Update laufende klinische Studien – Bereich CED und Zöliakie

Abteilungsfortbildung
29. November 2022

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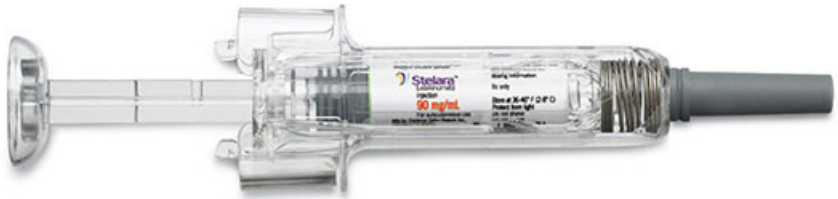
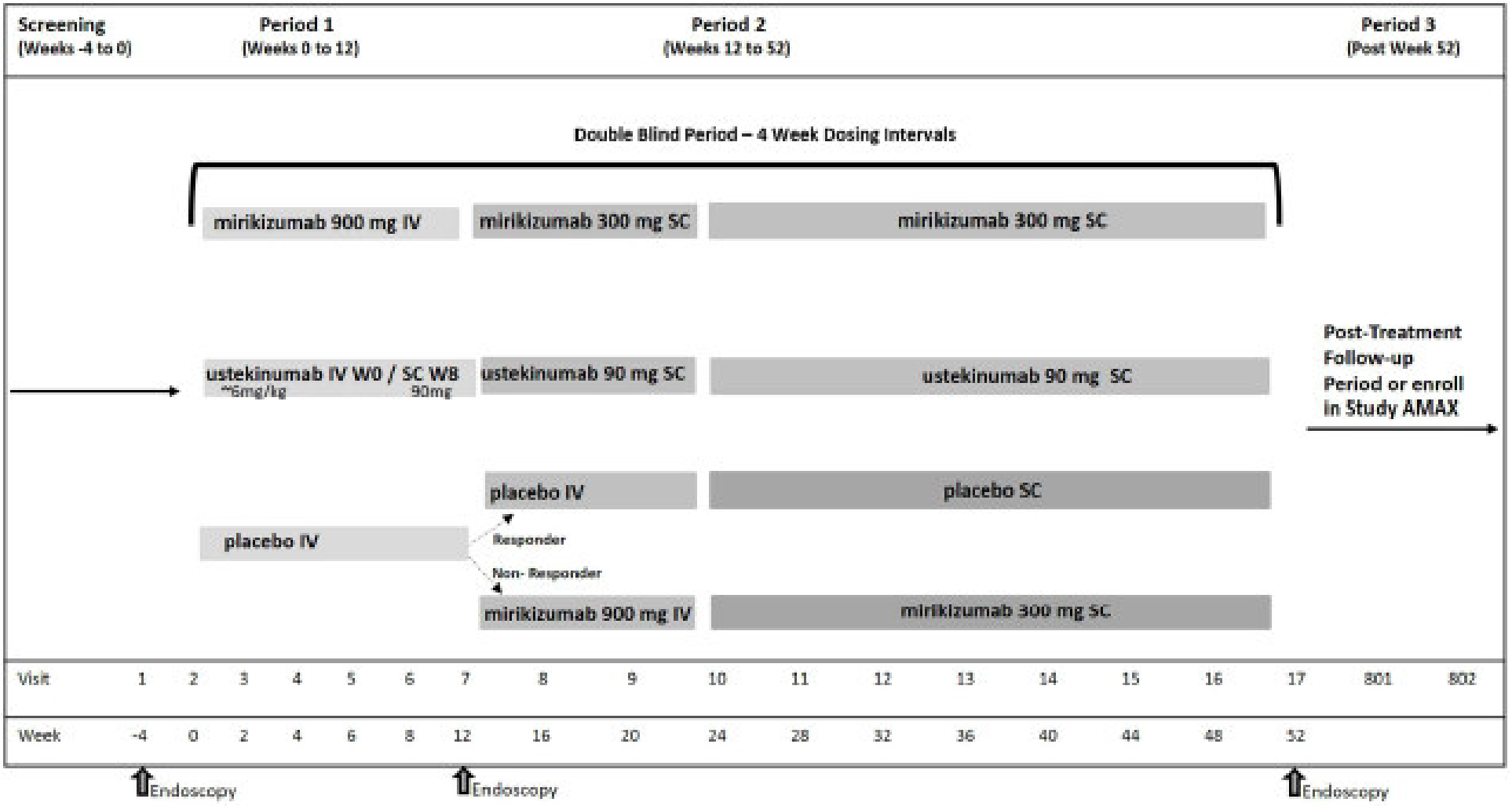
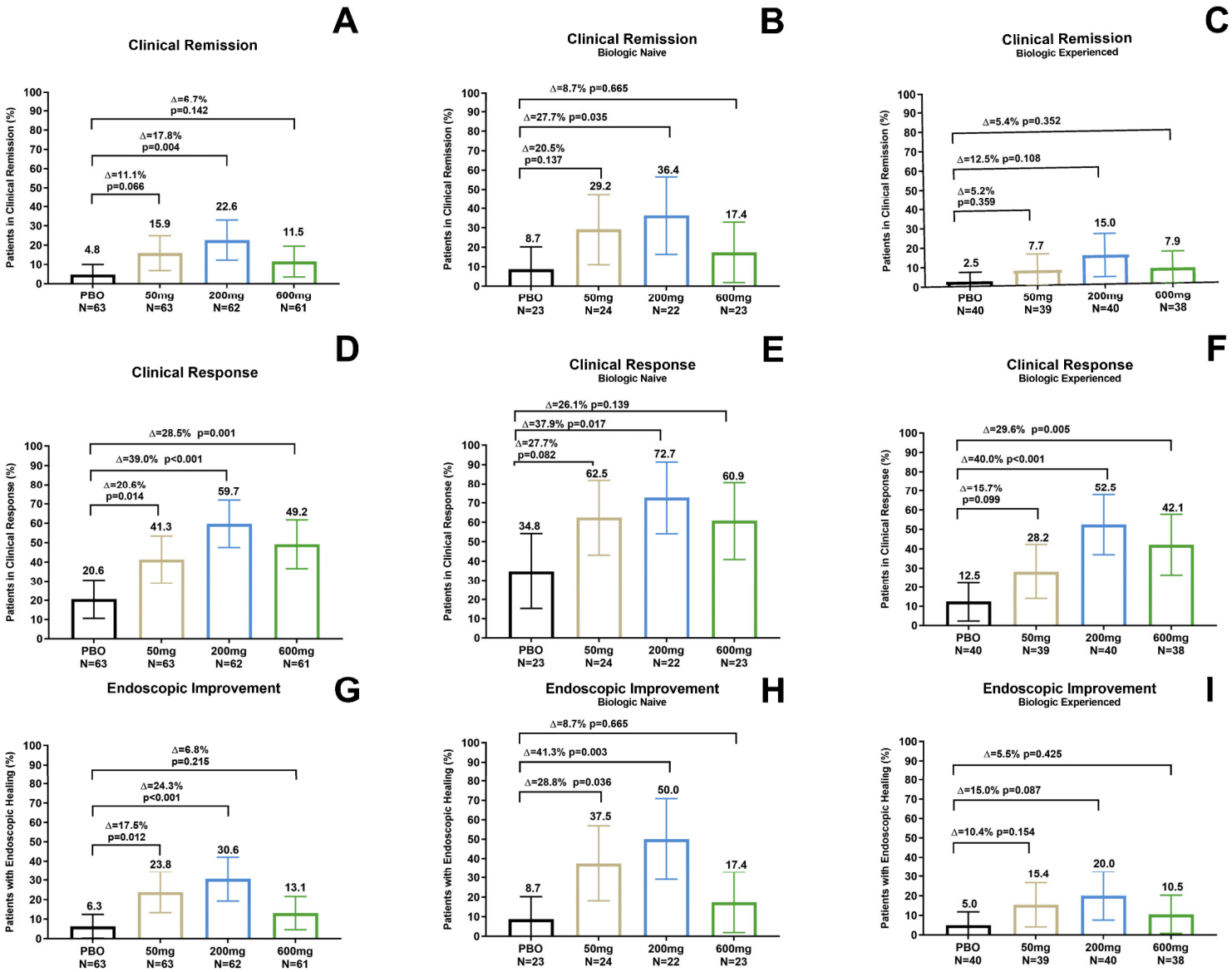
Klinische Abteilung für Gastroenterologie & Hepatologie

One time IV Infusion Induction Dose



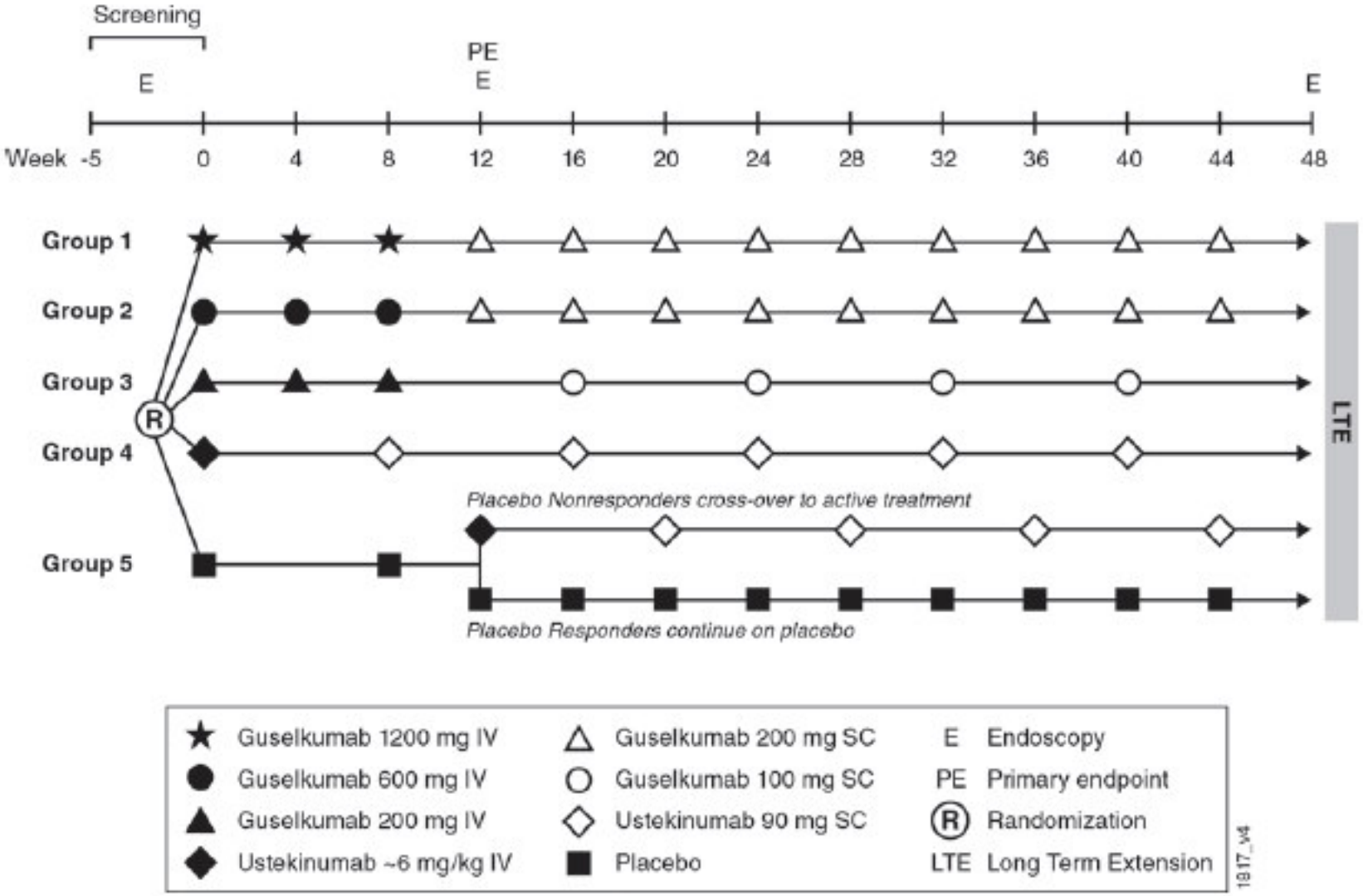
Subcutaneous Injection Maintenance Dose


Screening
(Weeks -4 to 0)
Period 1
(Weeks 0 to 12)
Period 2
(Weeks 12 to 52)
Period 3
(Post Week 52)
Double Blind Period – 4 Week Dosing Intervals
mirikizumab 900 mg IV
mirikizumab 300 mg SC
mirikizumab 300 mg SC
ustekinumab IV W0 / SC W8
~6mg/kg
90mg
ustekinumab 90 mg SC
ustekinumab 90 mg SC
Post-Treatment
Follow-up
Period or enroll
in Study AMAX
placebo IV
placebo SC
placebo IV
Responder
Non- Responder
mirikizumab 900 mg IV
mirikizumab 300 mg SC
Visit 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 801 802
Week -4 0 2 4 6 8 12 16 20 24 28 32 36 40 44 48 52
Endoscopy
Endoscopy
Endoscopy



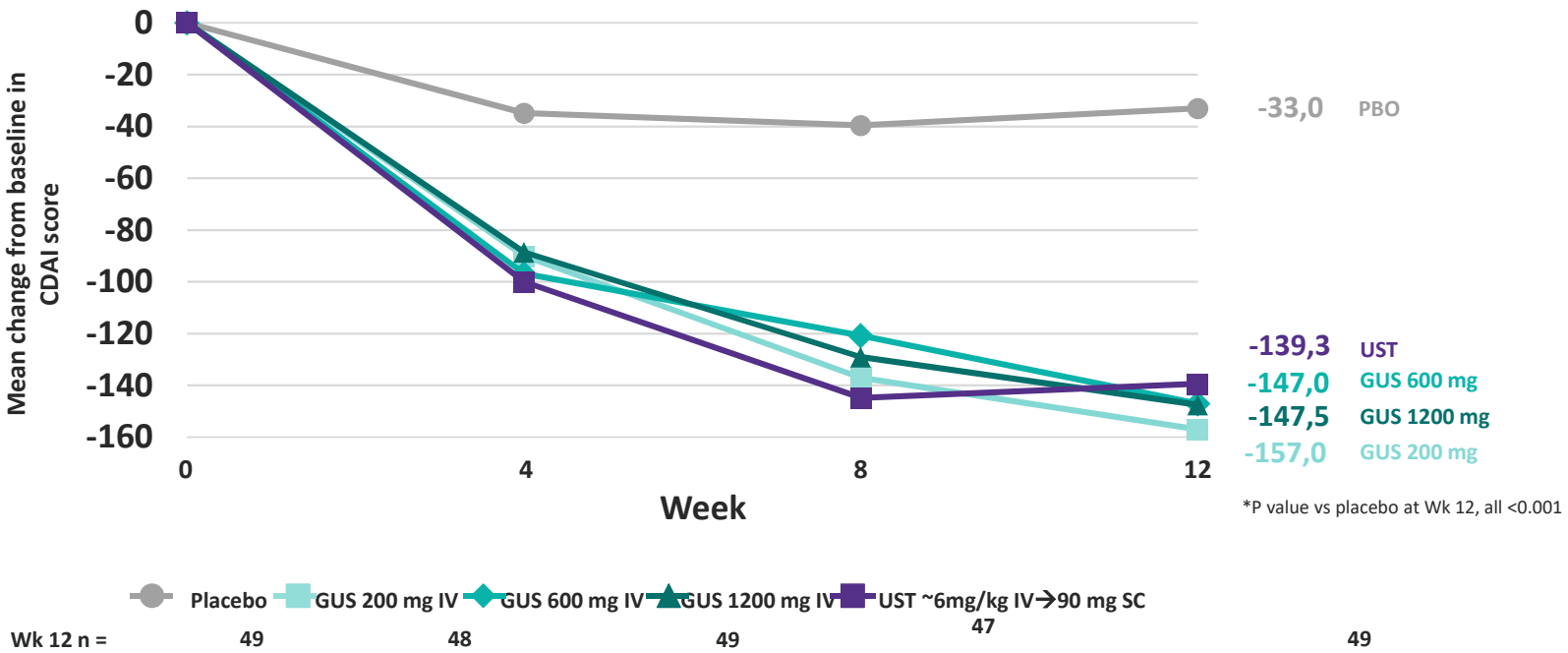
Gastroenterology 2020 158537-549.e10DOI: (10.1053/j.gastro.2019.08.043)

Figure 2: **Design schematic illustrating the dosing schemes for the 5 treatment groups from Week 0 to Week 48 in Phase 2 (ie, GALAXI 1)**



GALAXI Phase 2

Mean Change From Baseline in CDAI Score Through Week 12



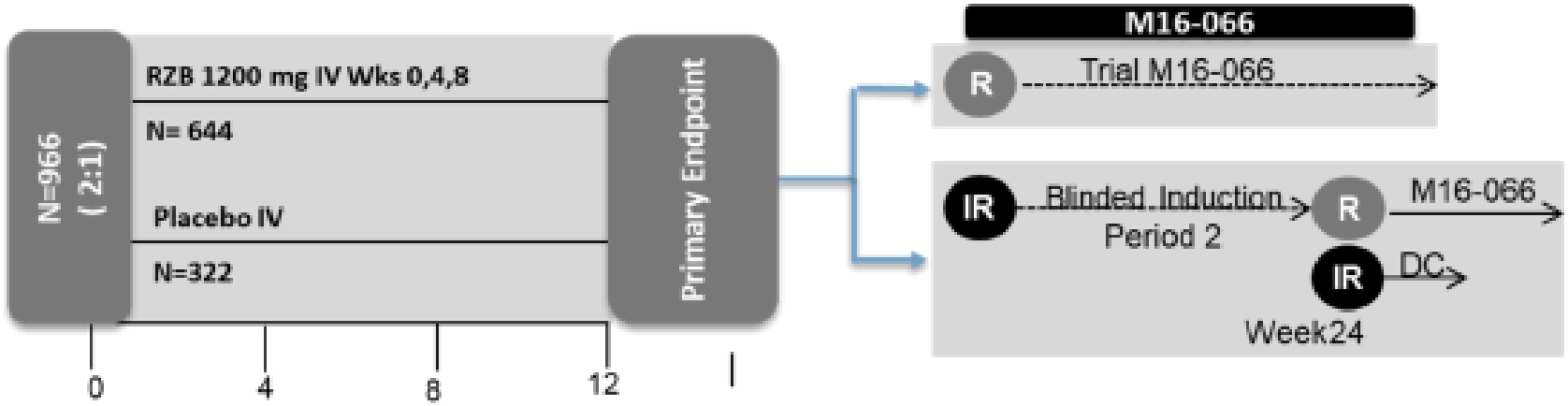
Patients who had a prohibited change in concomitant CD medication, a CD-related surgery, or discontinued study agent due to lack of efficacy or an AE of worsening CD prior to Week 12 had their baseline value carried forward. Patients who had insufficient data to calculate the CDAI Score at Week 12 did not have their missing data imputed.

*The comparisons versus placebo at the interim analysis were not controlled for multiplicity; nominal p values are presented.

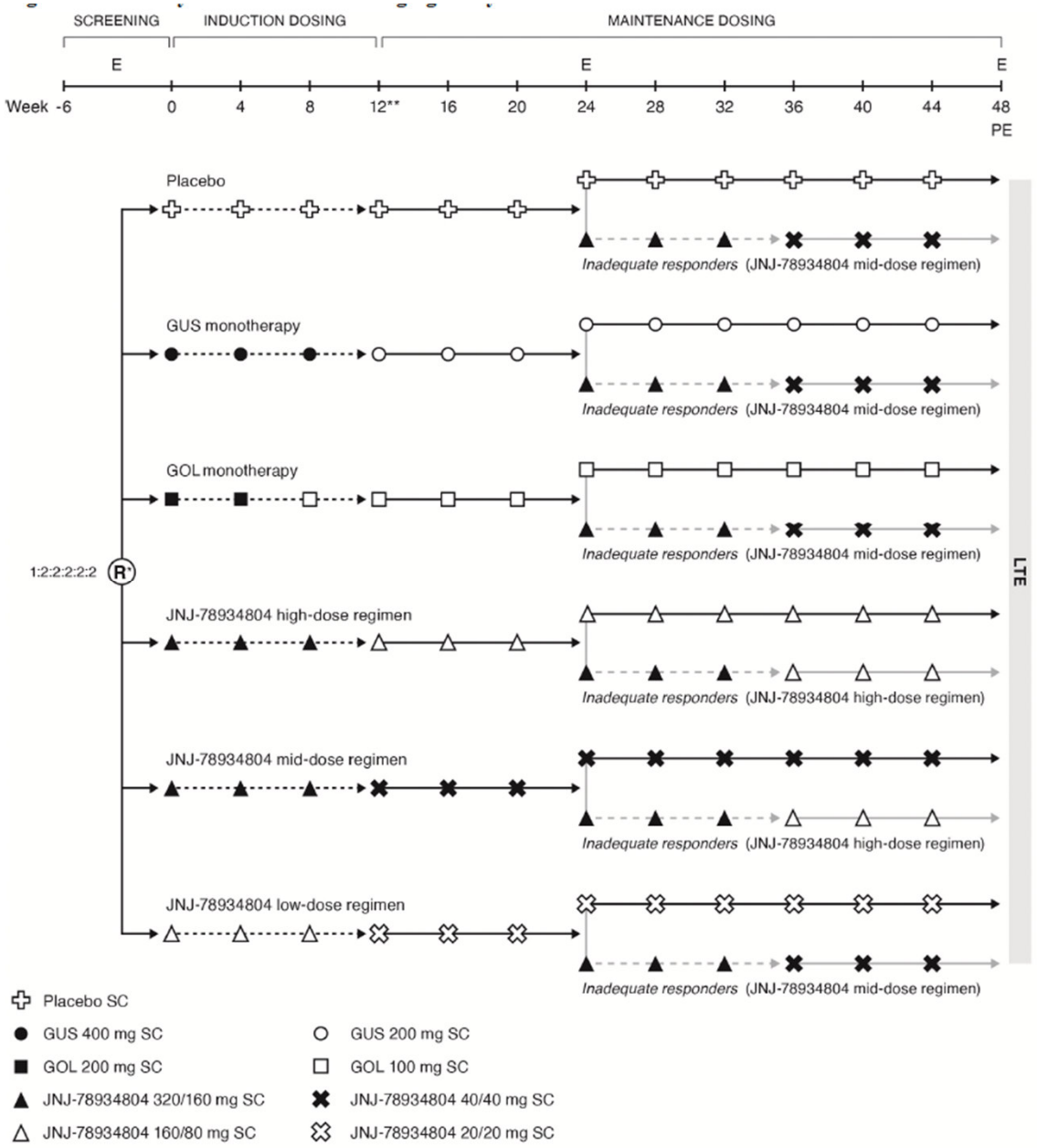
Sandborn WJ et al. UEGW Virtual 2020; 11–13 Oct 2020; Abstract OP089.

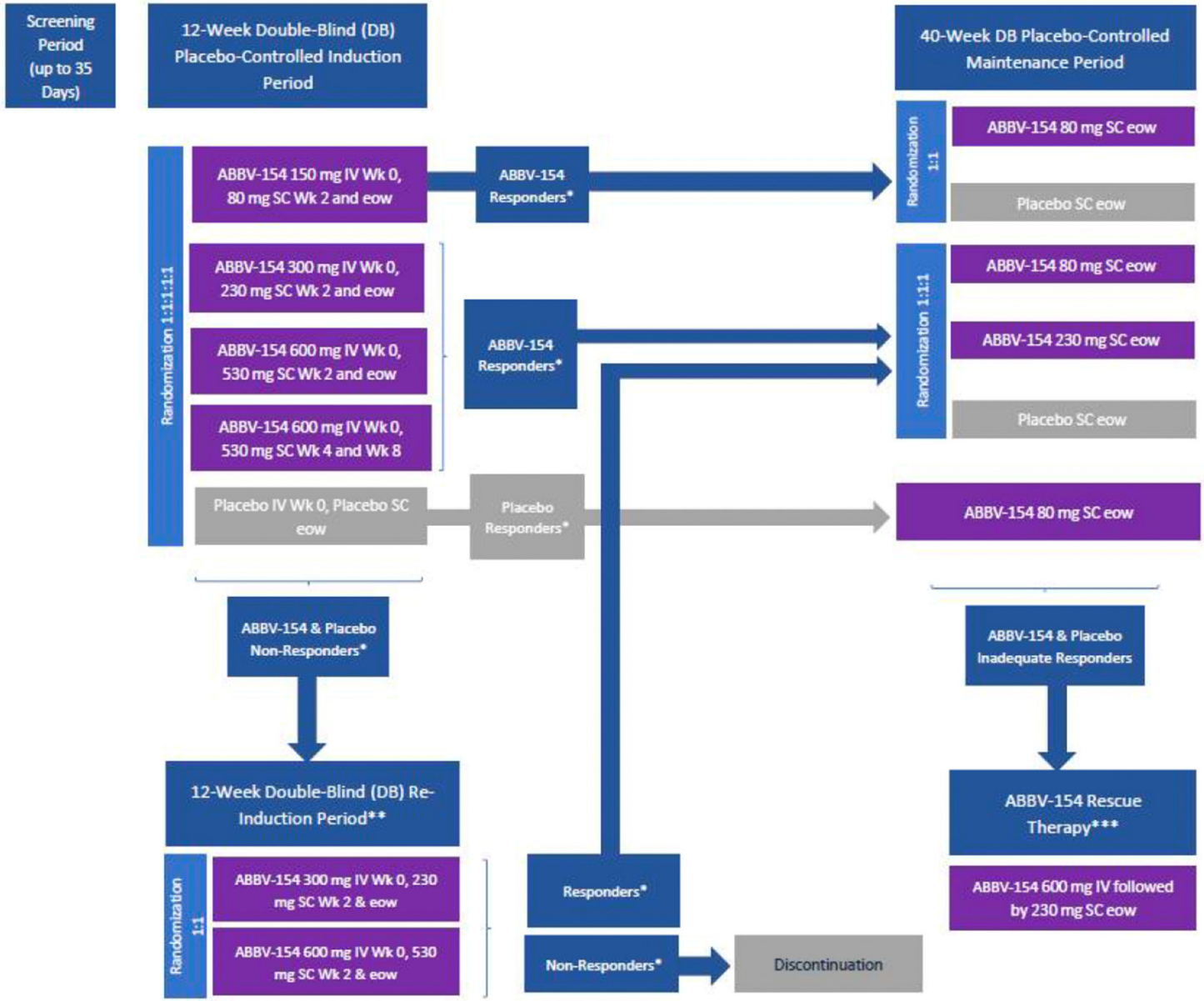
Risankizumab UC

Figure 3. Induction Period 1 of Study M16-067 Sub-Study 2 (Phase 3)

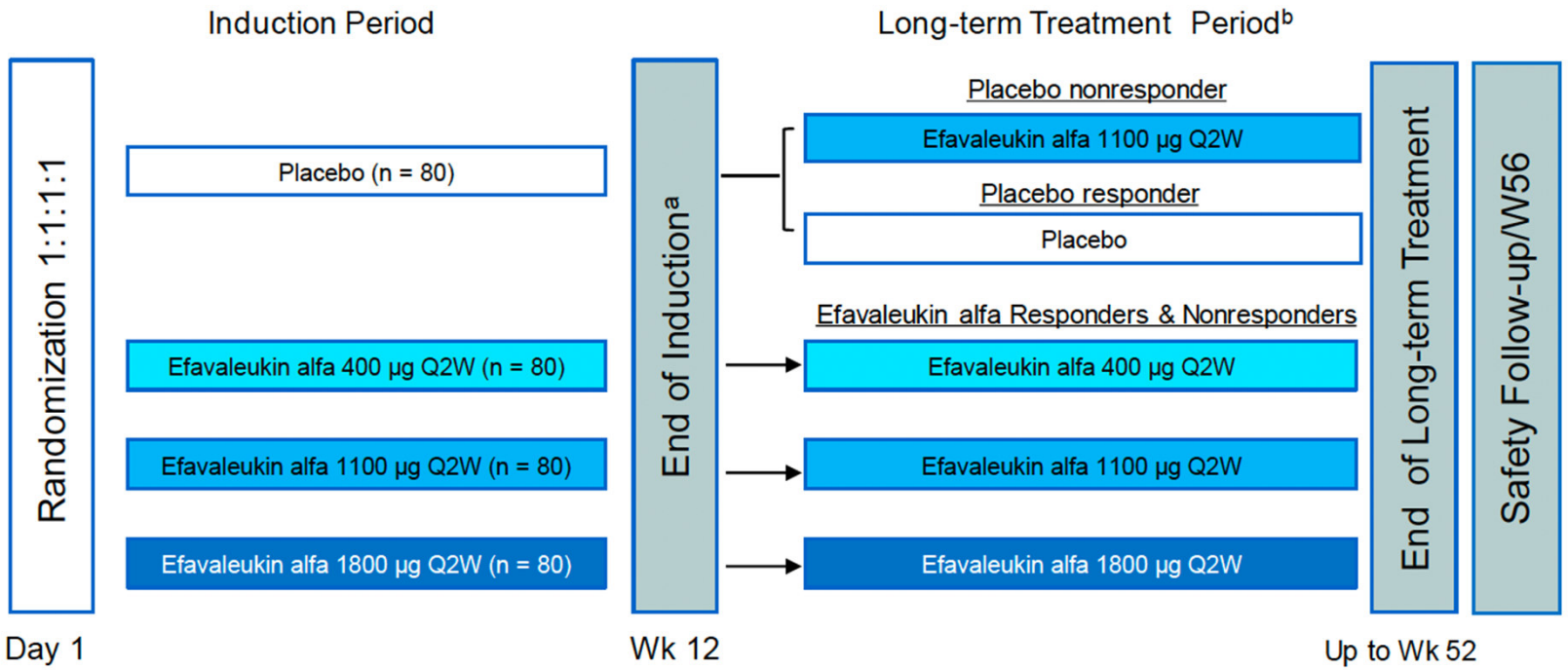


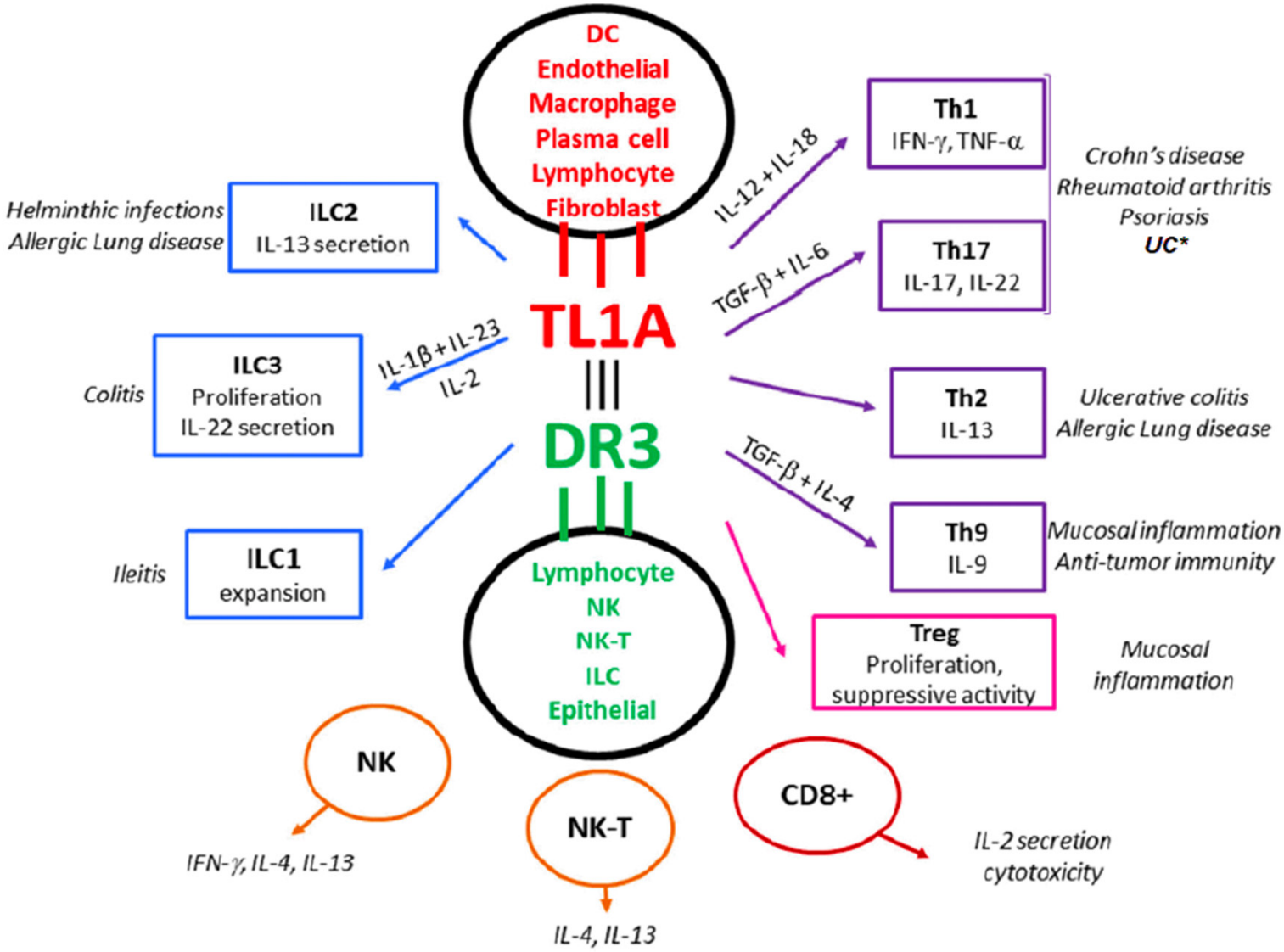
DC = discontinue; IR = subjects with inadequate clinical response; R = subjects with clinical response; SS-2 = Sub-study 2

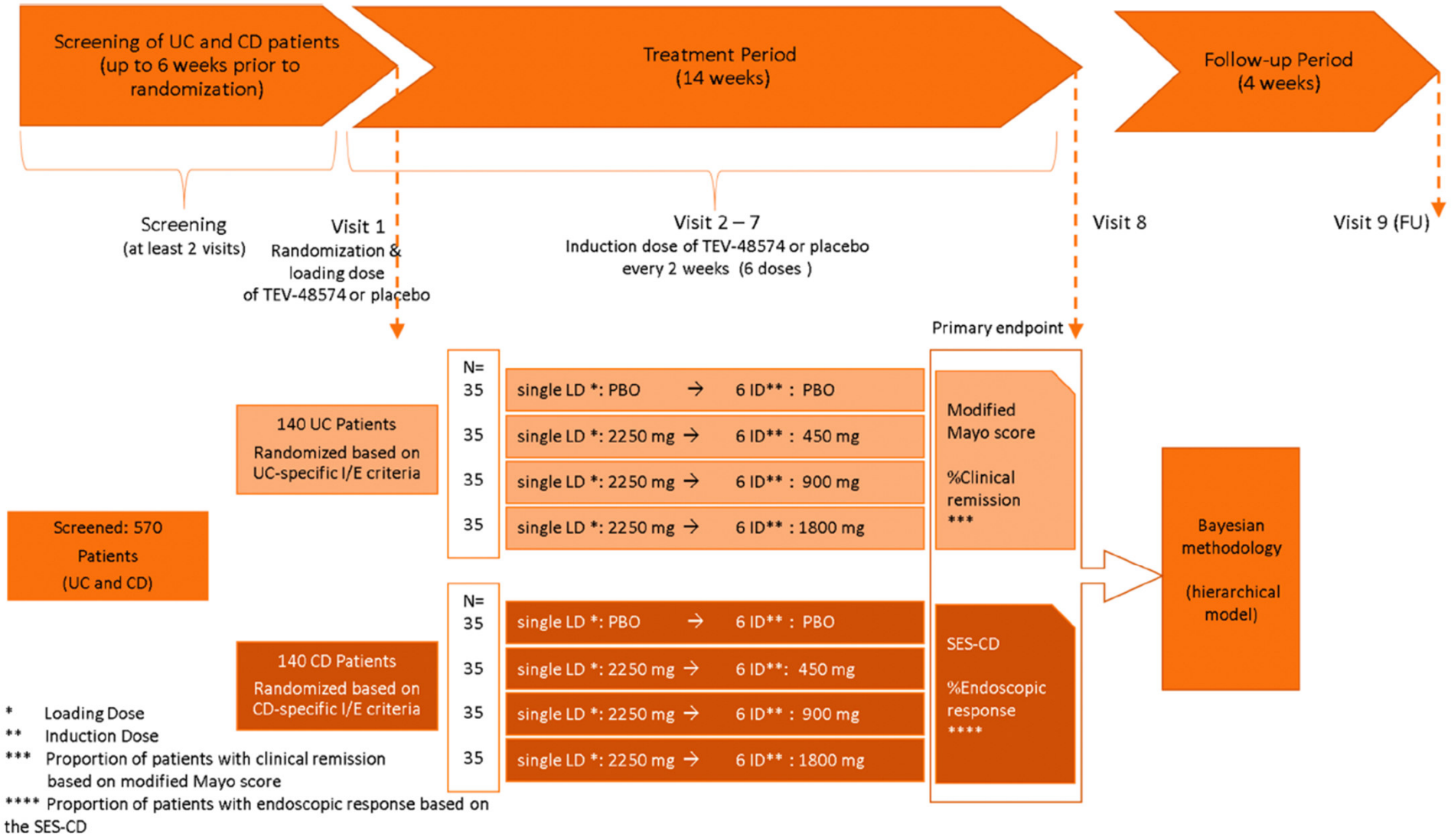

SCREENING
INDUCTION DOSING
MAINTENANCE DOSING
E
E
E
Week -6
0
4
8
12**
16
20
24
28
32
36
40
44
48
PE
Placebo
Inadequate responders (JNJ-78934804 mid-dose regimen)
GUS monotherapy
Inadequate responders (JNJ-78934804 mid-dose regimen)
GOL monotherapy
Inadequate responders (JNJ-78934804 mid-dose regimen)
1:2:2:2:2:2
R*
JNJ-78934804 high-dose regimen
Inadequate responders (JNJ-78934804 high-dose regimen)
JNJ-78934804 mid-dose regimen
Inadequate responders (JNJ-78934804 high-dose regimen)
JNJ-78934804 low-dose regimen
Inadequate responders (JNJ-78934804 mid-dose regimen)
LTE
Placebo SC
GUS 400 mg SC
GUS 200 mg SC
GOL 200 mg SC
GOL 100 mg SC
JNJ-78934804 320/160 mg SC
JNJ-78934804 40/40 mg SC
JNJ-78934804 160/80 mg SC
JNJ-78934804 20/20 mg SC

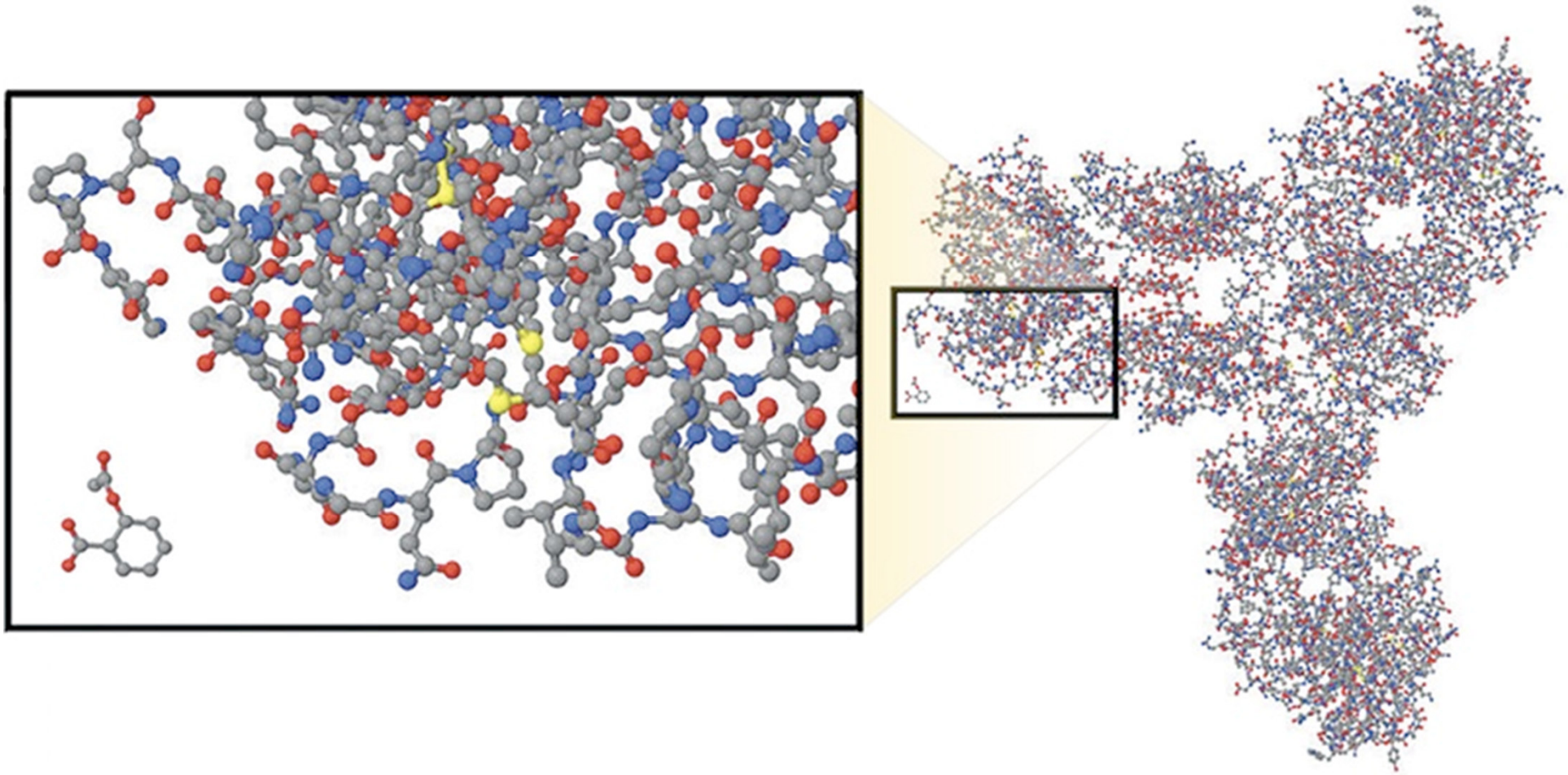

Screening Period (up to 35 Days)
12-Week Double-Blind (DB) Placebo-Controlled Induction Period
40-Week DB Placebo-Controlled Maintenance Period
Randomization 1:1:1:1:1
ABBV-154 150 mg IV Wk 0, 80 mg SC Wk 2 and eow
ABBV-154 Responders*
Randomization 1:1
ABBV-154 80 mg SC eow
Placebo SC eow
ABBV-154 300 mg IV Wk 0, 230 mg SC Wk 2 and eow
ABBV-154 600 mg IV Wk 0, 530 mg SC Wk 2 and eow
ABBV-154 600 mg IV Wk 0, 530 mg SC Wk 4 and Wk 8
ABBV-154 Responders*
Randomization 1:1:1
ABBV-154 80 mg SC eow
ABBV-154 230 mg SC eow
Placebo SC eow
Placebo IV Wk 0, Placebo SC eow
Placebo Responders*
ABBV-154 80 mg SC eow
ABBV-154 & Placebo Non-Responders*
ABBV-154 & Placebo Inadequate Responders
12-Week Double-Blind (DB) Re-Induction Period**
ABBV-154 Rescue Therapy***
Randomization 1:1
ABBV-154 300 mg IV Wk 0, 230 mg SC Wk 2 & eow
ABBV-154 600 mg IV Wk 0, 530 mg SC Wk 2 & eow
Responders*
ABBV-154 600 mg IV followed by 230 mg SC eow
Non-Responders*
Discontinuation

Efavaleukin Alfa

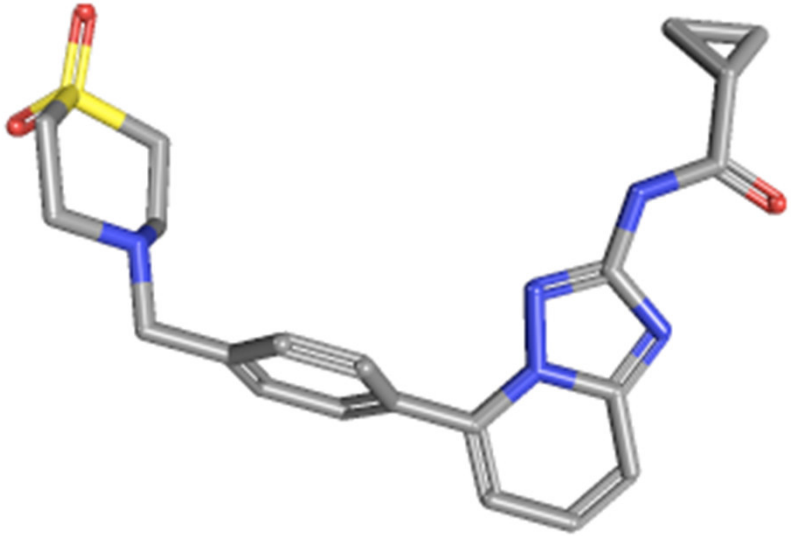


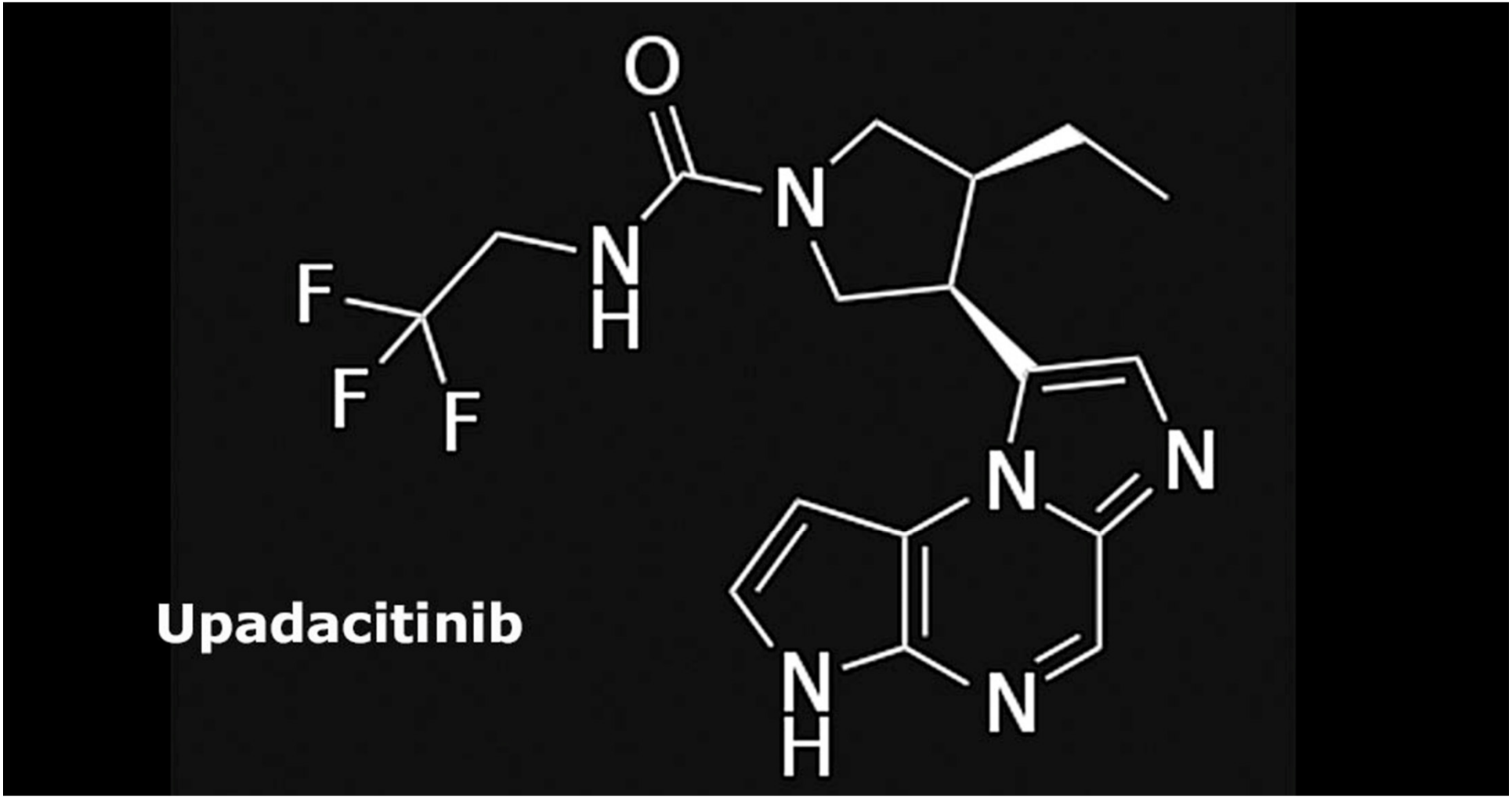

DC
Endothelial
Macrophage
Plasma cell
Lymphocyte
Fibroblast
TL1A
DR3
Lymphocyte
NK
NK-T
ILC
Epithelial
IL-12 + IL-18
Th1
IFN-γ, TNF-α
Crohn's disease
Rheumatoid arthritis
Psoriasis
UC*
TGF-β + IL-6
Th17
IL-17, IL-22
Helminthic infections
Allergic Lung disease
ILC2
IL-13 secretion
IL-1β + IL-23
IL-2
Colitis
ILC3
Proliferation
IL-22 secretion
Th2
IL-13
Ulcerative colitis
Allergic Lung disease
TGF-β + IL-4
Th9
IL-9
Mucosal inflammation
Anti-tumor immunity
Ileitis
ILC1
expansion
Treg
Proliferation,
suppressive activity
Mucosal
inflammation
NK
IFN-γ, IL-4, IL-13
NK-T
IL-4, IL-13
CD8+
IL-2 secretion
cytotoxicity


Screening of UC and CD patients (up to 6 weeks prior to randomization)
Treatment Period (14 weeks)
Follow-up Period (4 weeks)
Screening (at least 2 visits)
Visit 1 Randomization & loading dose of TEV-48574 or placebo
Visit 2 – 7 Induction dose of TEV-48574 or placebo every 2 weeks (6 doses)
Visit 8
Visit 9 (FU)
Primary endpoint
Screened: 570 Patients (UC and CD)
140 UC Patients Randomized based on UC-specific I/E criteria
N= 35 single LD *: PBO → 6 ID** : PBO
35 single LD *: 2250 mg → 6 ID** : 450 mg
35 single LD *: 2250 mg → 6 ID** : 900 mg
35 single LD *: 2250 mg → 6 ID** : 1800 mg
Modified Mayo score
%Clinical remission ***
140 CD Patients Randomized based on CD-specific I/E criteria
N= 35 single LD *: PBO → 6 ID** : PBO
35 single LD *: 2250 mg → 6 ID**: 450 mg
35 single LD *: 2250 mg → 6 ID** : 900 mg
35 single LD *: 2250 mg → 6 ID** : 1800 mg
SES-CD
%Endoscopic response ****
Bayesian methodology (hierarchical model)
* Loading Dose
** Induction Dose
*** Proportion of patients with clinical remission based on modified Mayo score
**** Proportion of patients with endoscopic response based on the SES-CD



Filgotinib




O
N
N
H
F
F
F
N
N
N
H
N
Upadacitinib

Bundesamt für
Sicherheit im
Gesundheitswesen
BASG

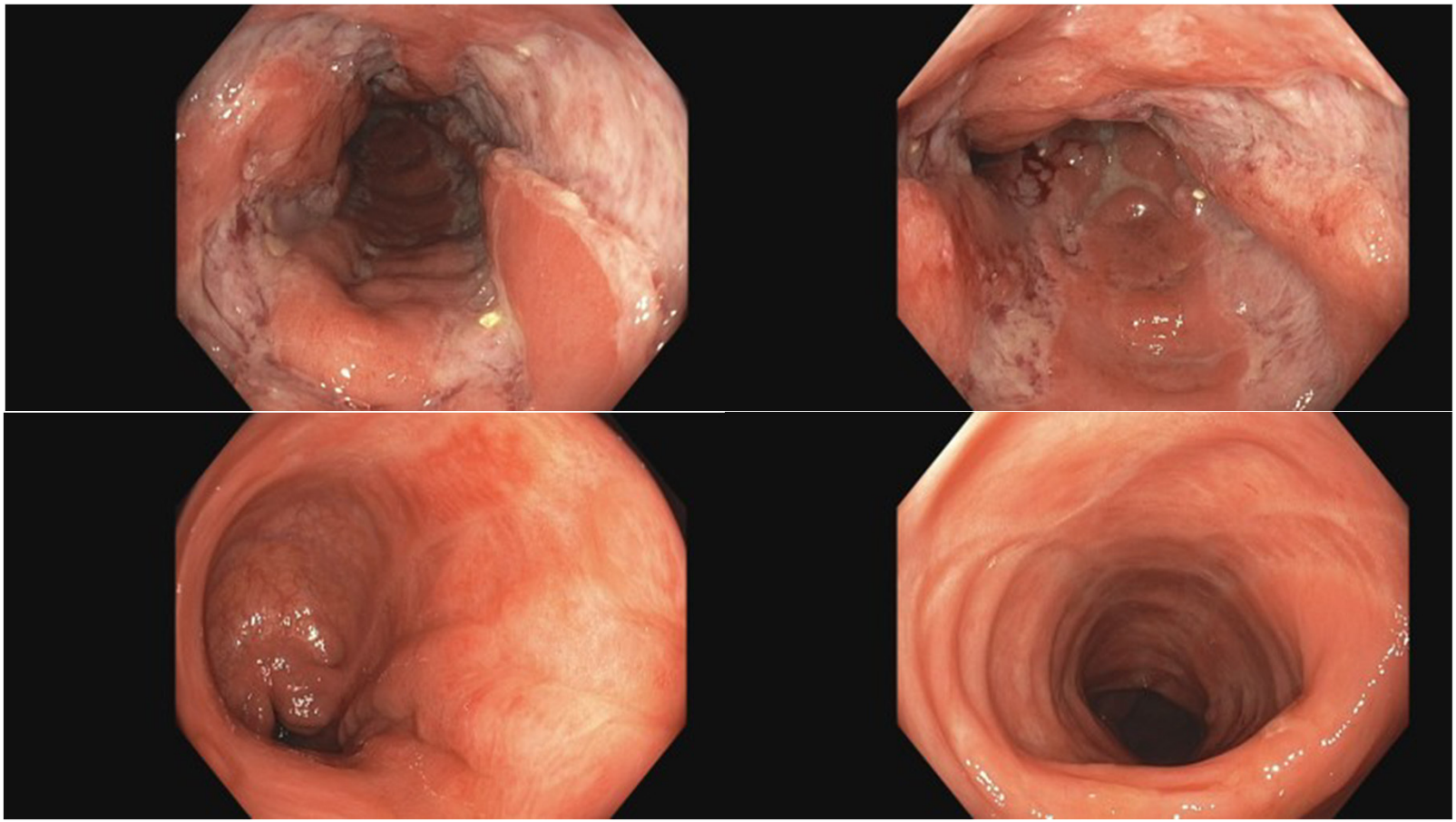
Landeshauptleute; Landessanitätsdirektionen;
Österreichische Apothekerkammer; Österreichische
Ärztekammer; Landesärztekammern;
Anstaltsapotheken der Universitätskliniken

Datum: 08.07.2021
Kontakt: Mag. Rudolf Schranz
Tel: +43 505 55-36246
E-Mail: rudolf.schranz@ages.at

Mitteilung des Bundesamts für Sicherheit im Gesundheitswesen über Maßnahmen zur Gewährleistung der Arzneimittelsicherheit:

Wichtige Information des Bundesamtes für Sicherheit im Gesundheitswesen über ein erhöhten Risiko für schwerwiegende unerwünschte Kardiovaskuläre Ereignisse und maligne Erkrankungen (außer nicht-melanozytärem Hautkrebs/NMSC) unter der Anwendung von Tofacitinib im Vergleich zu TNF-Alpha-Inhibitoren

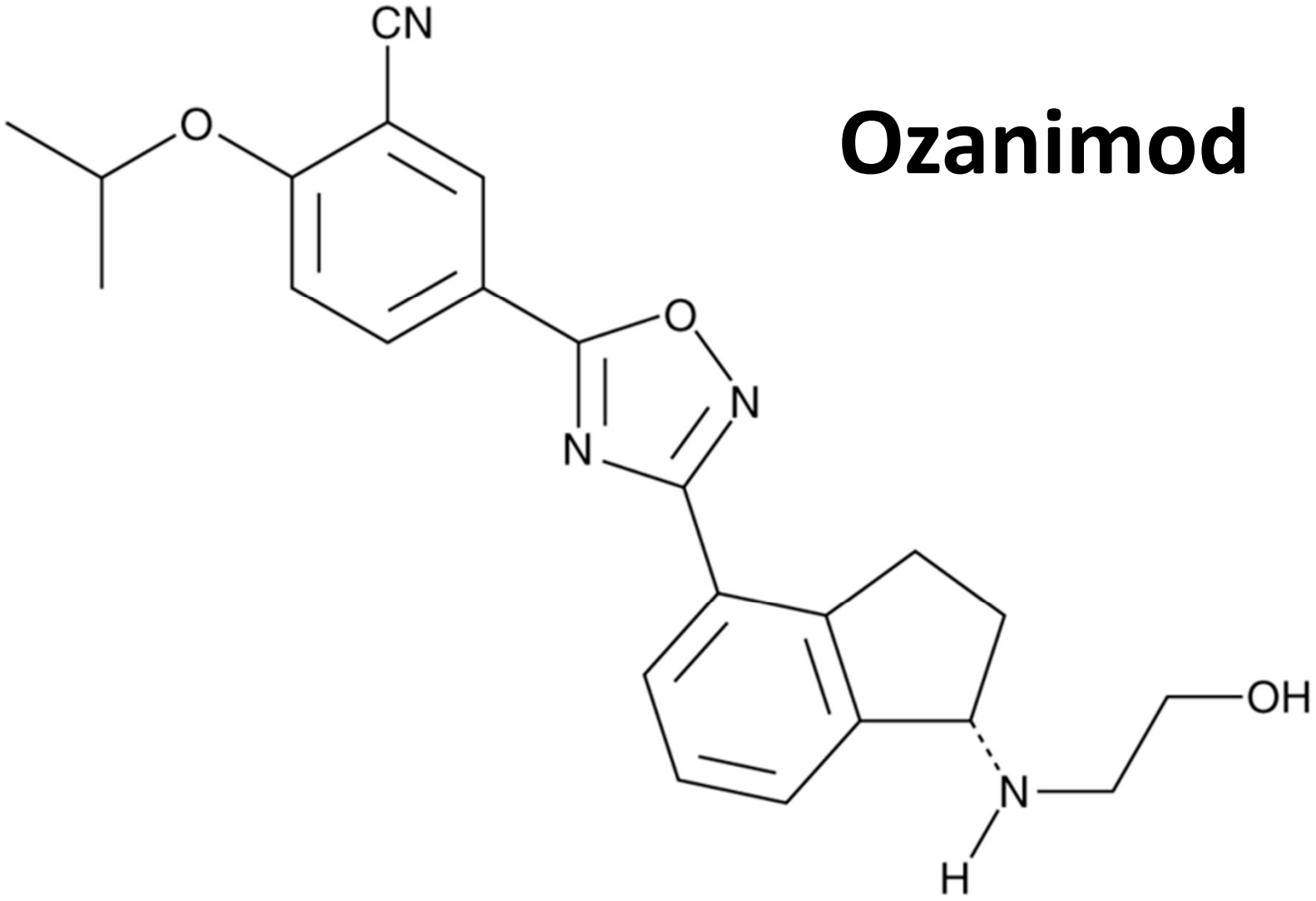
Upadacitinib…

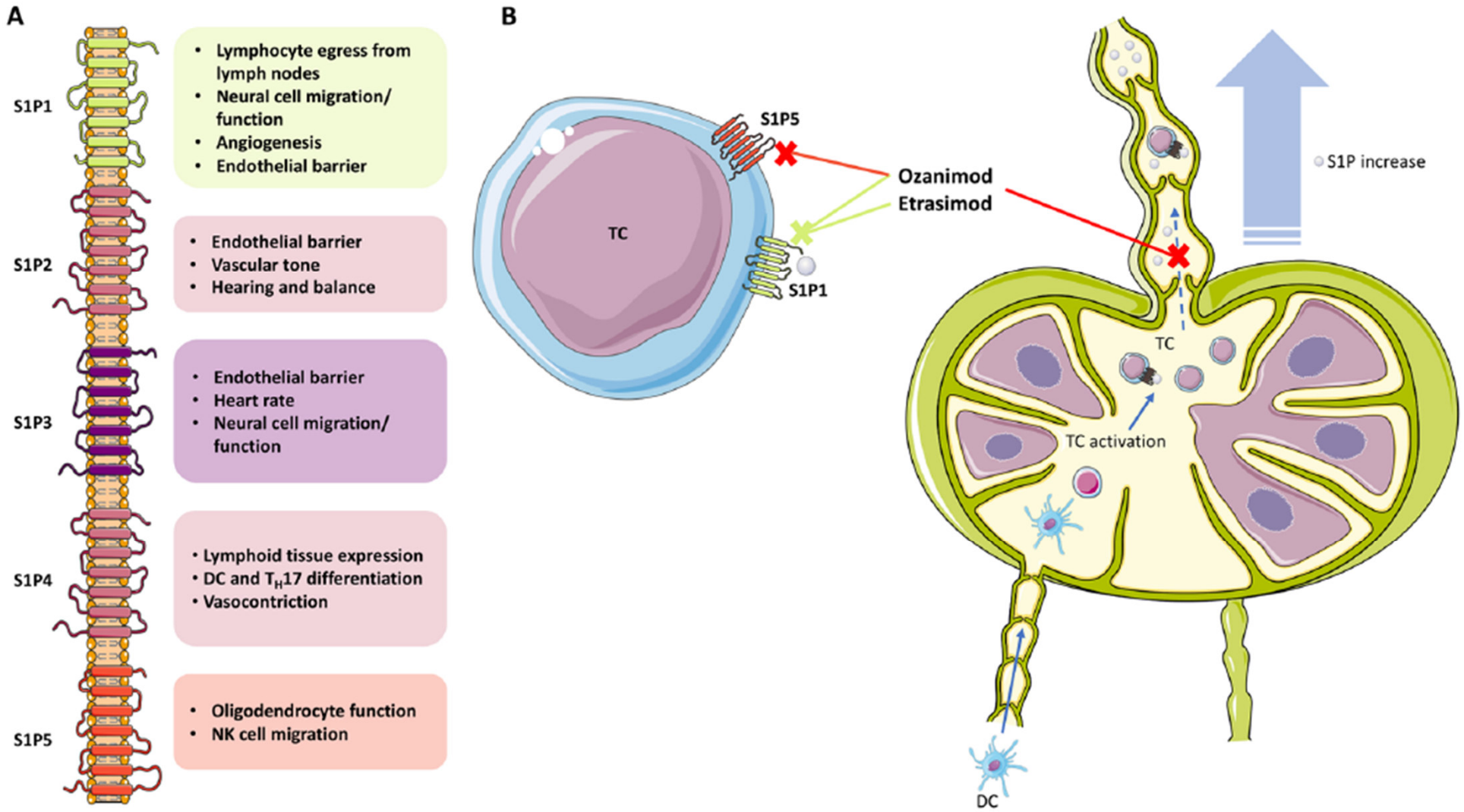


Kolo
29.03.2019

Kolo
10.07.2019

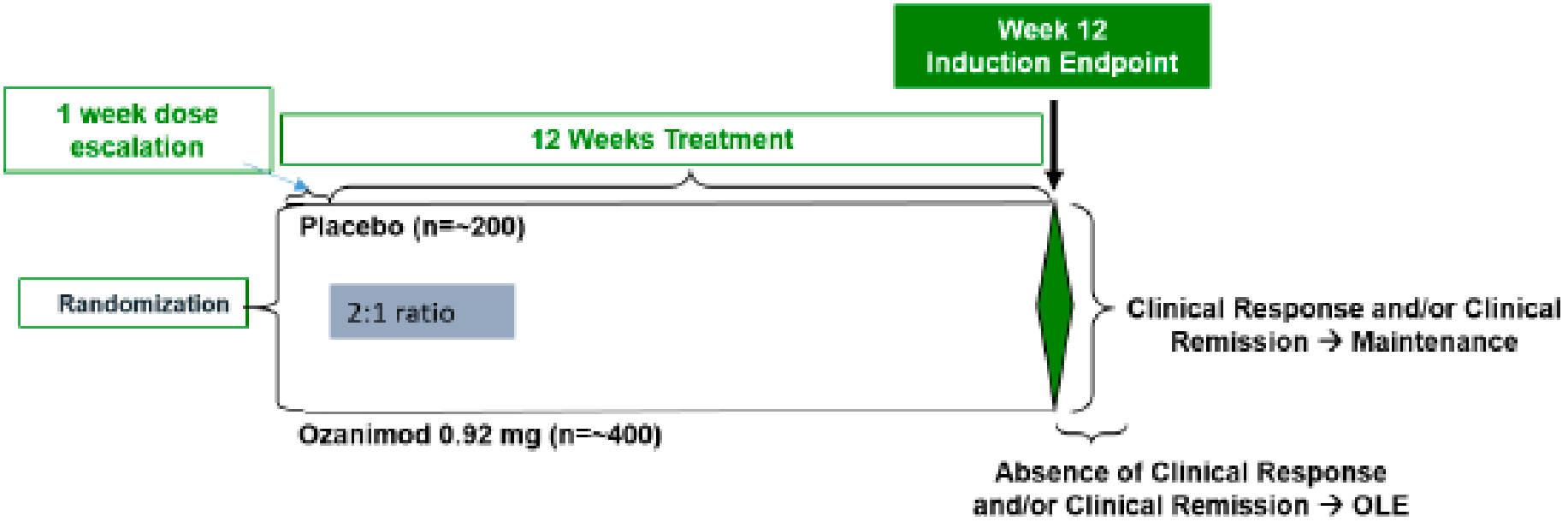
Ozanimod



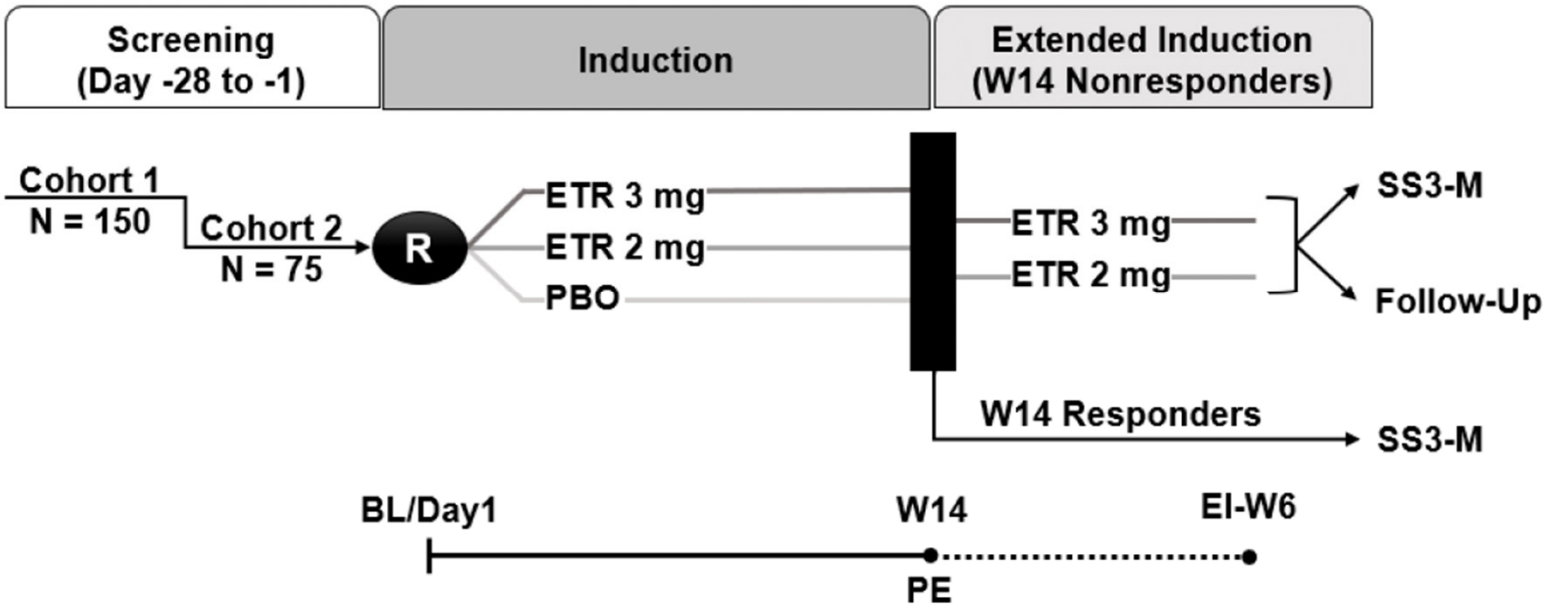

A
S1P1
• Lymphocyte egress from lymph nodes
• Neural cell migration/ function
• Angiogenesis
• Endothelial barrier
S1P2
• Endothelial barrier
• Vascular tone
• Hearing and balance
S1P3
• Endothelial barrier
• Heart rate
• Neural cell migration/ function
S1P4
• Lymphoid tissue expression
• DC and T_H17 differentiation
• Vasocontriction
S1P5
• Oligodendrocyte function
• NK cell migration
B
S1P5
TC
S1P1
Ozanimod
Etrasimod
S1P increase
TC
TC activation
DC

Ozanimod

Figure 1: Overall Study Design



Etrasimod


Screening
(Day -28 to -1)
Induction
Extended Induction
(W14 Nonresponders)
Cohort 1
N = 150
Cohort 2
N = 75
R
ETR 3 mg
ETR 2 mg
PBO
ETR 3 mg
ETR 2 mg
SS3-M
Follow-Up
W14 Responders
SS3-M
BL/Day1
W14
PE
EI-W6

A phase IIb, double-blind, randomised, placebo-controlled trial to evaluate the efficacy and tolerability of ZED1227 in celiac disease subjects experiencing symptoms despite gluten-free diet

Short title: ZED1227 for treatment of symptomatic celiac disease subjects

Investigational drug:	ZED1227 (10/25/50 mg capsules)
Reference drug:	Placebo capsules
Indication:	Treatment of celiac disease
Phase of trial:	IIb

- **Run-in Phase (Trial Period A):**
  Subjects will receive a 5-week, single-blind placebo treatment with:
  Placebo capsules TID 30 minutes before each meal
  3 x Placebo capsule

  First IMP intake: In the morning after Baseline Visit A (V1)
  Last IMP intake: In the morning of Baseline Visit B (V3)

- **Treatment Phase (Trial Period B):**
  Subjects will be randomised (1:1:1:1) to receive a 12-week, double-blind treatment with:

Treatment group	Investigational medicinal product
A	10 mg ZED1227 (TID) 30 minutes before each major meal 3 x ZED1227 10 mg capsule
B	25 mg ZED1227 (TID) 30 minutes before each major meal 3 x ZED1227 25 mg capsule
C	50 mg ZED1227 (OD) 30 minutes before breakfast; placebo capsules 30 minutes before lunch and dinner. 1 x ZED1227 50 mg capsule, 2 x Placebo capsule
D	Placebo capsules (TID) 30 minutes before each major meal 3 x Placebo capsule