European Crohn's and Colitis Organisation

Maintenance of clinical effect in patients with moderate-to-severe Crohn's disease treated with Filgotinib, a selective JAK1 inhibitor

Exploratory 20-week data analysis of the Phase 2 FITZROY study

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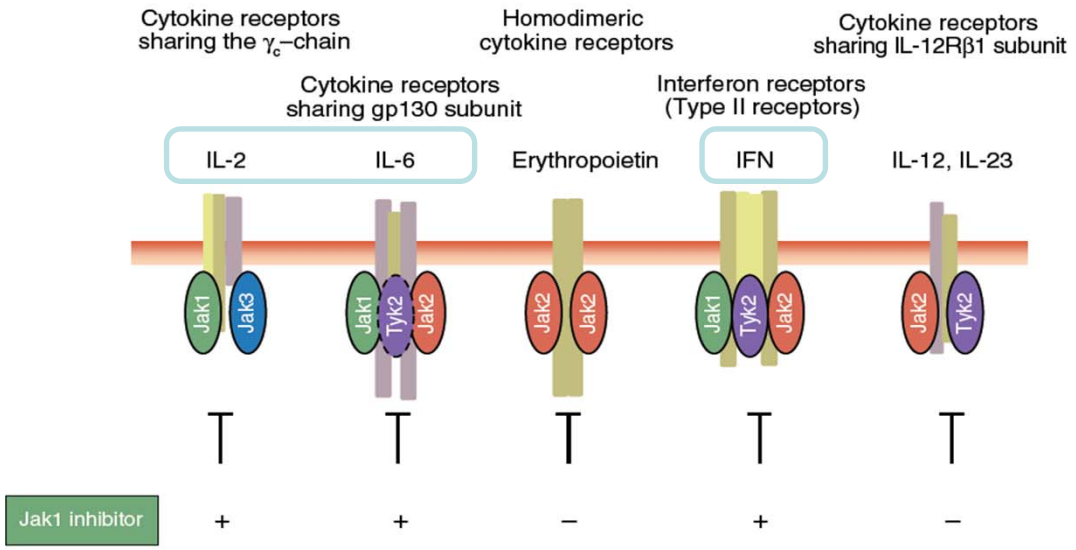
Janus family tyrosine kinases (JAKs)

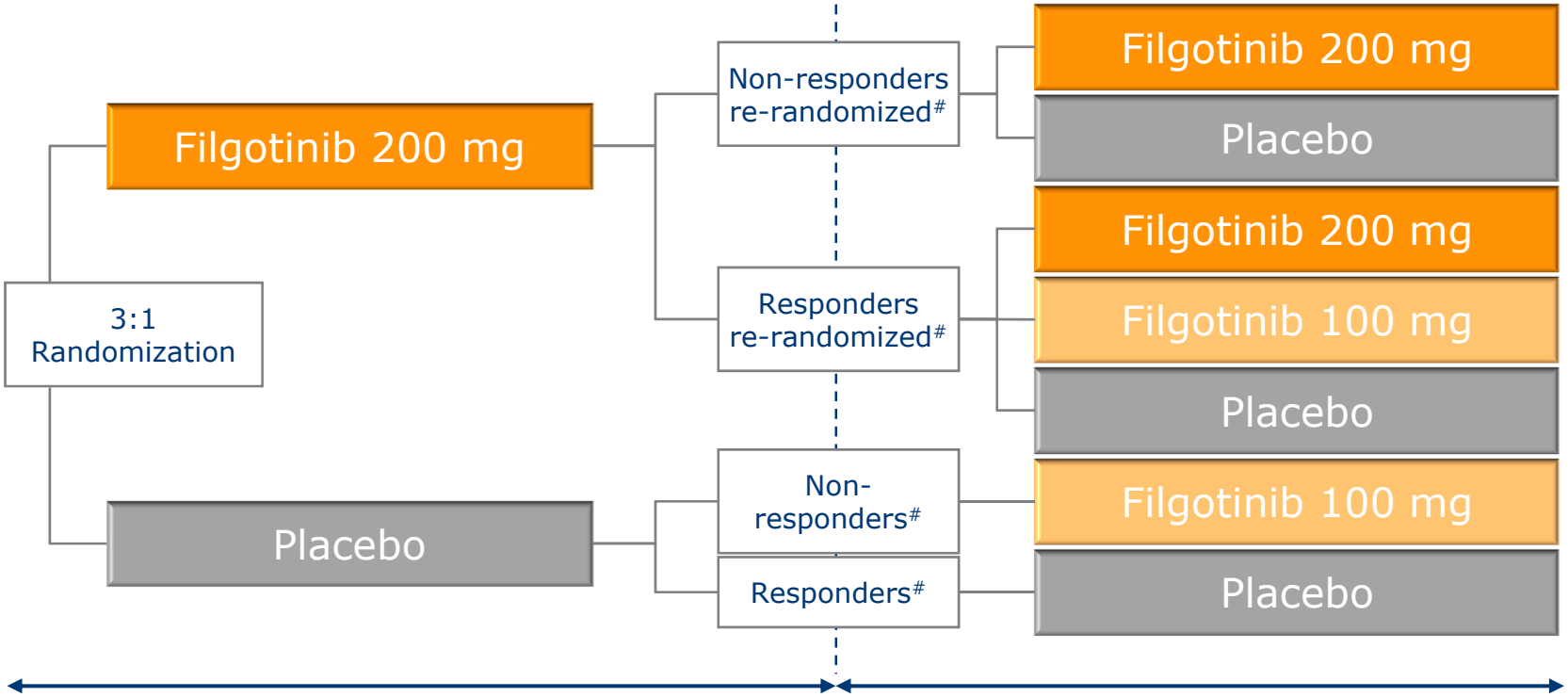


- JAK1 inhibition suppresses signaling for (pro)inflammatory cytokines
- JAK2 inhibition also suppresses GM-CSF, EPO, TPO, GH, PRL signaling
- JAK3 inhibition has an effect on γ-chain IL-s, critical for lymphocyte function

- Filgotinib is a highly selective inhibitor of Janus kinase 1 (JAK1)
- Biochemical IC50 ~10nM
- 30-fold selective over JAK2 in human whole blood
- >10-fold selective over Tyk2
- >50-fold selective over non-JAK kinases and JAK3

Ghoreschi K, et al. *Nature Immunol* 2009;10:356–360

FITZROY: study design



Primary endpoint: CDAI remission (CDAI <150) at W10

Secondary endpoints: CDAI, endoscopy, histopathology, QoL, CRP

Exploratory endpoints: CDAI, QoL, CRP

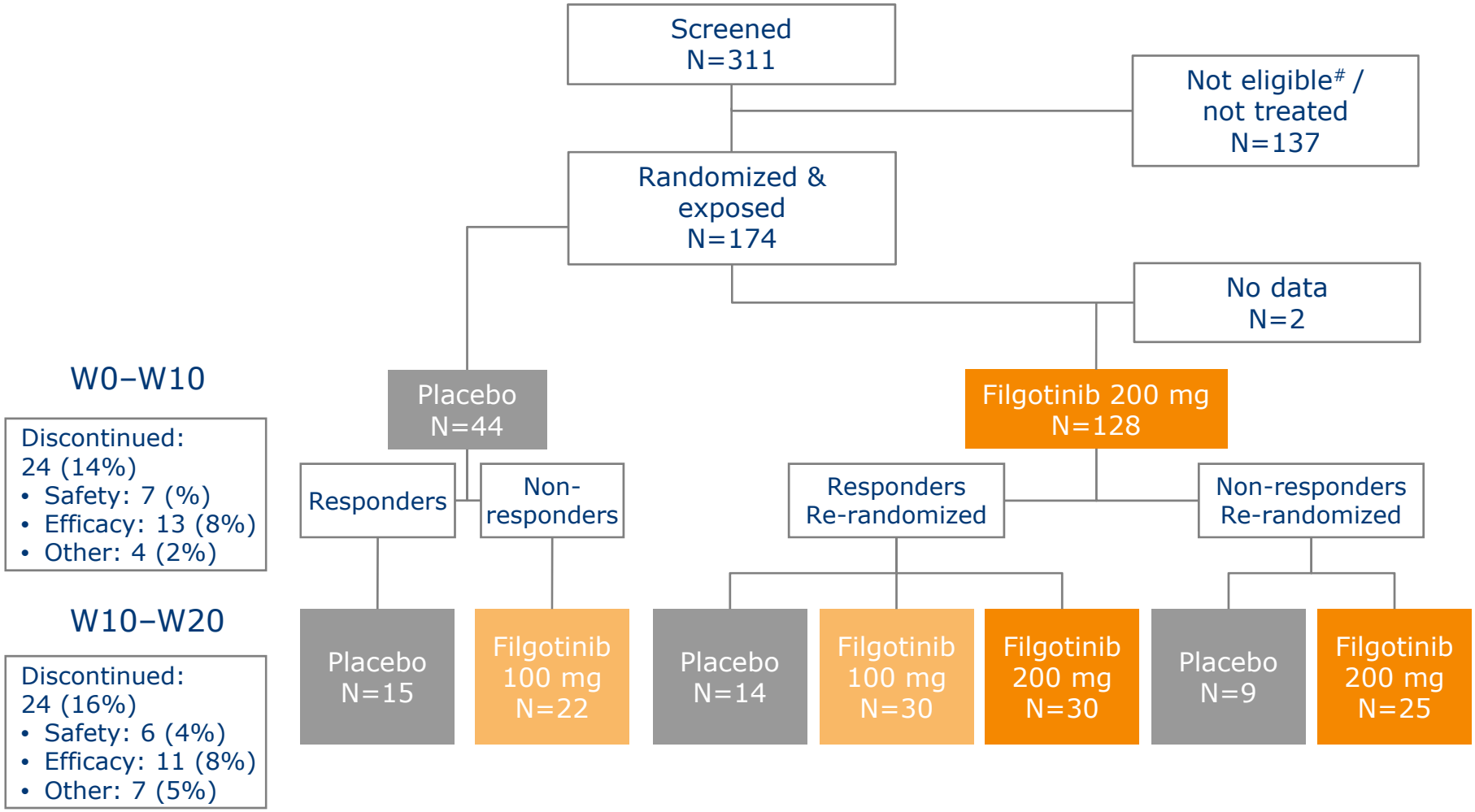
#Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

FITZROY: key eligibility criteria

- Inclusion:
  - ileal, colonic, or ileocolonic Crohn's Disease (on colonoscopy and histology)
  - Crohn's Disease Activity Index (CDAI) 220–450
  - endoscopic confirmation of active disease, ulceration (score of 2 or 3[#] in at least 1 out of 5 of the ileocolonic segments - SES-CD, total score of at least 7, central reading)
- Exclusion:
  - indeterminate colitis, ulcerative colitis
  - surgical bowel resection within past 6 months
- Concomitant medications:
  - allowed: stable doses of oral steroids (≤30 mg prednisolone eq/day), mesalazine, CD-related antibiotics, and probiotics
  - not allowed: anti-TNFs, immuno-modulators (AZA, MTX and 6-MP)

[#]Amended during the study to score of 1

FITZROY: patient disposition



#47% failures were due to SES-CD

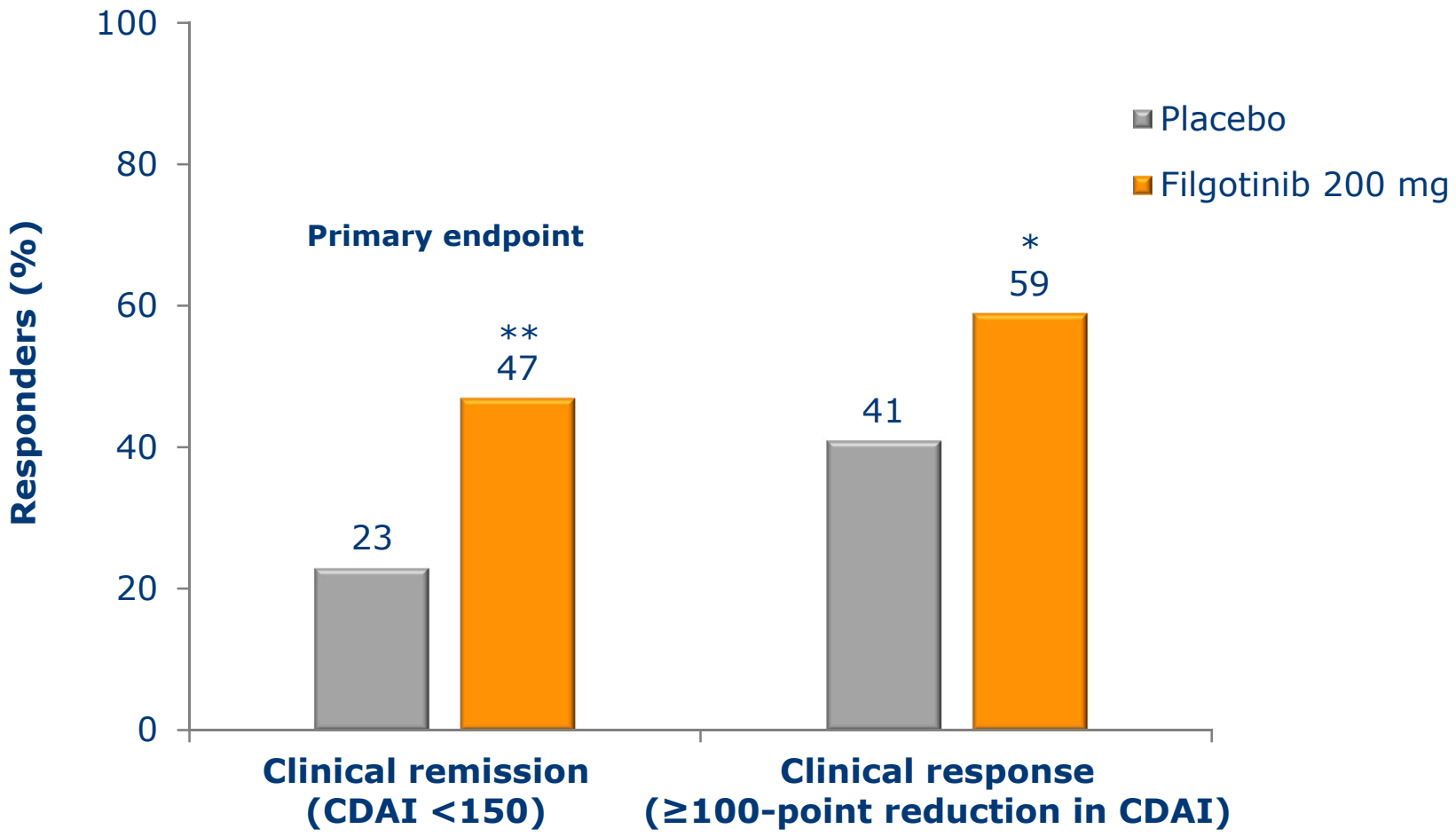
FITZROY: baseline characteristics

Safety population

	Placebo (N=44)	Filgotinib 200 mg (N=130)
Age, mean, years	35.1	37.4
Female, %	59	55
Duration of CD, median, years	5.4	6.3
CDAI, mean	299	291
IBDQ, mean	120.8	123.0
SES-CD, mean	15.8	14.2
CRP, median, mg/L	8.1	8.2
CRP >10mg/L, %	41	42
Concomitant oral corticosteroids, %	52	48
mean daily dose, mg	21.3	20.7
Anti-TNF experienced, %	64	56

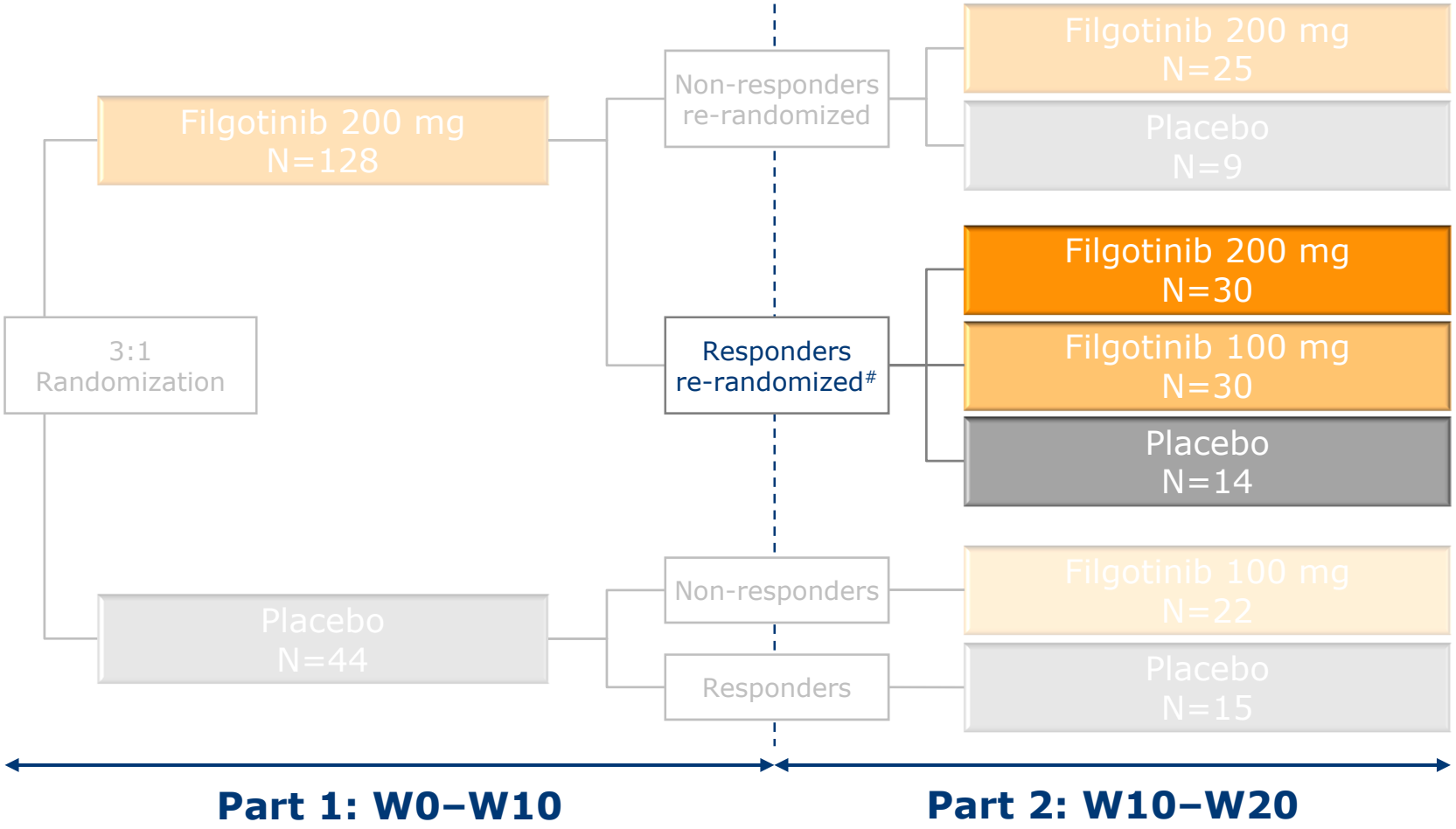
FITZROY: CDAI remission and response

ITT-NRI, W10



*p<0.05; **p<0.01

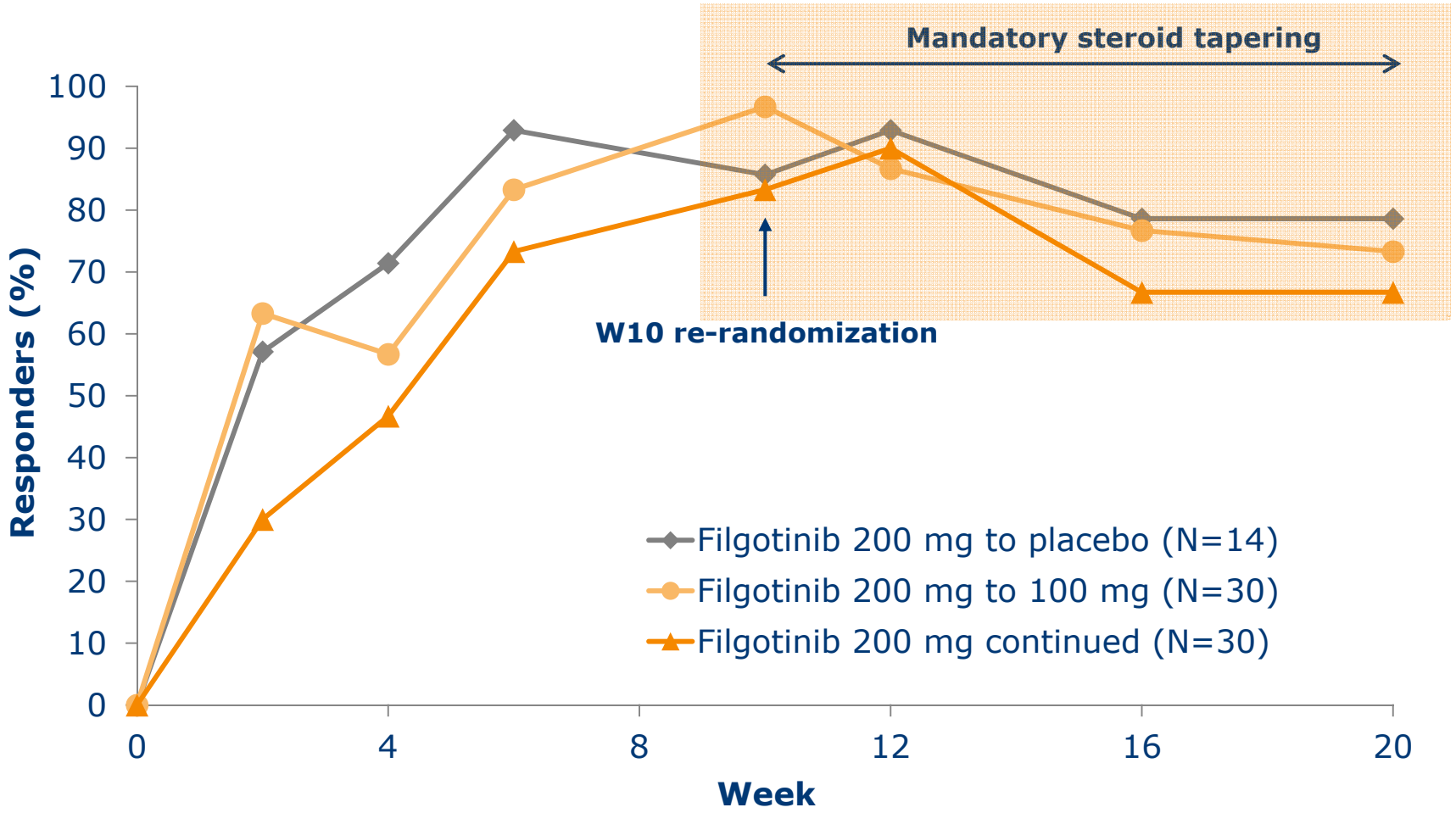
FITZROY: 10 week 'maintenance' period



#Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

FITZROY: clinical response

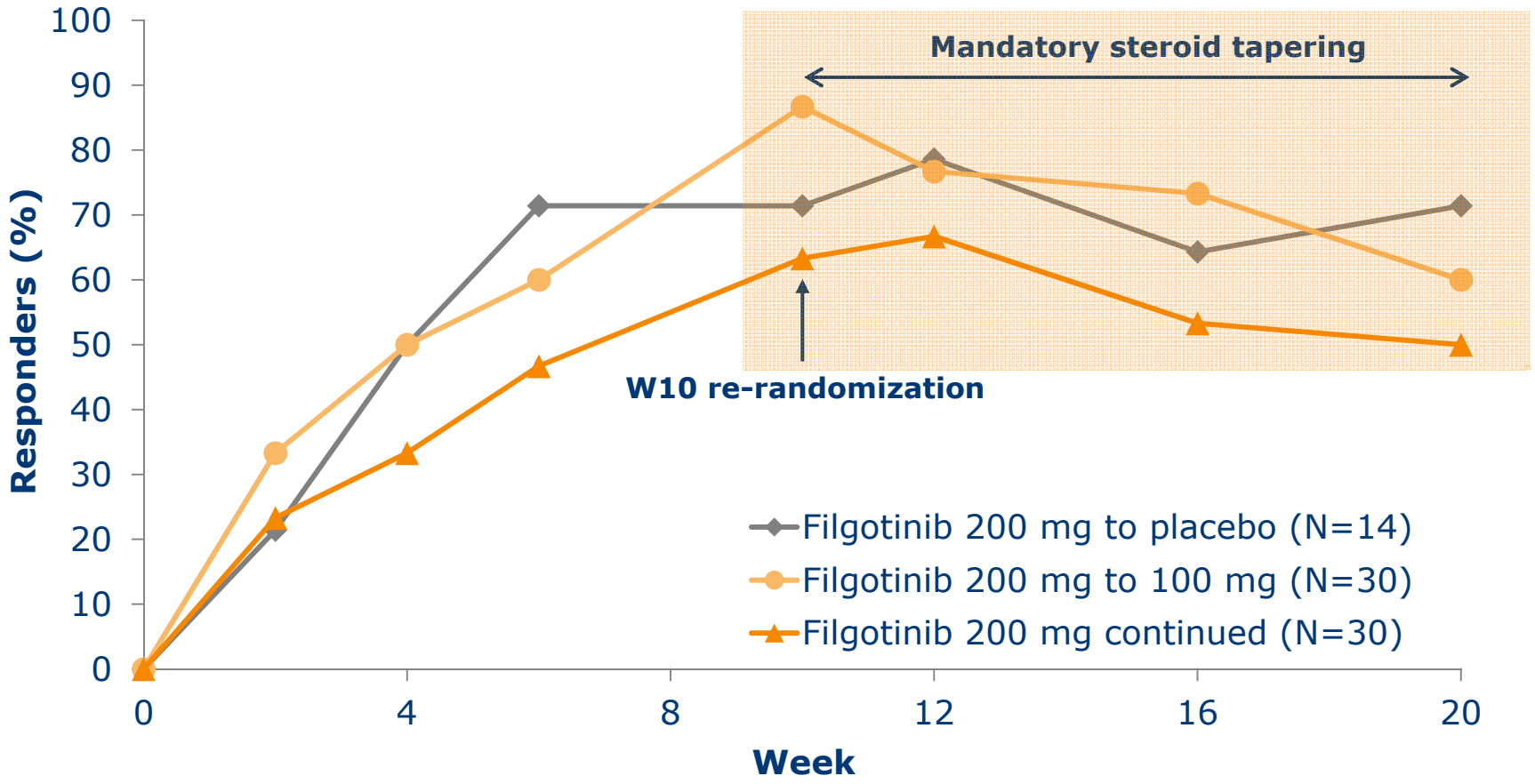
ITT-NRI, initial filgotinib 200 mg responders[#]



[#]Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

FITZROY: clinical remission

ITT-NRI, initial filgotinib 200 mg responders[#]

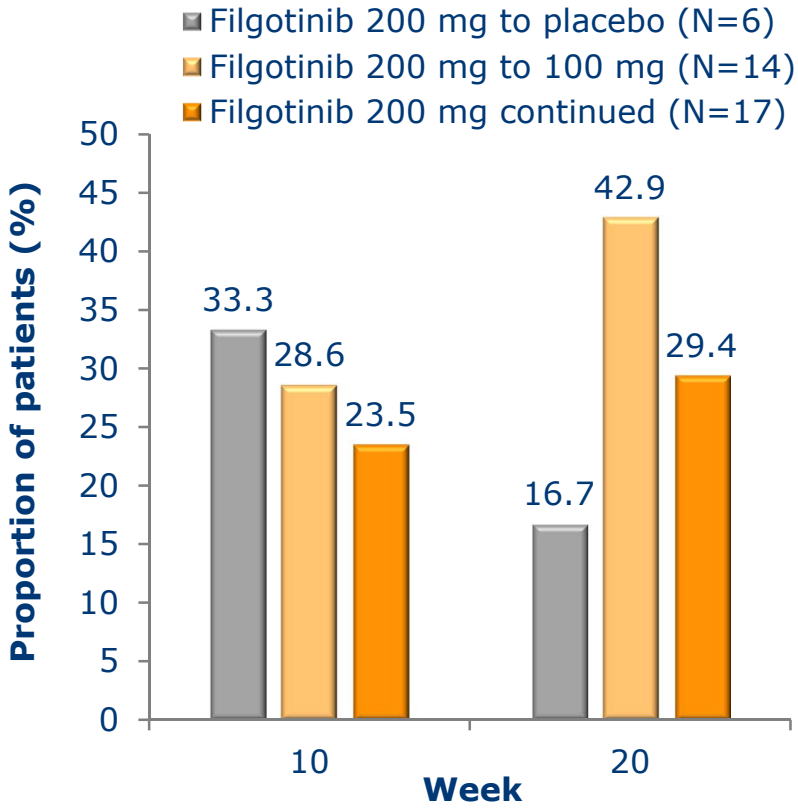


[#]Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

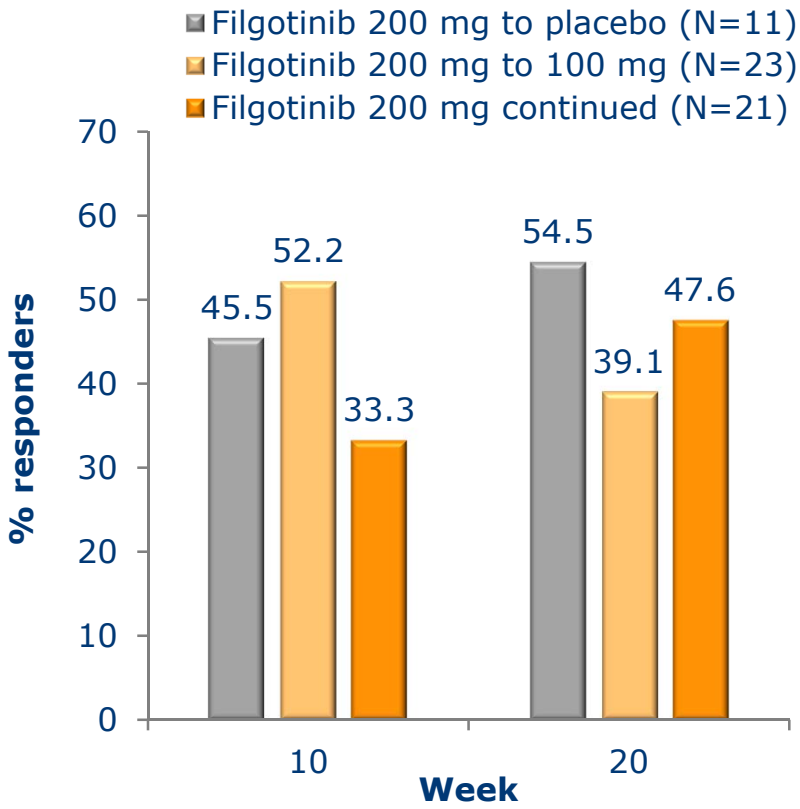
FITZROY: CRP normalization and biological response

ITT-LOCF, initial filgotinib 200 mg responders[#]

CRP normalization##



Combined clinical remission / biological response



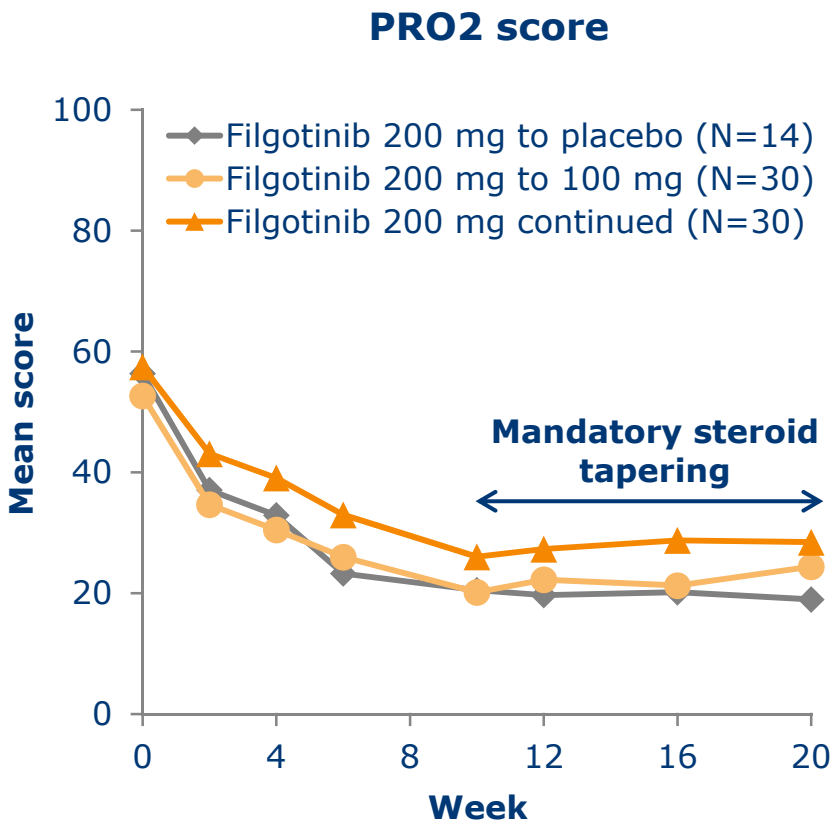
Combined clinical remission / biological response: CDAI-score <150 points and CRP decrease >50% and/or fecal calprotectin decrease >50% from baseline

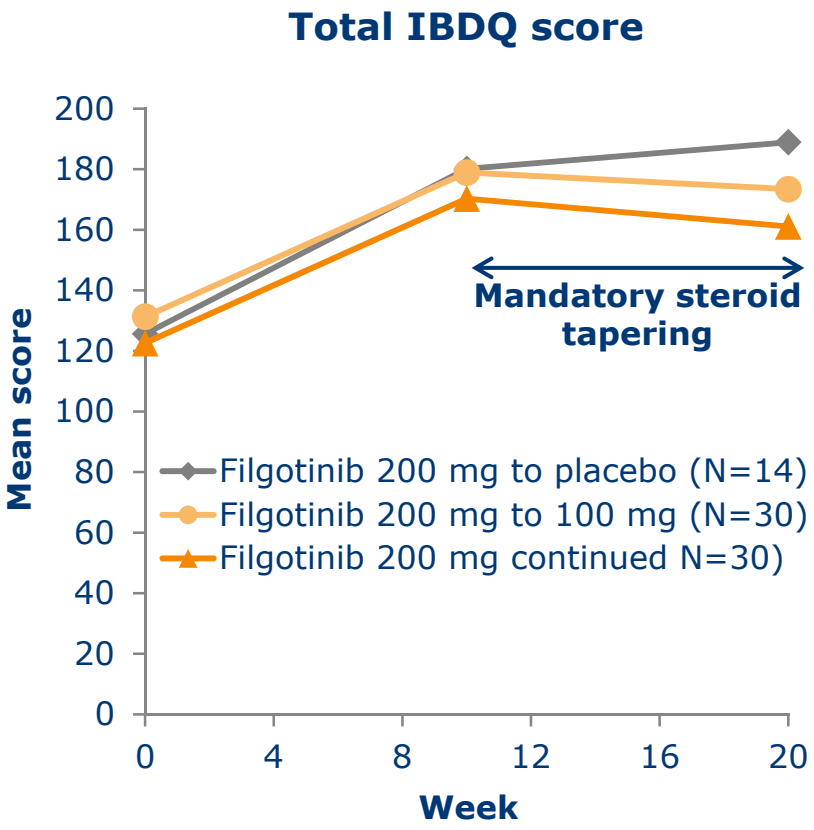
[##]subjects with high baseline CRP ≥8mg/L

[#]Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

FITZROY: PRO2 score and QoL

ITT-LOCF, initial filgotinib 200 mg responders[#]

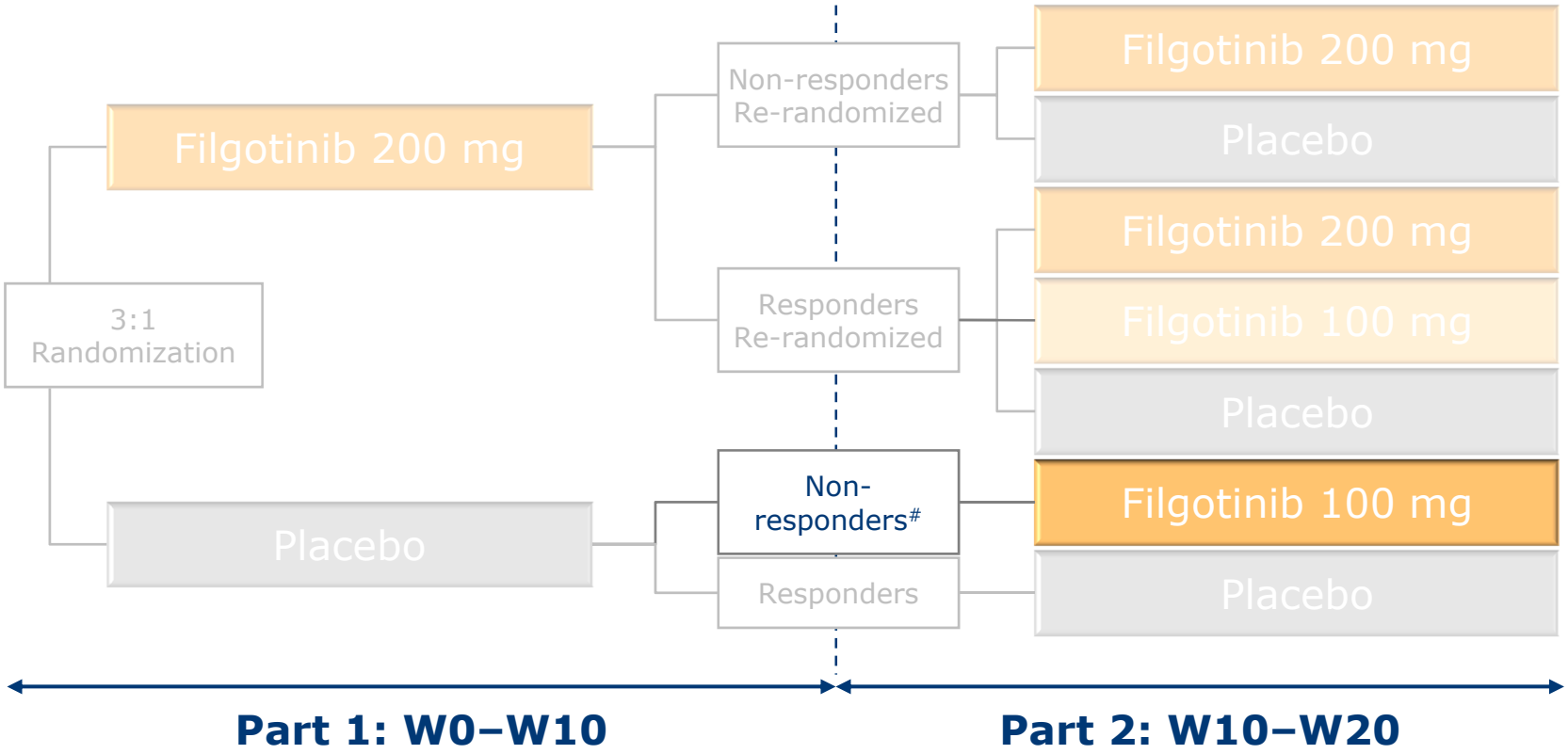




PRO2: a composite score based on daily stool frequency and self-reported abdominal pain, with remission defined as "7 × (mean daily number of liquid or very soft stools) + 7 × (mean daily self-reported abdominal pain)" ≤28

[#]Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

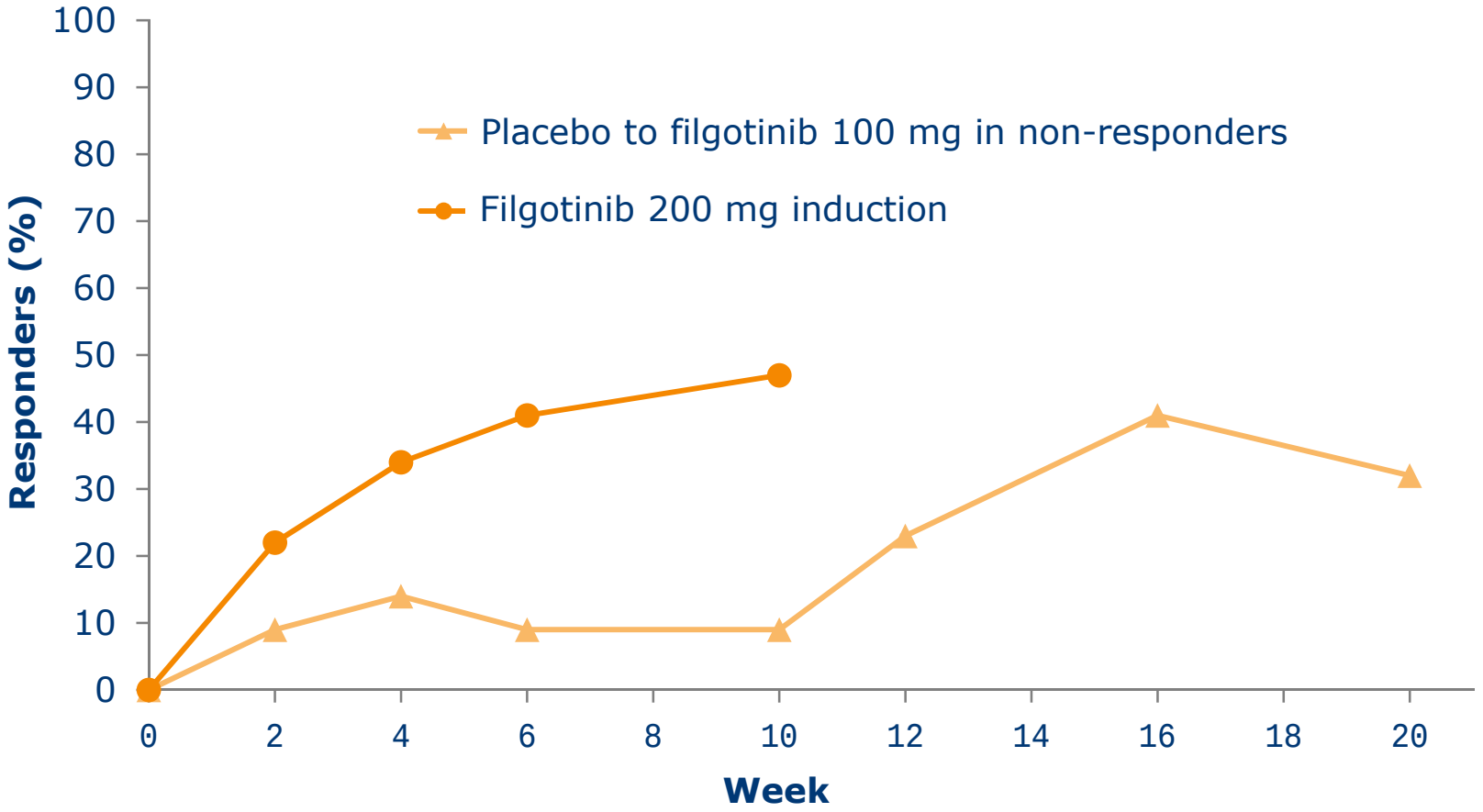
FITZROY: placebo non-responders re-randomized to filgotinib 100 mg



#Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

FITZROY: clinical remission

ITT-NRI, initial placebo non-responders#



Biased comparison as groups were assessed during different study periods (W10–W20 study period versus W0–W10 study period); clinical remission: CDAI score <150 points; 2nd part non-responders stay on stable steroids

#Responder status based on investigator calculation of CDAI score at week 10: non-responder = CDAI reduction of <100 points from baseline; responder = CDAI reduction of ≥100 points from baseline

FITZROY: safety summary

Over 20 weeks, pooled groups

n (%)	Placebo periods (N=67)	Filgotinib periods (N=152)
TE AE	45 (67)	114 (75)
Infections and infestations	17 (25)	48 (32)
Gastrointestinal disorders	19 (28)	53 (35)
Nervous system disorders	12 (18)	30 (20)
Serious TE AE	3 (4)	14 (9)
Serious TE infections	0 (0)	4 (3)
SAE leading to death	0 (0)	0 (0)
TE AE leading to discontinuation	6 (9)	27 (18)

Pooled placebo is the sum of: placebo to placebo + part 1 placebo from placebo switched to filgotinib 100 mg + part 2 placebo from filgotinib 200 mg switched to placebo. Pooled filgotinib is the sum of all remaining patients

FITZROY: conclusions

Week 20

- Filgotinib maintains, after 20 weeks of treatment, and despite mandatory steroid tapering
  - clinical efficacy
  - improvement in patient's quality of life (IBDQ)
- In patients who did not respond to placebo during weeks 0–10, filgotinib 100 mg also showed efficacy; further evaluation is warranted
- Favorable risk/benefit profile
- Data support currently ongoing Phase 3 program