Supplemental Online Content

Syversen SW, Jørgensen KK, Goll GL, et al. Effect of therapeutic drug monitoring vs standard therapy during maintenance infliximab therapy on disease control in patients with immune-mediated inflammatory diseases: a randomized clinical trial. *JAMA*. Published December 21, 2021. doi:10.1001/jama.2021.21316

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. The NOR-DRUM Steering Group

Principal Investigator	Professor Espen A. Haavardsholm, M.D., Ph.D.
Project leader	Silje W. Syversen, M.D., Ph.D.
National medical leaders	Professor emeritus Tore K. Kvien, M.D., Ph.D., Rheumatology
	Professor Jørgen Jahnsen, M.D., Ph.D., Gastroenterology
	Cato Mørk, M.D., Ph.D., Dermatology
National laboratory leader	Nils Bolstad, M.D., Ph.D.
Biostatisticians	Joseph Sexton, Ph.D.
	Inge Christoffer Olsen, Ph.D.
Clinical coordinators	Guro L. Goll, M.D., Ph.D., Rheumatology
	Kristin K. Jørgensen, M.D., Ph.D., Gastroenterology
	Øystein Sandanger, M.D., Ph.D., Dermatology
Laboratory coordinators	Johanna Gehin, M.D.
	David J. Warren, Ph.D.
PhD fellows	Marthe Kirkesæther Brun, M.D., Rheumatology
	Kristin Hammersbøen Bjørlykke, M.D., Gastroenterology
Patient representatives	Jon Hagfors, The Norwegian Rheumatism Association
	Bjørn Gulbrandsen, The Norwegian IBD Patient Organization
	Hilde Mellum, The Psoriasis and Eczema Association of Norway

eAppendix 2. Principal Investigators From Each Study Center

Silje Watterdal Syversen, Kristin Kaasen Jørgensen, Geir Noraberg, Trude Jannecke Bruun, Christian Kvikne Dotterud, Maud Kristine Aga Ljoså, Anne Julsrud Haugen, Rune Johan Njålla, Camilla Zettel, Øystein Sandanger, Carl Magnus Ystrøm, Yngvill Hovde Bragnes, Svanaug Skorpe, Turid Thune, Kathrine Aglen Seeberg, Brigitte Michelsen, Ingrid Marianne Blomgren, Eldri Kveine Strand, Pawel Mielnik, Roald Torp

eAppendix 3. Eligibility Criteria

Inclusion Criteria

1. A clinical diagnosis of one of the following; rheumatoid arthritis, spondyloarthritis (including ankylosing spondylitis), psoriatic arthritis[a], ulcerative colitis, Crohn disease or chronic plaque psoriasis
2. Male or non-pregnant female
3. ≥18 and <75 years of age at screening
4. On maintenance therapy with infliximab for a minimum of 30 weeks and a maximum of 3 years
5. A clinical indication for further infliximab treatment
6. Subject capable of understanding and signing an informed consent form

[a]Patients with psoriatic arthritis and predominantly axial manifestations should be included and assessed as spondyloartritis

Exclusion criteria

1. Major co-morbidities, such as previous malignancies within the last 5 years, severe diabetes mellitus, severe infections, uncontrollable hypertension, severe cardiovascular disease (NYHA class 3 or 4), severe respiratory diseases, demyelinating disease, significant chronic widespread pain syndrome, laboratory abnormalities or significant renal or hepatic disease and/or other diseases or conditions where treatment with infliximab is either found contra-indicated by the clinician or which make adherence to the protocol difficult
2. Inadequate birth control, pregnancy or subject considering becoming pregnant during the study period
3. Psychiatric or mental disorders, alcohol abuse or other substance abuse, language barriers or other factors which makes adherence to the study protocol difficult
4. For patients with UC and CD: Functional colostomy or ileostomy. Extensive colonic resection with less than 25 cm of the colon left in situ.

eTable 1. Details of Study Endpoints

Endpoint	Abbreviation	Diagnosis	Description
Primary endpoint			
Disease worsening		All	Disease worsening is defined according to the patient's diagnosis (see below).
		RA	Increase in Disease Activity Score 28 joints ≥1.2 and a minimum Disease Activity Score 28 joints of 3.2 or patient and investigator consensus on disease worsening. Separately, this endpoint is pre-specified as a secondary endpoint. More details are given below.
		SpA	Increase in Ankylosing Spondylitis Disease Activity Score-CRP of ≥1.1 and a minimum Ankylosing Spondylitis Disease Activity Score of 2.1 or patient and investigator consensus on disease worsening. Separately, this endpoint is pre-specified as a secondary endpoint. More details are given below.
		PsA	Increase in Disease Activity Score 28 joints ≥1.2 and a minimum Disease Activity Score 28 joints score of 3.2 or patient and investigator consensus on disease worsening. Separately, this endpoint is pre-specified as a secondary endpoint. More details are given below.
		UC	Increase in partial Mayo score of ≥ 3 points and a minimum partial Mayo score of 5 or patient and investigator consensus on disease worsening. Separately, this endpoint is pre-specified as a secondary endpoint. More details are given below.
		CD	Increase in Harvey-Bradshaw Index of ≥4 points and a minimum Harvey-Bradshaw Index of 7 points or patient and investigator consensus on disease worsening. Separately, this endpoint is pre-specified as a secondary endpoint. More details are given below.
		Ps	Increase in The Psoriasis Area and Severity Index of ≥3 points and a minimum The Psoriasis Area and Severity Index of 5 or patient and investigator consensus on disease worsening. Separately, this endpoint is pre-specified as a secondary endpoint. More details are given below.
Secondary efficacy endpoints			
Common disease activity endpoints			
Physician's global assessment of disease activity	PhGA	All	Physicians global assessment of disease activity range 0-100 on a visual analogue scale (VAS). 0 indicates no activity, 100 highest possible disease activity. MCID not defined.
Patient's global assessment of disease activity	PGA	All	Patients assessment of disease activity range 0-100 on a visual analogue scale (VAS). Patients are asked to rate their disease activity according to the following question: "We ask you to assess how active your (disease) has been during the last week. Considering all your symptoms, please mark a vertical line on the scale below." 0 indicates no activity, 100 highest possible disease activity. MCID not clearly defined, but within rheumatology it is generally accepted that a 10-point change on the 0–100 VAS corresponds to MCID.[1]
Erythrocyte sedimentation rate	ESR	All	Measured in mm/h, assessed by the Westergren method. Range 1-130 mm/h. Normal range 1-12 mm/h (men) and 1-17 mm/h (female). Higher value indicates worse disease.
C-reactive protein	CRP	All	Measured in mg/L. Range <1-1050 mg/L. Normal range 0-4 mg/L. Higher value indicates worse disease.

Endpoint	Abbreviation	Diagnosis	Description
Disease specific disease activity endpoints			
Disease Activity Score 28 joints[2]	DAS28	RA PsA	Disease activity score 28 joints includes the 28 tender and swollen joint count (SJC28 and TJC28), ESR and PGA. The DAS28 is calculated as follows: DAS28 = 0.56*sqrt (TJC28) + 0.28*sqrt (SJC28) + 0.70*Ln (ESR) + 0.014*PGA. Range 0-9.4. Higher values indicate worse disease; DAS28 < 2.6 remission, 2.6-<3.2 low disease activity, 3.2-5.1 moderate, >5.1 high disease activity. DAS28 is a recommended tool to be used for assessment of RA disease activity in clinical trials based on both psychometric properties and feasibility.[3] MCID is 1.2.[3]
Simple Disease Activity Index[4]	SDAI	RA PsA	The SDAI includes 28 tender and swollen joint count (SJC28 and TJC28), PGA, PhGA and CRP. The SDAI is calculated as follows: SDAI=TCJ28 + SJC28 + PGA/10 + PhGA/10 + CRP/10. Range 0-86. Higher values indicate worse disease. Remission <3.3, high disease activity >26. MCID 13.[3]
Modified Health Assessment Questionaire[5]	MHAQ	SpA RA PsA	The MHAQ consists of 8 questions evaluating the patient's physical function. Each item is scored on a categorical 0-3 scale and the sum score is divided by 8 to form the MHAQ score ranging 0.0 to 3.0. Higher values indicate worse physical function. MCID is 0.25.[1]
Disease Activity in Psoriatic Arthritis[6]	DAPSA	PsA	Disease Activity index for Psoriatic Arthritis (DAPSA) includes, 68 tender and 66 swollen joint count, CRP, PGA and VAS Pain and is calculated as follows: TJC68 + SJC66 + CRP (mg/L)/10 + PGA (0-100)/10+VAS Pain (0-100)/10. Range 0 and higher (depending on the CRP). Higher score indicates worse disease. MCID not defined.
Ankylosing Spondylitis Disease Activity Score[7]	ASDAS	SpA	Ankylosing Spondylitis Disease Activity Score includes components from the BASDAI, PGA and CRP: total back pain (VAS 0-100), PGA (VAS 0-100), peripheral pain/swelling (Numeric rating scale (NRS) 0-10), duration of morning stiffness (NRS 0-10) and CRP in mg/L. ASDAS is calculated as follows: ASDAS-CRP=0.121*total back pain + 0.011*patient global + 0.073*peripheral pain/swelling + 0.058*duration of morning stiffness + 0.579*ln (CRP+1). Range 0.6-7.7. Higher values indicate worse disease. Remission (inactive disease) <1.3, low disease activity 1.3-2.0, high disease activity 2.1-3.5, very high disease activity >3.5. ASDAS is the recommended tool to be used for assessment of SpA disease activity in clinical trials based on both psychometric properties and feasibility.[8] MCID is 1.1.[9]
The Bath Ankylosing Spondylitis Disease Activity Index[10]	BASDAI	SpA	BASDAI includes six questions pertaining to the five major symptoms of ankylosing spondylitis: fatigue, spinal pain, joint pain/swelling, areas of localized tenderness, morning stiffness duration and morning stiffness severity. Each question is scored on NRS (0-10). The two morning stiffness scores are averaged and added to the average of the other scores forming a total score in the range of 0-10 with larger values indicating worse disease. Components of BASDAI is included in ASDAS. MCID is 1.1.[11]

Endpoint	Abbreviation	Diagnosis	Description
Partial Mayo Score[12]	PMS	UC	Partial Mayo Score consists of three components (rectal bleeding, stool frequency and physician rating of disease activity) rated from 0–3 that are summed to give a total score that ranges from 0–9. Higher score indicates worse disease. Clinical remission ≤2 points. High activity is defined as >5 and severe activity >7 points. The non-invasive partial Mayo score is derived from the Mayo score (Range 0-12).[13] The partial Mayo score is more feasible as it does not require endoscopy and has been shown to perform as well as the full Mayo score to identify patient-perceived response in clinical trials.[12] MCID 3 points.[12]
Harvey-Bradshaw Index[14]	HBI	CD	Harvey-Bradshaw Index consists of five domains; general well-being (0-4), abdominal pain (0-3), number of liquid soft stools per day, abdominal mass (0-3) and number of predefined complications (0-8). The scores of each sub-domain are summed up to compute the HBI. The range of HBI score is from 0 with no upper limit. Higher values indicate worse disease. The HBI score of ≤ 4 points is well established as clinical remission. [15] There are two validated, clinical activity indices for Crohn disease, Crohn's disease activity index (CDAI) [16] and Harvey Bradshaw index.[14] These two indices are highly correlated.[15] Harvey Bradshaw index is often preferred to CDAI for assessment of CD disease activity in clinical trials due to feasibility (no need for diary card). MCID has not been defined, but a change of ≥ 3 points is suggested as a clinically meaningful change.[15]
Calprotectin		UC CD	Fecal calprotectin is measured in mg/kg. Fecal calprotectin is a marker of inflammation in the gut and widely used to monitor disease activity in inflammatory bowel disease.[17] The measurement range for fecal calprotectin is from <50 mg/kg to >2000 mg/kg. Validated cut-off values are still lacking[18], but a recent consensus agree on 150 mg/kg as a cut-off to identify endoscopic healing and levels between 150 and 250 mg/kg as a grey zone.[19]
Psoriasis Area and Severity Index[20]	PASI	Ps	The Psoriasis Area and Severity Index is a measure of redness, thickness and scaliness of lesions (each graded 0-4), weighted by the area and location of involvement. It scores from 0 (no disease) to 72 (maximal disease severity).The PASI score is the current "gold standard" for assessment of Ps disease activity in clinical trials.[21] The head, upper extremities, lower extremities, and trunk are assessed separately and then combined using weighting based on the surface area represented by each area (head = 0.1, upper extremities = 0.2, trunk = 0.3, and lower extremities = 0.4). The degree of erythema, induration, and scale in each area is judged on a 0–4 scale, the sum of which represents disease severity. The area of involvement of each area is graded from 0–6, depending on the estimated percentage of lesional area (0 = 0%, 1 = <10%, 2 = 10–29%, 3 = 30–49%, 4 = 50–69%, 5 = 70–89%, and 6 = 90–100%). These body scores are multiplied by the disease severity score and the weighting for each body area, yielding a score between 0 and 72. High scores indicate worse disease. In trials, PASI calculators are supplied to facilitate ease of scoring. MCID not defined.
Clinical remission			Remission is defined as follows: RA and PSA: A DAS 28 score of <2.6, SpA: An ASDAS score <1.3, UC: A PMS of ≤2 with no sub scores >1, CD: A HBI score of ≤4 and Ps: A PASI score of ≤4.[22]

Endpoint	Abbreviation	Diagnosis	Description
Quality of life and utility endpoints			
SF-36[23]	SF36	All	The SF-36 is a multi-purpose, short-form health survey with 36 questions. It has been scored according to 36-Item Health Survey 1.0 to form eight scores 0-100: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal/emotional problems, emotional well-being, social functioning, energy/fatigue (vitality), and general health perceptions. Scores on each item are summed; higher scores indicate worse disease. In addition, composite scores for physical and mental health summary measures are calculated according to the New England Medical Centre. The composite scores are computed according to 1998 US general population means/standard deviations. MCIDs according to disease are between 5-10 (total score) and 2.5-5 (subcomponents).[1,24,25]
SF-36 physical functioning		All	See above.
SF-36 bodily pain		All	See above.
SF-36 role limitation due to physical health problems		All	See above.
SF-36 role limitations due to personal/emotional problems		All	See above.
SF-36 emotional well-being		All	See above.
SF-36 social functioning		All	See above.
SF- vitality		All	See above.
SF-36 general health		All	See above.
SF-36 physical summary		All	The SF-36 physical component summary score is a weighted sum of the domain normalized scores using Norwegian specific weights. Higher values indicate better health.
SF-36 mental summary		All	See above.
EQ5D VAS[26]	EQ5D VAS	All	European Quality of life five dimensions visual analogue scale. The EQ VAS records the patient's self-rated health on a vertical visual analogue scale, where the endpoints are labelled 'The best health you can imagine' and 'The worst health you can imagine'. The VAS can be used as a quantitative measure of health outcome that reflect the patient's own judgement. 0 indicates no activity, 100 very severe activity. The MCID may differ according to disease subgroup. MCID is 9.2 for IBD.[24]

Endpoint	Abbreviation	Diagnosis	Description
EQ5D index (UK weighted) [26]	EQ-5D	All	European Quality of life five dimensions EQ-5D is a standardized instrument for use as a measure of health outcome. The EQ-5D index values are calculated according to the EQ-5D United Kingdom Time Trade-Off (TTO) value set and gives a utility score based on 5 questions, each with three response options Higher score means better health. MCID 0.03-0.52 across diseases.[27]
Work Productivity and Impairment Questionnaire Absenteeism[28]	WPAI absenteeism	All	WPAI absenteeism is the percent work time missed due to a specified problem. Range 0-100%. Score range:0 (no impairment) to 100 (completely impaired). MCID is 7%.[29]
Work Productivity and Impairment Questionnaire Presentism[28]	WPAI presentism	All	WPAI presentism is the percent impairment while working due to a specified problem. Range 0-100%. Score range:0 (no impairment) to 100 (completely impaired) MCID is 7%.[29]
Work Productivity and Impairment Questionnaire overall work impairment[28]	WPAI WI	All	WPAI overall work impairment is the percent overall work impairment due to a specified problem. Range 0-100%. Score range:0 (no impairment) to 100 (completely impaired). MCID is 7%.[29]
Work Productivity and Impairment Questionnaire activity impairment [28]	WPAI AI	All	WPAI activity impairment is the percent activity impairment due to a specified problem. Range 0-100%. Score range:0 (no impairment) to 100 (completely impaired). MCID is 7%.[29]
Rheumatoid Arthritis Impact of Disease total score[30]	RAID total	RA	The Rheumatoid Arthritis Impact of Disease (RAID) score was developed by EULAR and is calculated based on seven questions (pain, function, fatigue, sleep, emotional wellbeing, physical wellbeing and coping/self-efficacy), each scored 0-10 on a Numeric rating scale (NRS). The RAID total score is calculated as follows: RAID final value = 0.21*pain* 0.21 + 0.16*function + 0.15*fatigue + 0.12*physical wellbeing + 0.12*sleep + 0.12*emotional wellbeing + 0.12*coping. The range of the RAID total score is 0–10 where higher values indicate worse status. MCID is 3.[31]
Psoriatic Arthritis Impact of Disease total score[32]	PsAID	PsA	The PsAID questionnaire with 9 domains of health (PsAID-9) was developed by EULAR to calculate a score for clinical trials reflecting the impact of PsA from the patient's perspective. The nine domains with relative weights are: pain (0.174), fatigue (0.131), skin (0.121), work and/or leisure activities (0.110), function (0.107), discomfort (0.098), sleep (0.089), coping (0.087) and anxiety (0.085), each rated on an NRS (0-10). The rates of each domain are weighted and summed to form a score in the range of 0-10. Higher score indicates worse status. MCID not defined.

Endpoint	Abbreviation	Diagnosis	Description
Inflammatory Bowel Disease Questionnaire total score[33]	IBDQ	CD UC	The IBDQ is a tool to measure health-related quality of life in patients with inflammatory bowel diseases. The questionnaire consists of 32 questions scored in four domains: bowel symptoms, emotional health, systemic systems and social function. The response for each question ranges from one to seven with one corresponding to significant impairment and seven corresponding to no impairment. The total IBDQ score is the sum of all the question scores, ranging 32 to 224. Higher values indicate better quality-of-life. MCID is 9 points.[34]
Dermatology Life Quality Index total score[35]	DLQI	PS	The Dermatology Life Quality Index (DLQI) consists of 10 questions concerning patients' perception of the impact of skin diseases on their health-related quality of life over the last week. It has been validated for adult dermatology patients aged 16 years and older. The items of the DLQI encompass aspects of symptoms and feelings, daily activities, leisure, work/ school, personal relationships and side effects of treatment. Each question is scored on a 4-point Likert scale: Not at all/Not relevant=0, A little=1, A lot=2 and Very much=3. Scores of individual items (0-3) are added to yield a total score (0-30); higher scores mean greater impairment of patient's QoL. MCID is 3.3.[36,37]

eTable 2. Demographic and Baseline Characteristics in Disease Subgroups

eTable 2a: Demographic and Baseline Characteristics in Spondyloarthritis		
	Therapeutic Drug Monitoring (n=68)	**Standard Therapy (n=70)**
Demographics		
Age, mean, y	45.3 (14.2)	42.2 (12.4)
Sex, No. (%)		
Women	29 (42.6)	23 (32.9)
Men	39 (57.4)	47 (67.1)
Disease duration, median (IQR), y	7.1 (2.2-15.2)	4.5 (1.2-10.6)
Therapy		
Infliximab treatment duration, median (IQR), weeks	40.4 (38.0-52.0)	41.2 (38.0-52.0)
Exposed to TDM prior to randomization[a], No. (%)	24 (35.3)	24 (34.3)
Concomitant immunosuppressive therapy[b], No. (%)	15 (22.1)	17 (24.3)
Concomitant use of glucocorticoids, No. (%)	2 (2.9)	2 (2.9)
Use of biologic therapy[c] prior to infliximab, No. (%)	25 (36.8)	25 (35.7)
Use of TNF inhibitor[d] prior to infliximab, No. (%)	25 (36.8)	25 (35.7)
Use of other biologic therapy[e] prior to infliximab, No. (%)	2 (2.9)	3 (4.3)
General baseline characteristics		
Erythrocyte sedimentation rate[f], median (IQR), mm/h	5.0 (2.0-10.0)	6.0 (2.0-11.0)
C-reactive protein[g], median (IQR), mg/L	1.0 (1.0-3.0)	1.0 (1.0-3.0)
Physician's global assessment[h] of disease activity, mean	11.0 (12.3)	9.6 (10.7)
Patient's global assessment[h] of disease activity, mean	26.7 (22.2)	23.4 (18.6)

Abbreviations: IQR, interquartile range; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; SD, standard deviation.
[a]TDM prior to randomization defined as one or more assessments of serum drug levels during the last 3 infusions.
[b]Biologic therapy includes: Etanercept, adalimumab, certolizumab pegol, golimumab, infliximab, secukinumab and ustekinumab.
[c]Prior TNFi includes: Etanercept, adalimumab, certolizumab pegol, golimumab and infliximab.
[d]Other biologic therapy includes: Secukinumab and ustekinumab.
[e]Concomitant immunosuppressive medication includes: Methotrexate, leflunomide and sulfasalazine.
[f]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)
[g]C-reactive protein (mg/L), normal range 0-4 mg/mL
[h]Global assessment of disease activity range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity.

eTable 2b: Demographic and Baseline Characteristics in Ulcerative Colitis		
	Therapeutic Drug Monitoring (n=38)	**Standard Therapy (n=43)**
Demographics		
Age, mean, y	42.6 (13.9)	42.3 (15.7)
Sex, No. (%)		
Women	14 (36.8)	20 (46.5)
Men	24 (63.2)	19 (44.2)
Disease duration, median (IQR), y	4.2 (1.8-9.0)	3.4 (1.9-10.8)
Therapy		
Infliximab treatment duration, median (IQR), weeks	38.4 (37.0-60.0)	38.0 (36.0-83.0)
Exposed to TDM prior to randomization[a], No. (%)	17 (44.7)	21 (48.8)
Concomitant immunosuppressive therapy[b], No. (%)	17 (44.7)	19 (44.2)
Concomitant use of glucocorticoids, No. (%)	2 (5.3)	3 (7.0)
Use of biologic therapy[c] prior to infliximab, No. (%)	7 (18.4)	10 (23.3)
Use of TNF inhibitor[d] prior to infliximab, No. (%)	7 (18.4)	9 (29.9)
Use of other biologic therapy[e] prior to infliximab, No. (%)	0 (0.0)	1 (2.3)
General baseline characteristics		
Erythrocyte sedimentation rate[f], median (IQR), mm/h	7.0 (3.0-15.0)	5.0 (3.0-8.0)
C-reactive protein[g], median (IQR), mg/L	1.0 (1.0-3.0)	1.0 (1.0-3.0)
Physician's global assessment[h] of disease activity, mean	18.8 (20.1)	13.7 (16.4)
Patient's global assessment[h] of disease activity, mean	26.7 (22.7)	21.6 (19.8)

Abbreviations: IQR, interquartile range; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; SD, standard deviation.
[a]TDM prior to randomization defined as one or more assessments of serum drug levels during the last 3 infusions.
[b]Concomitant immunosuppressive medication includes: Methotrexate, azathioprine and sulfasalazine.
[c]Biologic therapy includes: Adalimumab, golimumab infliximab and vedolizumab.
[d]Prior TNFi includes: Adalimumab, golimumab and infliximab.
[e]Other biologic therapy includes: Vedolizumab.
[f]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)
[g]C-reactive protein (mg/L), normal range 0-4 mg/mL
[h]Global assessment of disease activity range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity.

eTable 2c: Demographic and Baseline Characteristics in Rheumatoid Arthritis

	Therapeutic Drug Monitoring (n=39)	Standard Therapy (n=40)
Demographics		
Age, mean, y	51.6 (15.5)	57.1 (12.3)
Sex, No. (%)		
Women	35 (89.7)	31 (77.5)
Men	4 (10.3)	9 (22.5)
Disease duration, median (IQR), y	6.2 (2.9-14.9)	8.2 (2.5-17.1)
Therapy		
Infliximab treatment duration, median (IQR), weeks	39.4 (38.0-62.0)	39.9 (38.1-46.0)
Exposed to TDM prior to randomization[a], No. (%)	13 (33.3)	15 (37.5)
Concomitant immunosuppressive therapy[b], No. (%)	38 (97.4)	38 (95.0)
Concomitant use of glucocorticoids, No. (%)	8 (20.5)	7 (17.5)
Use of biologic therapy[c] prior to infliximab, No. (%)	12 (30.8)	13 (32.5)
Use of TNF inhibitor[d] prior to infliximab, No. (%)	12 (30.8)	12 (30.0)
Use of other biologic therapy[e] prior to infliximab, No. (%)	2 (5.1)	2 (5.0)
General baseline characteristics		
Erythrocyte sedimentation rate[f], median (IQR), mm/h	10.0 (6.0-16.0)	7.0 (3.0-14.0)
C-reactive protein[g], median (IQR), mg/L	1.0 (1.0-3.0)	3.0 (1.0-4.5)
Physician's global assessment[h] of disease activity, mean	9.6 (10.4)	9.8 (9.8)
Patient's global assessment[h] of disease activity, mean	23.3 (19.6)	21.6 (20.9)

Abbreviations: IQR, interquartile range; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; SD, standard deviation.
[a]TDM prior to randomization defined as one or more assessments of serum drug levels during the last 3 infusions.
[b]Concomitant immunosuppressive medication includes: Methotrexate, leflunomide and sulfasalazine.
[c]Biologic therapy includes: Etanercept, adalimumab, certolizumab pegol, golimumab, infliximab, abatacept, rituximab, tocilizumab and in one patient tofacitinib (targeted synthetic DMARD).
[d]Prior TNFi includes: Etanercept, adalimumab, certolizumab pegol, golimumab and infliximab.
[e]Other biologic therapy includes: Abatacept, rituximab, tocilizumab and in one patient tofacitinib (targeted synthetic DMARD).
[f]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)
[g]C-reactive protein (mg/L), normal range 0-4 mg/mL
[h]Global assessment of disease activity range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity.

eTable 2d: Demographic and Baseline Characteristics in Crohn Disease		
	Therapeutic Drug Monitoring (n=34)	**Standard Therapy (n=32)**
Demographics		
Age, mean, y	39.6 (11.6)	36.5 (11.7)
Sex, No. (%)		
Women	19 (55.9)	11 (34.4)
Men	15 (44.1)	21 (65.6)
Disease duration, median (IQR), y	2.2 (1.4-11.9)	2.6 (1.7-9.2)
Therapy		
Infliximab treatment duration, median (IQR), weeks	38.5 (37.0-102.0)	38.0 (36.0-53.5)
Exposed to TDM prior to randomization[a], No. (%)	21 (61.8)	19 (59.4)
Concomitant immunosuppressive therapy[b], No. (%)	16 (47.1)	21 (65.6)
Concomitant use of glucocorticoids, No. (%)	1 (2.9)	0 (0.0)
Use of biologic therapy[c] prior to infliximab, No. (%)	4 (11.8)	5 (15.6)
Use of TNF inhibitor[d] prior to infliximab, No. (%)	4 (11.8)	5 (15.6)
Use of other biologic therapy[e] prior to infliximab, No. (%)	0 (0.0)	1 (3.1)
General baseline characteristics		
Erythrocyte sedimentation rate[f], median (IQR), mm/h	7.0 (5.0-13.0)	6.0 (2.0-10.0)
C-reactive protein[g], median (IQR), mg/L	2.0 (1.0-5.0)	1.0 (1.0-3.5)
Physician's global assessment[h] of disease activity, mean	23.2 (21.3)	17.4 (16.2)
Patient's global assessment[h] of disease activity, mean	30.5 (25.3)	26.0 (20.6)

Abbreviations: IQR, interquartile range; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; SD, standard deviation.

[a]TDM prior to randomization defined as one or more assessments of serum drug levels during the last 3 infusions.

[b]Biologic therapy includes: Adalimumab, golimumab, infliximab and vedolizumab.

[c]Prior TNFi includes: Adalimumab, golimumab and infliximab.

[d]Other biologic therapy includes: Vedolizumab.

[e]Concomitant immunosuppressive medication includes: Methotrexate and azathioprine.

[f]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)

[g]C-reactive protein (mg/L), normal range 0-4 mg/mL

[h]Global assessment of disease activity range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity.

eTable 2e: Demographic and Baseline Characteristics in Psoriatic Arthritis		
	Therapeutic Drug Monitoring (n=28)	**Standard Therapy (n=25)**
Demographics		
Age, mean, y	45.3 (13.0)	44.9 (10.7)
Sex, No. (%)		
Women	14 (50.0)	11 (44.0)
Men	14 (50.0)	14 (56.0)
Disease duration, median (IQR), y	7.1 (2.6-11.9)	7.6 (2.4-10.5)
Therapy		
Infliximab treatment duration, median (IQR), weeks	40.0 (37.5-44.5)	54.0 (38.3-83.0)
Exposed to TDM prior to randomization[a], No. (%)	11 (39.3)	8 (32.0)
Concomitant immunosuppressive therapy[b], No. (%)	23 (82.1)	23 (92.0)
Concomitant use of glucocorticoids, No. (%)	2 (7.1)	1 (4.0)
Use of biologic therapy[c] prior to infliximab, No. (%)	12 (42.9)	8 (32.0)
Use of TNF inhibitor[d] prior to infliximab, No. (%)	12 (42.9)	8 (32.0)
Use of other biologic therapy[e] prior to infliximab, No. (%)	2 (7.1)	3 (12.0)
General baseline characteristics		
Erythrocyte sedimentation rate[f], median (IQR), mm/h	4.0 (2.0-10.0)	4.0 (2.0-7.0)
C-reactive protein[g], median (IQR), mg/L	1.0 (1.0-2.5)	1.0 (1.0-2.0)
Physician's global assessment[h] of disease activity, mean	7.8 (8.0)	7.4 (8.7)
Patient's global assessment[h] of disease activity, mean	24.5 (18.2)	22.7 (18.4)

Abbreviations: IQR, interquartile range; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; SD, standard deviation.
[a]TDM prior to randomization defined as one or more assessments of serum drug levels during the last 3 infusions.
[b]Biologic therapy includes: Etanercept, adalimumab, certolizumab pegol, golimumab, infliximab, secukinumab and ustekinumab.
[c]Prior TNFi includes: Etanercept, adalimumab, certolizumab pegol, golimumab and infliximab.
[d]Other biologic therapy includes: Secukinumab and ustekinumab.
[e]Concomitant immunosuppressive medication includes: Methotrexate, leflunomide and sulfasalazine.
[f]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)
[g]C-reactive protein (mg/L), normal range 0-4 mg/mL
[h]Global assessment of disease activity range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity.

eTable 2f: Demographic and Baseline Characteristics in Psoriasis		
	Therapeutic Drug Monitoring (n=20)	**Standard Therapy (n=17)**
Demographics		
Age, mean, y	45.6 (14.8)	46.4 (14.0)
Sex, No. (%)		
Women	6 (30.0)	3 (17.6)
Men	14 (70.0)	15 (88.2)
Disease duration, median (IQR), y	20.6 (15.2-31.7)	23.9 (13.2-28.5)
Therapy		
Infliximab treatment duration, median (IQR), weeks	47.4 (38.4-116.0)	43.4 (38.7-83.0)
Exposed to TDM prior to randomization[a], No. (%)	5 (25.0)	7 (41.2)
Concomitant immunosuppressive therapy[b], No. (%)	14 (70.0)	12 (70.6)
Concomitant use of glucocorticoids, No. (%)	0 (0.0)	0 (0.0)
Use of biologic therapy[c] prior to infliximab, No. (%)	2 (10.0)	2 (11.8)
Use of TNF inhibitor[d] prior to infliximab, No. (%)	2 (10.0)	2 (11.8)
Use of other biologic therapy[e] prior to infliximab, No. (%)	0 (0.0)	2 (11.8)
General baseline characteristics		
Erythrocyte sedimentation rate[f], median (IQR), mm/h	6.0 (2.0-9.0)	3.5 (2.0-8.5)
C-reactive protein[g], median (IQR), mg/L	2.0 (1.0-2.5)	1.0 (1.0-2.0)
Physician's global assessment[h] of disease activity, mean	13.9 (14.9)	9.1 (8.1)
Patient's global assessment[h] of disease activity, mean	19.9 (19.2)	15.4 (11.5)

Abbreviations: IQR, interquartile range; TDM, therapeutic drug monitoring; TNF, tumor necrosis factor; SD, standard deviation.
[a]TDM prior to randomization defined as one or more assessments of serum drug levels during the last 3 infusions.
[b]Biologic therapy includes: Etanercept, adalimumab, infliximab and efalizumab.
[c]Prior TNFi includes: Etanercept, adalimumab and infliximab.
[d]Other biologic therapy includes: Efalizumab.
[e]Concomitant immunosuppressive medication includes: Methotrexate and leflunomide.
[f]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)
[g]C-reactive protein (mg/L), normal range 0-4 mg/mL
[h]Global assessment of disease activity range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity.

eTable 3. Disease Worsening According to Different Parts of the Definition

	Therapeutic Drug Monitoring N=60	Standard Therapy N=100
Disease worsening according to disease-specific composite measures	38 (16.7%)	55 (24.2%)
Disease worsening according to consensus about disease worsening between investigator and patient leading to a major change in treatment	16 (7.0%)	44 (19.3%)
Disease worsening due to study discontinuation before week 26	6 (2.6%)	1 (0.4%)

eTable 4. Sensitivity Analyses of the Primary Endpoint

eTable 4a: Pre-specified Sensitivity Analyses of the Primary Endpoint			
Analysis	**Therapeutic Drug Monitoring**	**Standard Therapy**	**Difference (95% CI)**
Primary analyses	167/227 (73.6)	127/227 (55.9)	17.6% (9.0, 26.2)
Baseline adjusted[a]	167/227 (73.6)	127/227 (55.9)	18.5% (9.9, 27.0)
Worst-case imputation	166/227 (73.1)	125/227 (55.1)	18.1% (9.5, 26.7)
Best-case imputation	173/227 (76.2)	128/227 (56.4)	19.9% (1.5, 28.3)
Complete-case analyses	160/214 (74.8)	119/218 (54.6)	20.3% (1.5, 29.0)
Last observation carried forward	173/227 (76.2)	128/227 (56.4)	19.7% (1.3, 28.2)
Patients with high adherence to the protocol[b]	143/186 (76.9)	119/209 (56.9)	20.0% (1.1, 29.0)
Center adjusted (fixed effect)	167/227 (73.6)	127/227 (55.9)	16.0% (7.5, 24.5)
Center adjusted (random effect)	167/227 (73.6)	127/227 (55.9)	17.7% (8.8, 26.5)
Disease worsening by definition[c]	183/227 (80.6)	171/227 (75.3)	7.8% (0.5,15.1)

Data are No. (%). CI, Confidence interval.
[a]Adjusted for the following baseline factors: age, gender, use of immunomodulation medication (methotrexate, azathioprine, sulfasalazine, leflunomide, prednisolone ≥ 15 mg), duration of infliximab treatment at baseline, serum infliximab at baseline and disease activity at baseline. The latter done via an interaction term with diagnosis.
[b]Patients with high adherence to the protocol defined as patients without study withdrawals prior to the week 52 visit, deviations to eligibility criteria, intervals between infusions >12 weeks, or deviations to the TDM strategy.
[c]Analysis excluding disease worsening solely by patient-investigator consensus

eTable 4b: Post-Hoc Sensitivity Analyses of the Primary Endpoint			
Analysis	**Therapeutic Drug Monitoring**	**Standard Therapy**	**Difference (95% CI)**
Primary analyses	167/227 (73.6)	127/227 (55.9)	17.6% (9.0, 26.2)
Patients on concomitant[a] immunosuppressive therapy (Post hoc)	89/123 (72.4)	71/130 (54.6)	17.5% (5.9,29.2)
Patients without concomitant[a] immunosuppressive therapy (Post hoc)	78/104 (75.0)	56/97 (57.7)	18.4% (5.6, 31.1)

Data are No. (%). CI, Confidence interval.
[a]Concomitant immunosuppressive therapy includes: Methotrexate, leflunomide, sulfasalazine, and azathioprine.

eTable 5. Results Secondary Endpoints

	Baseline		Week 52		Adjusted Difference at 52 weeks (95% CI)
	Therapeutic Drug Monitoring	Standard Therapy	Therapeutic Drug Monitoring	Standard Therapy	
	Observed values		Change from baseline		
Continuous endpoints					
Measures of disease activity					
Physician's global assessment[a]	13.8 (15.8)	11.2 (12.6)	-1.5 (18.5)	0.2 (15.6)	0.5 (-2.0,3.0)
Patient's global assessment[b]	25.8 (21.6)	22.5 (19.1)	-0.3 (21.3)	2.4 (20.2)	0.9 (-2.4,4.2)
Erythrocyte sedimentation rate[c], mm/hr	7.0 (3.0,12.0)	5.0 (2.0,11.0)	0.0 (6.0)	1.5 (9.9)	0.6 (-0.5,1.8)
C-reactive protein[d], mg/L	1.0 (1.0,3.0)	1.0 (1.0,3.0)	0.1 (3.8)	0.8 (15.6)	0.9 (-0.3,2.0)
Disease Activity Score 28 joints[e] RA/PsA	2.3 (1.0)	2.0 (1.2)	-0.1 (0.9)	0.1 (1.0)	0.1 (-0.2,0.3)
Simple Disease Activity Index[f] RA/PsA	5.6 (5.0)	5.3 (5.0)	-0.9 (4.8)	-0.1 (5.4)	1.0 (-0.6,2.7)
Modified Health Assessment Questionnaire[g] RA/PsA/SpA	0.3 (0.3)	0.2 (0.3)	-0.0 (0.3)	-0.0 (0.2)	0.0 (-0.0,0.1)
Disease Activity in Psoriatic Arthritis[h] PsA	10.2 (9.0)	6.2 (5.1)	-2.2 (8.1)	1.2 (5.0)	1.4 (-1.6,4.4)
The Bath Ankylosing Spondylitis Disease Activity[i] SpA	2.7 (1.9)	2.6 (1.7)	0.0 (1.3)	-0.0 (1.5)	-0.0 (-0.4,0.4)
Ankylosing Spondylitis Disease Activity Score[j] SpA	1.6 (0.8)	1.5 (0.8)	-0.1 (0.7)	-0.0 (0.7)	0.0 (-0.2,0.2)
Harvey-BradshawIndex[k] CD	3.6 (2.7)	3.1 (2.2)	-0.3 (1.4)	0.5 (3.7)	0.4 (-0.7,1.6)
Partial Mayo Score[m] UC	1.1 (1.3)	1.0 (1.6)	-0.1 (1.5)	0.3 (1.4)	0.6 (-0.0,1.1)
Calprotectin[n], mg/kg	43.0 (16.0,95.0)	75.0 (28.0,187.0)	32.5 (257.3)	20.5 (672.5)	346.7 (-23.8,717.3)
Psoriasis Area and Severity Index[o] Ps	2.4 (1.7)	2.3 (1.4)	0.1 (1.6)	0.2 (1.5)	0.1 (-0.9,1.2)
Quality of life and utility endpoints					
SF-36 physical functioning[p]	82.0 (18.2)	83.8 (19.0)	1.1 (13.5)	0.3 (12.9)	-0.5 (-2.6,1.6)
SF-36 bodily pain	74.4 (20.7)	75.8 (20.3)	-4.8 (24.1)	-4.3 (22.5)	0.8 (-2.6,4.2)
SF-36 role limitation due to physical health problem	57.8 (42.2)	63.9 (40.6)	6.8 (36.1)	-0.6 (33.6)	-5.4 (-11.1,0.4)
SF-36 role limitation due to emotional problem	72.5 (39.7)	72.3 (38.8)	1.9 (40.4)	-1.3 (40.5)	-2.9 (-8.7,2.9)
SF-36 general health	57.7 (21.4)	61.0 (21.7)	-0.3 (15.5)	-2.3 (13.7)	-1.4 (-3.8,1.0)
SF-36 emotional well-being	77.5 (14.8)	77.3 (15.5)	-0.6 (11.4)	-0.3 (12.0)	0.6 (-1.5,2.6)

Baseline	Baseline		Week 52		Adjusted Difference at 52 weeks (95% CI)
	Therapeutic Drug Monitoring	Standard Therapy	Therapeutic Drug Monitoring	Therapeutic Drug Monitoring	Standard Therapy
	Observed values		Change from baseline		
SF-36 social functioning	80.1 (22.3)	81.9 (20.3)	0.6 (17.9)	-2.2 (17.9)	-1.5 (-4.5,1.4)
SF-36 vitality	48.3 (22.7)	51.0 (22.3)	0.5 (15.4)	-0.6 (17.9)	-0.7 (-3.5,2.1)
SF-36 physical component summary	46.7 (9.0)	48.2 (8.2)	0.0 (7.8)	-0.9 (6.1)	-0.5 (-1.6,0.6)
SF-36 mental component summary	48.7 (10.1)	48.7 (10.5)	0.1 (8.4)	-0.3 (8.6)	-0.2 (-1.6,1.1)
EQ5D VAS[q]	71.1 (19.1)	72.7 (19.1)	-0.7 (17.6)	0.3 (17.4)	1.4 (-1.5,4.4)
EQ5D index[r] (UK weighted)	0.77 (0.20)	0.78 (0.20)	-0.01 (0.21)	-0.01 (0.21)	0.01 (-0.02,0.04)
WPAI[s] Percent work missed due to specified problem (Absenteeism)	12.4 (27.3)	8.0 (22.0)	-3.0 (31.7)	2.4 (25.4)	0.2 (-5.0,5.4)
WPAI Percent impairment while working due to specified problem (Presenteeism)	22.4 (23.3)	16.9 (19.2)	-1.5 (21.5)	2.6 (19.2)	1.1 (-3.0,5.2)
WPAI Percent overall work impairment due to specified problem	26.5 (26.6)	18.7 (21.9)	-3.3 (24.4)	4.1 (24.8)	2.5 (-2.5,7.5)
WPAI Percent activity impairment due to specified problem	27.8 (25.8)	24.4 (24.0)	-0.4 (22.0)	2.6 (20.0)	1.7 (-1.8,5.2)
RAID[t] RA	2.8 (2.1)	2.5 (2.0)	-0.7 (1.7)	0.1 (1.4)	0.8 (0.2,1.5)
PsAID[u] PsA	2.4 (1.3)	2.3 (1.6)	0.3 (1.2)	0.1 (1.3)	-0.2 (-0.7,0.4)
IBDQ[v] CD/UC	176.2 (25.9)	178.1 (26.8)	-0.3 (16.0)	0.7 (17.2)	2.5 (-2.8,7.8)
DLQI[w] Ps	2.5 (3.6)	2.7 (3.9)	0.2 (3.5)	0.1 (3.3)	-0.1 (-1.3,1.1)
State endpoints					
Measures of disease activity	**Baseline No. (%)**	**Baseline No. (%)**	**Week 52 No. (%)**	**Week 52 No. (%)**	**Adjusted Difference at 52 weeks (95% CI)**
Remission status[x]	136 (59.9)	149 (65.9)	145 (66.8)	144 (65.5)	0.8% (-6.9,8.5)
DAS28 remission RA	25 (64.1)	24 (60.0)	30 (76.9)	28 (73.7)	-2.6% (-19.7,14.4)
DAS28 remission PsA	20 (71.4)	21 (84.0)	18 (64.3)	19 (79.2)	12.0% (-9.1,33.2)
ASDAS remission SpA	26 (38.2)	31 (44.3)	32 (49.2)	34 (49.3)	2.1% (-12.8,17.1)
HBI remission CD	21 (61.8)	24 (77.4)	21 (65.6)	22 (68.8)	7.5% (-13.1,28.2)
PMS remission UC	28 (73.7)	34 (79.1)	29 (80.6)	28 (68.3)	-9.9% (-27.2,7.3)
PASI remission Ps	16 (80.0)	15 (88.2)	15 (88.2)	13 (81.3)	-12.5% (-38.8,13.8)

Data are mean at baseline and mean change (follow-up minus baseline) from baseline. Difference is adjusted treatment difference at week 52 with 95% confidence interval. Data are N (%) of state at study end. Adjusted difference at week 52" gives differences adjusted for diagnosis and prior TDM/participation in NOR-DRUM A (stratification factors), and for continuous outcomes, baseline outcome values. CI, Confidence interval; SF-36, Short Form Health Survey t-scores using Norwegian norms; EQ-5D, EuroQol questionnaire; WPAI, Work Productivity and Impairment questionnaire; RAID, Rheumatoid Arthritis Impact of Disease; PsAID, Psoriatic Arthritis Impact of Disease; IBDQ, Inflammatory Bowel Disease Questionnaire; DLQI, Dermatology Life Quality Index; RA, Rheumatoid Arthritis; SpA, Spondyloarthritis; PsA psoriatic arthritis, CD; Crohn disease, UC; Ulcerative colitis, Ps; Psoriasis.

[a]Physician's global assessment (Range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity. MCID not defined.)

[b]Physician's global assessment (Range 0-100 on a visual analogue scale. 0 indicates no activity, 100 highest possible disease activity. MCID not defined.)

[c]Erythrocyte sedimentation rate (mm/h), normal range 0-12 (men), 0-17 (women)

[d]C-reactive protein (mg/L), normal range 0-4 mg/L

[e]Disease Activity Score 28 joints (Range 0-9.4. Higher values indicate worse disease. MCID 1.2)

[f]Simplified Disease Activity Index (Range 0-86. Higher values indicate worse disease. Remission <3.3, high disease activity >26. MCID 13.)

[g]Modified Health Assessment Questionnaire (Range 0.0 to 3.0. Higher values indicate worse physical function. MCID is 0.25.)

[h]Disease Activity in Psoriatic Arthritis (Range 0 and higher. Higher score indicates worse disease. MCID not defined.)

[i]Bath Ankylosing Spondylitis Disease Activity Index

[j]Ankylosing Spondylitis Disease Activity Score (Range 0.6-7.7. Higher values indicate worse disease. MCID is 1.1.)

[k]Harvey-Bradshaw Index (Range 0 with no upper limit. Higher values indicate worse disease. MCID not defined, 3 points suggested as a clinically meaningful change.)

[m]Partial Mayo Score (Range 0–9. Higher scores indicate worse disease. MCID 3).

[n]Fecal calprotectin (Range <50 mg/kg to >2000 mg/kg. Validated cut-off values are still lacking, but a recent consensus agree on 150 mg/kg as a cut-off to identify endoscopic healing with levels between 150 mg/kg and 250 mg/kg as a grey zone.)

[o]Psoriasis Area and Severity Index (Range 0-72. Higher scores indicate worse disease. MCID is not defined.)

[p]SF-36 Eight measures scores 0-100: physical functioning, bodily pain, role limitations due to physical health problems, role limitations due to personal or emotional problems, emotional well-being, social functioning, energy/fatigue (vitality), and general health perceptions. Scores on each item are summed; higher scores indicate worse disease. In addition, composite scores for physical and mental health summary measures are calculated according to the New England Medical Centre scoring instructions. MCID for SF-36 differ according to disease subgroup between 5-10 points in the total score and 2.5-5 points in the subcomponents (physical- and mental component).

[q]EQ-5D VAS (Range 0-100, 0 indicates no activity, 100 very severe activity. The MCID may differ according to disease subgroup. MCID is 9.2 for IBD.)

[r]EQ5D index (Range 1 full health – 0 death. MCID 0.03-0.52 across diseases.)

[s]Work Productivity and Impairment questionnaire (Range 0-100%. Score range:0 (no impairment) to 100 (completely impaired). MCID is 7%.)

[t]RAID, Rheumatoid Arthritis Impact of Disease (Range 0–10 where higher values indicate worse status. MCID is 3.)

[u]PsAID, Psoriatic Arthritis Impact of Disease (Range 0-10. Higher score indicates worse status. MCID not defined.)

[v]IBDQ, Inflammatory Bowel Disease Questionnaire (Range 32 to 224. Higher values indicate better quality-of-life. MCID is 9 points.)

[w]DLQI, Dermatology Life Quality Index (Range 0-30; higher scores mean greater impairment of patient's quality-of-life. MCID is 3.3.)

[x]Remission is defined as follows: RA and PSA: A DAS 28 score of <2.6, SpA: An ASDAS score <1.3, UC: A PMS of ≤2 with no sub scores >1, CD: A HBI score of ≤4 and Ps: A PASI score of ≤4

eTable 6. Change in Treatment at Disease Worsening

	Therapeutic Drug Monitoring n=60	Standard Therapy n=100
Increase in infliximab dose, no. (%)	19 (31.6)	51 (51.0)
Infliximab discontinuation with initiation of biological/targeted synthetic drug[a], no. (%)	5 (8.3)	12 (12.0)
Infliximab discontinuation without initiation of biological/targeted synthetic drug[a] no. (%)	3 (5.0)	5 (5.0)
Add corticosteroids (administration iv., sc., po., or ia.), no. (%)	2 (3.3)	2 (2.0)
Add or increase dose of concomitant immunosuppressive medication[b], no. (%)	10 (16.7)	7 (7.0)
No change in therapy, no. (%)	13 (21.7)	21 (21.0)

Iv. denotes intravenous, sc. subcutaneous, po. per oral, and ia intra articular.
[a]Biological/targeted synthetic drug includes: Etanercept, adalimumab, certolizumab pegol, golimumab, abatacept, efalizumab, rituximab, secukinumab, tocilizumab, tofacitinib, ustekinumab, and vedolizumab.
[b]Concomitant immunosuppressive medication includes: Methotrexate, leflunomide, azathioprine, and sulfasalazine.

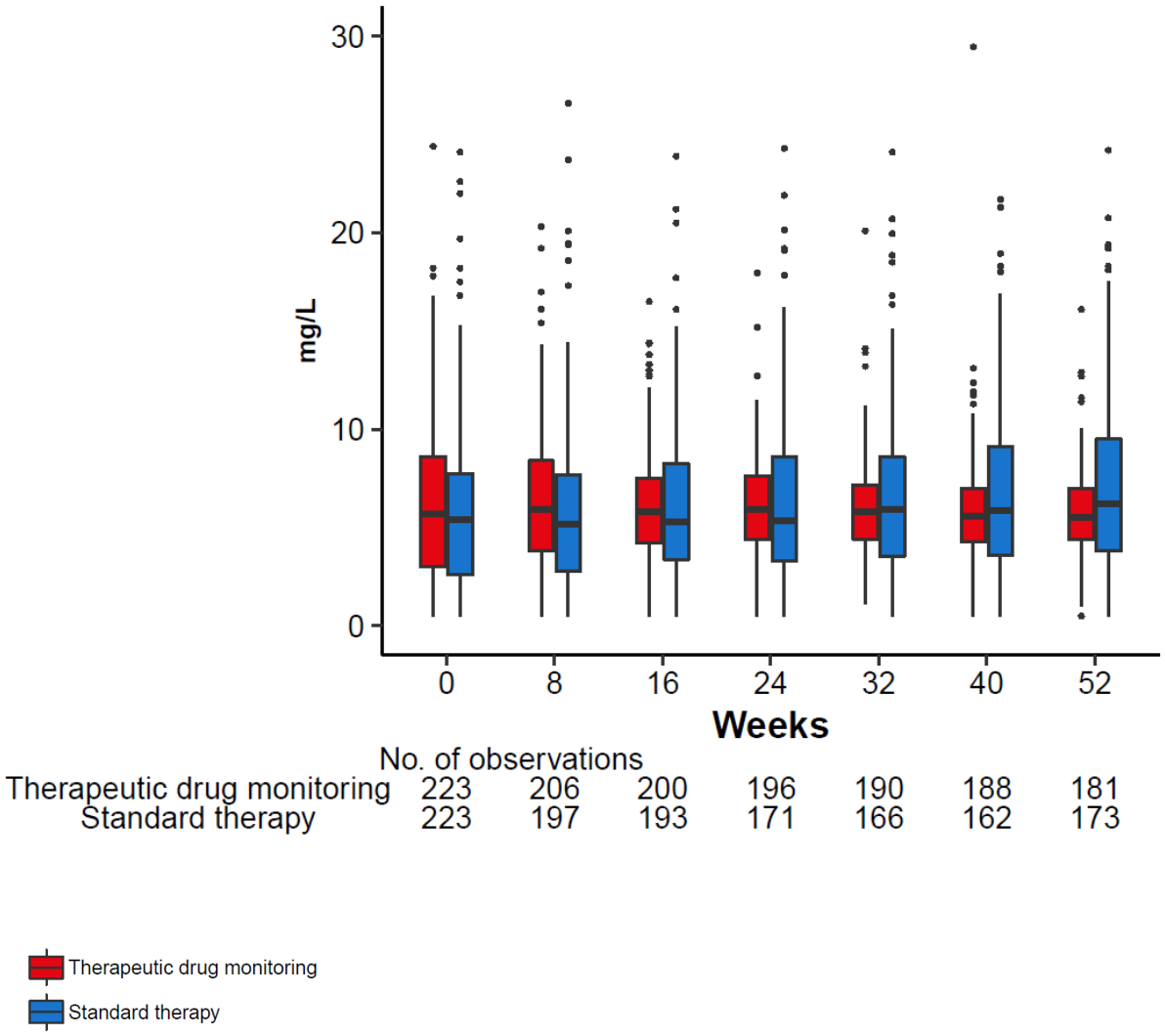
eFigure 1. Treatment Algorithm in the Therapeutic Drug Monitoring Group

Serum infliximab	**≤2.0 mg/L** **Increase dose** If ADAb[a] ≤50 µg/L Or **Switch therapy** if ADAb[a] >50 µg/L	**2.1 – 2.9 mg/L** **Consider increasing dose**	**3.0 – 8.0 mg/L** **No action** Within target range	**8.1 – 10.0 mg/L** **Consider decreasing dose**	**>10.0 mg/L** **Decrease dose**

Guideline for action: Increase the dose preferably by increasing the given dose by 2-2,5 mg/kg to a maximum dose of 10 mg/kg or by shortening the infusion interval by 2 weeks to a minimum of 4 weeks. Decrease the dose preferably by increasing the infusion interval by 2 weeks to a maximum of 10 weeks or by decreasing the given dose by 2-2,5 mg/kg

[a]ADAb= Anti-drug antibodies

eFigure 2. Serum Infliximab Level



Red color denotes the therapeutic drug monitoring group, blue color denotes the standard therapy group. Boxes mark first and third quartiles (range), the band inside the box is the second quartile (the median), while the whiskers indicate the highest and lowest values within 1.5 x the interquartile range. Dots denote individual patients (outliers).

eReferences

1. Strand V, Boers M, Idzerda L, et al. It's good to feel better but it's better to feel good and even better to feel good as soon as possible for as long as possible. Response criteria and the importance of change at OMERACT 10. J Rheumatol 2011;38(8):1720-7.DOI: 10.3899/jrheum.110392.
2. Prevoo ML, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, van Riel PL. Modified disease activity scores that include twenty-eight-joint counts. Development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis and rheumatism 1995;38(1):44-8. DOI: 10.1002/art.1780380107.
3. England BR, Tiong BK, Bergman MJ, et al. 2019 Update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures. Arthritis Care Res (Hoboken) 2019;71(12):1540-1555. DOI: 10.1002/acr.24042.
4. Aletaha D, Smolen J. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): a review of their usefulness and validity in rheumatoid arthritis. Clin Exp Rheumatol 2005;23(5 Suppl 39):S100-8.
5. Pincus T, Summey JA, Soraci SA, Jr., Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. Arthritis and rheumatism 1983;26(11):1346-53. DOI: 10.1002/art.1780261107.
6. Nell-Duxneuner VP, Stamm TA, Machold KP, Pflugbeil S, Aletaha D, Smolen JS. Evaluation of the appropriateness of composite disease activity measures for assessment of psoriatic arthritis. Annals of the rheumatic diseases 2010;69(3):546-9. DOI: 10.1136/ard.2009.117945.
7. Lukas C, Landewé R, Sieper J, et al. Development of an ASAS-endorsed disease activity score (ASDAS) in patients with ankylosing spondylitis. Annals of the rheumatic diseases 2009;68(1):18-24. DOI: 10.1136/ard.2008.094870.
8. Machado PM, Landewé RB, van der Heijde DM. Endorsement of definitions of disease activity states and improvement scores for the Ankylosing Spondylitis Disease Activity Score: results from OMERACT 10. J Rheumatol 2011;38(7):1502-6. DOI: 10.3899/jrheum.110279.
9. Machado P, Landewé R, Lie E, et al. Ankylosing Spondylitis Disease Activity Score (ASDAS): defining cut-off values for disease activity states and improvement scores. Annals of the rheumatic diseases 2011;70(1):47-53. DOI: 10.1136/ard.2010.138594.
10. Garrett S, Jenkinson T, Kennedy LG, Whitelock H, Gaisford P, Calin A. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21(12):2286-91.
11. Kviatkovsky MJ, Ramiro S, Landewé R, et al. The Minimum Clinically Important Improvement and Patient-acceptable Symptom State in the BASDAI and BASFI for Patients with Ankylosing Spondylitis. J Rheumatol 2016;43(9):1680-6. DOI: 10.3899/jrheum.151244.
12. Lewis JD, Chuai S, Nessel L, Lichtenstein GR, Aberra FN, Ellenberg JH. Use of the noninvasive components of the Mayo score to assess clinical response in ulcerative colitis. Inflammatory bowel diseases 2008;14(12):1660-6. DOI: 10.1002/ibd.20520.
13. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. The New England journal of medicine 1987;317(26):1625-9. DOI: 10.1056/nejm198712243172603.
14. Harvey RF, Bradshaw JM. A simple index of Crohn's-disease activity. Lancet (London, England) 1980;1(8167):514. DOI: 10.1016/s0140-6736(80)92767-1.
15. Vermeire S, Schreiber S, Sandborn WJ, Dubois C, Rutgeerts P. Correlation between the Crohn's disease activity and Harvey-Bradshaw indices in assessing Crohn's disease severity. Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association 2010;8(4):357-63. DOI: 10.1016/j.cgh.2010.01.001.
16. Best WR, Becktel JM, Singleton JW, Kern F, Jr. Development of a Crohn's disease activity index. National Cooperative Crohn's Disease Study. Gastroenterology 1976;70(3):439-44.
17. Sipponen T, Kolho KL. Fecal calprotectin in diagnosis and clinical assessment of inflammatory bowel disease. Scand J Gastroenterol 2015;50(1):74-80. DOI: 10.3109/00365521.2014.987809.
18. Vernia F, Di Ruscio M, Stefanelli G, Viscido A, Frieri G, Latella G. Is fecal calprotectin an accurate marker in the management of Crohn's disease? J Gastroenterol Hepatol 2020;35(3):390-400. DOI: 10.1111/jgh.14950.
19. Turner D, Ricciuto A, Lewis A, et al. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. Gastroenterology 2021;160(5):1570-1583. DOI: 10.1053/j.gastro.2020.12.031.
20. Fredriksson T, Pettersson U. Severe psoriasis--oral therapy with a new retinoid. Dermatologica 1978;157(4):238-44. DOI: 10.1159/000250839.
21. Schmitt J, Wozel G. The psoriasis area and severity index is the adequate criterion to define severity in chronic plaque-type psoriasis. Dermatology 2005;210(3):194-9.DOI: 10.1159/000083509.
22. Syversen SW, Goll GL, Jørgensen KK, et al. Effect of Therapeutic Drug Monitoring vs Standard Therapy During Infliximab Induction on Disease Remission in Patients With Chronic Immune-Mediated Inflammatory Diseases: A Randomized Clinical Trial. Jama 2021;325(17):1744-1754. DOI: 10.1001/jama.2021.4172.
23. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30(6):473-83.
24. Coteur G, Feagan B, Keininger DL, Kosinski M. Evaluation of the meaningfulness of health-related quality of life improvements as assessed by the SF-36 and the EQ-5D VAS in patients with active Crohn's disease. Alimentary pharmacology & therapeutics 2009;29(9):1032-41. DOI: 10.1111/j.1365-2036.2009.03966.x.
25. Feagan BG, Coteur G, Tan S, Keininger DL, Schreiber S. Clinically meaningful improvement in health-related quality of life in a randomized controlled trial of certolizumab pegol maintenance therapy for Crohn's disease. The American journal of gastroenterology 2009;104(8):1976-83. DOI: 10.1038/ajg.2009.199.
26. Brooks R. EuroQol: the current state of play. Health Policy 1996;37(1):53-72. DOI: 10.1016/0168-8510(96)00822-6.
27. Coretti S, Ruggeri M, McNamee P. The minimum clinically important difference for EQ-5D index: a critical review. Expert Rev Pharmacoecon Outcomes Res 2014;14(2):221-33. DOI: 10.1586/14737167.2014.894462.
28. Reilly MC, Zbrozek AS, Dukes EM. The validity and reproducibility of a work productivity and activity impairment instrument. Pharmacoeconomics 1993;4(5):353-65. DOI: 10.2165/00019053-199304050-00006.

29. Reilly MC, Brown MC, Brahant Y, Gerlier L, Tan SC, Sandborn WJ. Defining the minimally important difference for WPAI: CD Scores: What is a relevant impact on work productivity in active Crohn's disease? Gut 2007;56(Suppl 3): A159.
30. Gossec L, Dougados M, Rincheval N, et al. Elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative. Annals of the rheumatic diseases 2009;68(11):1680-5. DOI: 10.1136/ard.2008.100271.
31. Dougados M, Brault Y, Logeart I, van der Heijde D, Gossec L, Kvien T. Defining cut-off values for disease activity states and improvement scores for patient-reported outcomes: the example of the Rheumatoid Arthritis Impact of Disease (RAID). Arthritis Res Ther 2012;14(3):R129. DOI: 10.1186/ar3859.
32. Gossec L, de Wit M, Kiltz U, et al. A patient-derived and patient-reported outcome measure for assessing psoriatic arthritis: elaboration and preliminary validation of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, a 13-country EULAR initiative. Annals of the rheumatic diseases 2014;73(6):1012-9. DOI: 10.1136/annrheumdis-2014-205207.
33. Guyatt G, Mitchell A, Irvine EJ, et al. A new measure of health status for clinical trials in inflammatory bowel disease. Gastroenterology 1989;96(3):804-10.
34. Irvine EJ, Zhou Q, Thompson AK. The Short Inflammatory Bowel Disease Questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's Relapse Prevention Trial. The American journal of gastroenterology 1996;91(8):1571-8.
35. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19(3):210-6. DOI: 10.1111/j.1365-2230.1994.tb01167.x.
36. Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. Br J Dermatol 2008;159(5):997-1035. DOI: 10.1111/j.1365-2133.2008.08832.x.
37. Basra MK, Salek MS, Camilleri L, Sturkey R, Finlay AY. Determining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. Dermatology 2015;230(1):27-33. DOI: 10.1159/000365390.