Table. Primary and key secondary outcomes at 24 weeks (ITT)

	Active conventional therapy (ACT)	Certolizumab +MTX	Abatacept +MTX	Tocilizumab +MTX
No of pts (ITT)	200	203	204	188[§]
		Crude remission and response rates		
CDAI remission	**42.0%**	**47.8%**	**52.5%**	**41.0%**
ACR/EULAR Boolean remission	34.0%	38.4%	37.3%	31.4%
DAS28 remission	63.5%	68.5%	69.6%	63.3%
SDAI remission	41.5%	49.8%	51.5%	42.6%
EULAR good response	71.5%	76.9%	79.9%	71.3%
		Difference (95% CI) in rates with Arm 1 as reference (adjusted)		
CDAI remission	**Ref**	**4% (-5 to 13%)**	**9% (0.1 to 19%)**	**-1% (-10 to 9%)**
ACR/EULAR Boolean remission	Ref	4% (-6 to 13%)	5% (-5 to 14%)	-4% (-13 to 6%)
DAS28 remission	Ref	3% (-6 to 11%)	5% (-4 to 13%)	-1% (-10 to 8%)
SDAI remission	Ref	6% (-3 to 18%)	9% (-0.3 to 18%)	1% (-8 to 11%)
EULAR good response	Ref	4% (-4 to 14%)	8% (-2 to 18%)	0.4% (-10 to 11%)

[§]17 patients allocated to Tocilizumab did not receive it due to its unavailability and were excluded from ITT.

remission and response rates (superiority analysis). Differences in remission and response rates with CZP and TCZ, but not with ABA, remained within the pre-defined non-inferiority margin versus ACT, Fig 2.

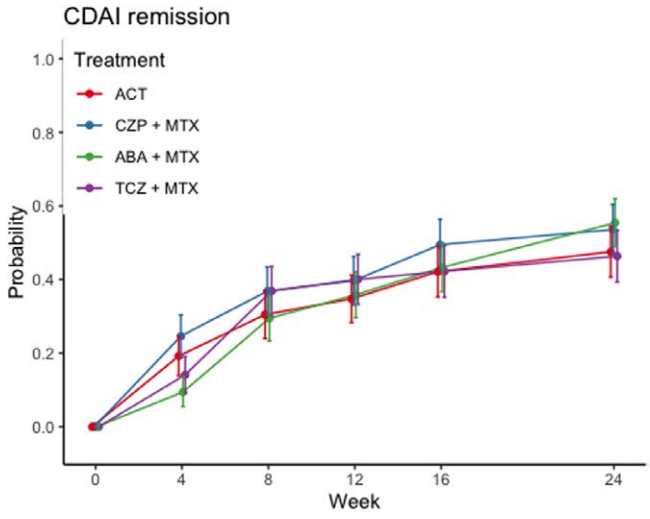
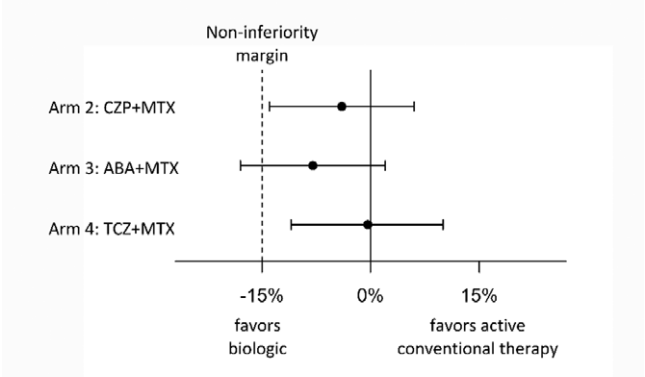


Figure 1. CDAI remission over time (adj. estimates with 95% CI)



Non-inferiority analysis, per protocol population. Estimated differences in CDAI remission rates between Arm 1 (active conventional therapy) and Arms 2, 3 and 4 (biologic arms) as reference with 95% confidence intervals, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP. ABA, abatacept; CZP, certolizumab-pegol; MTX, methotrexate; TCZ, tocilizumab.

Figure 2. Non-inferiority analysis of protocol population. Estimated differences in CDAI remission rates between Arm 1 (active conventional therapy) and Arms 2, 3, and 4 (biologic arms) as reference with 95% confidence intervals, adjusted for gender, ACPA status, country, age, body-mass index and baseline DAS28-CRP. ABA, abatacept; CZP, certolizumab-pegol; MTX, methotrexate; TCZ, tocilizumab.

Conclusion: High remission rates were found across all four treatment arms at 24 wks. Higher CDAI remission rate was observed for ABA versus ACT (+9%) and for CZP (+4%), but not for TCZ (-1%). With the predefined 15% margin, ACT was non-inferior to CZP and TCZ, but not to ABA. This underscores the efficacy of active conventional therapy based on MTX combined with glucocorticoids and may guide future treatment strategies for early RA.

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OP0019

STABLE VERSUS TAPERED AND WITHDRAWN TREATMENT WITH TUMOR NECROSIS FACTOR INHIBITOR IN RHEUMATOID ARTHRITIS REMISSION (ARCTIC REWIND): A RANDOMISED, OPEN-LABEL, PHASE 4, NON-INFERIORITY TRIAL

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Background: Remission is the preferred treatment target in rheumatoid arthritis (RA), and many patients require biologic DMARDs to reach this state. It is debated whether tapering of tumor necrosis factor inhibitor (TNFi) treatment to discontinuation should be considered in RA patients who sustain remission on treatment (1).

Objectives: The primary study objective was to assess the effect of tapering and withdrawal of TNFi on the risk of flares in RA patients in clinical remission.

Methods: In the non-inferiority ARCTIC REWIND trial, RA patients in remission for at least 12 months on stable TNFi therapy were randomly assigned to continued stable TNFi or tapering (half-dose TNFi for 4 months, thereafter withdrawal of TNFi), with visits every four months. csDMARD co-medication was kept stable in both arms. Patients had to be in DAS remission at inclusion with 0/44 swollen joints. The primary endpoint was the proportion of patients with disease flare during the 12-month study period (defined as DAS>1.6, change in DAS>0.6 and 2 or more swollen joints, or the physician and patient agreed that a clinically significant flare had occurred). Full-dose TNFi was reinstated in case of flares in the tapering arm. The non-inferiority margin was 20%, with a predefined superiority test if non-inferiority was not shown. The inferiority null-hypothesis was tested in the per-protocol population by mixed effect logistic regression. Radiographs were scored by van der Heijde modified Sharp score (0 and 12 months, average of two readers, progression: ≥1 unit change). Clinicaltrials NCT01881308.

Results: We randomised 99 patients, 92 received the allocated treatment strategy, 84 were included in the per-protocol population. Baseline characteristics, clinical and ultrasound disease activity were balanced (Table). csDMARD co-medication was used by 93% in the stable and 88% in the tapering arm. In the primary analysis, 5% of patients in the stable TNFi arm experienced a flare during 12 months, compared to 63% in the tapering TNFi arm. The risk difference (95% CI) was 58% (42% to 74%, Fig 1), with stable treatment being deemed superior to tapering. 90% in the stable and 81% in the tapering arm did not show progression of radiographic joint damage, difference (95% CI) -9% (-24%, 6%). At 12 months, DAS scores, DAS remission and function were similar between groups (Fig 2). The numbers of adverse events (AE)/serious AE in the stable and tapering arm were 57/2 and 50/3, respectively, with 26 and 15 infections.

Conclusion: In a randomised clinical trial assessing patients in prolonged and deep RA remission, we observed a large increase in the flare rate in patients who tapered and discontinued TNFi. Patients responded well to reinstated treatment and remission rates in the two study arms were comparable at 12 months.

References:

[1] Smolen et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. ARD 2020

Table. Baseline values – n (%), mean (SD), or median (IQR)

	Stable, n=45	Tapering, n=47
Age, yrs	57 (11)	58 (13)
Female	30 (67%)	25 (53%)
ACPA+	35 (78%)	36 (77%)
Symptom duration, yrs	10 (7)	12 (7)
DAS	0.9 (0.4)	0.8 (0.3)
CRP mg/L	1 (1 – 2)	1 (1 – 3)
No ulttrasound power Doppler signal in any of 32 joints	42 (96%)	44 (94%)

Figure 1: Non-inferiority plot of stable vs tapered TNFi treatment in per protocol population, per protocol patients with csDMARD co-medication, and in the full analysis set. The broken vertical line represents the non-inferiority margin.

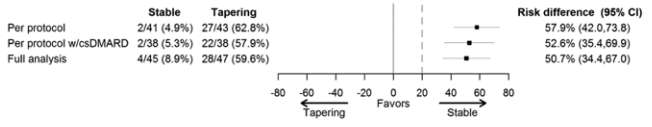
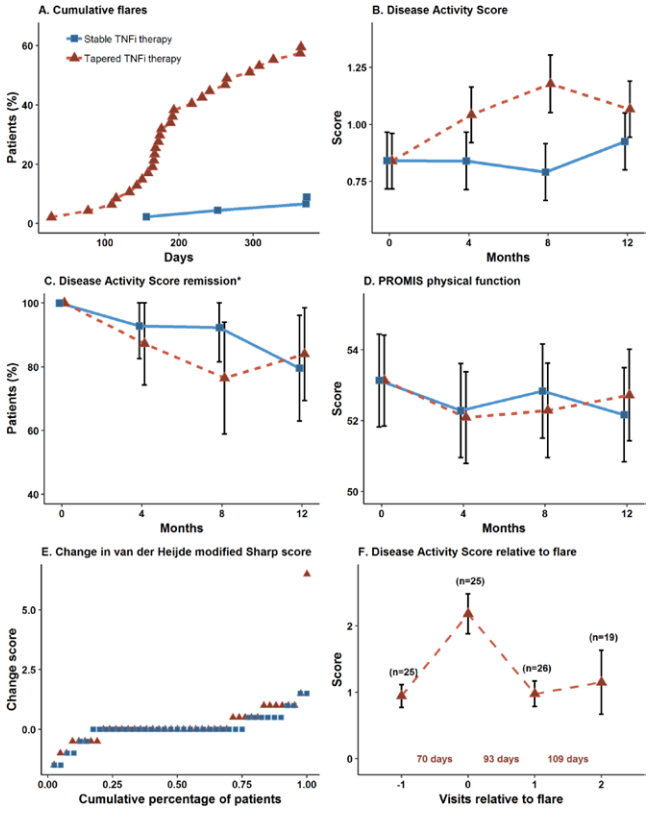


Figure 2: Secondary endpoints



Disclosure of Interests: Siri Lillegraven: None declared, Nina Paulshus Sundlisæter: None declared, Anna-Birgitte Aga: None declared, Joe Sexton: None declared, Inge Olsen: None declared, Åse Lexberg: None declared, Tor Magne Madland: None declared, Hallvard Fremstad: None declared, Christian A. Høili Consultant of: Novartis, Gunnstein Bakland Consultant of: Novartis, UCB, Cristina Spada: None declared, Hilde Haukeland Consultant of: Novartis, Inger M. Hansen: None declared, Ellen Moholt: None declared, Till Uhlig Consultant of: Lilly, Pfizer, Speakers bureau: Grünenthal, Novartis, Daniel Solomon Grant/research support from: Funding from Abbvie and Amgen unrelated to this work, Désirée van der Heijde Consultant of: AbbVie, Amgen, Astellas, AstraZeneca, BMS, Boehringer Ingelheim, Celgene, Cyxone, Daiichi, Eisai, Eli-Lilly, Galapagos, Gilead Sciences, Inc., Glaxo-Smith-Kline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, UCB Pharma; Director of Imaging Rheumatology BV, Tore K. Kvien Grant/research support from: Received grants from Abbvie, Hospira/Pfizer, MSD and Roche (not relevant for this abstract)., Consultant of: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Paid instructor for: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Speakers bureau: Have received personal fees from Abbvie, Biogen, BMS, Celltrion, Eli Lily, Hospira/Pfizer, MSD, Novartis, Orion Pharma, Roche, Sandoz, UCB, Sanofi and Mylan (not relevant for this abstract)., Espen A Haavardsholm Grant/research support from: AbbVie, UCB Pharma, Pfizer Inc, MSD Norway, Roche Norway, Consultant of: Pfizer, AbbVie, Janssen-Cilag, Gilead, UCB Pharma, Celgene, Lilly, Paid instructor for: UCB Pharma, Speakers bureau: Pfizer, AbbVie, UCB Pharma, Celgene, Lilly, Roche, MSD

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OP0020

IMPACT OF BDMARDS WITH DIFFERENT MODES OF ACTION ON FATIGUE IN RA PATIENTS

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