Infliximab（レミケード）の特徴

- 用量と投与期間の調整
- 関節破壊抑制効果
- 血中濃度と抗体
- TNF-α血中濃度
- MTXの併用
- csDMARDs vs Infliximab
- 副作用(Infusion reaction, 感染症)
- 減量・中止

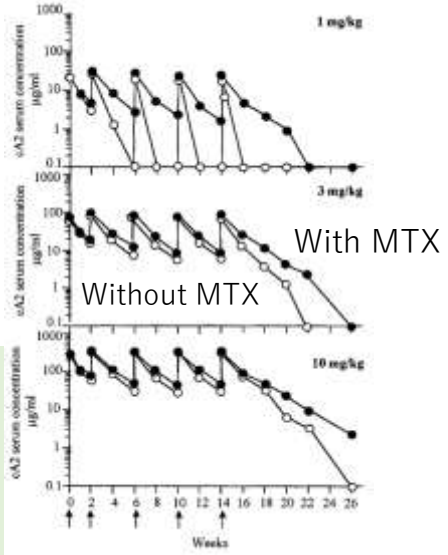
ARTHRITIS & RHEUMATISM

THERAPEUTIC EFFICACY OF MULTIPLE INTRAVENOUS INFUSIONS OF ANTI-TUMOR NECROSIS FACTOR α MONOCLONAL ANTIBODY COMBINED WITH LOW-DOSE WEEKLY METHOTREXATE IN RHEUMATOID ARTHRITIS

RAVINDER N. MAINI, FERDINAND C. BREEDVELD, JOACHIM R. KALDEN, JOSEF S. SMOLEN, DIANA DAVIS, JOHN D. MACFARLANE, CHRISTIAN ANTONI, BURKHARD LEEB, MICHAEL J. ELLIOTT, JAMES N. WOODY, THOMAS F. SCHAIBLE, and MARC FELDMANN

MTX-IRに対してMTX併用IFXの初のRCT.
MTX併用IFXの有効性を証明.
MTX併用(7.5mg/wk)で抗体産生を抑制.

[Arthritis Rheum 1998 ;41(9):1552-63.]



6施設110名のMTX-IRのRA.

IFX 1mg/kg, 3mg/kg, 10mg/kg, PBO＋MTX 7.5mg(固定)

IFX 1mg/kg, 3mg/kg, 10mg/kg＋PBOの7群

投与サイクル：0,2,6,10,14

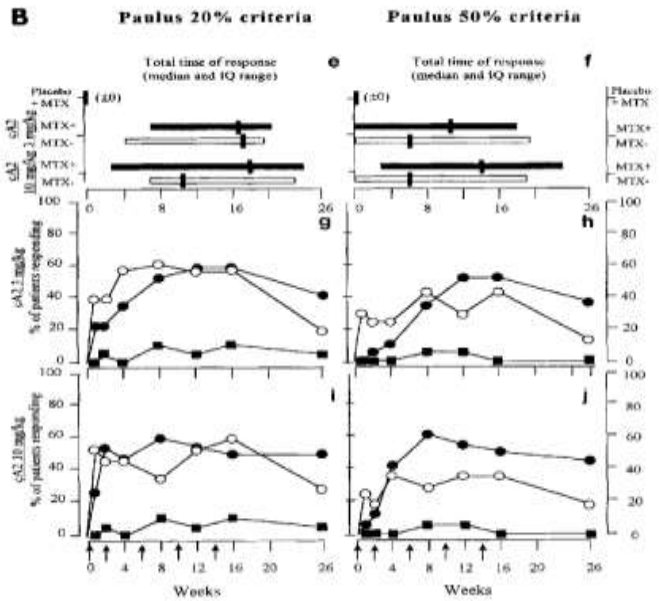
Outcome: 26週までのPaulus 20% indexの総時間

MTX併用の方が抗体の出現率は低い
(全体: 1mg 53%,3mg 21%,10mg 7%,
MTX併用 1mg 15%,3mg 7%,10mg 0%),
MTX併用でIFX血中濃度が安定.

Table 2. Statistical analysis of clinical response rates (% of patients responding) based on Paulus 20% and 50% criteria*

	1 mg/kg of cA2 at week					3 mg/kg of cA2 at week					10 mg/kg of cA2 at week				
	4	8	12	16	26	4	8	12	16	26	4	8	12	16	26
20% Paulus criteria															
cA2 with MTX	<0.001	0.021	0.009	0.017	0.512	0.014	0.008	0.001	0.005	0.010	0.001	0.003	0.001	0.011	0.004
cA2 without MTX	0.091	0.962	0.535	0.528	0.949	<0.001	0.002	0.001	0.008	0.239	0.005	0.132	0.003	0.004	0.083
50% Paulus criteria															
cA2 with MTX	0.003	0.026	0.026	0.001	0.161	0.016	0.018	0.002	0.001	0.005	0.003	<0.001	0.001	0.001	0.002
cA2 without MTX	0.176	0.317	1.000	0.317	0.317	0.035	0.010	0.062	0.003	0.083	0.022	0.101	0.047	0.010	0.085

* *P* values are for comparisons of groups of patients treated with cA2, with or without methotrexate (MTX), versus placebo plus MTX at each dosage level (see Figures 1A panels c and d and 1B panels g–j).



○IFX without MTX ●IFX with MTX ■PBO＋MTX

1mg/3mgMTX+はPBO/MTX＋と有意差あり(P<0.001).

1mg/MTX-,+はPBO/MTX+と26wのPaulus 20%/50%で有意差なし.

3mgはMTX有無に関わらずPBO/MTXと比べてPaulus 20,50の反応性良好.

3mg or 10mgでもMTX±に関わらずPaulus50の期間は有意差なし.

MTX併用した方が26wまでのPaulus20,50 criteriaで反応性はよい.

Individualized Monitoring of Drug Bioavailability and Immunogenicity in Rheumatoid Arthritis Patients Treated With the Tumor Necrosis Factor α Inhibitor Infliximab

Klaus Bendtzen,[1] Pierre Geborek,[2] Morten Svenson,[1] Lotta Larsson,[2] Meliha C. Kapetanovic,[2] and Tore Saxne[2]

MTX併用の有無で6カ月後のIFX抗体出現率は関連なし.

[Arthritis Rheum. 2006;54(12):3782-9.]

IFXの血中濃度と抗体産生の関連を調査した研究

IFX投与されている106名(MTX使用 63名)とBio投与歴がない206名を比較.

抗IFX抗体保有率:1.5か月後 13%, 3か月後 30%, 6か月後 44%

抗体発生と抗体濃度上昇はIFX血中濃度低下と関連していた.

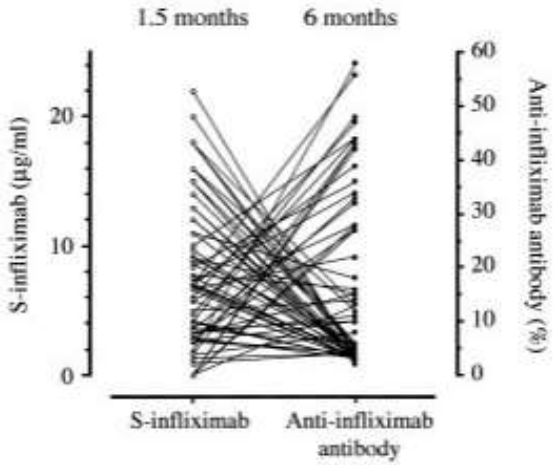
IFX抗体とETN,ADAの結合率はIFXと比較して0.001倍.

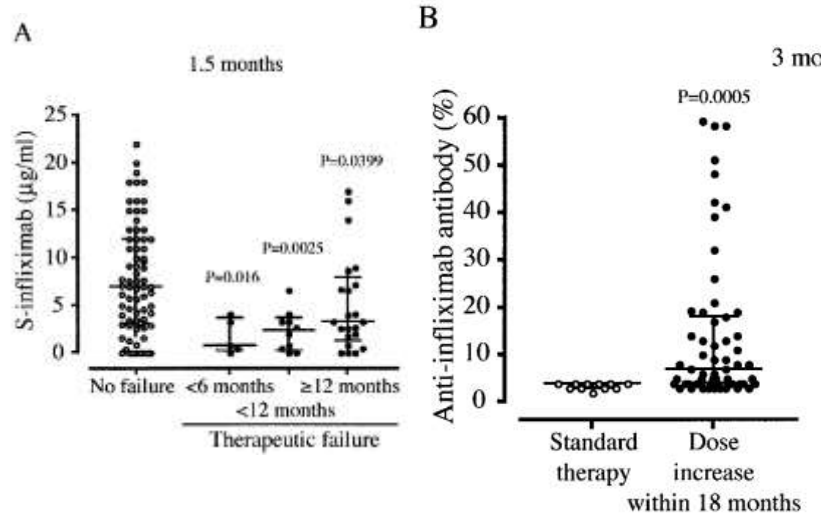
血中濃度の低さは治療失敗と関連(A).

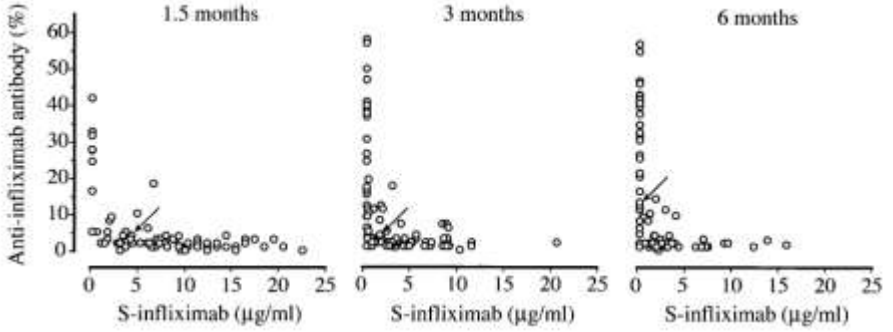
3カ月以内に抗体出現すると効果不十分のためIFX増量された(B).

治療失敗と抗体出現は関連(P=0.009).

- IFX2回目投与後のトラフが低いことは抗体出現は関連.
- CRP>40μg/mlはトラフ低値と関連(P=0.004)
- **6か月後のIFX抗体産生とMTX併用の有無は関連なし(MTX＋ 40%, MTX- 50%).**







CONCISE REPORT

Methotrexate polyglutamation in relation to infliximab pharmacokinetics in rheumatoid arthritis

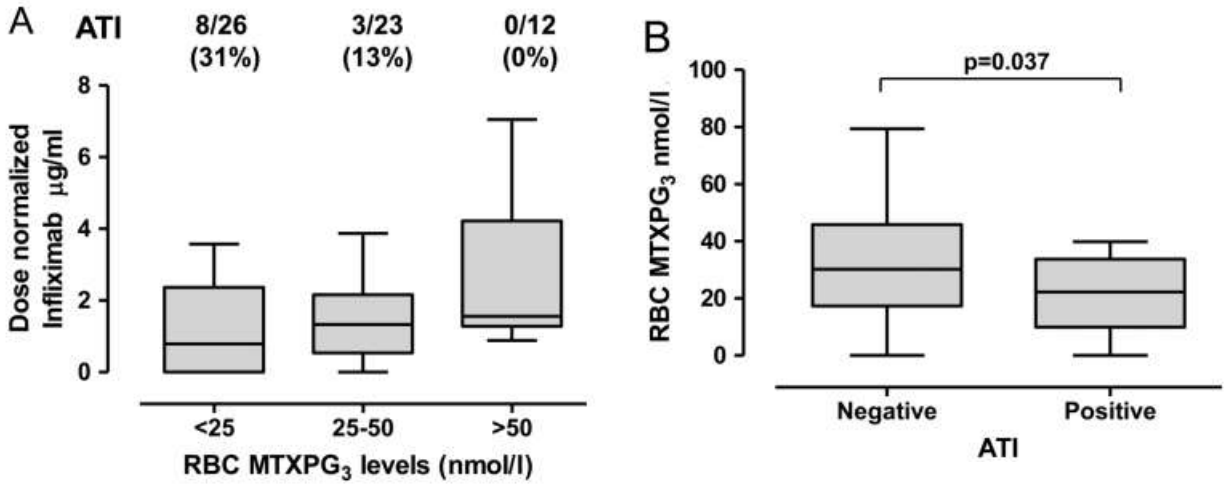
Thierry Dervieux,[1] Michael E Weinblatt,[2] Alan Kivitz,[3] Joel M Kremer[4]

RBC MTXPG$_3$濃度が高いほどIFX抗体の産生率は下がる

[Ann Rheum Dis. 2013;72(6):908-10.]

MTX→MTXPGとなることでIFX抗体産生を抑制する仮説を検証.
アメリカの3施設.
IFX 3カ月,MTX 4カ月の投与量が安定しているRA(n=61).

RBC MTXPG$_3$の中央値 28 nmol/l (IQR 16-40)
infliximabの中央値 3.3 mg/ml (IQR1.4-7.7), MTX投与量 15mg/wk.
ATI(antibodies against IFX)は11例 (18%, ATI>0.9 U/l)検出
MTXの投与量が多いほどRBC MTXPG$_3$濃度は高い
・IFXトラフの低下は, IFX投与量, ATIの存在, RBC MTXPG$_3$低下, MTX投与期間の短さと関連.
・RBC MTXPG$_3$濃度>25ならATI陽性率は4.7倍下がる(OR=4.7; 95% CI 1.1 to 20.8; p=0.02). >50にはATI陽性者(n=12)はいなかった.



RBC MTXPG$_3$濃度 <5 nmol/lの4人中3人(75%)がATIあり.

Table 2 Stepwise multivariate linear regression analysis for infliximab trough levels

Variable	Step	Global R^2	Partial R^2	Estimate	p Value
Intercept				0.189±2.1	
Infliximab (mg/kg/8 weeks)	1	0.364	0.364	3.48±0.62	<0.001
ATI positivity	2	0.436	0.072	−4.14±1.85	0.029
RBC MTXPG$_3$ (nmol/l)	3	0.469	0.033	0.08±0.04	0.032
Duration of MTX therapy (months)	4	0.494	0.025	−0.02±0.01	0.100

Table 1 Patient characteristics

Characteristic	Value
Age (years)	64 (54–71)
Gender (female)	77%
Duration of disease (years)	11 (6–20)
BMI	27.4 (22.3–32.6)
Anti-MCV positivity (>20 U)	83.6%
Smokers, n (%)	7 (12%)
Duration of MTX therapy (months)	112 (65–150)
MTX dose (mg/week)	15 (10–20)
Infliximab dose (mg/kg/8 weeks)	6.0 (4.4–8.4)
Duration of infliximab therapy (months)	70 (29–107)
Previous anti-TNFs	36%
CDAI	8 (4–13)

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- 減量・中止

Addition of infliximab compared with addition of sulfasalazine and hydroxychloroquine to methotrexate in patients with early rheumatoid arthritis (Swefot trial): 1-year results of a randomised trial

MTX-IRならIFX追加がcsDMARD追加より臨床所見は改善

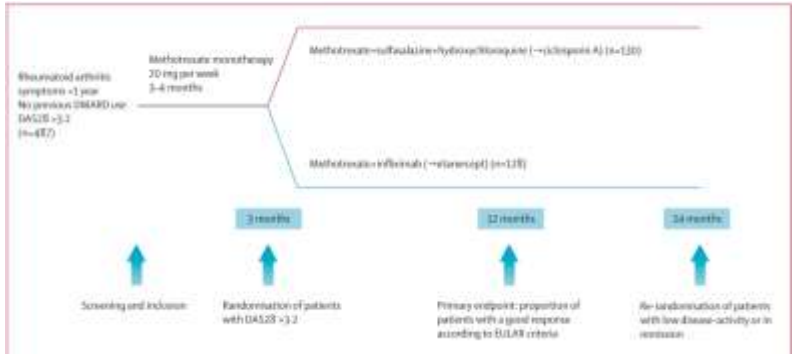
[Lancet. 2012;379(9827):1712-20.]

MTX-IRのearly RAにcsDMARD(SASP,HCQ) vs IFXの追加をRCT(open label)で検証.

罹病期間1年未満でDAS28＞3.2, csDMARDsでの治療歴がないRA(n=487)

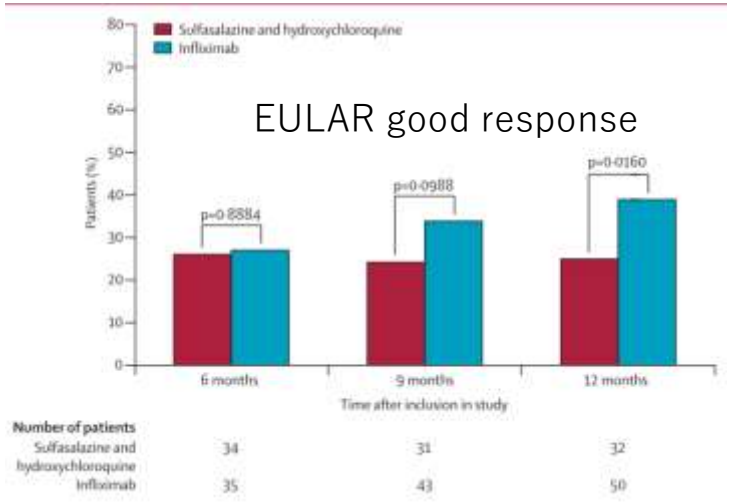
MTX開始し(MAX20mg),3~4か月後のDAS28＞3.2ならIFX群(3mg/kg, q8w, n=128) or SASP(1g/日)＋HCQ(400mg/日), n=130.

アウトカム：12か月後のEULAR good responseの割合で評価



- 12か月後のEULAR good response: IFX 39%vsSASP＋HCQ 25%(p=0.016)
- ACR20,50,70でもIFXで有意差あり.
- 有害事象は両群で同じ.

	Sulfasalazine and hydroxychloroquine (n=130)	Infliximab (n=128)
Total adverse events	48	32
Number of patients with at least one adverse event	33 (25%)	26 (21%)
Blood and lymphatic system	5	1
Liver	1	5
Infectious	0	5
Skin and allergic reactions	3	11
Gastrointestinal	15	1
Respiratory system	2	2
Hypertension	2	0
Eyes	2	0
Ears	1	0
Central and peripheral nervous system	6	1
Musculoskeletal	0	1
Psychiatric	4	0
General	2	3
Neoplasms	0	0
Abnormal blood test	1	1
Unspecified	4	1
Serious adverse events	1 (generalised symptoms*)	1(persistentfever)



	Sulfasalazine and hydroxychloroquine (n=130)	Infliximab (n=128)	Risk ratio (95% CI)	p
Responses compared with randomisation				
EULAR good response	32 (25%)	50 (39%)	1·59 (1·10—2·30)	0·0160
EULAR good or moderate response	64 (49%)	77 (60%)	1·22 (0·98—1·53)	0·0817
ACR 20	37 (28%)	54 (42%)	1·48 (1·06—2·08)	0·0266
ACR 50	19 (15%)	32 (25%)	1·71 (1·02—2·86)	0·0424
ACR 70	9 (7%)	15 (12%)	1·69 (0·77—3·73)	0·2044
Responses compared with inclusion				
EULAR good response	41 (32%)	61 (47%)	1·51 (1·11—2·06)	0·0107
EULAR good or moderate response	75 (58%)	91 (71%)	1·23 (1·03—1·48)	0·0275
ACR 20	59 (45%)	76 (59%)	1·31 (1·03—1·66)	0·0257
ACR 50	44 (34%)	62 (48%)	1·43 (1·06—1·93)	0·0226
ACR 70	20 (15%)	36 (28%)	1·83 (1·12—2·98)	0·0156

Conventional combination treatment versus biological treatment in methotrexate-refractory early rheumatoid arthritis: 2 year follow-up of the randomised, non-blinded, parallel-group Swefot trial

Ronald F van Vollenhoven, Pierre Geborek, Kristina Forslind, Kristina Albertsson, Sofia Ernestam, Ingemar F Petersson, Katerina Chatzidionysiou, Johan Bratt, for the Swefot study group

MTXにcsDMARDsを追加すると18・24カ月でIFXと同等の臨床効果を認めるが, 関節破壊は進行する.

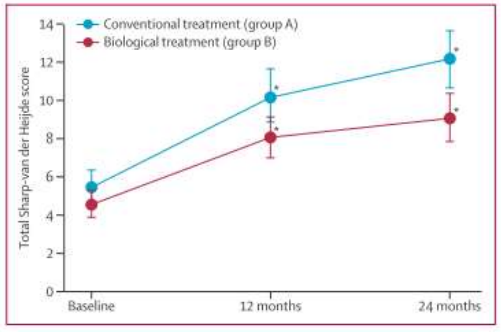
[Lancet. 2012;379(9827):1712-20.]

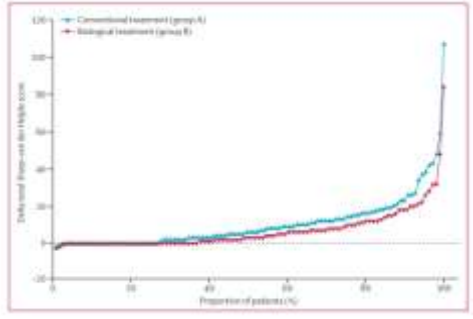
罹病期間1年未満でDAS28＞3.2, csDMARDsでの治療歴がないRA(n=487)
MTX開始し(MAX20mg),3~4か月後のDAS28＞3.2ならIFX群(3mg/kg, q8w, n=128) or SASP(1g/日)＋HCQ(400mg/日), n=130.
12か月後のEULAR good response: IFX 39%vsSASP＋HCQ 25%(p=0.016)
ACR20,50,70でもIFXで有意差あり.

このSwefot trialの18カ月, 24か月後の臨床所見とX線を評価した研究

	12 months				18 months			24 months		
	Conventional treatment (n=130)	Biological treatment (n=128)	Risk ratio (95% CI)	p value	Conventional treatment (n=130)	Biological treatment (n=128)	Risk ratio (95% CI)	Conventional treatment (n=130)	Biological treatment (n=128)	p value
ACR20 response	37 (28%)	54 (42%)	1·48 (1·06–2·08)	0·0266	44 (34%)	58 (45%)	1·34 (0·99–1·82)	43 (33%)	51 (40%)	0·259
ACR50 response	19 (15%)	32 (25%)	1·71 (1·02–2·86)	0·0424	25 (19%)	39 (30%)	1·58 (1·02–2·46)	28 (22%)	38 (30%)	0·134
ACR70 response	9 (7%)	15 (12%)	1·69 (0·77–3·73)	0·2044	14 (11%)	22 (17%)	1·60 (0·86–2·98)	18 (14%)	21 (16%)	0·566
EULAR good response	32 (25%)	50 (39%)	1·59 (1·10–2·30)	0·0160	38 (29%)	49 (38%)	1·31 (0·93–1·85)	40 (31%)	49 (38%)	0·204
EULAR good to moderate response	64 (49%)	77 (60%)	1·22 (0·98–1·53)	0·0817	61 (47%)	74 (58%)	1·23 (0·97–1·56)	65 (50%)	75 (59%)	0·166

	Increase from baseline to 12 months					Increase from 12 months to 24 months					Increase from baseline to 24 months				
	Conventional treatment (n=104)		Biological treatment (n=102)		Treatment difference (95% CI)	Conventional treatment (n=107)		Biological treatment (n=102)		Treatment difference (95% CI)	Conventional treatment (n=109)		Biological treatment (n=106)		Treatment difference (95% CI); p value
	Mean (SE)	Median (IQR)	Mean (SD)	Median (IQR)		Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)		Mean (SD)	Median (IQR)	Mean (SE)	Median (IQR)	
Total score	5·04 (10·64)	1 (0–6·5)	2·95 (6·07)	0 (0–5)	2·09 (–0·30 to 4·48)	2·21 (6·39)	0 (0–3)	1·05 (5·57)	0 (0–1)	1·16 (–0·48 to 2·80)	7·23 (12·72)	3 (0–11·25)	4·00 (10·05)	1 (0–5)	3·23 (0·14 to 6·32); 0·009
Erosion score	1·93 (5·28)	0 (0–2)	1·02 (2·93)	0 (0–2)	0·91 (–0·27 to 2·09)	0·69 (4·28)	0 (0–1)	0·25 (2·67)	0 (0–0)	0·44 (–0·54 to 1·42)	2·82 (6·69)	0 (0–3)	1·29 (4·73)	0 (0–1)	1·53 (–0·03 to 3·09); 0·039
Joint-space narrowing	3·12 (6·04)	0 (0–4)	1·84 (3·71)	0 (0–3)	1·28 (–0·10 to 2·66)	1·53 (3·09)	0 (0–2)	0·96 (3·74)	0 (0–1)	0·57 (–0·22 to 1·36)	4·45 (7·10)	2 (0–8)	2·79 (6·25)	0 (0–4)	1·66 (–0·14 to 3·46); 0·026





- cs群では多くが脱落した.
- 24か月後のIFX群 vs cs群 ACR20 40% vs 33% (p=0.259), ACR50 30% vs 22% (p=0.134),
- 有意差はないがIFXは24カ月後でも臨床効果はcs群より高い.
- mTSS IFX群 4.0 vs cs群 7.2 (p=0.009)
- IFX群の方がmTSSの増加が少ない.
- 2年目の進行もIFX群で低い.

Clinical and epidemiological research

EXTENDED REPORT

Infliximab for 6 months added on combination therapy in early rheumatoid arthritis: 2-year results from an investigator-initiated, randomised, double-blind, placebo-controlled study (the NEO-RACo Study)

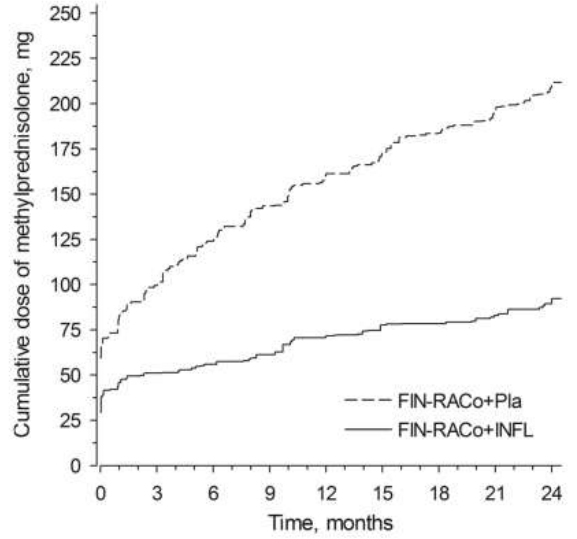
Marjatta Leirisalo-Repo,[1,2] Hanna Kautiainen,[3,4] Leena Laasonen,[5] Markku Korpela,[6] Markku J Kauppi,[7,8] Dili Kaipiainen-Seppänen,[9] Riitta Luosujärvi,[1,2] Reijo Luukkainen,[10] Anna Karjalainen,[11] Harri Blåfield,[12] Toini Utunela,[13] Kirsti Ilva,[14] Heikki A Julkunen,[15] Leena Peltomaa,[2] Kari Puolakka,[16] Eeva Moilanen,[17] Pekka J Hannonen,[18] Timo Möttönen,[19,20] for the NEO-RACo Study Group

寛解を目指すT2Tで, csDMARD剤にIFXを追加すると持続的寛解が高くなり, X線の関節破壊抑制効果あり

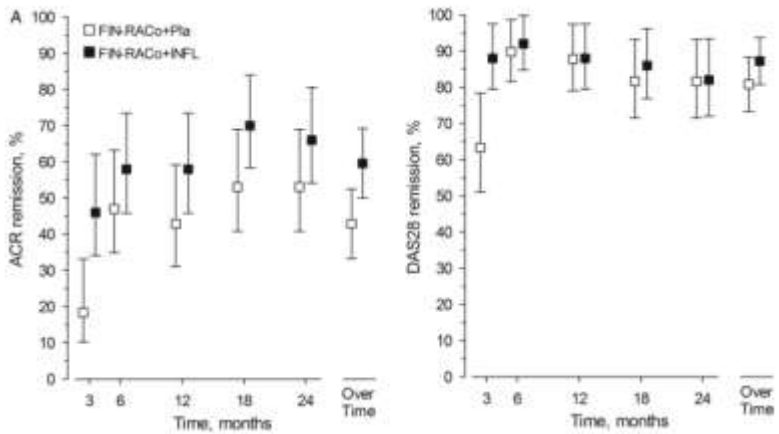
[Ann Rheum Dis. 2013 ;72(6):851-7.]

3剤のcsDMARDsにIFXを加えるとX線で関節破壊抑制があるか検討したRCT.
フィンランドの15施設
罹病期間1年未満のDMARD naïveの102名,寛解を目指し治療を強化.寛解達成後も漸減はしない.
MTX25mg＋SASP 2g+HCQ 35mg/kg/wk+PSL 7.5mg+PBO(n=49)
MTX25mg＋SASP 2g+HCQ 35mg/kg/wk+PSL 7.5mg+IFX(n=50)
MTXは10mg/wkで開始, 14wには25mg/wkを目指す.
アウトカム：24カ月後のACR remissionとX線の変化

- 24カ月後のACR 50/70, ACR remissonは有意差なし
- しかし,sustained ACR/DAS28 remissionは有意差あり(p=0.042,0.019)
- X線で関節破壊が進行しなかった割合：IFX群 80%, PBO群 53% (p=0.006)
- 関節内ステロイド累積投与量：PBO 212mg>IFX 92mg
- 有害事象は両群で差はない(IFX 6% vs PBO 8%)



Outcome measure	Treatment group: FIN-RACo+infliximab	FIN-RACo+placebo	p Value
ACR50 (%, 95% CI)	96 (86 to 100)	92 (80 to 98)	0.436
ACR70 (%, 95% CI)	86 (73 to 94)	71 (57 to 83)	0.090
Modified ACR remission (%, 95% CI)	66 (51 to 81)	53 (38 to 67)	0.19
Sustained modified ACR remission from 6 to 24 months (%, 95% CI)	26 (15 to 40)	10 (3 to 22)	0.042
DAS28 remission (%, 95% CI)	82 (72 to 93)	82 (71 to 93)	NS
Sustained DAS28 remission from 6 to 24 months (%, 95% CI)	72 (58 to 84)	49 (34 to 64)	0.019
Sharp-van der Heijde score, change from baseline (mean, 95% CI)*			
Erosion score	0.1 (−0.7 to 0.6)†	1.0 (0.6 to 1.6)‡	0.018§
Narrowing score	−0.3 (−0.7 to 0)†	0.4 (0.1 to 0.9)‡	0.029
Total score	−0.2 (−1.2 to 0.4)†	1.4 (0.8 to 2.3)‡	0.0058
Larsen score, change from baseline (mean, 95% CI)	0.4 (−0.5 to 1.3)†	1.7 (0.8 to 2.8)‡	0.079



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- TNF-α血中濃度
- MTXの併用
- csDMARDs vs Infliximab
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- 減量・中止

Extended report

Postmarketing surveillance of the safety profile of infliximab in 5000 Japanese patients with rheumatoid arthritis

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日本のIFX市販後調査の結果

[Ann Rheum Dis. 2008;67(2):189-94.]

重篤な副作用：6.2%

●infusion reaction
発熱(118例, 2.4%), ほてり(78例, 1.6%),
発疹(77例, 1.5%)
重篤な反応は24例(0.5%)
MTX >8mg/wkはリスク因子(p=0.004)

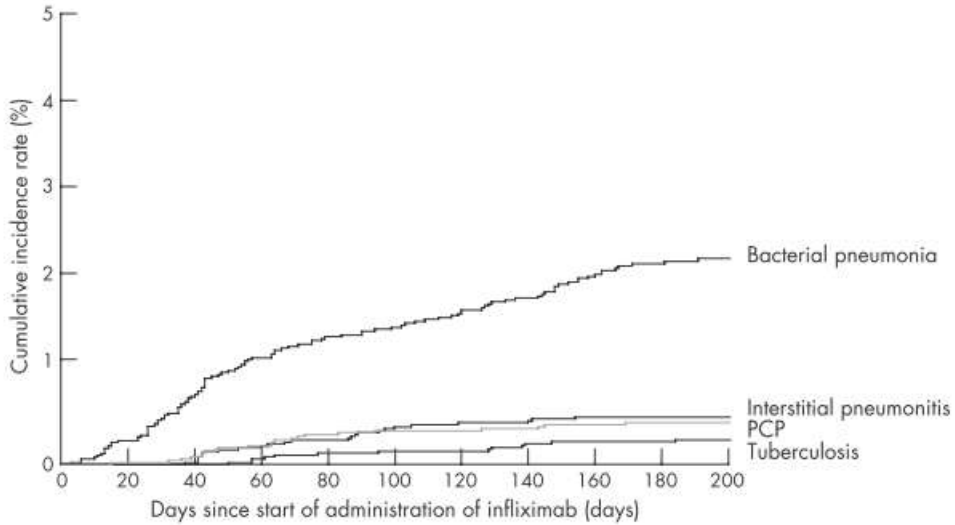
●間質性肺炎
25例(0.5%)
平均2.8回投与後に発症

●結核
14例(0.3%), 全例が重症.
7例(50%)が肺外結核

●PCP
22例(0.4%)
22例中21例がBALのPCRで診断.

●細菌性肺炎
108例(2.2%)
40歳未満にはいなかった.

- 初回投与から結核, PCP, 細菌性肺炎, 間質性肺炎が発生するまでの平均日数は, それぞれ103.1日, 70.0日, 72.1日, 76.8日.
- これらのADRの累積発生率をKaplan-Meiermethodでプロットすると, 細菌性肺炎は投与開始直後から, 結核, PCP, 間質性肺炎は投与開始後約1カ月から発生し始めた.



CONCISE REPORT

Study of the tolerance of infliximab infusions with or without betamethasone premedication in patients with active rheumatoid arthritis

J Sany, M J Kaiser, C Jorgensen, G Trape

GCsの前投与はinfusion reactionの発生率や重症度軽減に寄与しない.

[Ann Rheum Dis. 2005;64(11):1647-9.]

背景：IFX投与の5%にInfusion reactionが起こるとされている.
アセトアミノフェン, 抗ヒスタミン薬, ステロイド, 投与速度減量などで改善.

MTX併用しているRA
IFX 3mg/kgを 2 時間かけて投与
A:投与前にベタメタゾン(n=179), B:PBO(n=176)
Infusion reaction:投与 2 時間以内に悪寒, そう痒, 蕁麻疹, 胸痛, 呼吸困難, 低血圧, 血圧上昇, 呼吸困難, 頻脈と定義

Infusion reaction発生率：3.8%
ベタメタゾン投与群では30/179例(16.8%), PBO 18/176例(10.2%)
発生時期は, inductionとmaintenanceで差はない
ベタメタゾンはinfusion reactionの重症度に影響しなかった.

アトピー性皮膚炎の既往や経口PSLでも差はない.

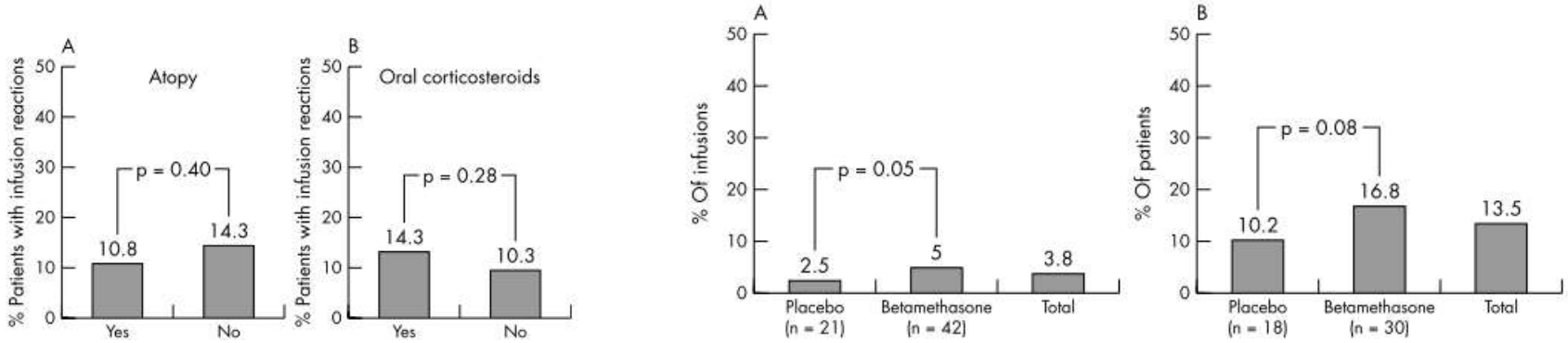


Figure 1 (A) Percentage of infusions in which infusion reactions occurred. (B) Percentage of patients in whom infusion reactions occurred.

START study

The Safety of Infliximab, Combined With Background Treatments, Among Patients With Rheumatoid Arthritis and Various Comorbidities

A Large, Randomized, Placebo-Controlled Trial

Rene Westhovens,[1] David Yocum,[2] John Han,[3] Alberto Berman,[4] Ingrid Strusberg,[5] Piet Geusens,[6] and Mahboob U. Rahman,[7] for the START Study Group

10mg/kgに増量すると感染症が増える

[Arthritis Rheum. 2006;54(4):1075-86.]

基礎疾患を有する活動性のRAでMTX＋IFX(3mg/kg or 10mg/kg)の安全性を検討したRCT.

MTX-IRで圧痛・腫脹関節が6か所以上が対象

PBO群(n=363), 3mg/kg群(n=360), 10mg/kg群(n=361) (それぞれq8w)

3mg/kgは22wにベースラインから20%の改善が乏しい,

または50%悪化あれば1.5mg/kg増量,MTXはMax25mg/wk, csDMARDS併用可

アウトカム：22wでの重篤な感染症の割合(PSL有無で層別化)

- ベースラインの各群の基礎疾患に差はなかった.
- DAS28,ACR responseなどの臨床効果は3mgと10mgで差はない.
- 22wでの重篤な感染症：relative risk 3mg/kg 1.0[p=0.995], 10mg/kg 3.1[p=0.013]
- PBO群 1.6%, 3mg/kg群 1.7%, 10mg/kg 5.0%
- 種類：肺炎, Tb, 蜂窩織炎, UTI
- 22w~54wでは重篤な感染症の発生率は各群で差はなかった.

Table 2. Serious infections through week 22*

Category	Placebo + MTX	Infliximab + MTX		
		3 mg/kg	10 mg/kg	Combined
No. of patients treated	361	360	361	721
Weeks of followup, mean	21.7	21.9	21.7	21.8
Weeks of treatment, mean	13.6	13.6	13.3	13.5
Patients with ≥1 serious infection	6 (1.7)	6 (1.7)	18 (5.0)	24 (3.3)
Serious infections reported				
Pneumonia	0 (0.0)	3 (0.8)	4 (1.1)	7 (1.0)
Active tuberculosis	0 (0.0)	0 (0.0)	3 (0.8)	3 (0.4)
Newly detected latent tuberculosis	1 (0.3)	1 (0.3)	0 (0.0)	1 (0.1)
Cellulitis	0 (0.0)	1 (0.3)	1 (0.3)	2 (0.3)
Urinary tract infection	0 (0.0)	0 (0.0)	2 (0.6)	2 (0.3)
Bronchitis	2 (0.6)	1 (0.3)	0 (0.0)	1 (0.1)
Corneal ulceration	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Viral infection	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Influenza	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Injection site inflammation†	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Otitis media	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Pleurisy	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Pneumocystis carinii infection	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Sepsis	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Sinusitis	0 (0.0)	0 (0.0)	1 (0.3)	1 (0.1)
Septic arthritis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Diverticulitis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Pyelonephritis	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)

Infliximab（レミケード）の特徴

- 用量と投与期間の調整
- 関節破壊抑制効果
- 血中濃度と抗体
- TNF-α血中濃度
- MTXの併用
- csDMARDs vs Infliximab
- 副作用(Infusion reaction, 感染症)
- 減量・中止

Extended report

Discontinuation of infliximab after attaining low disease activity in patients with rheumatoid arthritis: RRR (remission induction by Remicade in RA) study

Y Tanaka,[1] T Takeuchi,[2] T Mimori,[3] K Saito,[1] M Nawata,[1] H Kameda,[4] T Nojima,[3] N Miyasaka,[5] T Koike[6]; for the RRR study investigators

24wでDAS28<3.2(LDA)ならIFX中止すると, 55%でLDAを維持

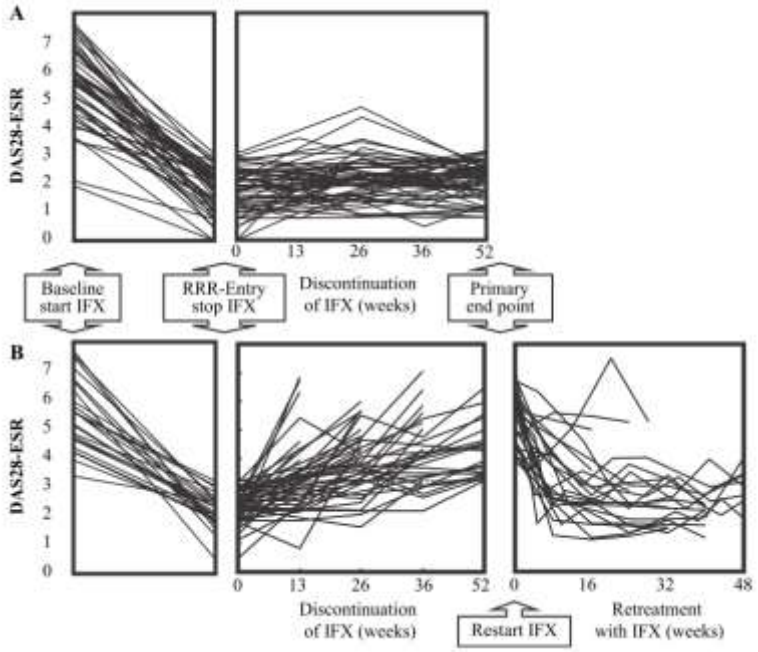
[Ann Rheum Dis. 2010;69(7):1286-91.]

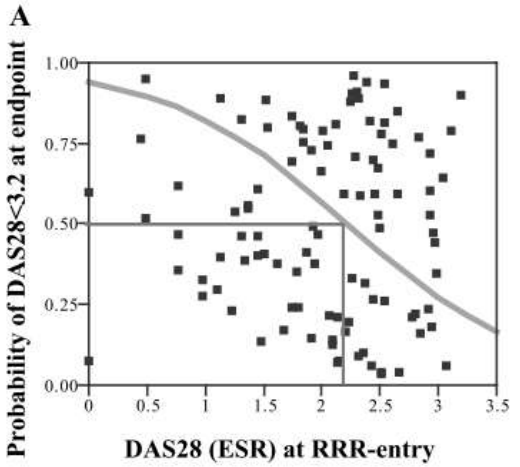
日本26施設.
DAS28(CRP/ESR)でLDA<3.2を24w継続したIFX使用中のRA(102名).
中止後2年間, 症状とDAS28を4-13w毎にフォローする.MTXは固定.
アウトカム：IFX中止後1年後、DAS28-ESR <3.2, mTSSの進行 <0.5
再燃時(RRR failed)は中止前の同じdoseのIFXを開始.

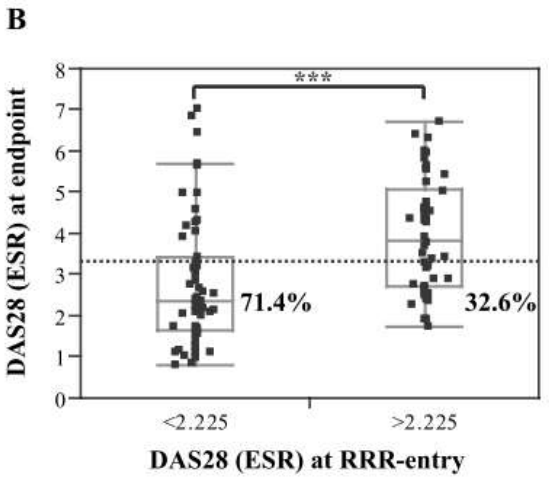
56/102名(55%)がIFX中止1年後もDAS28-ESR<3.2を達成.
さらに44/56名がDAS28-ESR<2.6となった.
IFX中止後29名が再発, 17名がDAS28-ESR≥3.2で46名(45%)が失敗.
IFX再投与で大半は24w以内にDAS28-ESR<3.2となった.

IFX中止成功因子
・若年(49yo vs 56yo)
・短い罹病期間(4.8 vs 7.8)
・mTSS低値(46.9 vs 97.2)
多変量解析：罹病期間とRF(p=0.0019, 0.0128)

IFX中止前のDAS28が以降1年間の寛解と相関
特に<2.225の深い寛解なら71.4%がDAS28-ESR<3.2を維持.







Extended report

Discontinuing treatment in patients with rheumatoid arthritis in sustained clinical remission: exploratory analyses from the BeSt study

N B Klarenbeek,[1] S M van der Kooij,[1] M Güler-Yüksel,[1] J H L M van Groenendael,[2] K H Han,[3] P J S M Kerstens,[4] T W J Huizinga,[1] B A C Dijkmans,[4 5] C F Allaart[1]

Early RAでDAS44<1.6後にIFX中止すると15%は中止を維持.

[Ann Rheum Dis. 2011;70(2):315-9.]

活動性のあるearly RA(罹病期間2年未満)
Group 1(n=126): MTX→SASP→LEF→MTX＋IFX....
Group 2(n=121): MTX→MTX＋SASP→MTX＋SASP+HCQ→ MTX＋SASP+HCQ+PSL...
Group 3(n=133):MTX＋SASP+PSL60mg→ MTX＋CyA+PSL→...
Gropu 4(n=128):MTX＋IFX
DAS44<2.4(LDA)を３カ月毎に評価し,未達成なら治療を変更していく.
DAS44<2.4(LDA)を6カ月継続すると維持量(MTX 10mg/wk,SASAP 2gなど)とする.
さらに６カ月以上DAS44<1.6なら中止.

5年後115/508例(23%)でdrug freeを達成(群間差なし, p=0.2)
Group 4 (MTX＋IFX)は15%(19/128)でdrug freeを維持.
53/115例が中央値 5カ月で治療再開している.
26/53例(47%)は3カ月以内に維持量DMARD再開で寛解を達成.
初診時のCCP抗体,RF, HAQ低値, VAS global health低下は中止後の治療再開と相関.
寛解時の特徴とは関連なし.

Table 1 Overview of the distribution of patients who achieved drug-free remission during 5 years of follow-up in the four treatment groups

	Sequential monotherapy (n=126)	Step-up therapy (n=121)	Initial combination with prednisone (n=133)	Initial combination with infliximab (n=128)
Drug-free ever	31	24	24	36
Still drug-free at 5 years	14 (45)	14 (58)	10 (42)	21 (58)
Restarted DMARD monotherapy	15 (48)	9 (38)	14 (58)	15 (42)
Lost to follow-up	2 (6)	1 (4)	0 (0)	0 (0)

Table 2 Treatment details of the 115 patients who discontinued all DMARDs due to sustained clinical remission

	Sustained drug-free remission (n=59)	Restarted (n=53)	Lost to follow-up (n=3)
Sequential monotherapy			
MTX monotherapy*	11	9	1
SSA monotherapy†	0	4	1
Leflunomide monotherapy‡	3	0	0
MTX + IFX§	0	2	0
Next steps	0	0	0
Step-up combination therapy			
MTX monotherapy*	8	4	1
MTX + SSA¶	4	3	0
MTX + SSA + HCQ¶	2	1	0
MTX + SSA + HCQ + pred¶	0	1	0
Next steps	0	0	0
Initial combination with prednisone			
MTX + SSA + pred**	10	12††	0
MTX + CSA + pred‡‡	0	2	0
Next steps	0	0	0
Initial combination with infliximab			
MTX + IFX§	19	13	0
SSA monotherapy†	2	2	0
Next steps	0	0	0