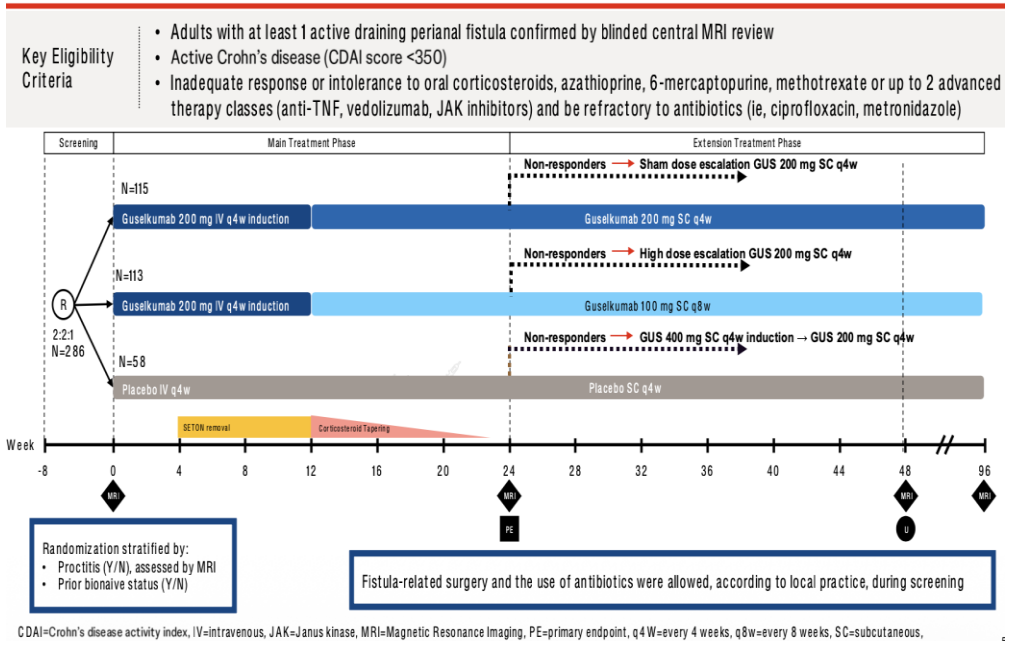
## Design

### Phase 3, Double-Blind, Treat-Through Study




CDAI=Crohn's disease activity index, IV=intravenous, JAK=Janus kinase, MRI=Magnetic Resonance Imaging, PE=primary endpoint, q4W=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous,

## Issues semaine 24

### Endpoints through Week 24*

| Primary Endpoint* | Multiplicity-Controlled Secondary Endpoints* | Key Secondary Endpoints |
|---|---|---|
| Combined fistula remission at week 24 (clinically and radiologically assessed) | • Clinically assessed fistula remission at week 24<br>• Clinically assessed fistula response at week 24 | • Clinically assessed fistula response at week 12 |

| Assessment Type | Outcome | Definition |
|---|---|---|
| Clinical | Clinically assessed fistula remission | 100% closure of all treated external openings, without development of new fistulas or abscesses and without any drainage by the external openings, occurring spontaneously or after gentle finger compression |
| | Clinically assessed fistula response | ≥50% reduction from baseline in number of open or draining perianal fistulas |
| Radiological | Absence of collections >2cm | Absence of collections >2 cm of the perianal fistulas, confirmed by a blinded central review of the MRI results |

*In the statistical testing procedure, guselkumab 200 mg q4w dose then the 100 mg q8w dose were sequentially tested versus placebo for the primary endpoint then for the multiplicity-controlled secondary endpoints.

# GUSELKUMAB FOR PERIANAL FISTULIZING CROHN'S DISEASE: WEEK 24 RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER FUZION STUDY

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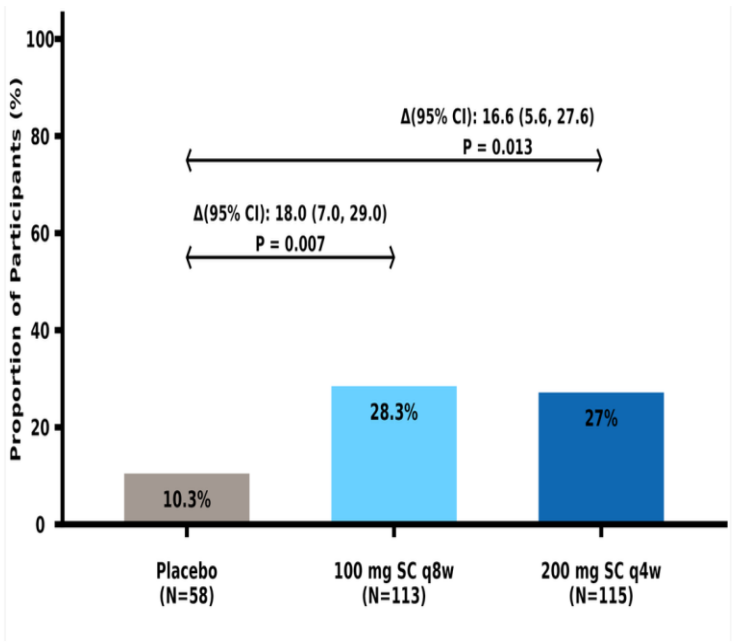
## Combined Fistula Remission at Week 24

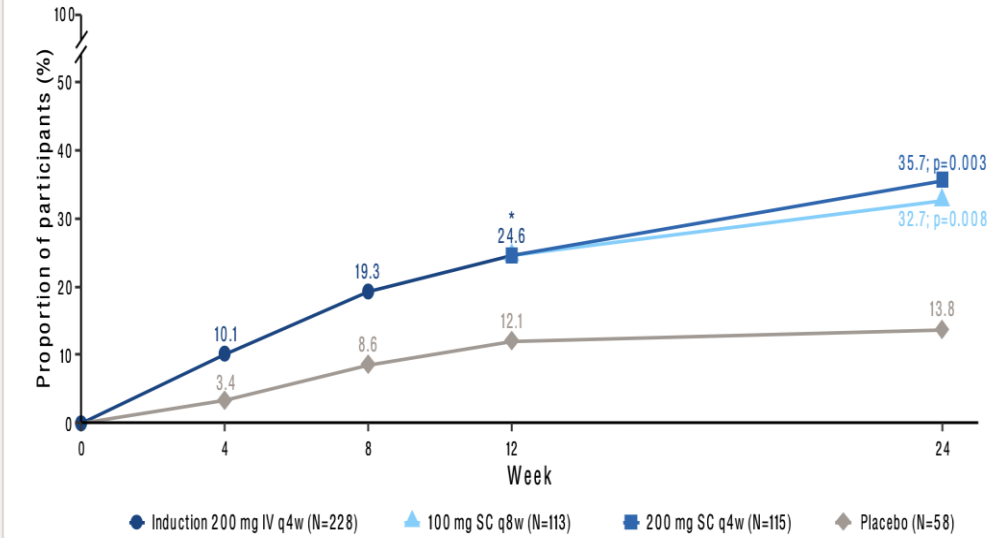
### Primary Endpoint




Combined Fistula Remission: 100% closure of all treated external openings, without development of new fistulas or abscesses and without any drainage by the external openings, occurring spontaneously or after gentle finger compression AND absence of collections >2 cm of the perianal fistulas, confirmed by a blinded central review of the MRI results

## Clinically Assessed Fistula Response through Week 24

### Guselkumab showed meaningful difference versus placebo during induction




Clinically Assessed Fistula Response: ≥50% reduction from baseline in number of open or draining perianal fistulas

*Nominal p=0.041

Missing Data Imputation: After applying the ICE strategy, missing data were imputed as not having achieved a combined fistula remission at Week 24. The adjusted risk difference and CI were based on Wald statistics using Mantel-Haenszel stratum weights stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no). The p-values are based on the CMH test, stratified by baseline proctitis (yes, no) and baseline bio-naïve status (yes, no). CI=confidence interval, CMH=Cochran-Mantel-Haenszel, ICE=intercurrent event, IV=intravenous, MRI=magnetic resonance imaging, q4w=every 4 weeks, q8w=every 8 weeks, SC=subcutaneous.

# GUSELKUMAB FOR PERIANAL FISTULIZING CROHN'S DISEASE: WEEK 24 RESULTS FROM THE PHASE 3, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER FUZION STUDY

11:45 a.m. - 12:00 p.m. HAE

mardi, mai 5, 2026

## Conclusions

- FUZION est une étude de phase 3 internationale évaluant une issue primaire combinant la clinique et l'imagerie par IRM
- Guselkumab démontré efficace à 24 semaines chez une population bio-naïve et bio-exposée avec un Crohn périanal vs pbo
- Aucun nouveau signal d'innocuité

# 624 - GLP-1 RECEPTOR AGONISTS REDUCE LONG-TERM STEROID, BIOLOGIC, AND ACUTE CARE UTILIZATION IN ULCERATIVE COLITIS AND CROHN'S DISEASE: A 5-YEAR TRINETX STUDY WITH LANDMARK ANALYSIS

9:00 a.m. - 9:15 a.m. HAE

lundi, mai 4, 2026

# 624 - GLP-1 RECEPTOR AGONISTS REDUCE LONG-TERM STEROID, BIOLOGIC, AND ACUTE CARE UTILIZATION IN ULCERATIVE COLITIS AND CROHN'S DISEASE: A 5-YEAR TRINETX STUDY WITH LANDMARK ANALYSIS

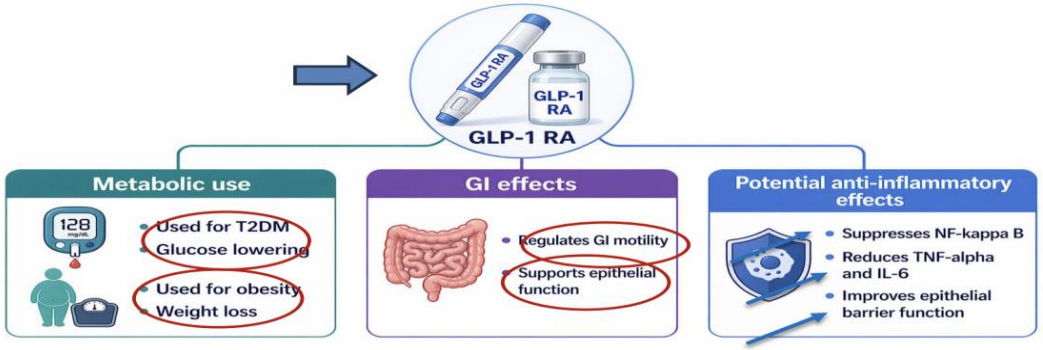
9:00 a.m. - 9:15 a.m. HAE
lundi, mai 4, 2026

## Contexte

- Études récentes suggérant que les agonistes GLP-1 peuvent être associés à certaines issues favorables chez les patients MII
- Données provenant de cohortes limitées
- Efficacité pour la perte de poids chez nos patients avec MII pour qui des conditions métaboliques peuvent coexister

## Objectif

- Large cohorte real-world
- Évaluer l'association entre l'utilisation de GLP-1 et certaines issues MII avec un focus particulier sur l'innocuité et les marqueurs de progression de la maladie



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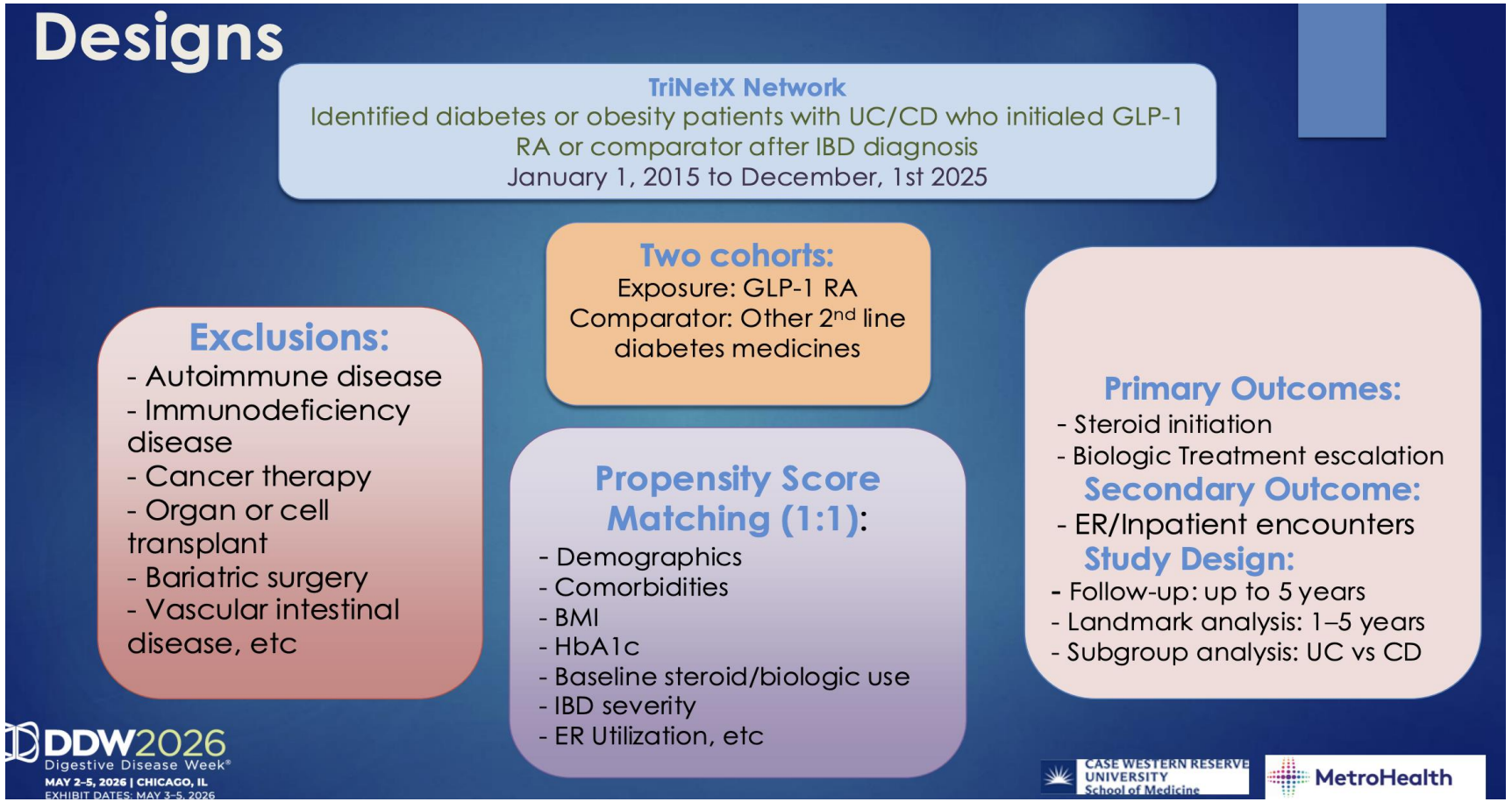

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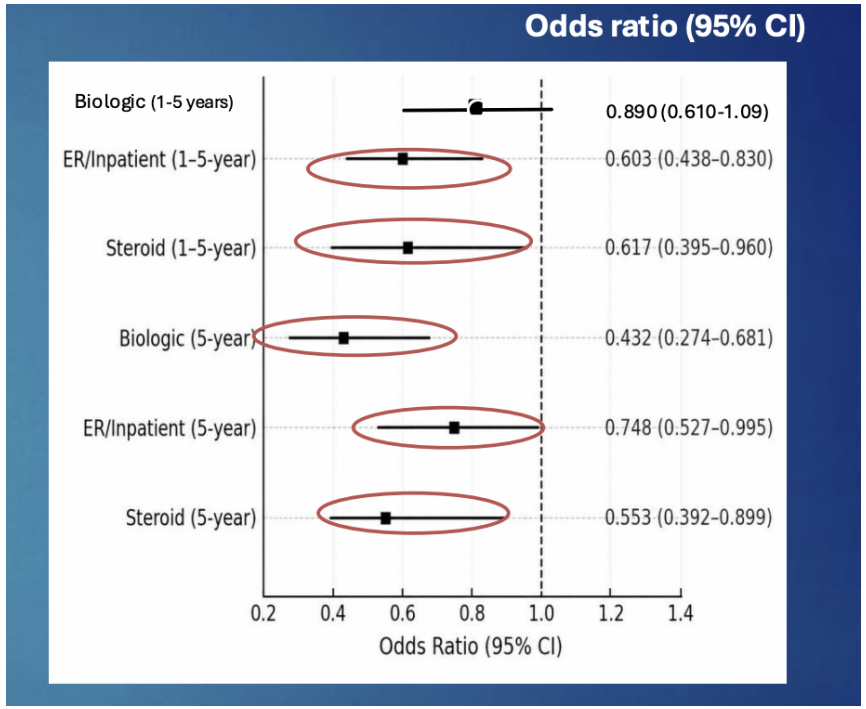
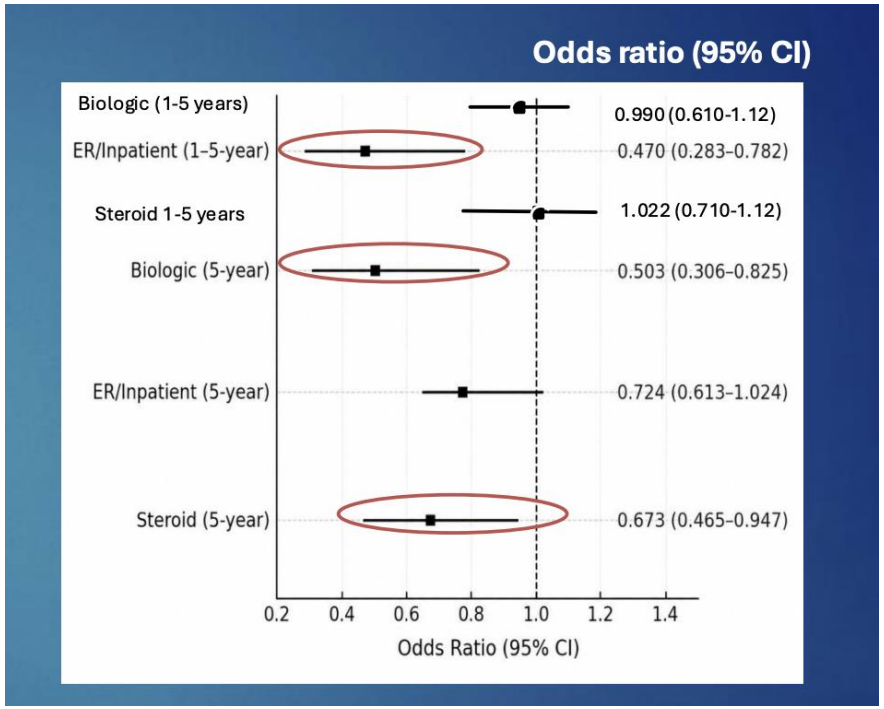
## Colite ulcéreuse




## Crohn



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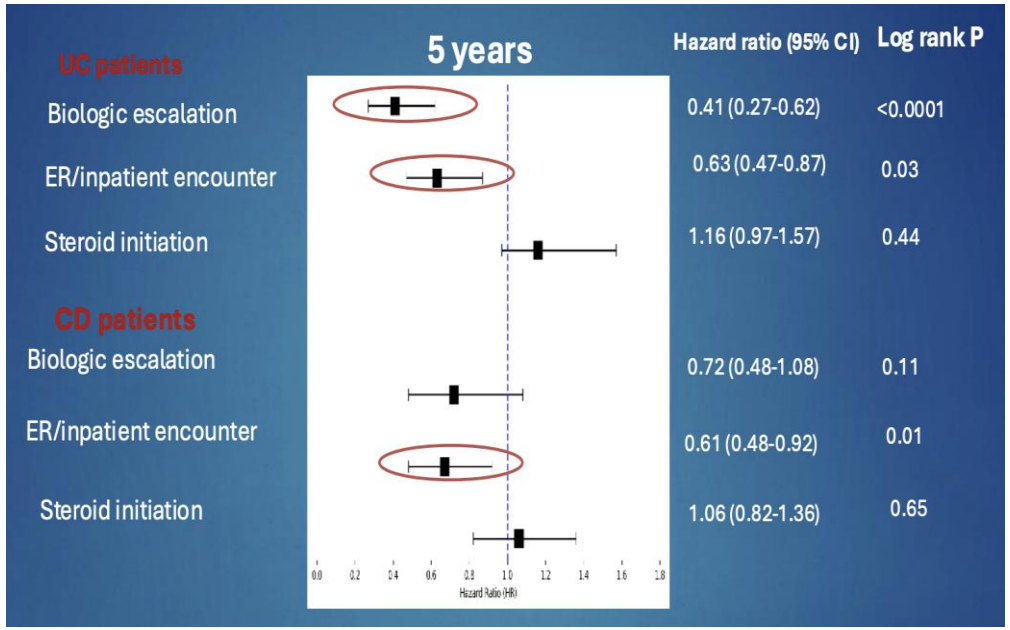



## Conclusions

- GLP-1 associés à des issues favorables chez les patients MII ayant des comorbidités métaboliques, particulièrement en colite ulcéreuse
- Études prospectives requises afin de déterminer si les GLP-1 peuvent modifier le cours de la MII
- Pas de signal d'innocuité

# THÉRAPEUTIQUE

Efficacité comparative

Combinaison

Nouveautés d'intérêt

# 538 - COMPARATIVE EFFECTIVENESS OF JAK INHIBITORS VERSUS IL-23 INHIBITORS IN USTEKINUMAB FAILURES IN MODERATE-TO-SEVERE CROHN'S DISEASE

5:45 p.m. - 6:00 p.m. HAE

dimanche, mai 3, 2026

Mass General Brigham

# Comparative Effectiveness of JAK Inhibitors Versus Il-23 Inhibitors in Ustekinumab Failures in Moderate-to-Severe Crohn's Disease: A COMPARE-IBD Study

**Maryam K Ibrahim**, Wasuwit Wanchaitanawong, Ryan Stidham, Nisha Mathur, Benjamin Click, Manasi Agrawal, Adam S. Faye, Siddharth Singh, Ashwin Ananthakrishnan

# 538 - COMPARATIVE EFFECTIVENESS OF JAK INHIBITORS VERSUS IL-23 INHIBITORS IN USTEKINUMAB FAILURES IN MODERATE-TO-SEVERE CROHN'S DISEASE

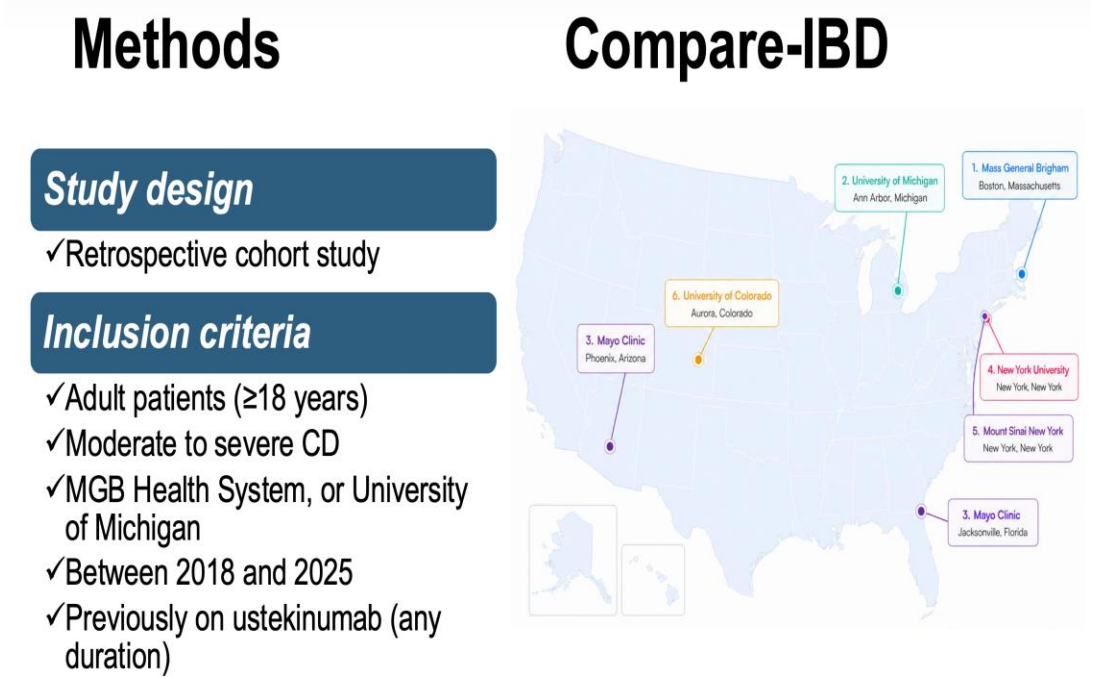
5:45 p.m. - 6:00 p.m. HAE

dimanche, mai 3, 2026

## Objectif

Évaluer l'efficacité comparative JAKi vs IL23i en termes de rémission clinique à 3 et 12 mois et la rémission endoscopique chez les pts avec Crohn modéré à sévère précédemment exposés à l'ustekinumab

## Étude de cohorte rétrospective



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5:45 p.m. - 6:00 p.m. HAE

dimanche, mai 3, 2026

## Primary Outcome

- Steroid-free clinical remission at **3 months**
- Defined by:
  - Physician's global assessment of clinical remission (clinical symptoms, physical exam, inflammatory biomarkers, radiology) OR
  - CDAI score <150 OR
  - HBI <5
  - AND no use of oral corticosteroids at assessment

## Secondary Outcomes

- Steroid-free clinical remission at **12 months**
- Endoscopic remission on post-treatment endoscopy
  - Defined by:
    - Normal endoscopy (absence of any endoscopic evidence of inflammation) OR
    - SES-CD 0-2

# 538 - COMPARATIVE EFFECTIVENESS OF JAK INHIBITORS VERSUS IL-23 INHIBITORS IN USTEKINUMAB FAILURES IN MODERATE-TO-SEVERE CROHN'S DISEASE

5:45 p.m. - 6:00 p.m. HAE

dimanche, mai 3, 2026

N=430

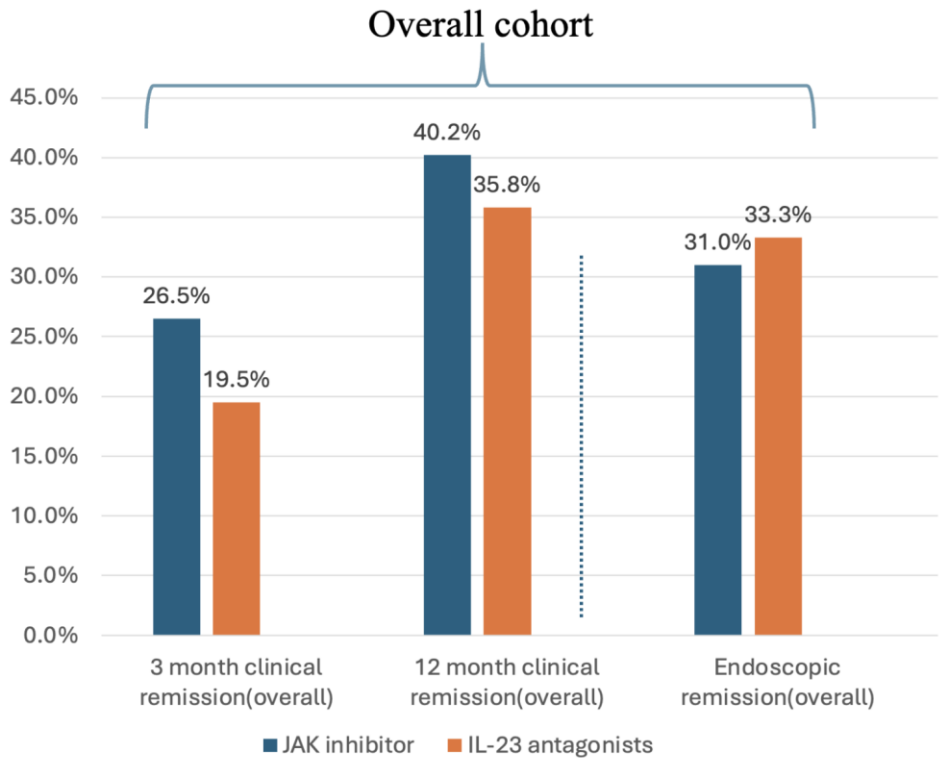



**Table 2: Comparison of JAK inhibitors and IL-23 antagonists on achieving clinical and endoscopic outcomes using stabilized IPTW models**

| Outcome | IPTW-OR (JAK-inhibitor vs IL-23) [95% CI] † | p-value |
|---|---|---|
| Clinical remission at 3 months | 1.58 [0.97, 2.6] | 0.066 |
| Clinical remission at 12 months | 1.57[0.99,2.48] | 0.055 |
| Endoscopic remission | 0.87 [0.5, 1.5] | 0.6 |

† Stabilized IPTW-weighted model using age, sex, race, smoking, disease location, disease phenotype, perianal disease, disease duration, history of IBD surgery, prior TNF, prior vedolizumab, steroid at baseline, study site, reason for stopping ustekinumab, escalation of ustekinumab dose

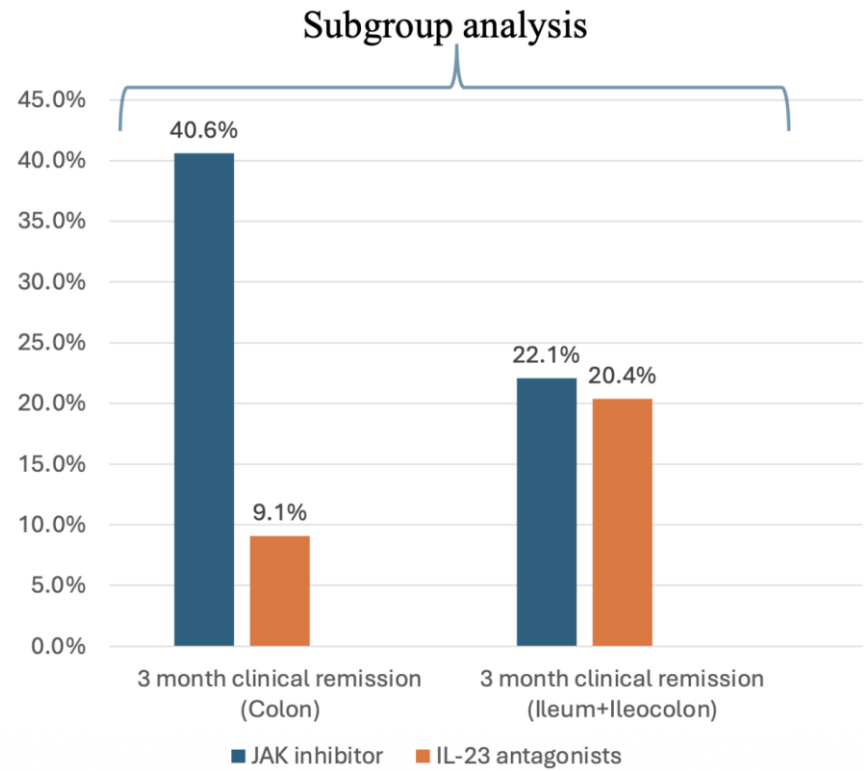
# 538 - COMPARATIVE EFFECTIVENESS OF JAK INHIBITORS VERSUS IL-23 INHIBITORS IN USTEKINUMAB FAILURES IN MODERATE-TO-SEVERE CROHN'S DISEASE

5:45 p.m. - 6:00 p.m. HAE

dimanche, mai 3, 2026

| Outcome | Variable | | No. of patients | OR (JAK-inhibitor vs IL-23) [95% CI] † | p-interaction |
|---|---|---|---|---|---|
| Clinical remission at 3 months | Disease location | L2(colon) | 76 | 9.2 [2.5, 34.3] | 0.004 |
| | | L1 (Ileum)+L3 (Ileocolon) | 354 | 1.1[0.64, 1.91] | |
| | Disease phenotype | Inflammatory (B1) | 107 | 2.1 [0.85, 5.17] | 0.42 |
| | | Complicated phenotype (B2/B3) | 323 | 1.3[0.75, 2.41] | |
| | History of IBD surgery | Yes | 228 | 1.1[0.53, 2.11] | 0.093 |
| | | No | 202 | 2.5[1.2, 5.0] | |
| | Reason for stopping ustekinumab | Loss of efficacy | 371 | 1.8[1.1, 3.1] | 0.190 |
| | | Other* | 59 | 0.74[0.22, 2.58] | |
| | Escalation of ustekinumab dose | Yes | 323 | 1.6[0.89, 2.87] | 0.91 |
| | | No | 107 | 1.5[0.62, 3.65] | |
| | Steroid at baseline | Yes | 148 | 1.5[0.62, 3.57] | 0.87 |
| | | No | 282 | 1.6[0.9, 2.9] | |
| | Site | Mass General Brigham | 334 | 1.6[0.91, 2.70] | 0.95 |
| | | University of Michigan | 96 | 1.6[0.54, 4.94] | |

† Propensity score model with IPTW stabilized weights using age, sex, race, smoking, disease location, disease phenotype, perianal disease, disease duration, history of IBD surgery, prior TNF, prior vedolizumab, steroid at baseline, study site, reason for stopping ustekinumab, escalation of ustekinumab dose



# 538 - COMPARATIVE EFFECTIVENESS OF JAK INHIBITORS VERSUS IL-23 INHIBITORS IN USTEKINUMAB FAILURES IN MODERATE-TO-SEVERE CROHN'S DISEASE

5:45 p.m. - 6:00 p.m. HAE

dimanche, mai 3, 2026

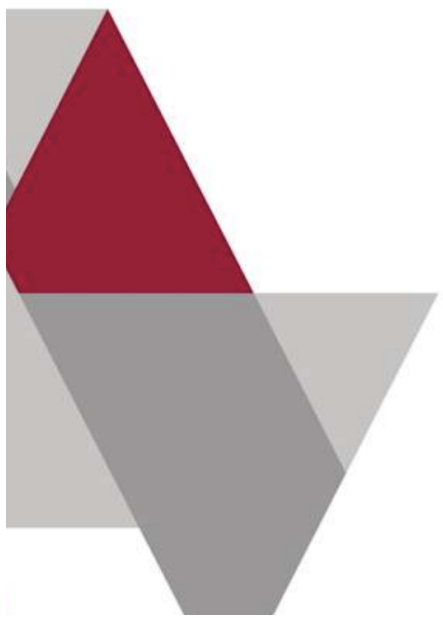
## Conclusions

- Tendance vers la supériorité des JAKi vs IL23i pour induire la rémission clinique à 3 et 12 moins chez les pts avec échec antérieur à l'ustekinumab
- Avantage en Crohn colique à favoriser les JAKi
- Toutefois, absence de différences au niveau des issues endoscopiques ce qui suggère que les 2 thérapies représentent des options adéquates après un échec à l'ustekinumab
- Nécessité d'obtenir d'autres études sans caractère rétrospectif

# REAL WORLD OUTCOMES OF UPADACITINIB COMPARED WITH USTEKINUMAB, RISANKIZUMAB, MIRIKIZUMAB, AND GUSELKUMAB AS SECOND-LINE THERAPY IN ULCERATIVE COLITIS AFTER INFLIXIMAB EXPOSURE

6:15 p.m. - 6:30 p.m. HAE

dimanche, mai 3, 2026



**Real-World Outcomes Of Upadacitinib Versus IL-23–Based Therapies as Second-Line Therapy in Ulcerative Colitis After Infliximab Exposure**

**Adalberto E Guzman, Lina AlQirem, Urveesh Sharma, Manesh Kumar Gangwani, Yash Shah*, Evelyn J Calderon Martinez, Mohammad Alomari**

University of Arkansas for Medical Sciences, Little Rock, AR
Cedars-Sinai Medical Center, Los Angeles, CA

**DDW — May 2026 | Oral Presentation**

UAMS
University of Arkansas for Medical Sciences

# REAL WORLD OUTCOMES OF UPADACITINIB COMPARED WITH USTEKINUMAB, RISANKIZUMAB, MIRIKIZUMAB, AND GUSELKUMAB AS SECOND-LINE THERAPY IN ULCERATIVE COLITIS AFTER INFLIXIMAB EXPOSURE

6:15 p.m. - 6:30 p.m. HAE

dimanche, mai 3, 2026

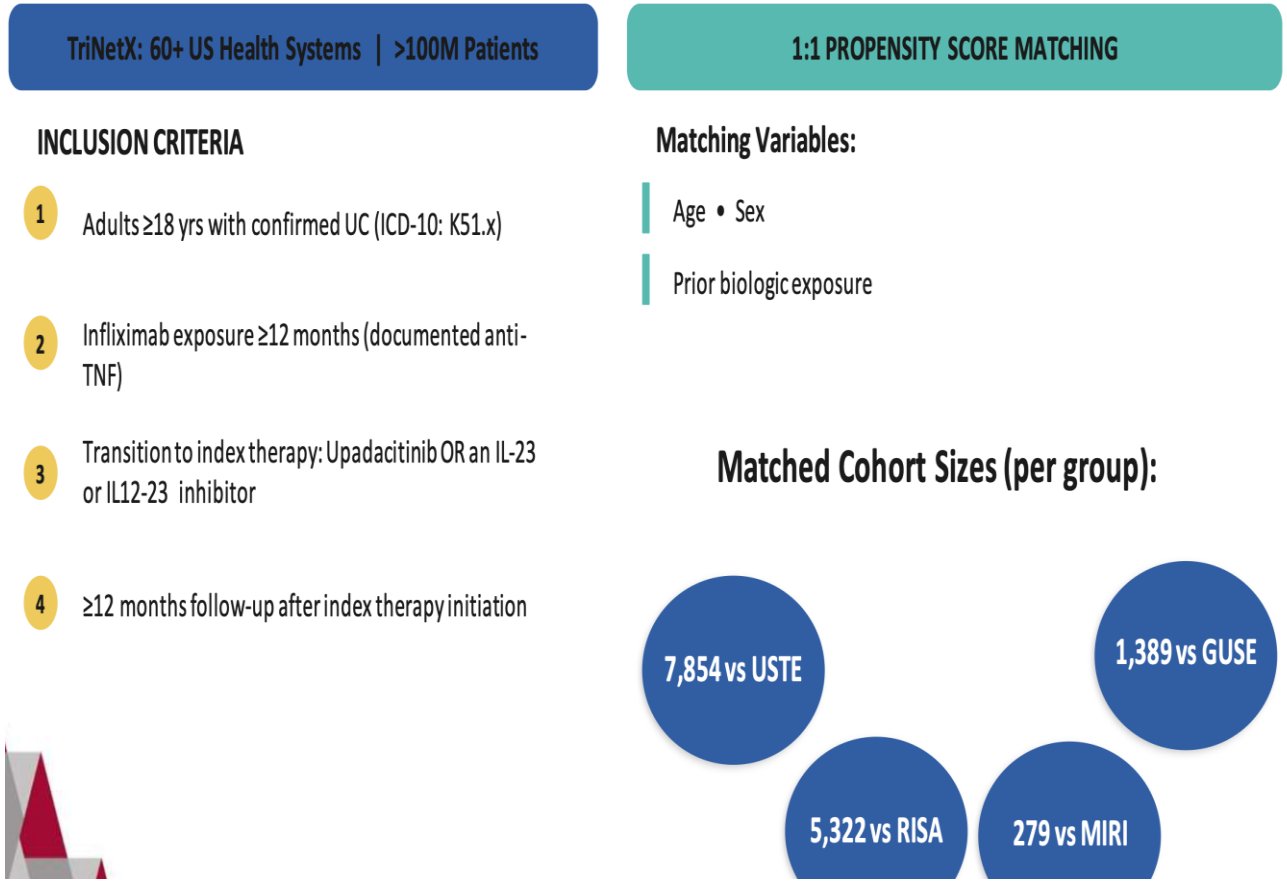
## Objectif

Comparer les issues à 12 mois

JAKi vs ustekinumab, risankizumab, mirikizumab, guselkumab

chez les patients avec CU

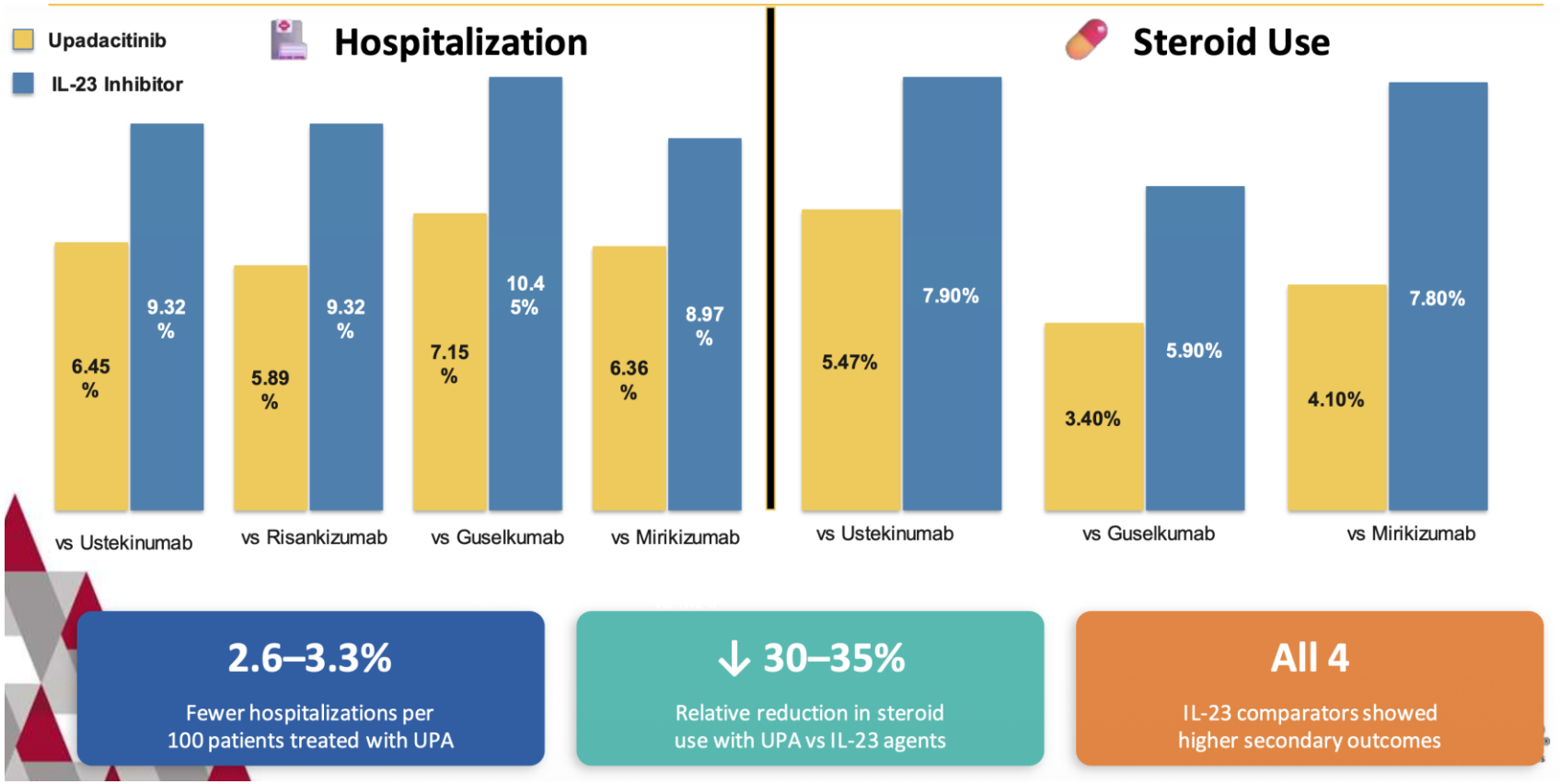
en utilisant le TriNetX Research Network



# REAL WORLD OUTCOMES OF UPADACITINIB COMPARED WITH USTEKINUMAB, RISANKIZUMAB, MIRIKIZUMAB, AND GUSELKUMAB AS SECOND-LINE THERAPY IN ULCERATIVE COLITIS AFTER INFLIXIMAB EXPOSURE

6:15 p.m. - 6:30 p.m. HAE

dimanche, mai 3, 2026



# REAL WORLD OUTCOMES OF UPADACITINIB COMPARED WITH USTEKINUMAB, RISANKIZUMAB, MIRIKIZUMAB, AND GUSELKUMAB AS SECOND-LINE THERAPY IN ULCERATIVE COLITIS AFTER INFLIXIMAB EXPOSURE

6:15 p.m. - 6:30 p.m. HAE

dimanche, mai 3, 2026

## RESULTS: Complete Outcome Summary

UPA vs Each IL-23 Inhibitor | 12-Month Follow-Up

| Outcome | vs UST (n=7,854) | | vs RISA (n=5,322) | | vs GUSE (n=1,181) | | vs MIRI (n=279) | | All Favor |
|---|---|---|---|---|---|---|---|---|---|
| | UPA | IL-23 | UPA | IL-23 | UPA | IL-23 | UPA | IL-23 | |
| Surgery | **1.45%** | 1.67% | **2.23%** | 3.57% | **1.39%** | 2.69% | **1.79%** | 3.99% | UPA ✓ |
| Steroid Use | **5.48%** | 7.90% | — | — | **3.4%** | 5.9% | **4.1%** | 7.8% | UPA ✓ |
| Hospitalization | **6.45%** | 9.32% | **5.89%** | 9.32% | **7.15%** | 10.5% | **6.36%** | 8.97% | UPA ✓ |
| Biomarkers (CRP >10, ESR >30, Fecal Calprotectin >150) | ↓ | ↑ | ↓ | ↑ | ↓ | ↑ | ↓ | ↑ | UPA ✓ |

*— = not reported for this comparison | ↓ = lower in UPA group | UPA values in gold; IL-23 in blue*

# REAL WORLD OUTCOMES OF UPADACITINIB COMPARED WITH USTEKINUMAB, RISANKIZUMAB, MIRIKIZUMAB, AND GUSELKUMAB AS SECOND-LINE THERAPY IN ULCERATIVE COLITIS AFTER INFLIXIMAB EXPOSURE

6:15 p.m. - 6:30 p.m. HAE

dimanche, mai 3, 2026


Conclusions

- Ces données comparatives supportent l'utilisation JAKi chez un pt avec CU réfractaire à un TNFi
- L'utilisation d'un IL23i ou IL12-23i demeure une option adéquate mais semble avoir des issues inférieures vs upadacitinib

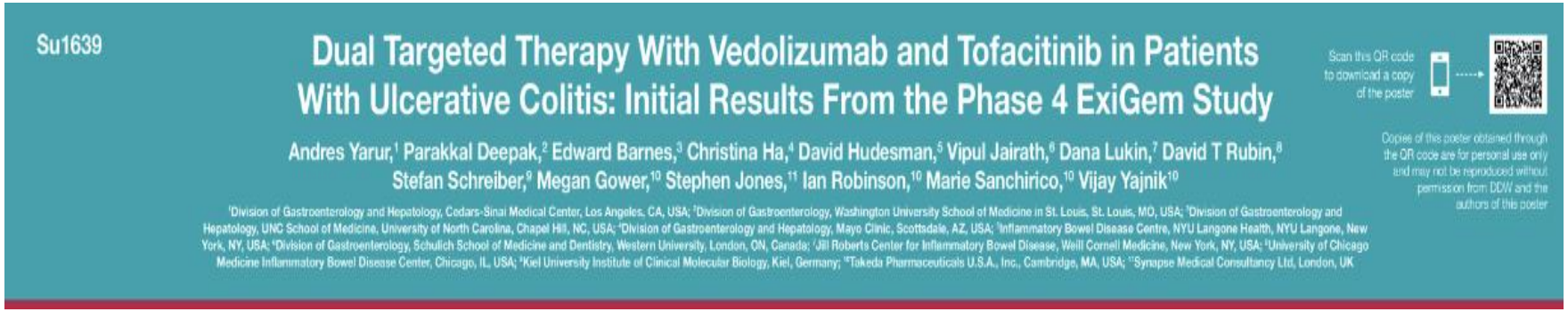
# COMBINAISON DE THÉRAPIES AVANCÉES (DAT)

Therapeutic Synergy of Combined IL-23 and JAK-I Inhibition in Difficult-To-Treat Crohn's Disease

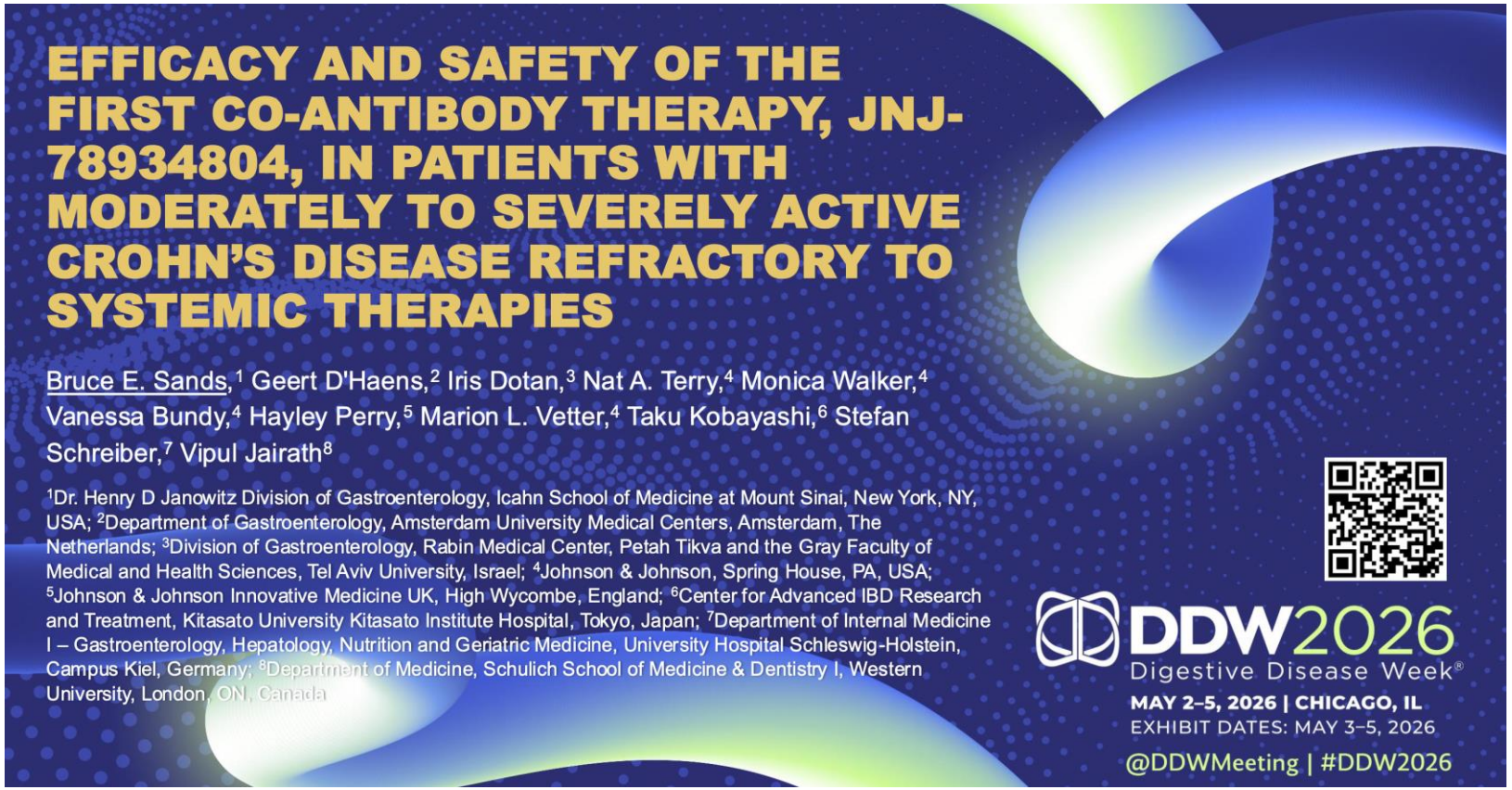
Patricia M. Hughes, Shouli Tung, Elizabeth A. Spencer, Marla C. Dubinsky

Department of Pediatrics, Susan and Leonard Feinstein IBD Clinical Center, Icahn School of Medicine at Mount Sinai, New York

Icahn School of Medicine at Mount Sinai

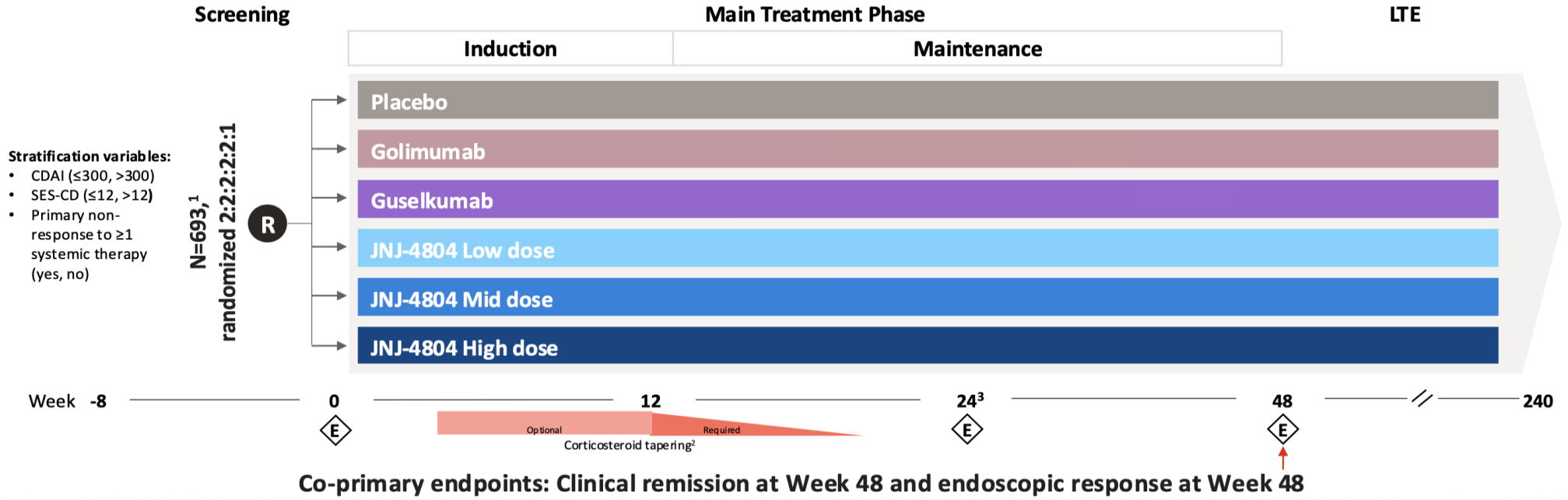


# COMBINAISON DE THÉRAPIES AVANCÉES (DAT)



# PHASE 2B DUET CD

- Moderately to severely active CD
- Inadequate response or intolerance to ≥1 systemic therapy mechanism (anti-TNF, IL-12/23, IL-23p19, integrin, or JAK inhibitors)
- Caps for prior systemic therapy mechanisms: 1 (50%), 2 (35%), >2 (15%)
- All study medications were administered subcutaneously




[1]Full Analysis Set.
[2]All participants taking corticosteroids at Week 0 could begin tapering as early as Week 4 but no later than Week 12.
[3]Patients who met inadequate response criteria, regardless of treatment assignment, received a JNJ-4804 regimen based on their initial study intervention group assignment.
***CD**=Crohn's disease, **CDAI**=Crohn's Disease Activity Index, **E**=endoscopy, **JAK**=Janus kinase, **LTE**=long-term extension, **R**=randomization, **SES-CD**=Simple Endoscopic Score for Crohn's Disease, **TNF**=tumor necrosis factor.*

# PHASE 2B DUET CD

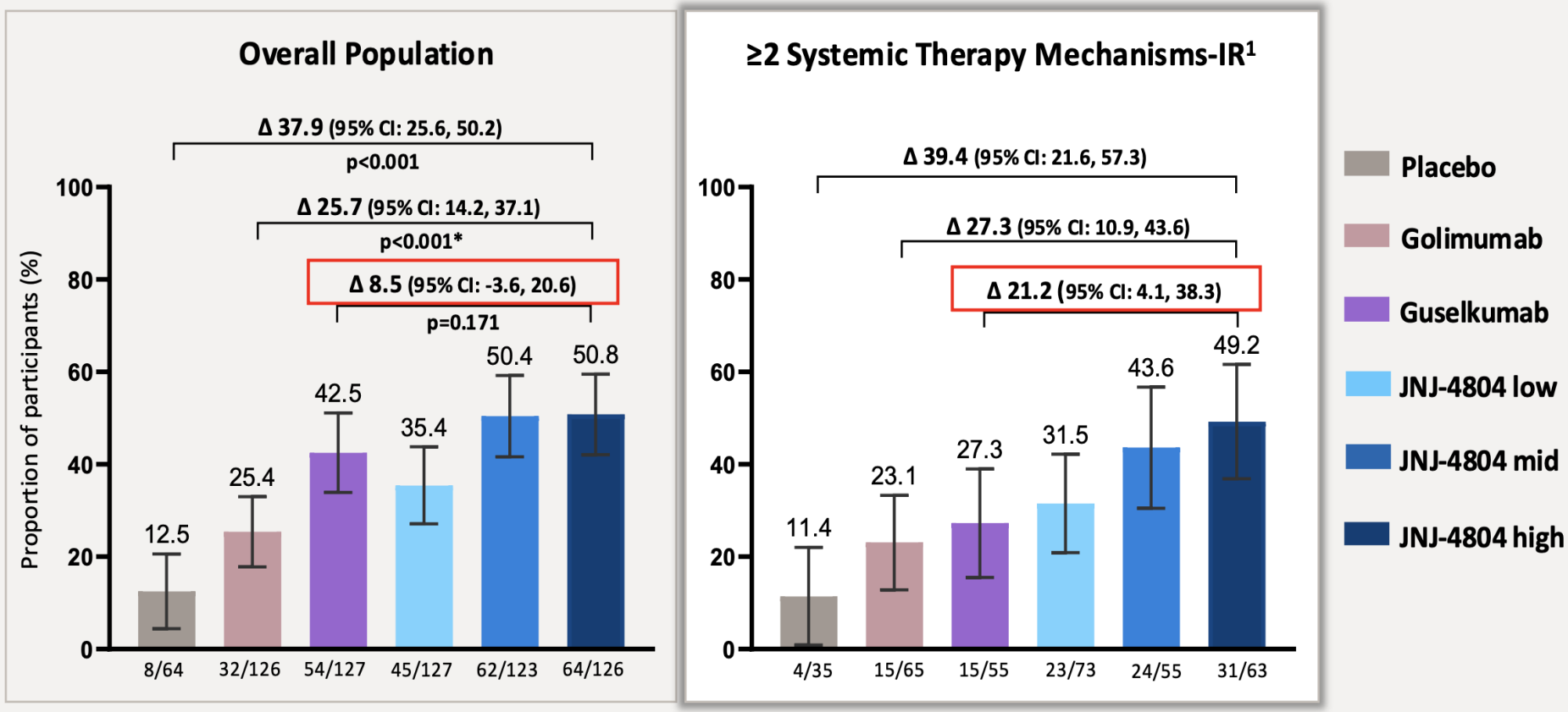
| | | Placebo | Golimumab | Guselkumab | JNJ-4804 Low dose | JNJ-4804 Mid dose | JNJ-4804 High dose | Total |
|---|---|---|---|---|---|---|---|---|
| **Analysis set, n** | | 64 | 126 | 127 | 127 | 123 | 126 | 693 |
| **Participants with inadequate response to 1 or more systemic therapy mechanisms[1], n (%)** | | | | | | | | |
| **Number of systemic therapy mechanisms - inadequate responders, n (%)[2]** | **1** | 29 (45.3%) | 61 (48.4%) | 72 (56.7%) | 53 (42.1%) | 68 (55.3%) | 63 (50.0%) | 346 (50.0%)[3] |
| | **≥2** | 35 (54.7%) | 65 (51.6%) | 55 (43.3%) | 73 (57.9%) | 55 (44.7%) | 63 (50.0%) | 346 (50.0%) |

History of inadequate response or intolerance by systemic therapy mechanism in the overall population

- Anti-TNF: 90% (82% of the 1 systemic therapy-IR subgroup)
- Anti-IL-12/23: 47% (8% of the 1 systemic therapy-IR subgroup)
- Anti-integrin: 26% (8% of the 1 systemic therapy-IR subgroup)
- JAK inhibitor: 3%
- Anti-IL-23p19: 3%

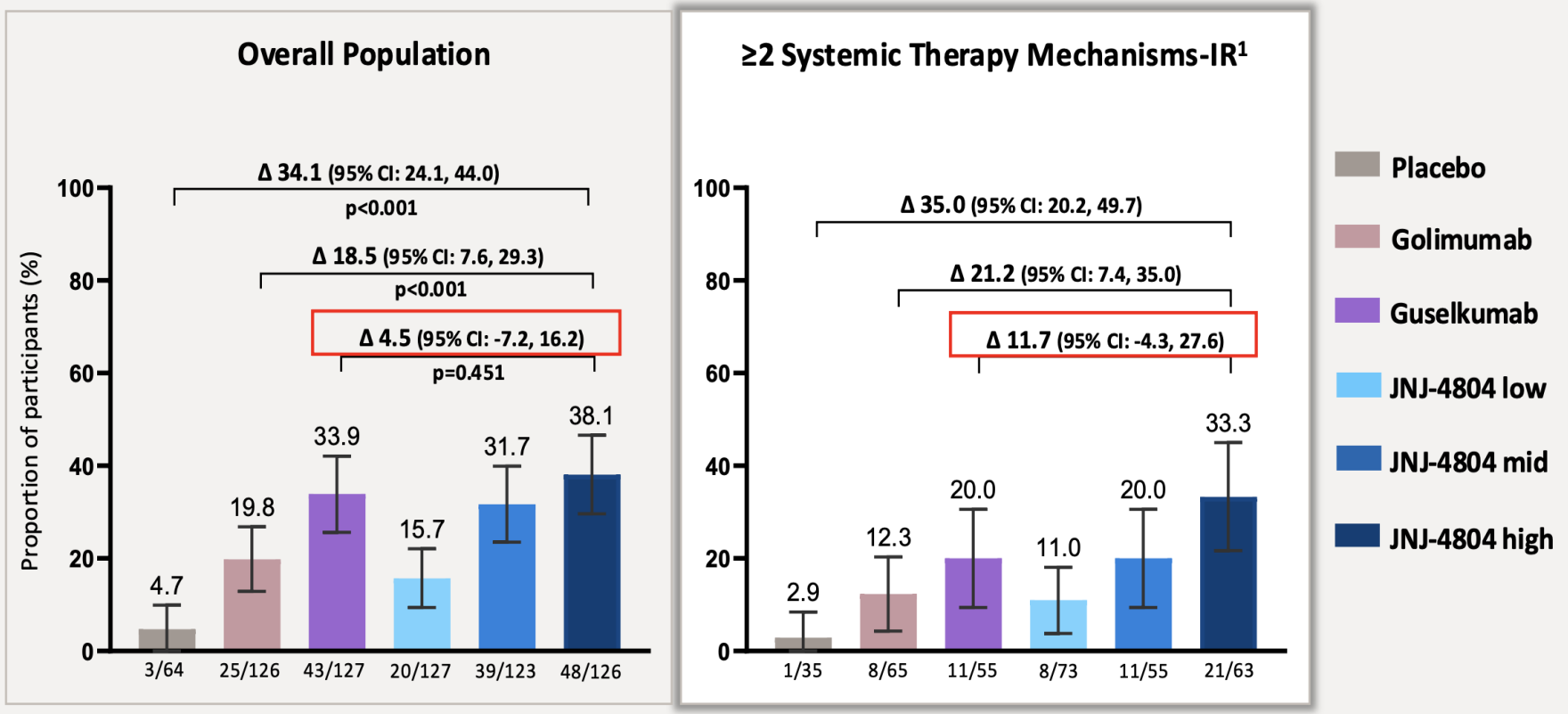
50% were refractory to
2 or more systemic therapy mechanisms

# DUET CD – RÉMISSION CLINIQUE SEM 48




**Clinical remission**: CDAI score of <150

# DUET CD – RÉPONSE ENDOSCOPIQUE SEM 48




**Endoscopic response**: >50% improvement from baseline in SES-CD or an SES-CD ≤2, as assessed by central endoscopy reading

# DUET CD

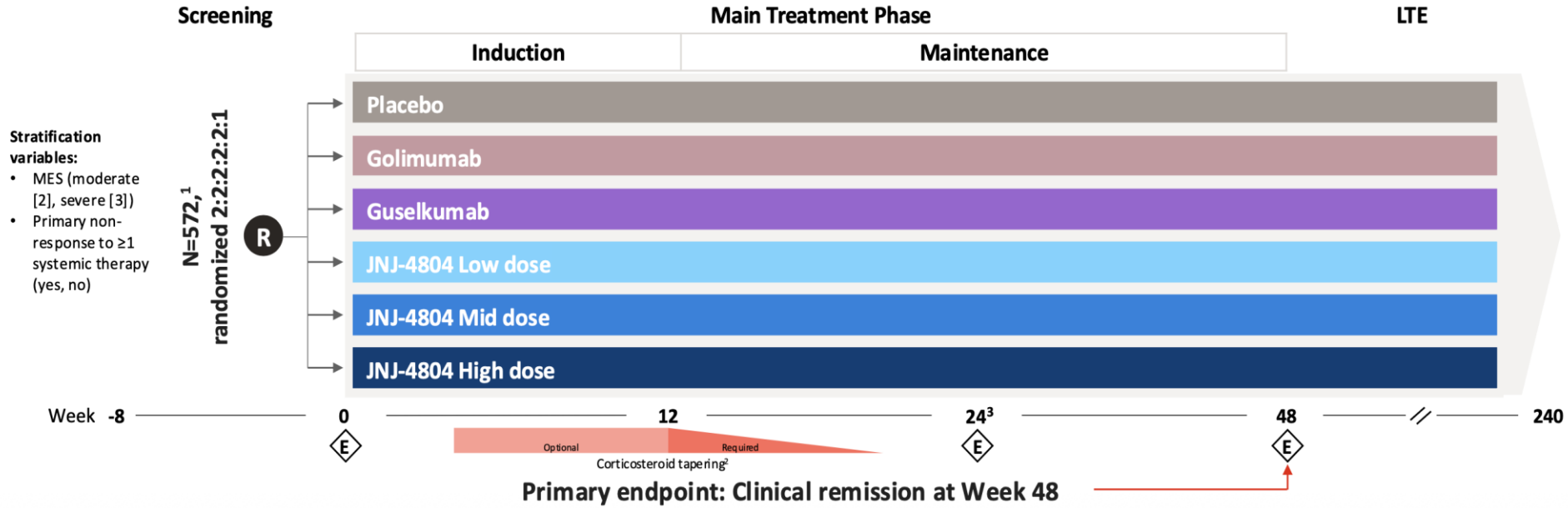
Conclusions

- Première co-thérapie en développement qui démontre une efficacité supérieure vs monothérapies chez les patients avec un Crohn réfractaire
- Supérieur au golimumab et numériquement vs guselkumab dans la population globale
- Chez les pts réfractaires à 2 ou plus thérapies : supérieur au golimumab et guselkumab
- Pas de nouveau signal d'innocuité vs profil de chacune des thérapies

# COMBINAISON DE THÉRAPIES AVANCÉES (DAT)

# PHASE 2B DUET UC

- Moderately to severely active UC
- Inadequate response or intolerance to ≥1 systemic therapy mechanism (anti-TNF, IL-12/23, IL-23p19, integrin, JAK inhibitor, or S1PR modulator)
- Caps for prior systemic therapy mechanisms: 1 (50%), 2 (35%), >2 (15%)
- All study medications were administered subcutaneously




[1]Full Analysis Set; 559 were included in the modified Full Analysis Set (13 did not meet mMayo inclusion criteria at baseline).
[2]Participants taking corticosteroids at Week 0 could begin tapering as early as Week 4 but no later than Week 12.
[3]Participants who met inadequate response criteria at Week 24 received a JNJ-4804 regimen (regardless of treatment assignment).
***E**=endoscopy, **IL**=interleukin, **JAK**=Janus kinase, **LTE**=long-term extension, **MES**=Mayo Endoscopic Score, **mMayo**=modified Mayo, **R**=randomization, **S1PR**=sphingosine-1-phosphate receptor, **TNF**=tumor necrosis factor, **UC**=ulcerative colitis.*

# PHASE 2B DUET UC

| | | Placebo | Golimumab | Guselkumab | JNJ-4804 Low dose | JNJ-4804 Mid dose | JNJ-4804 High dose | Total |
|---|---|---|---|---|---|---|---|---|
| **Full analysis set** | | 52 | 104 | 103 | 103 | 105 | 105 | 572 |
| **Participants with inadequate response to 1 or more systemic therapy mechanisms[1]** | | | | | | | | |
| **Number of systemic therapy mechanisms - inadequate responders, n (%)[2]** | **1** | 30 (58.8%) | 56 (53.8%) | 51 (49.5%) | 63 (61.2%) | 58 (55.2%) | 58 (55.8%) | 316 (55.4%) |
| | **≥2** | 21 (41.2%) | 48 (46.2%) | 52 (50.5%) | 40 (38.8%) | 47 (44.8%) | 46 (44.2%) | 254 (44.6%) |

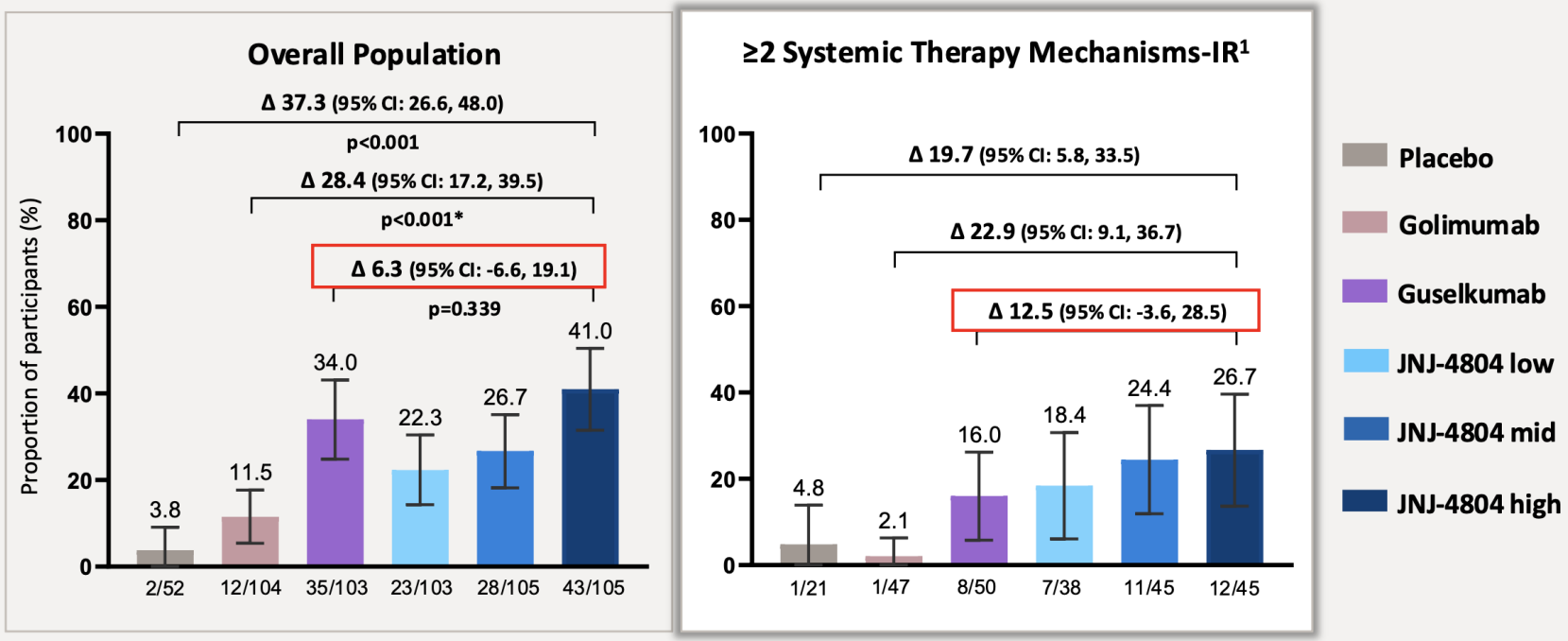
44.6% were refractory to 2 or more systemic therapy mechanisms

History of inadequate response or intolerance by system therapy mechanism in the overall population

- Anti-TNF: 74%
- Anti-integrin: 44%
- JAK inhibitor: 26%
- Ustekinumab: 19%
- S1PR modulator: 4%
- Anti-IL-23: 1%

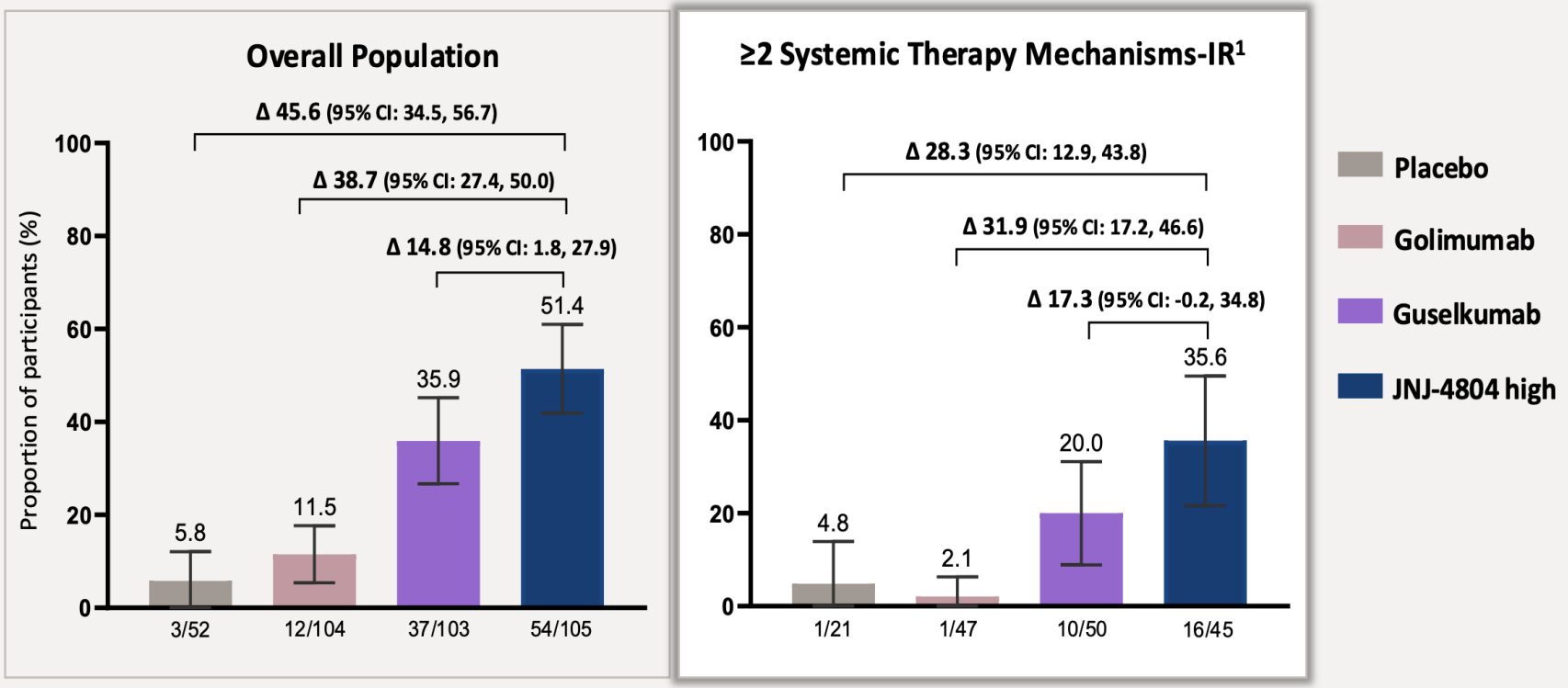
60% of participants with disease refractory to 1 systemic therapy had inadequate response to an anti-TNF only

# PHASE 2B DUET UC – RÉMISSION CLINIQUE SEM48



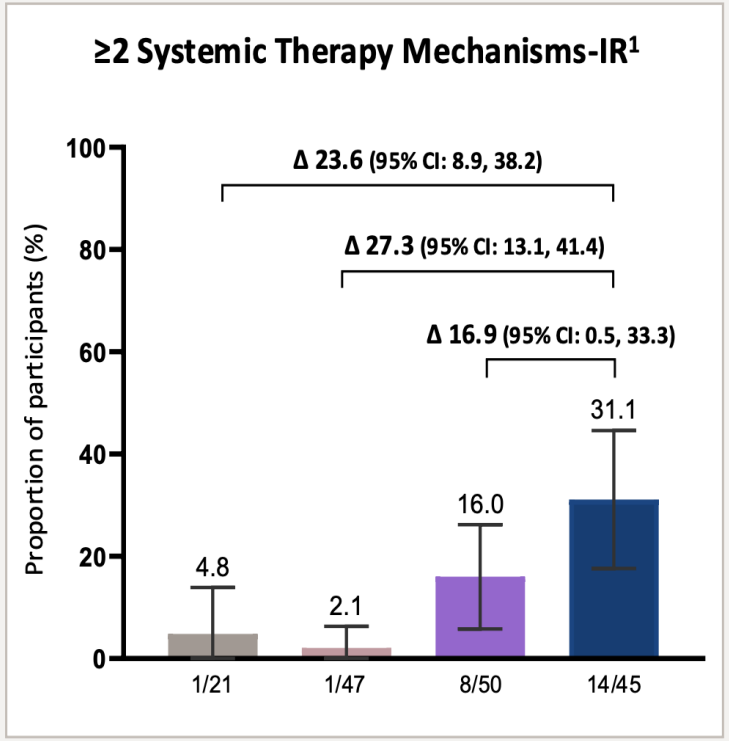

**Clinical remission**: stool frequency subscore of 0 or 1, rectal bleeding subscore of 0, and endoscopy subscore of 0 or 1 per central review of the video endoscopy

# PHASE 2B DUET UC – AMÉLIORATION ENDO SEM48




**Endoscopic improvement**: endoscopy subscore of 0 or 1 per central review of the video endoscopy

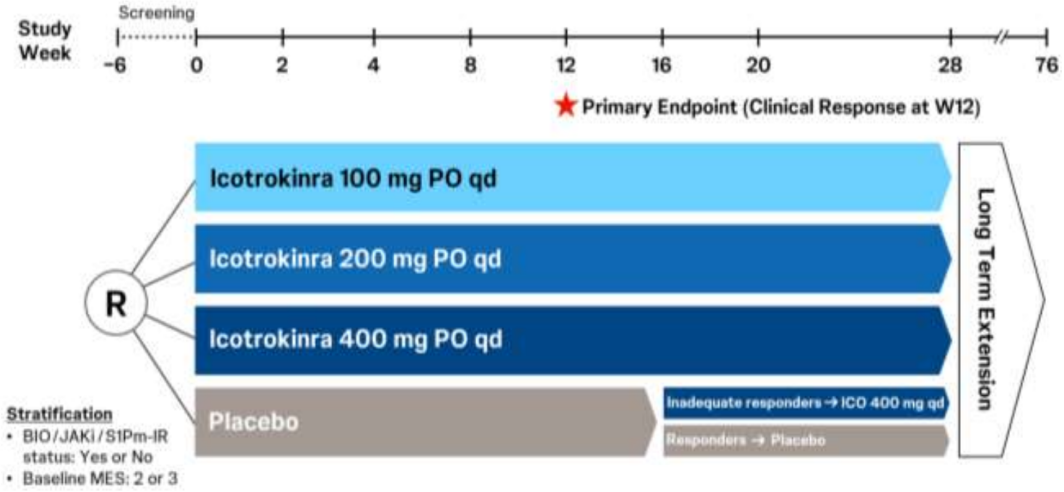
# PHASE 2B DUET UC – RÉMISSION HISTO ET AMÉLIORATION ENDO SEM 48




**Histologic remission AND endoscopic improvement**: absence of neutrophils from the mucosa (both lamina propria and epithelium), no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system, and an endoscopy subscore of 0 or 1 per central review of the video endoscopy

# NOUVEAUTÉS – INH IL23 ORAL

# ANTHEM-UC




**Key Eligibility Criteria**

- Diagnosed UC of ≥12 weeks duration
- Modified Mayo score of 5–9, inclusive
- Mayo endoscopic subscore (MES) ≥2 per central review
- Inadequate response/intolerance (IR) to CS, 6-MP, or AZA **OR** CS dependence **OR** IR to TNFα antagonists, ustekinumab, vedolizumab, JAK inhibitors, or S1P receptor modulators (BIO/JAKi/S1Pm-IR)

**Clinical inflammatory biomarkers:** C-reactive protein and fecal calprotectin

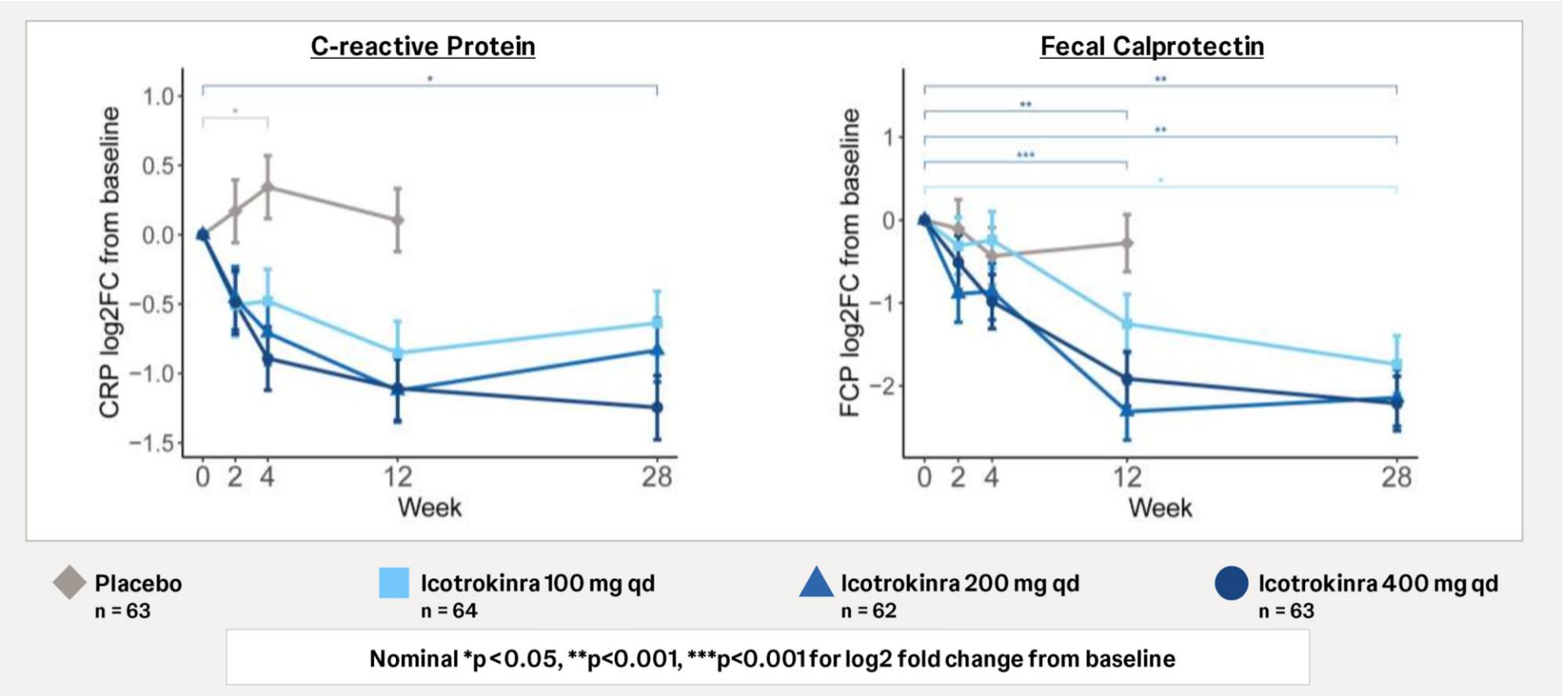
**Systemic IL-23 pathway biomarkers:** IL-22, IL-17A, and IL-17F

**Tissue biomarkers:** IL-23 pathway gene expression changes in colonic biopsies

- At screening, biopsies were collected from the colon/rectum (at least 15–20 cm from the anal verge) in a representative area that was consistent with the severity of inflammation
- Subsequent biopsies from the same location were collected at Weeks 12 and 28

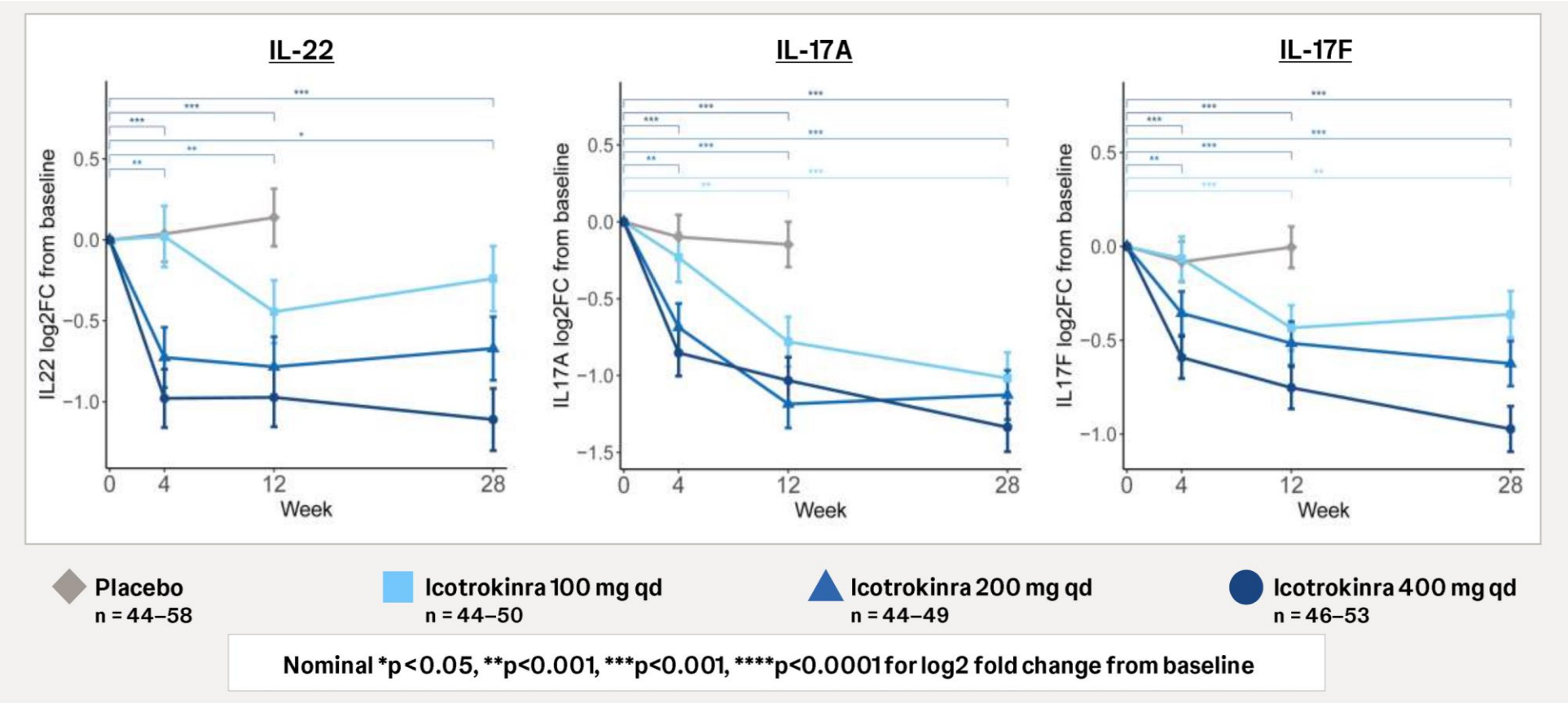
Statistical analyses of these biomarkers were not controlled for multiple comparisons

# ANTHEM-UC - BIOMARQUEURS



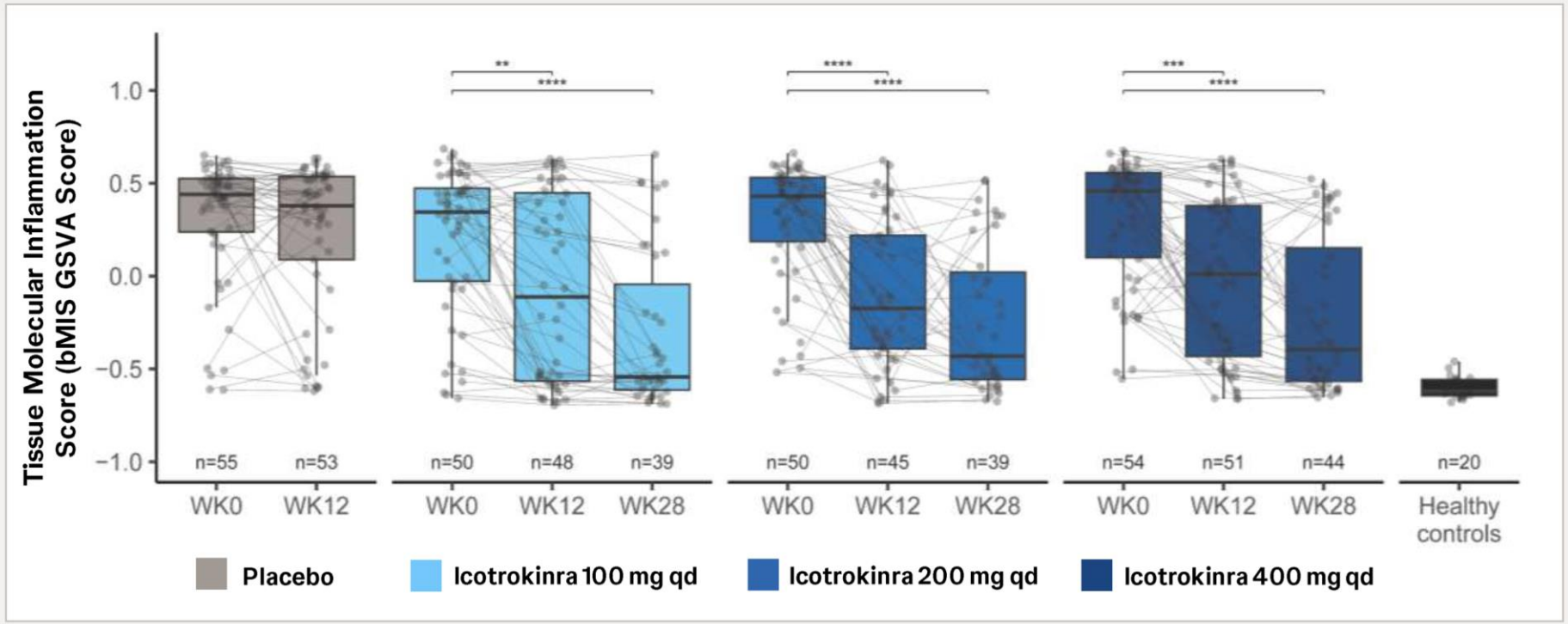

Plots track mean values (estimated marginal means) using a linear mixed effect model that accounts for treatment*time interaction, age, and sex, with subject as a random effect.
Error bars are model-based standard errors.

# ANTHEM-UC BIOMARQUEURS SYSTÉMIQUES VOIE IL23




Plots track mean values (estimated marginal means) using a linear mixed effect model that accounts for treatment*time interaction, age, and sex, with subject as a random effect.
Error bars are model-based standard errors.

# ANTHEM-UC CHARGE INFLAMMATOIRE TISSULAIRE




Quantification of biopsy molecular inflammation score (bMIS) using gene set variation analysis (GSVA) at the indicated time points after placebo or icotrokinra treatment. GSVA scores are depicted and compared at Week 0 and Week 12 or Week 28 with a t-test. Error bars are 95% confidence intervals. Data from healthy controls were generated from commercially obtained colonic biopsies.

# NOUVEAUTÉS – TL1A…AU-DELÀ DE L'INFLAMMATION !

## The Anti-TL1A Monoclonal Antibody Tulisokibart Inhibits Inflammatory and Fibrosis Pathways: Results From a Phase 2 Ulcerative Colitis Study

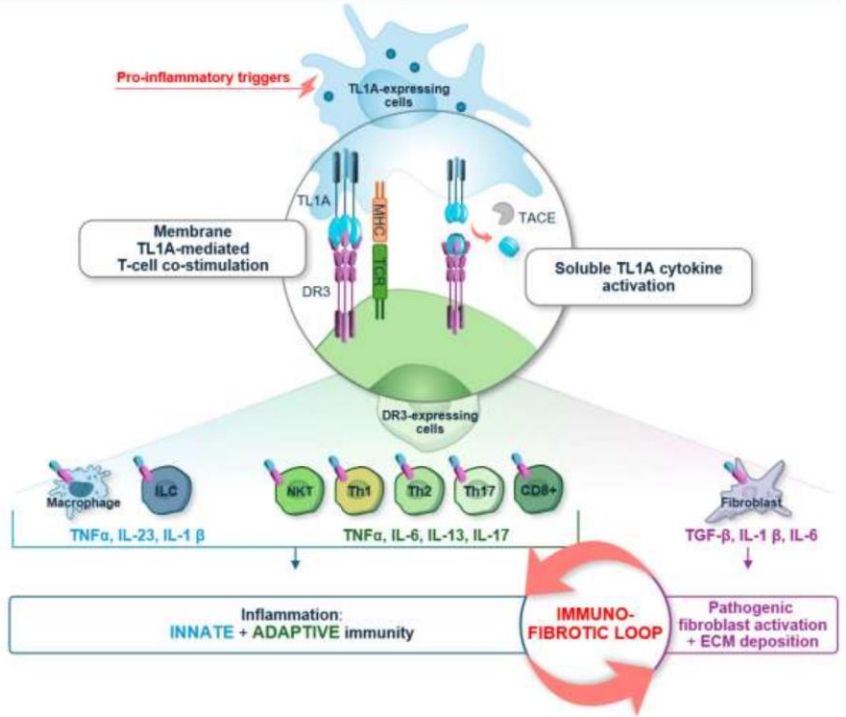
[1]Florian Rieder, [2]Richard Wnek, [2]Shiuli Agarwal, [2]Heather Llewellyn, [2]John Kang, [2]Peining Tao, [2]Wen Zhou, [2]Justin Klaff, [2]In Sock Jang, [2]Ernesto J. Muñoz-Elias, [3]Jean-Frederic Colombel

[1]Department of Gastroenterology, Hepatology and Nutrition, Digestive Diseases Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA; [2]Merck & Co., Inc., Rahway, New Jersey, USA; [3]Department of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, NY, USA

# CONTEXTE

## Tulisokibart Inhibits TL1A, a Central Amplifier of Inflammatory and Fibrotic Pathways in IBD Pathogenesis

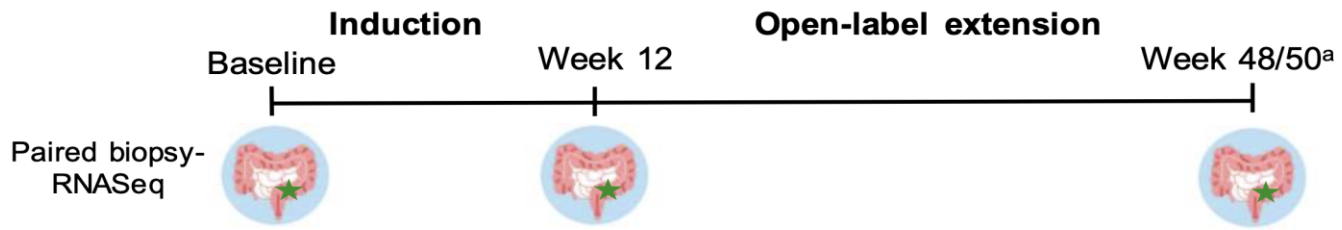
- Preclinical and translational data supported targeting TL1A for the treatment of IBD[1-7]
- Tulisokibart is a humanized monoclonal antibody that binds membrane and soluble TL1A and inhibits signaling through DR3 leading to reduction of inflammatory and fibrosis pathways[8,9,10]
- Phase 2 ARTEMIS-UC in moderately to severely active ulcerative colitis: tulisokibart induction treatment significantly improved clinical, endoscopic, and patient-reported outcomes vs placebo at week 12[11]; responses were maintained through week 50[12]




1. Bamias G, et al. *Gut*. 2025;74(4):652-668. 2. Lusetti F, et al. *Expert Rev Gastroenterol Hepatol*. 2025;19(1):15-25. 3. Solitano V, et al. *BioDrugs*. 2025;39(2):171-183. 4. Siakavellas SI, et al. *Inflamm Bowel Dis*. 2015;21(10)2441-2452. 5. Bamias G, et al. *Clin Immunol*. 2010;137(2):242-249. 6. Yamazaki K, et al. *Hum Mol Genet*. 2005;14(22):3499-3506. 7. Jostins L, et al. *Nature*. 2012;491(7422):119-124. 8. Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2025;10(8):715-725. 9. Fransson J, et al. Protein & Antibody Engineering Summit (PEGS) Europe; Lisbon, Portugal; 2023. 10. Danese S, et al. United European Gastroenterology (UEG) Week; Copenhagen, Denmark; 2023. 11. Sands B, et al. *N Engl J Med*. 2024;391:1119-1129. 12. Ma C, et al. United European Gastroenterology (UEG) Week; Vienna, Austria; 2024.

# ANALYSE POST-HOC

## Gene Expression Analysis of Mucosal Inflammatory and Fibrosis Pathways




**Biomarker Samples**
(Cohorts 1+2):

| Week 12 | N |
|---|---|
| Placebo | 73 |
| Tulisokibart | 77 |

| Week 50 | N |
|---|---|
| Tulisokibart 100 mg | 13 |
| Tulisokibart 250 mg | 25 |

**Mucosal transcriptomic signatures analyzed by GSVA[b,1]**

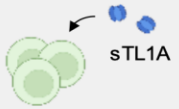
**Inflammatory pathways**

**T-helper 1**
*Th1 biology*

**T-helper 17**
*Th17 biology*

**Inflammatory monocytes**
*Produce IL23, IL1b, TNF*

**TL1A pathway**

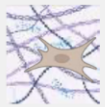



**TL1A Th1**
*TL1A-induced genes in Th1 cells*

**Profibrotic cell types**

**Fibroblast activation**
*IBD-activated fibroblasts*

**Fibroblast identity**
*Creeping-fat fibroblast*



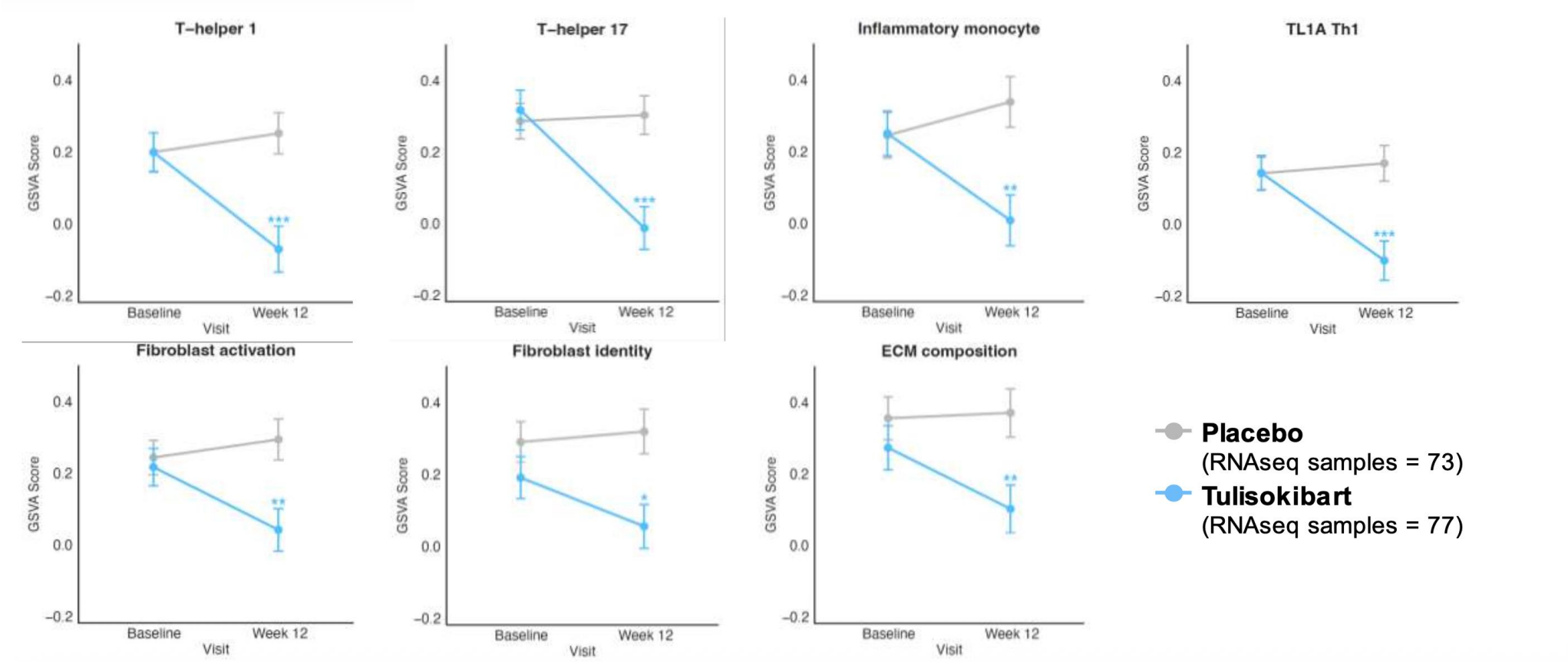
***ECM composition***
*ECM[c] fibroblast*

[1]Patients had either a week 48 or week 50 biopsy collection. [b]GSVA estimates pathway or gene-set activity at the sample level by summarizing coordinated expression of predefined gene sets in an unsupervised manner. [c]ECM composition: the overlap of genes between the fibroblast activation signature and the Core matrisome signature for ECM as identified in The Matrisome Project The Matrisome Project (mit.edu).

# SEMAINE 12

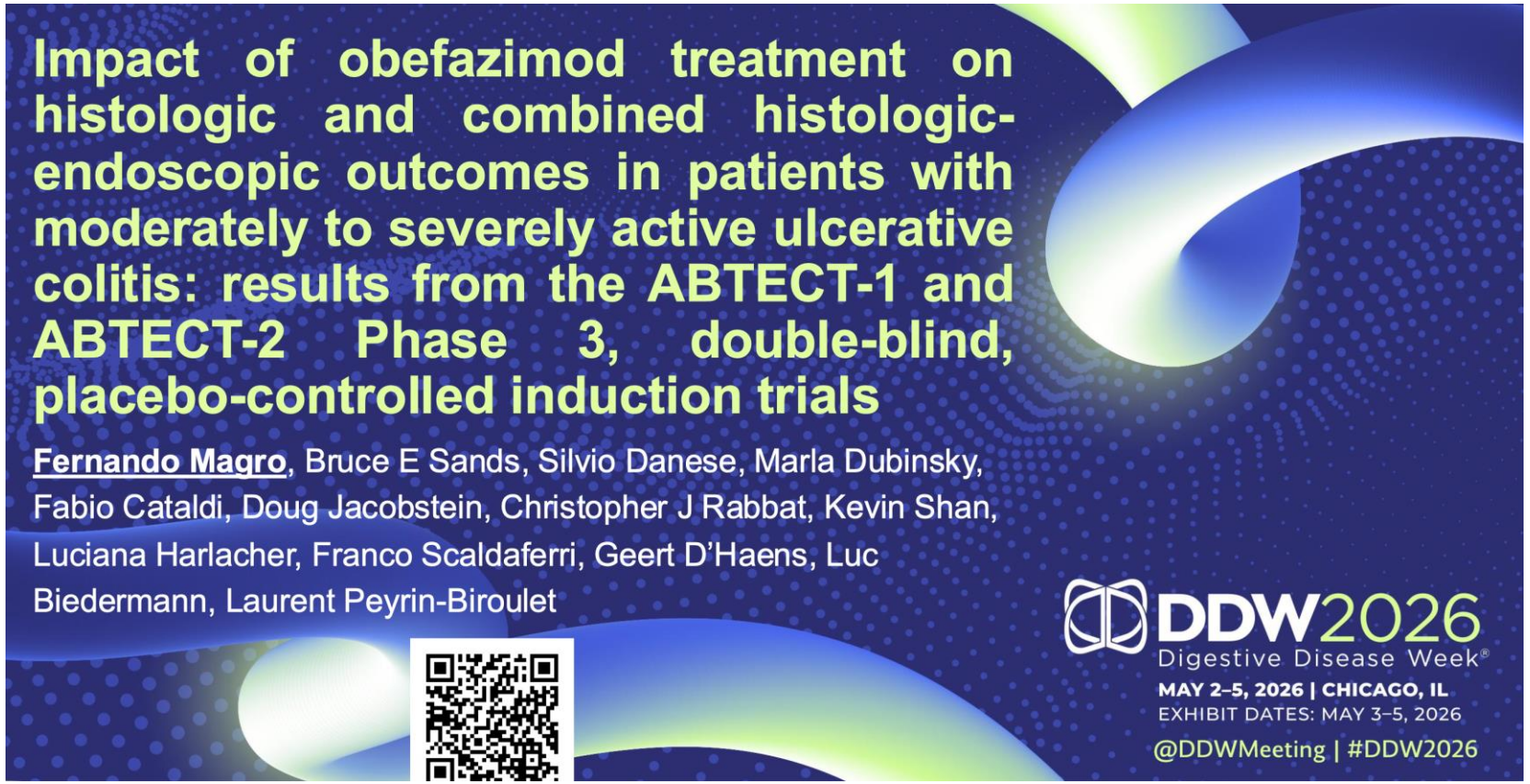
Molecular pathways modulated by tulisokibart treatment in intestinal mucosal biopsies of UC patients support a pleiotropic role for TL1A dysregulation in driving inflammatory and fibrotic pathways

- Tulisokibart suppressed Th1, Th17, TL1A-Th1, and fibrosis gene expression pathways
- Tulisokibart also suppressed gene expression pathways associated with inflammatory monocytes, which are known to produce TNFα, IL-1b, and IL-23

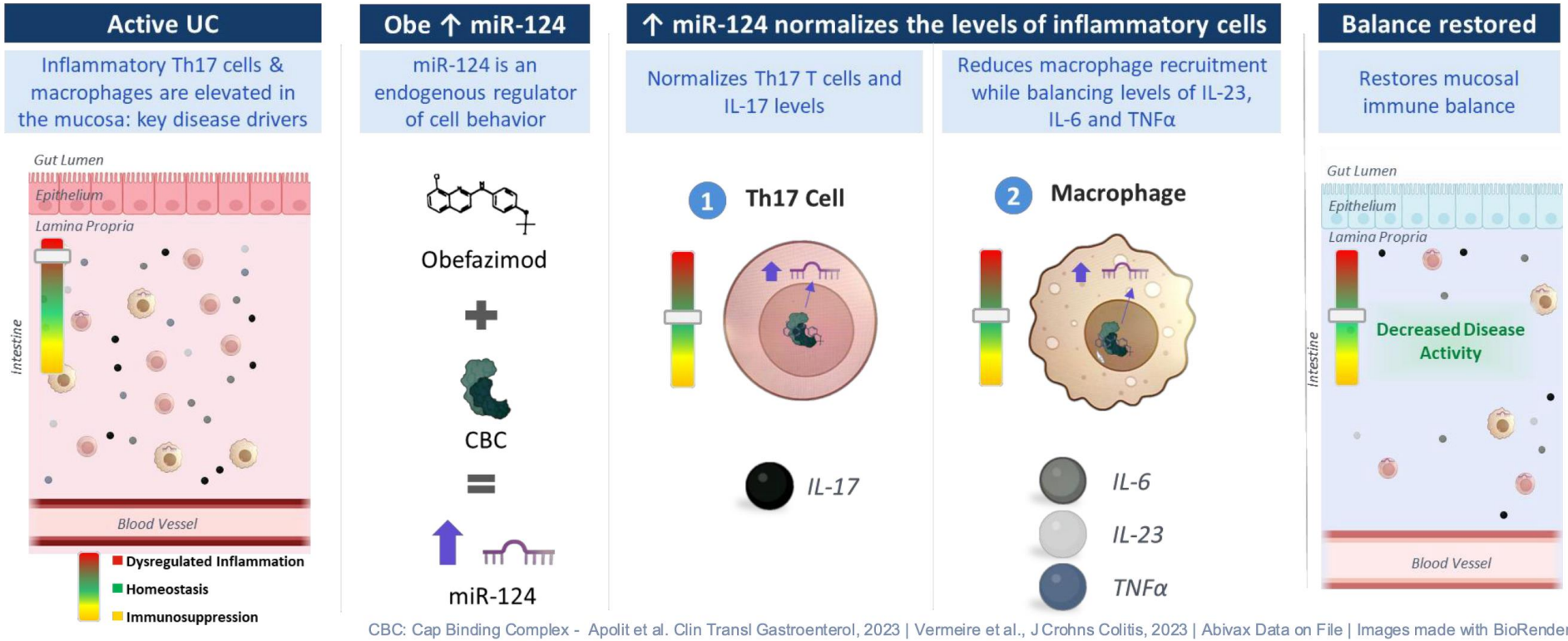



*P* values are for w eek 12 versus baseline; one-sided significance levels: **P* < 0.05; ** *P* < 0.01; *** *P* < 0.001. Paired analysis.
ECM, extracellular matrix; GSVA, gene set variation analysis; RNAseq, RNA sequencing; Th1, T-helper 1.

# NOUVEAUTÉS - OBEFAZIMOD



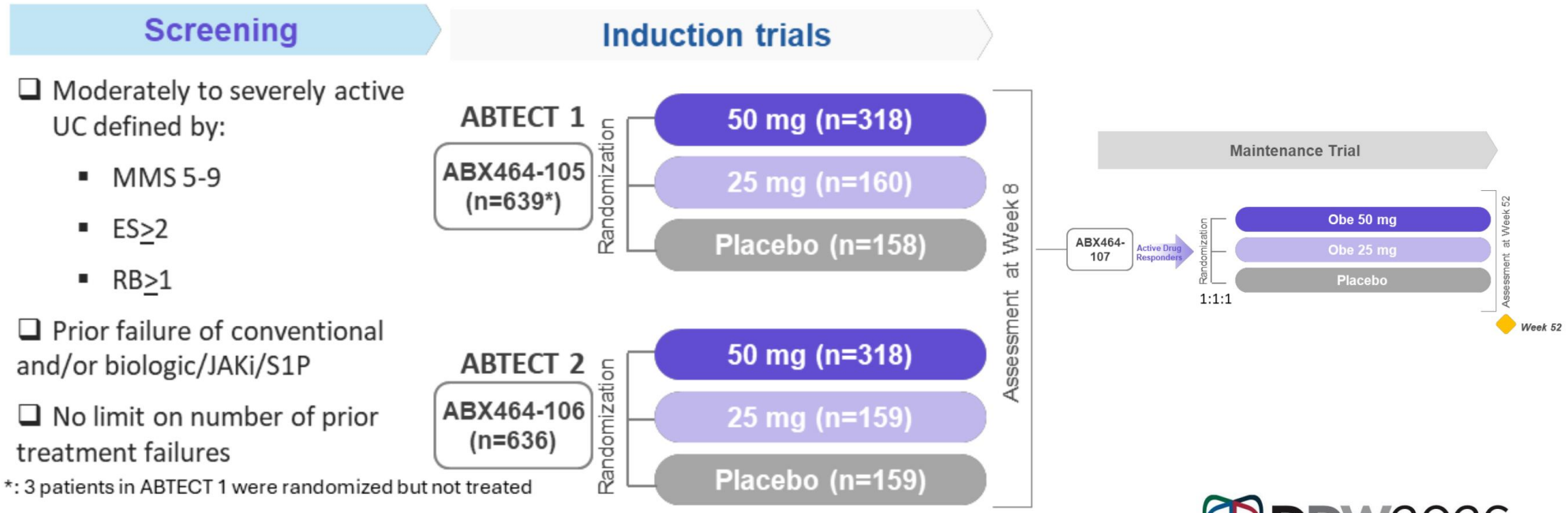
# OBEFAZIMOD




CBC: Cap Binding Complex - Apolit et al. Clin Transl Gastroenterol, 2023 | Vermeire et al., J Crohns Colitis, 2023 | Abivax Data on File | Images made with BioRender

**Obefazimod restores mucosal immune balance in ulcerative colitis through regulation of Th17 cells and macrophages**

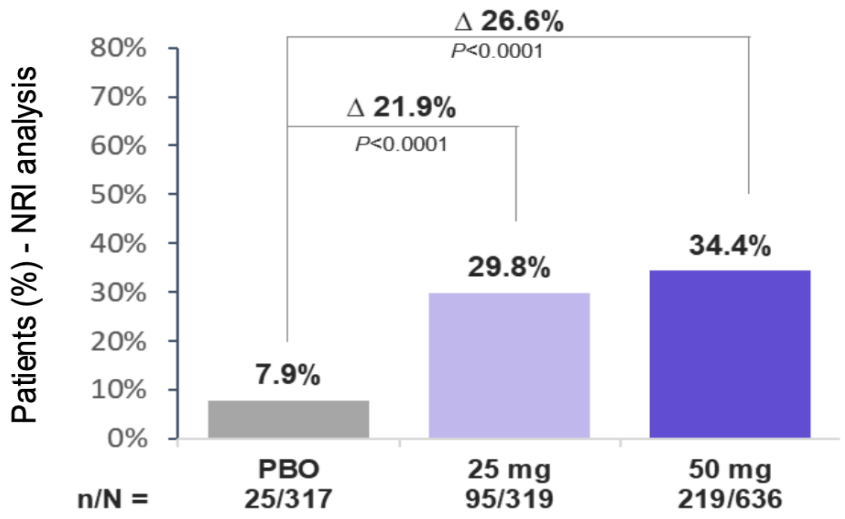
# ABTECT 1&2



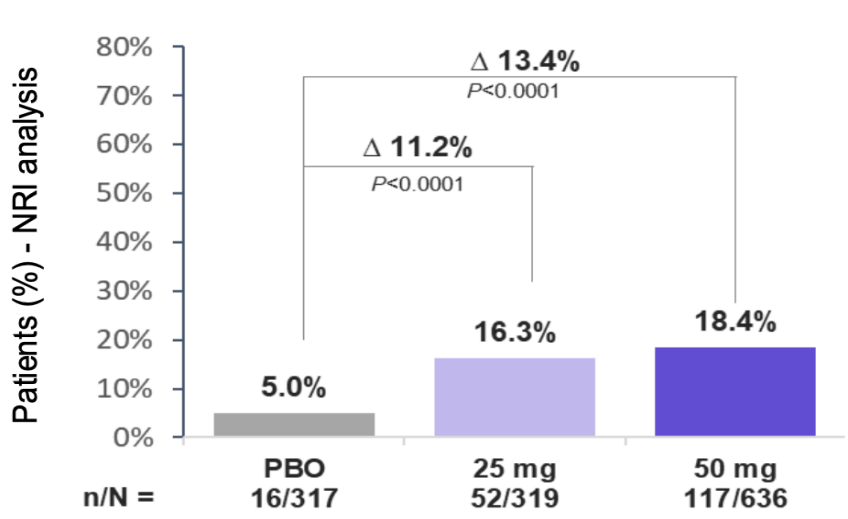

Rectal or sigmoidal biopsies from the most affected segment were collected during endoscopy at screening and Week 8

# SEMAINE 8 – ISSUES ENDOSCOPIQUES

**Endoscopic improvement**



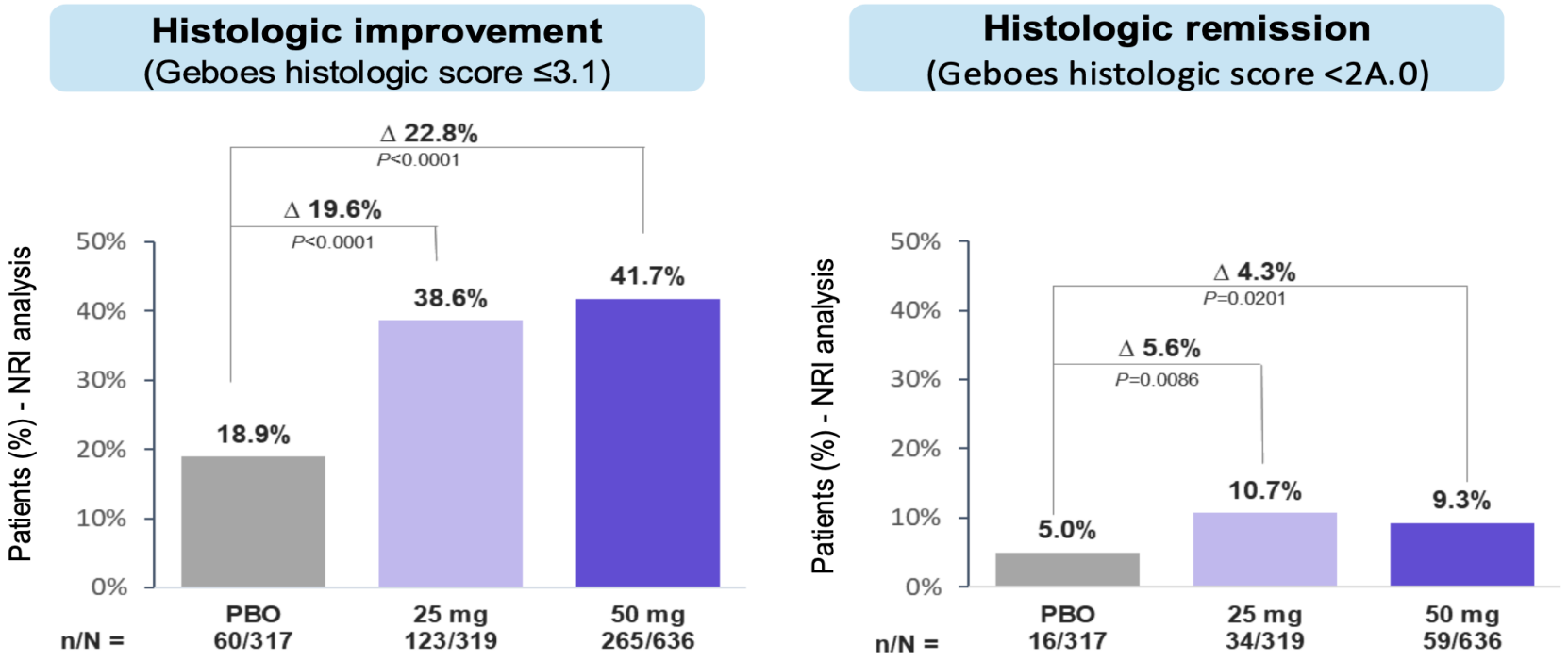

**Endoscopic remission**




* All p-values are nominal

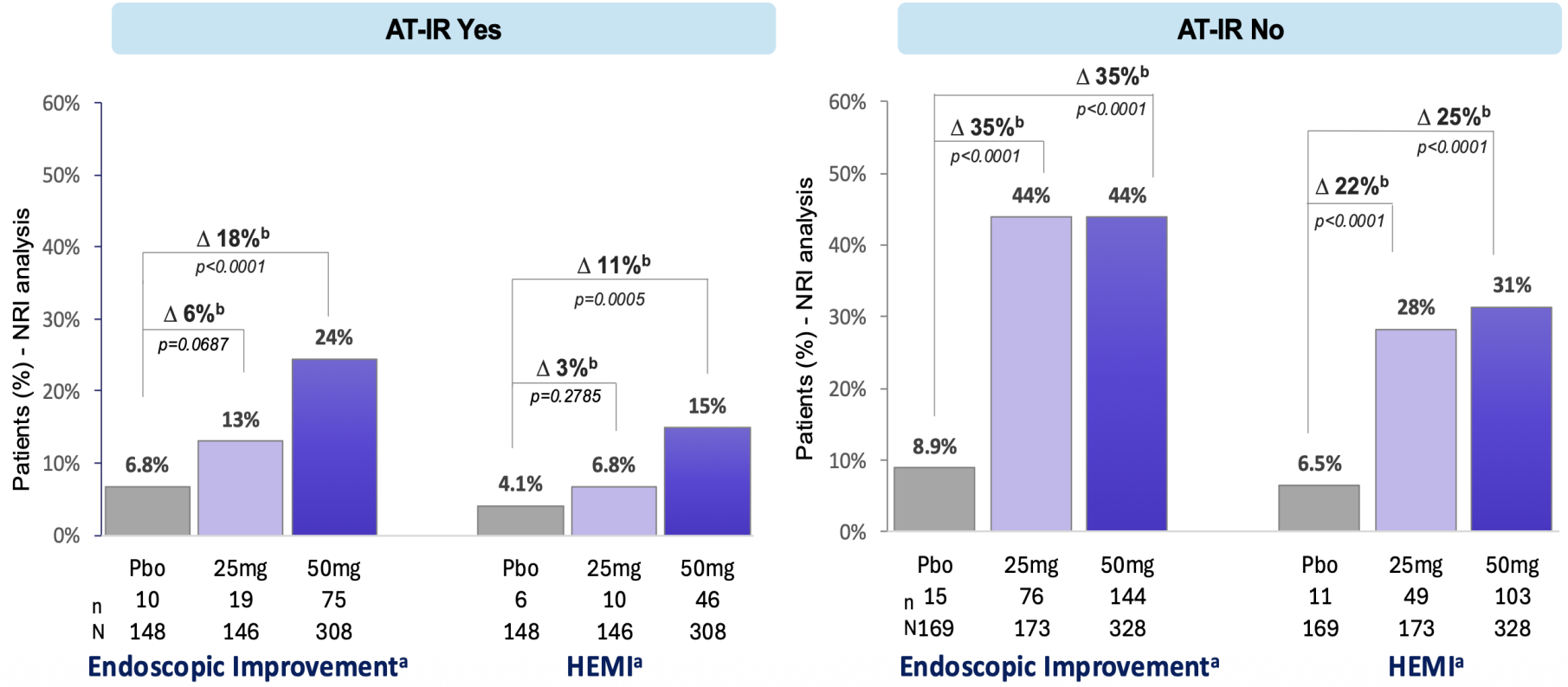
NRI is used for subjects with missing outcome at week 8 and subjects reporting any IE prior to week 8; % Difference is for Obe minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), baseline oral corticosteroids usage (yes/no), and pivotal study (ABX464-105/ABX464-106). All P values are 2-sided. Endoscopic improvement: endoscopic subscore ≤1. Endoscopic remission: endoscopic subscore=0. IE, intercurrent event; MES, Mayo Endoscopic Subscore; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo.

# SEMAINE 8 - HISTOLOGIE




*: All p-values are nominal; NRI is used for subjects with missing outcome at week 8 and subjects reporting any IE prior to week 8; % Difference is for Obe minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), baseline oral corticosteroids usage (yes/no), and pivotal study (ABX464-105/ABX464-106). All P values are 2-sided. Histological improvement: neutrophil infiltration in <5% of crypts, no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system (ie, Geboes histologic score ≤3.1). Histological remission: absence of neutrophils in the epithelial crypts or lamina propria and no increase in eosinophils, no crypt destruction, and no erosions, ulcerations, or granulation tissue, according to the Geboes grading system (ie, Geboes histologic score <2A.0). IE, intercurrent event; MES, Mayo Endoscopic Subscore; NRI, non-responder imputation; Obe, obefazimod; PBO, placebo.

# SEMAINE 8

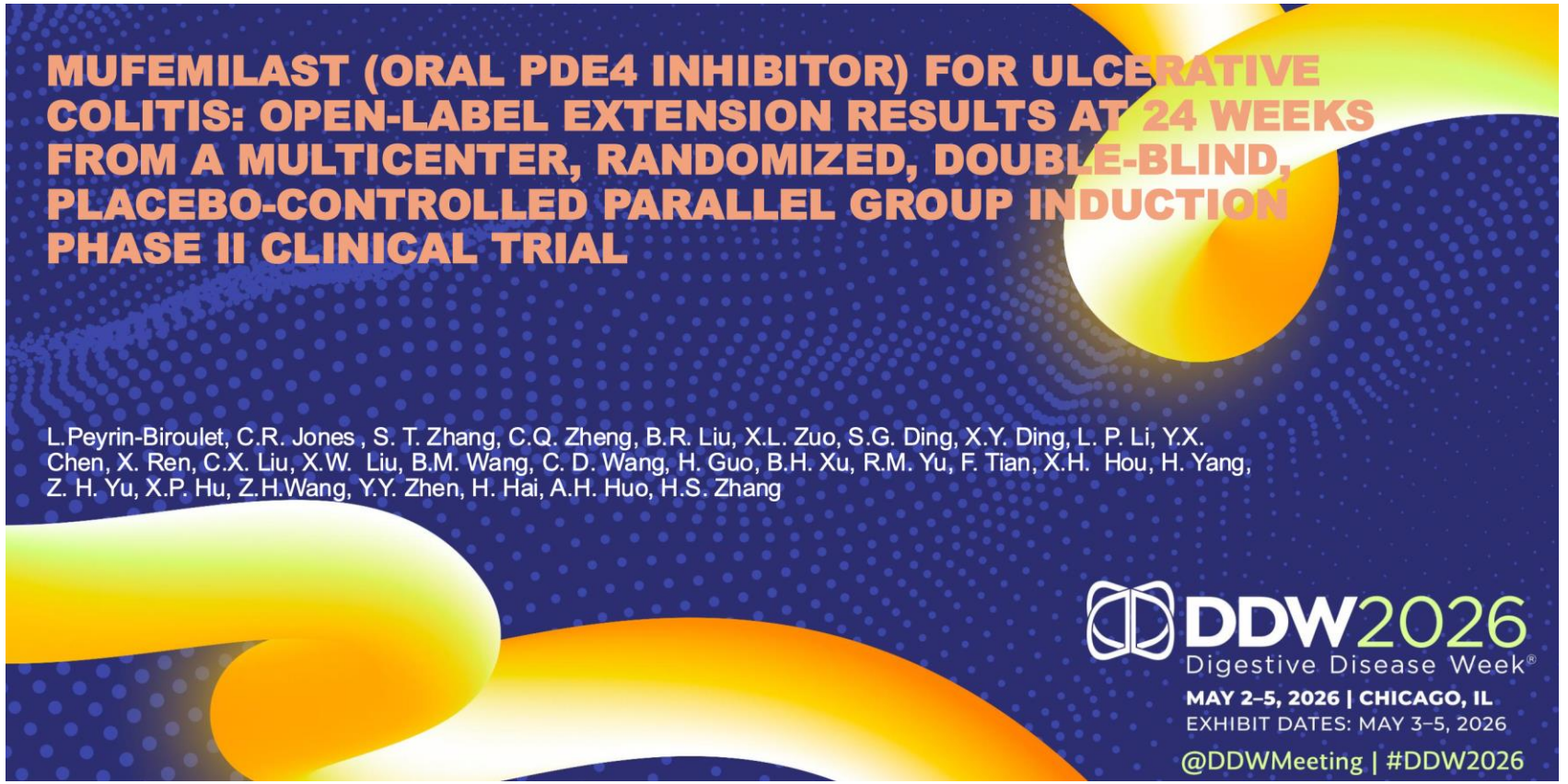



AT-IR: inadequate response to advanced therapies

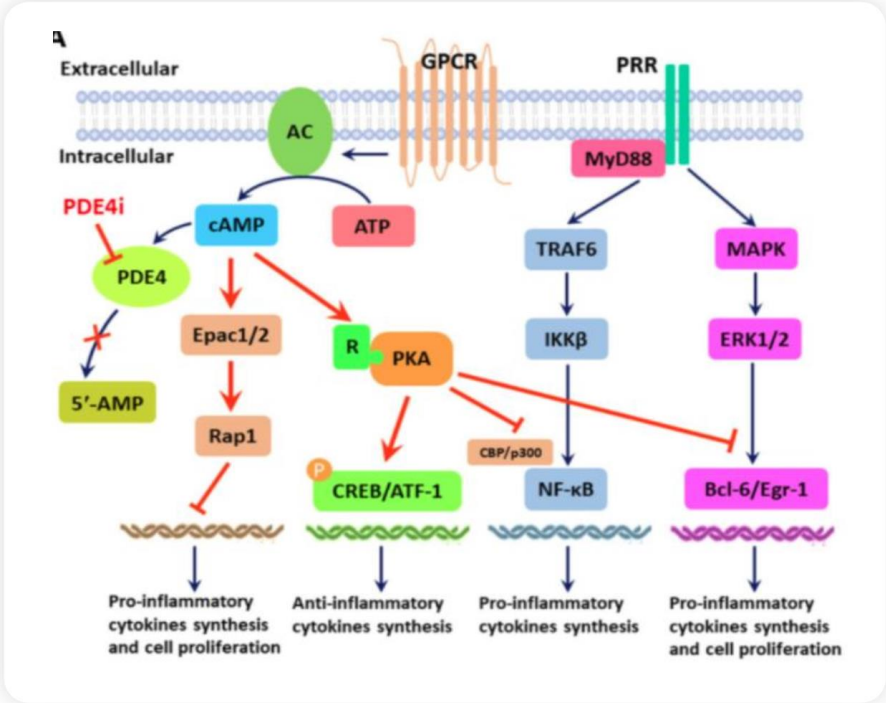
All p-values are nominal; [a] Endoscopic improvement is defined as MES = 0 or 1 (MES of 1 modified to exclude friability). HEMI is defined as MES = 0 or 1 and Geboes Index score ≤3.1; [b] % Difference is for obefazimod minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), Baseline oral corticosteroids usage (yes/no). P-values are two sided. NRI is used for subjects with missing outcome at Week 8 and subjects reporting any IE prior to Week 8.

# AUTRE ALLIÉ CONTRE LA FIBROSE!

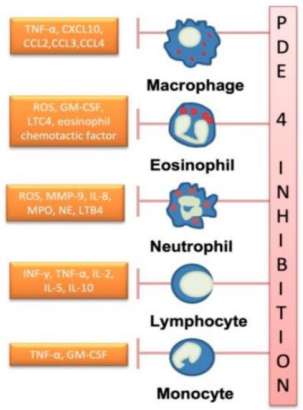
# NOUVEAUTÉS - MUFEMILAST



# MUFEMILAST




**Mufemilast works beyond the axis of specific cytokines blocked by biologics (IL12/23; IL17) without additional safety concerns. This includes targeting NF-κB, MAPK, neutrophil trafficking, and PDE4b expression inhibition**




**Multiple target cells**



DOI:10.3389/fphar.2018.01048 Corpus ID: 53167673
***Phosphodiesterase-4 Inhibitors for the Treatment of Inflammatory Diseases***

# CE QUI A RETENU MON ATTENTION!

- IL23i – emphase sur la durabilité et l'innocuité à long-terme
- Innovation liée à la commodité module la compétition dans la classe des IL23i
  - Icotrokinra (oral)
  - Induction sous-cutanée
  - SPY003 (liaison FcRn qui permet une extension de la demi-vie)
  - XmAb412 (dual IL23i/TL1Ai avec extension de la demi-vie)
- TL1Ai font déplacer la conversation au-delà de l'inflammation : fibrose!
- Nouveaux MoA :
  - Obefazimod (upreg miR-124)
  - Mufemilast (PDE4i)
- Combinaison de thérapies avancées – préparez-vous!

Merci de votre attention!

joannie.ruel@usherbrooke.ca