Immunomodulateurs & anti-TNFalpha pour le traitement des uvéites

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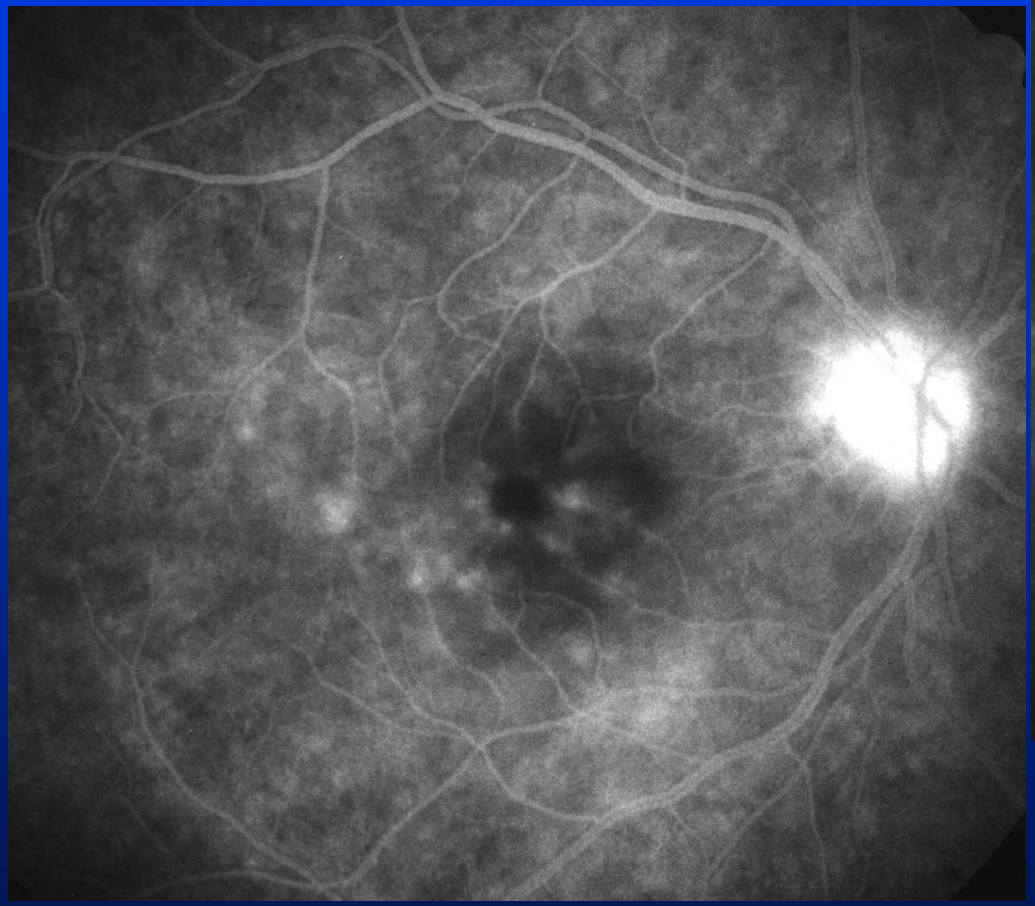
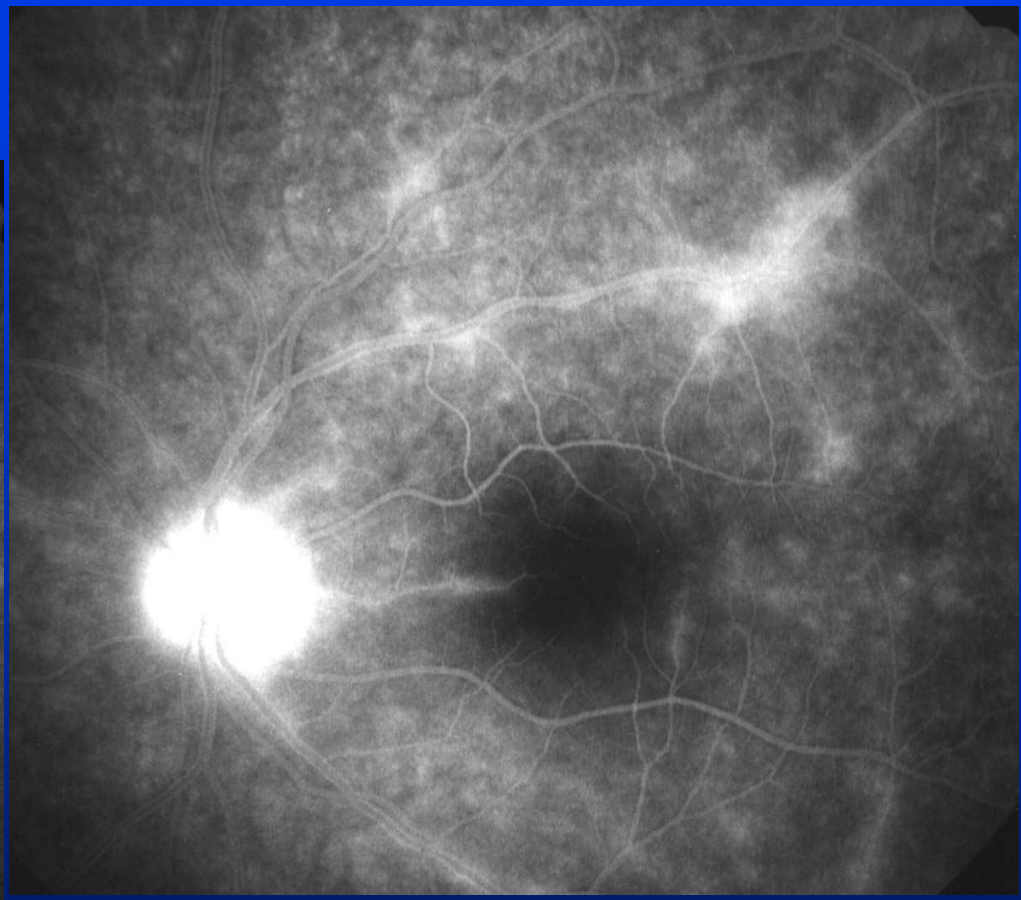




Les corticoïdes

CORTICOIDES

- **Education thérapeutique**
- **Prévention des complications**
  - **Recommandations EULAR 2007**

EULAR evidence-based recommendations on the management of systemic glucocorticoid therapy in rheumatic diseases

J N Hoes, J W G Jacobs, M Boers, D Boumpas, F Buttgereit, N Caeyers, E H Choy, M Cutolo, J A P Da Silva, G Esselens, L Guillevin, I Hafstrom, J R Kirwan, J Rovensky, A Russell, K G Saag, B Svensson, R Westhovens, H Zeidler, J W J Bijlsma

Ann Rheum Dis 2007;**66**:1560–1567. doi: 10.1136/ard.2007.072157

  - **Ostéoporose et biphosphonates**

Les immunosuppresseurs

Niveaux de preuve

Ia	Evidence obtained from meta-analysis of RCTs
Ib	Evidence obtained from at least one RCT
IIa	Evidence obtained from at least one well-designed study without randomization
IIb	Evidence obtained from at least one other type of well-designed quasi-experimental study
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

Immunosuppresseurs

- **Immunosuppresseurs**
  - Azathioprine
  - Cyclophosphamide
  - Ciclosporine
  - Méthotrexate
  - Mycophénolate mofétil
  - Tacrolimus, FK506
  - Chlorambucil
- **Immunomodulation**
  - IgIV
  - IFN-alpha
- **Biothérapies**
  - Anti-TNF-alpha
  - Anti-IL2R
  - Anti-IL1RA
  - Anti-CD52
  - Anti CD20

Immunosuppresseurs

- **Multiples agents disponibles…**

- **Choix en fonction :**
  - **Du terrain (âge, insuffisances d'organe…)**
  - **Des risques liés à ces traitements (♀ en âge de procréer, enfants, immunodéprimés…)**
  - **De l'éventuelle maladie systémique sous-jacente**
  - **Des résultats des études disponibles**

AZATHIOPRINE

AMM formes sévères de maladies auto-immunes

Effets secondaires :

- **Toxicité hématologique** (dose dépendante, réversible - dosage TPMT)
- **Toxicité hépatique**
- **Choc hypovolémique, diarrhée, vomissements, pancréatite, fièvre**

(possible si grossesse)

CYCLOPHOSPHAMIDE

- Prodrogue, alkylant, diminuant la prolifération lymphocytaire T CD4 et CD8, B
- per os: 2 mg/kg/j (peu utilisé)
- IV: 600 à 750 mg/m^2 (maxi 1.2 g)
  - **J1 J15 J30**
  - **puis toutes les 3 à 4 sem**

TOXICITE DU CYCLOPHOSPHAMIDE

La majorité des effets indésirables sont dose-dépendants

Toxicité fréquente (> 10 %)

- **nausées** (IV > PO)
- stomatite (fortes doses)
- **myélosuppression** (16-66 %) : neutropénie (nadir 8-12ème jour IV), lymphopénie
- **infections**: bactériennes, parasitaires, virales et en particulier opportunistes (PCP, zona, aspergillose, mycobactérioses …)
- **cystite** (prévenue par l 'administration de Mesna et hydratation)
- **aménorrhée** par insuffisance ovarienne (20-66 % des cas au cours des maladies systémiques), **stérilité définitive** surtout femmes âgées >25 ans et en cas de traitements prolongés
- azoospermie (jusqu'à 60 % après 6 mois de traitement), parfois réversible
- alopécie

TOXICITE DU CYCLOPHOSPHAMIDE

Toxicité rare (1-10%)

- **cancers secondaires** (RR 2,4):
  - vessie (3-5%) RR 33,
  - leucémies (<1% au cours des maladies systémiques, pour des doses cumulées > 50 g),
  - lymphomes (RR 11)
- **myélodysplasie** (2 %)
- **cardiotoxicité** (pour les fortes doses : troubles du rythme, myocardite, insuffisance cardiaque congestive)

CICLOSPORINE

- Action sur les lymphocytes T activés
- Deux formes principales per os:
  - Sandimmun® : formulation conventionnelle
  - Néoral ® : microémulsion

- 2 à 5 voire 10 mg/kg, PO
- **Taux sérique thérapeutique** : 150-250 ng/ml, puis 80-150 ng/ml après 1 an

- Intravitréen ? Microsphères ? *(He, 2006, Invest Ophthalmol Vis Sci)*

CICLOSPORINE

Effets secondaires :

- **Neurologiques : tremblements, convulsions, encéphalopathies**
- **HTA +++, insuffisance rénale, fibrose rénale**
- **Vasculaires : microangiopathie thrombotique**
- **Métaboliques : hyperlipidémie, diabète**
- **Hyperplasie gingivale**
- **Hypertrichose**
- **Tumeurs cutanées, lymphomes**

METHOTREXATE

- **Antimétabolite, analogue de l'acide folique, inhibant la DHFR, la synthèse d'ADN et la prolifération des lymphocytes T**
- **Activité anti-inflammatoire**

- **0,2 à 0,3 mg/kg/semaine, PO ou IM**

METHOTREXATE

Toxicité

- **Hépatite** fibrosante (cirrhose)
- **Pneumopathie d'hypersensibilité**
- **Toxicité hématologique** (rare aux doses utilisées)
- **Toxicité gonadique et tératogénicité,** risque abortif. Contraception obligatoire +++
- Toxicité tubulaire rénale (attention si IR)

- Troubles digestifs: stomatite, diarrhée

  → Acide folinique (5 mg/j-sans MTX ou 25 mg/sem)

MYCOPHÉNOLATE MOFÉTIL

Effets secondaires :

- **Digestifs:** diarrhées, dl abdo, vomissements
- **Hématologiques :** leucopénie, thrombopénie, anémie
- Hypersensibilité
- Pneumopathie interstitielle
- Aucun effet cardio-vasculaire ou métabolique
- Pas de néphrotoxicité

TACROLIMUS

- **FK506 - Macrolide inhibant l'activité lymphocytaire T (10-100 x plus puissant que CsA)**
- **Interactions nombreuses, absorption variable**

- **0,03 - 0,1 voire 0,3 mg/kg/j, PO**
- **Taux sérique efficace, non toxique <15ng/ml**

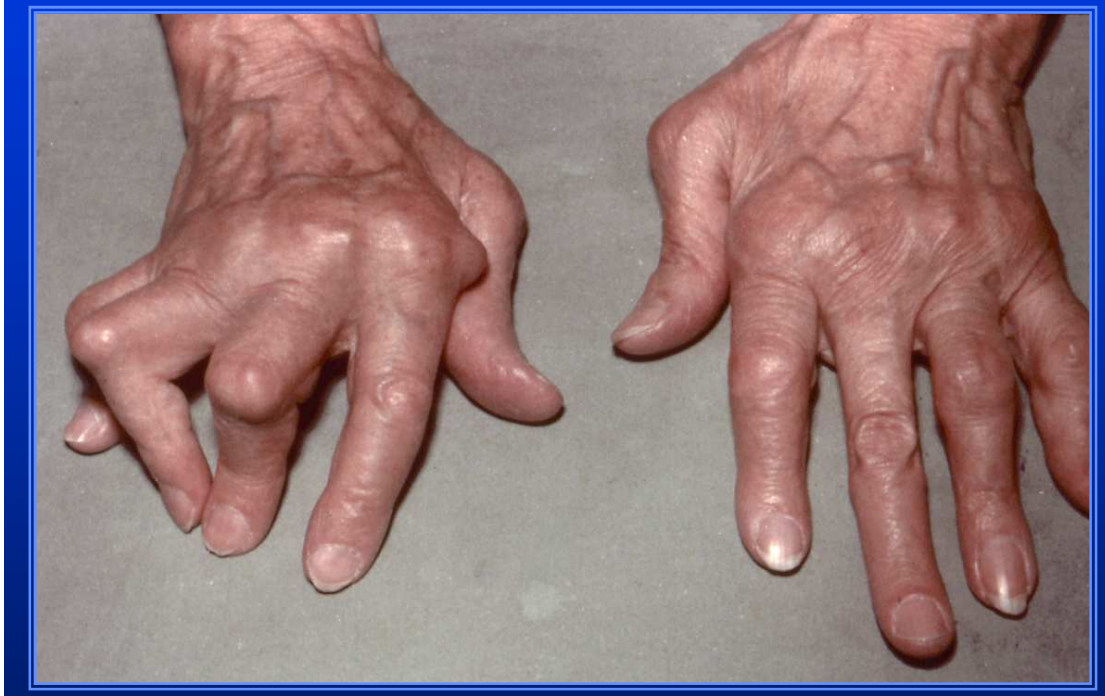
- **Moins toxique sur le plan rénal que la CsA**
- **Intravitréen ?** (modèle animal - *Oh-i, 2007, Br J Ophthalmol*)

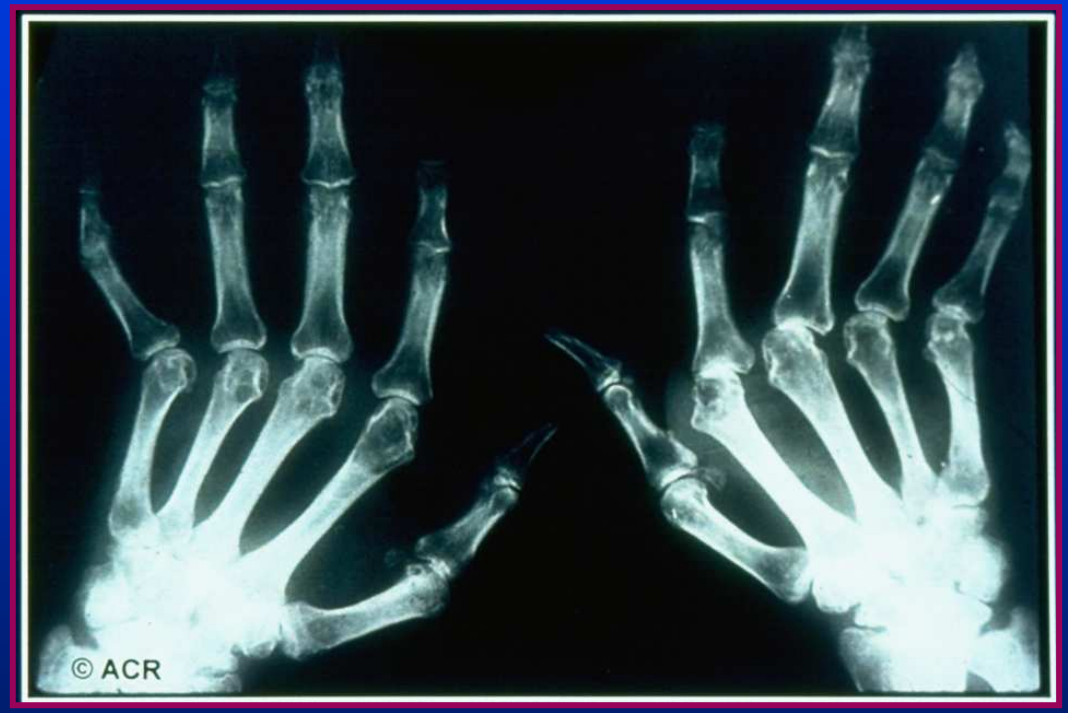

Nouveaux agents biologiques

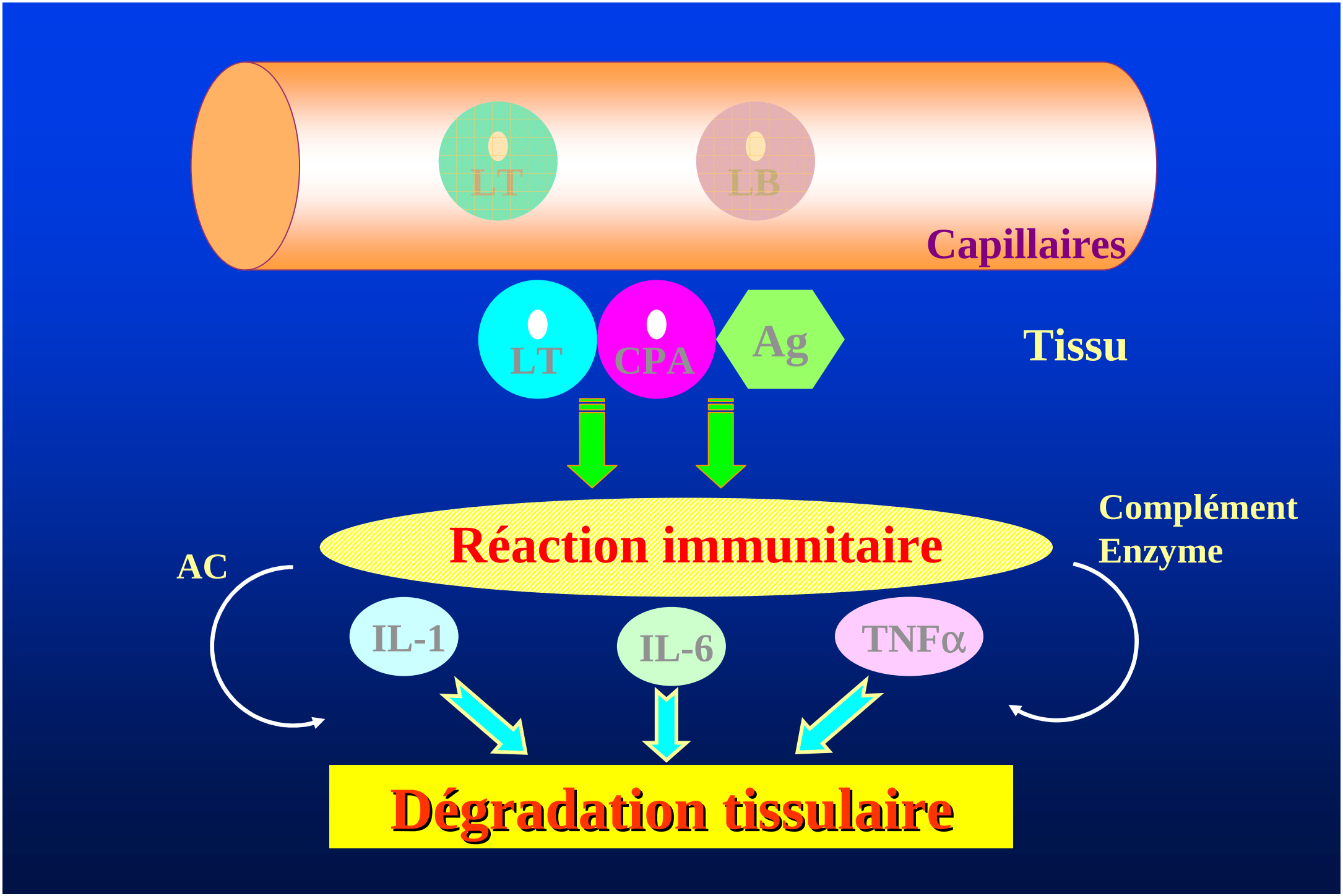

Nomenclature des Ac monoclonaux

Espèce	Lettre	Suffixe
Humain	U	umab
Souris	O	omab
Rat	E	
Hamster	E	
Primate	i	
Chimère	Xi	ximab
Humanisé	zu	zumab

La Polyarthrite Rhumatoïde : maladie modèle

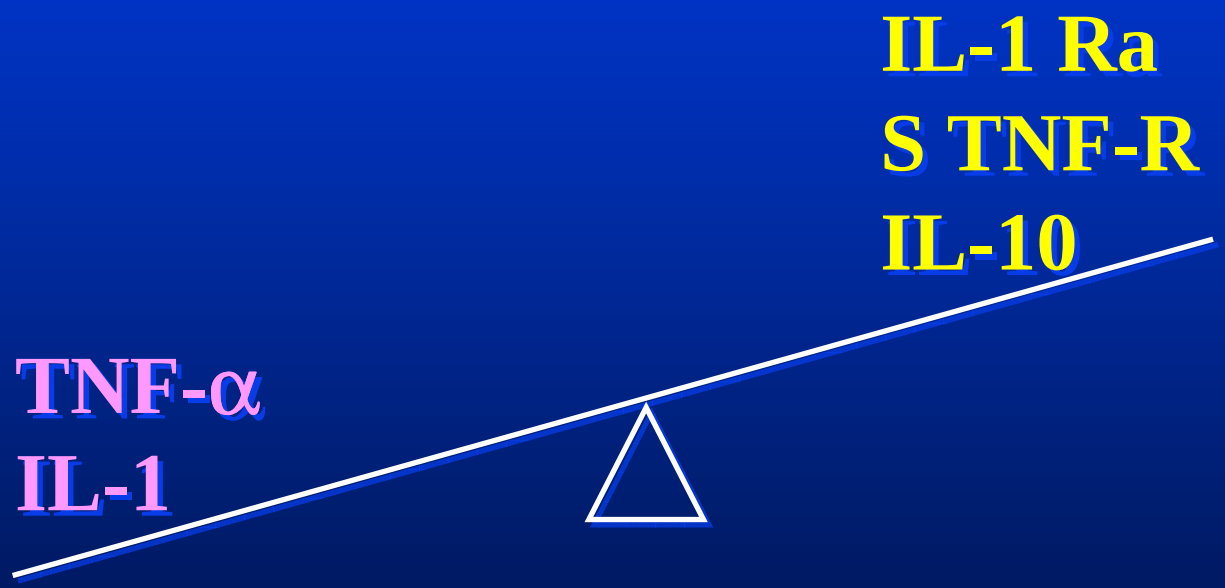




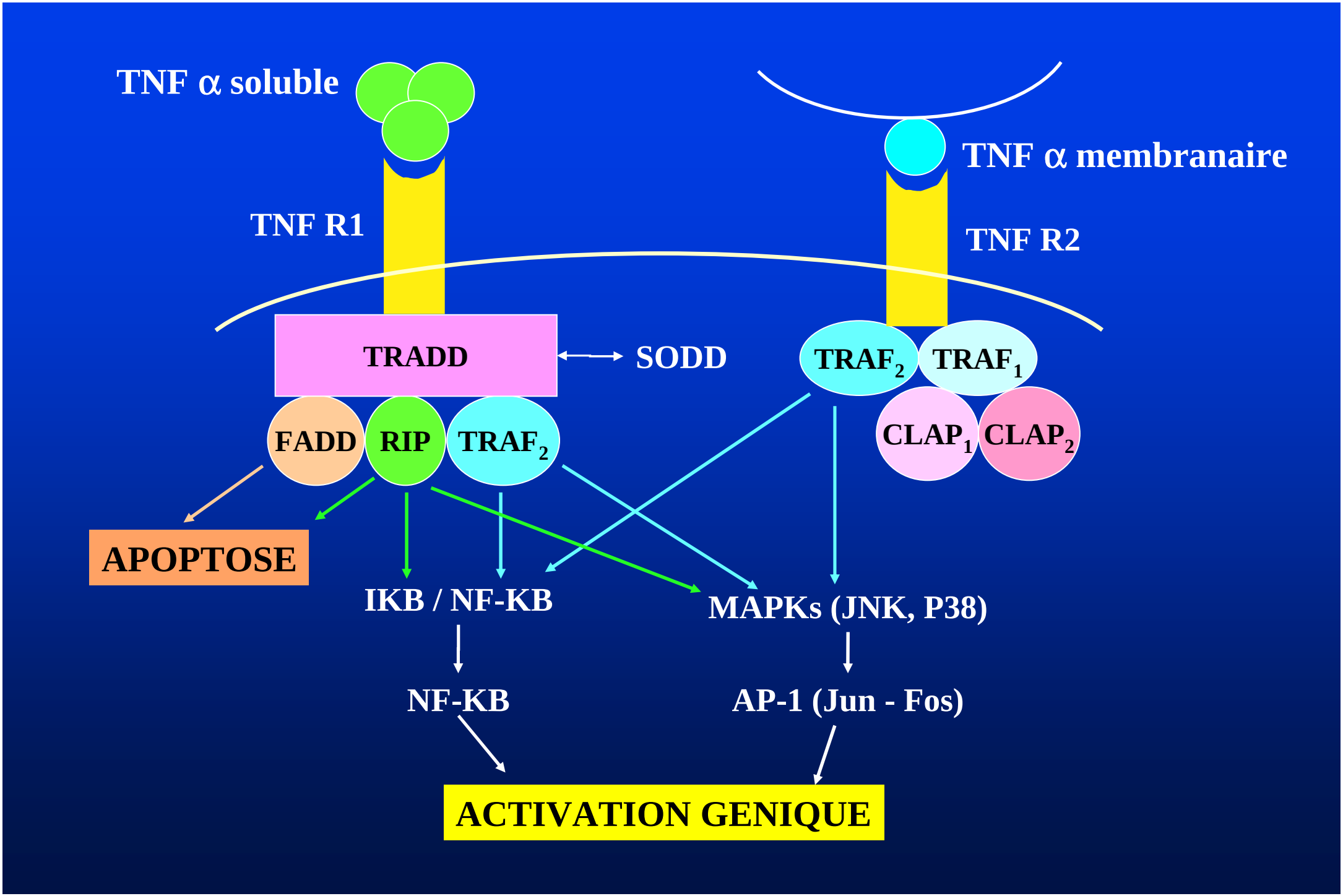

LT
LB
Capillaires
LT
CPA
Ag
Tissu
Réaction immunitaire
AC
Complément
Enzyme
IL-1
IL-6
TNFα
Dégradation tissulaire

Immunopathologie de la polyarthrite rhumatoïde

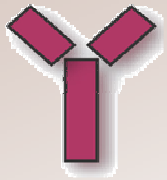
- **Rupture d'équilibre cytokinique**



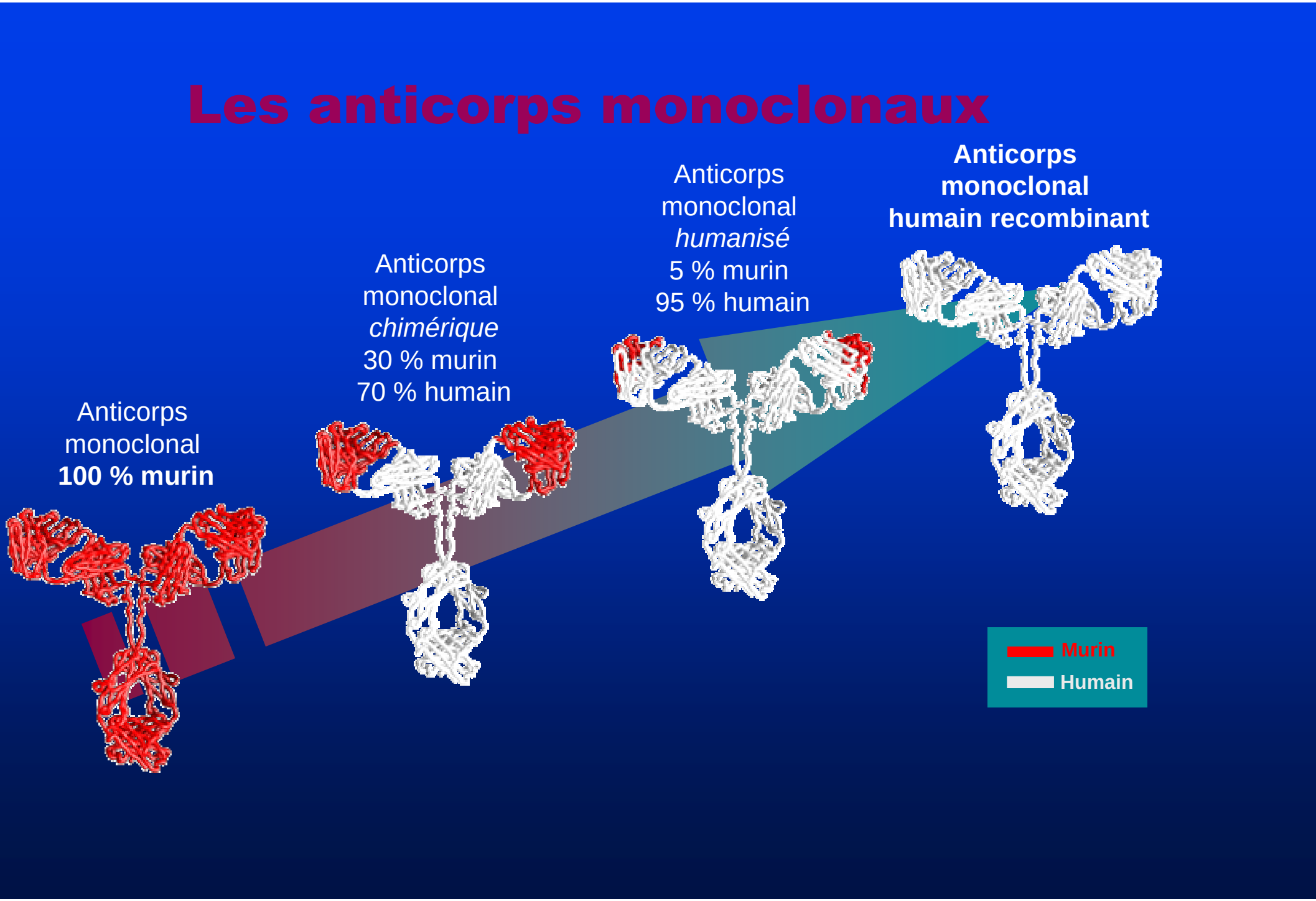
Feldmann et al. Cell 1996; 85 : 307.


TNF α soluble
TNF α membranaire
TNF R1
TNF R2
TRADD
SODD
TRAF2
TRAF1
FADD
RIP
TRAF2
CLAP1
CLAP2
APOPTOSE
IKB / NF-KB
MAPKs (JNK, P38)
NF-KB
AP-1 (Jun - Fos)
ACTIVATION GENIQUE

Biothérapies ayant obtenu une autorisation de mise sur le marché pour le traitement de la PR

Antagonistes des récepteurs à l'IL-1 recombinants	Anticorps monoclonal chimérique anti-TNF alpha	Fragments solubles de récepteurs au TNF (4,6)	Anticorps monoclonal anti-TNF alpha humain recombinant (1,2,6)
Anakinra Kineret® 	Infliximab Remicade® 	Etanercept Enbrel® 	Adalimumab Humira® 
Antagoniste du récepteur de l'interleukine 1 humaine (r-metHuIL-1ra) produit par la technique de l'ADN recombinant.	Fraction variable d'un anticorps monoclonal anti-TNF de souris couplée à une fraction constante d'une IgG1 humaine	Protéine de fusion composée : - du domaine de liaison extracellulaire du récepteur TNFR2/p75 au TNF - associé au fragment Fc d'une IgG1 humaine	Séquences peptidiques et structure 100 % humaines IgG1 humaine recombinante

Les anticorps monoclonaux



Uvéites et Infliximab

Etudes	n	Indications en ADJUVANT	% efficacité
Prospectives ouvertes			
Suhler, Arch Ophtalmol, 2005	23	Uvéites post réfract.	78%
Tugal-Tutkun, Arthritis Rheum, 2005	13	Uvéites Behçet + AZA CS	30% sans poussées mais 70% à l'arrêt (AV idem S54)
Joseph, 2004, Ophtalmology	5	Uvéites post Behçet ou idiopathique réfractaires	4/5 (1 Tuberculose)
Ohno, 2004, J Rheumatol	13	Uvéorétinite réfractaire Behçet	↓ du nb de poussées de 75%
Rétrospectives			
Lindstedt, 2005, Br J Ophtalmol	13	Uvéites sévères	100% infl, 84% AV
Bodaghi, 2005, Ann Rheum Dis	12	Uvéites sévères réfract.	100% réponse, 83% AV, 33% rechutes (>8s)
Murphy, 2004, Ophtalmology	7	3 uvéites réfract. + autres	86%

A Prospective Trial of Infliximab Therapy for Refractory Uveitis

Preliminary Safety and Efficacy Outcomes

Eric B. Suhler, MD; Justine R. Smith, MBBS, PhD; Michael S. Wertheim, MBChB, MRCOphth; Andreas K. Lauer, MD; Daryl E. Kurz, MD; Terri D. Pickard, COT; James T. Rosenbaum, MD

Objective: Infliximab, a monoclonal antibody against tumor necrosis factor α, is approved by the US Food and Drug Administration for treatment of numerous autoimmune disorders. We conducted a prospective, open-label phase 2 clinical trial to assess the effectiveness of infliximab in treating refractory autoimmune uveitis.

Methods: We prospectively enrolled 23 patients from the uveitis clinic of the Casey Eye Institute, Portland, Ore, into this trial. All patients meeting eligibility criteria received 3 infliximab infusions at weeks 0, 2, and 6. Clinical success was ascertained at week 10. Patients meeting initial criteria for success received an infusion at week 14 and every 8 weeks thereafter, with dose escalation permitted for breakthrough inflammation, and underwent outcome measurements at week 50.

Results: All patients underwent outcome assessment at week 10. Eighteen (78%) of these subjects met criteria for clinical success at this time. Success was judged by the composite clinical end point of visual acuity, control of intraocular inflammation, ability to taper concomitant medication therapy, and improvement in inflammatory signs on fluorescein angiography and/or ocular coherence tomography. Successful grading required improvement in at least 1 of 4 subcomponents and worsening in none. Seven of 14 patients enrolled for 1 year continued infliximab therapy and maintained their successful grading. Five did not complete 1 year of treatment because of significant adverse events, and 2 terminated treatment early for reasons unrelated to the study. Serious adverse events that were potentially related to infliximab included pulmonary embolus, congestive heart failure, lupus-like reaction in 2, and vitreous hemorrhage in 2 patients. Antinuclear antibodies developed in 15 of 20 enrolled patients receiving 3 or more infusions.

Conclusions: Infliximab was an effective short-term immunosuppressive agent in most of the patients, with 18 of 23 meeting criteria for clinical success at week 10. Infliximab was effective in the long term in all patients able to complete 50 weeks of therapy. Although some patients achieved clear benefit, the rate of serious toxic effects was unexpectedly high. Further long-term studies are warranted to determine the safety and efficacy of infliximab in treating intraocular inflammation.

Arch Ophthalmol. 2005;123:903-912

Infliximab Therapy for the Treatment of Refractory Ocular Inflammatory Disease

Lucia Sobrin, MD; Eva C. Kim, MD; William Christen, PhD; Thekla Papadaki, MD; Erik Letko, MD; C. Stephen Foster, MD

Objective: To report the outcomes of infliximab therapy in the treatment of ocular inflammatory disease refractory to traditional immunomodulatory therapy (IMT).

Methods: We retrospectively reviewed the medical records of 27 patients. All patients had noninfectious ocular inflammatory disease refractory to traditional IMT and received 5 mg/kg of infliximab at 2-week to 8-week intervals. Main outcome measures were clinical response, reduction in concomitant IMT, and adverse effects. Cumulative incidences of inflammation control and vision change were calculated using life-table methods.

Results: Twenty-one patients experienced sustained improvement in inflammation with their initial course of infliximab therapy. Cumulative incidence of inflammation resolution at 12 months was greater than 90%. Sixteen patients were able to decrease the dose of their concomitant IMT medication or stop all other IMT. Four patients were able to discontinue all other IMT while receiving infliximab therapy. Three patients with scleritis were eventually able to remain inflammation-free while not taking any medication. At 12 months, 56% and 65% of left and right eyes, respectively, showed visual acuity improvement by 2 or more Snellen lines. Only 1 patient developed an adverse event requiring therapy discontinuation.

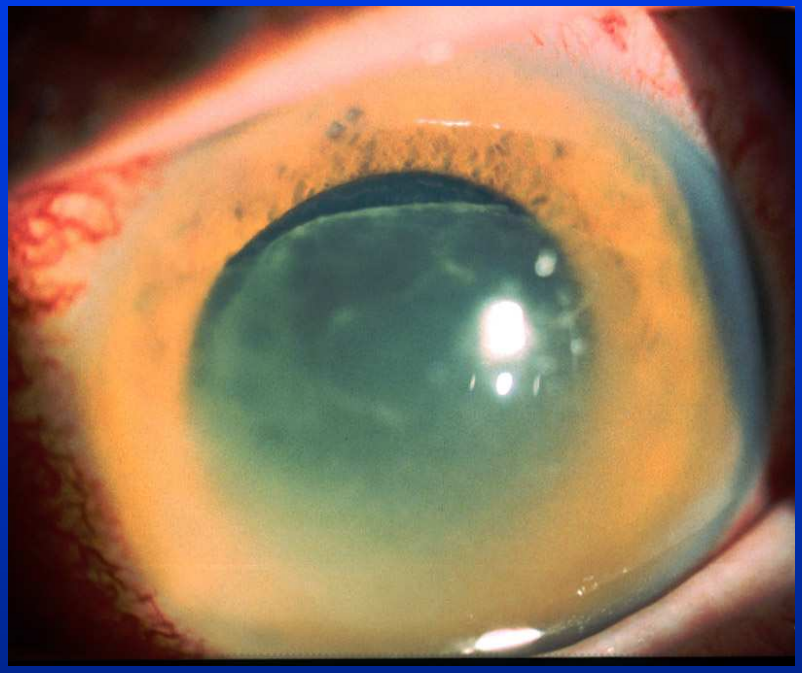
Conclusions: We found a high rate of ocular inflammation control with infliximab therapy. The incidence of adverse effects in this study was low.

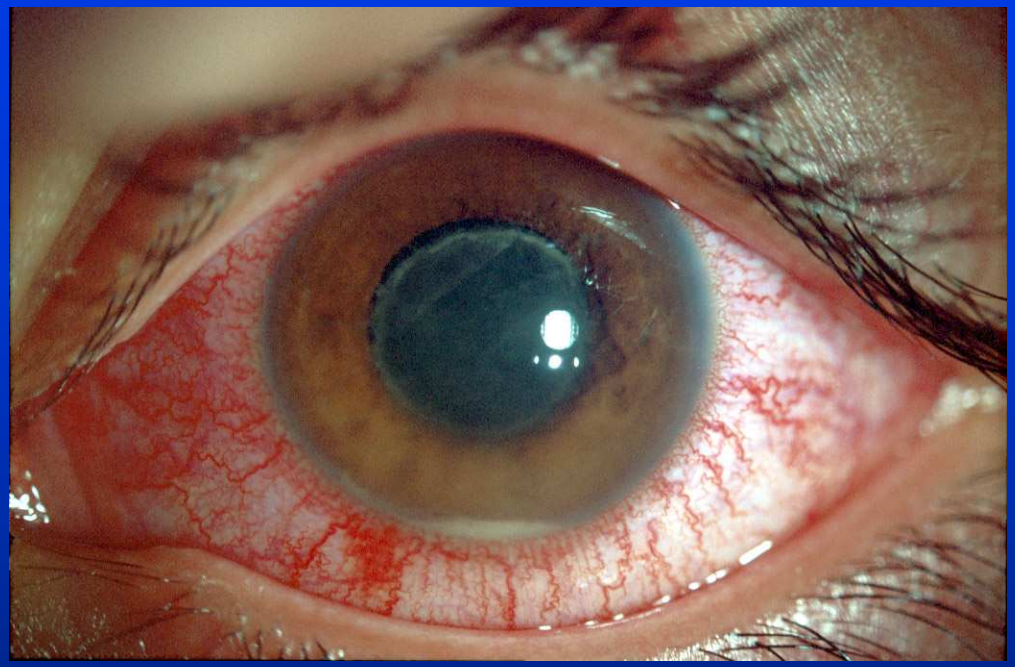
Arch Ophthalmol. 2007;125(7):895-900

Uvéites et Etanercept

Etudes	n	Indications	% efficacité	Mais…
Prospectives				
Foster, Arch Ophtalmol, 2003	10 ETA vs 10 P	Uvéites diverses en entretien sous MTX	+ Rechutes 3 vs 5	NS 2 arrêt pour EII
Smith, Arth Rheum, 2005	7 ETA vs 5 P	Uvéite ACJ	+ 3 (43%) vs 2 (40%)	NS
Baughman, Chest, 2002	9 ETA vs 9 P	Uvéite BBS réfractaire MTX	- 2 vs 3 p	NS
Prospectives ouvertes				
Reiff, Arth Rheum, 2001	10 ETA	Uvéite réfractaire, enfants (ACJ 7)	63%, Améliorat° AV 40%	1 aggravat°
Rétrospectives				
Smith, Arth Rheum, 2001	14 ETA, 2 IFL (9 uvéites, 7 sclérites)	Divers, SPA	38%	31% développées sous ttt

Uvéites associées à l ’HLA B27





Traitement de la poussée aiguë

Traitement de fond, préventif

ARTHRITIS & RHEUMATISM
Vol. 52, No. 8, August 2005, pp 2447–2451
DOI 10.1002/art.21197

Decreased Incidence of Anterior Uveitis in Patients With Ankylosing Spondylitis Treated With the Anti–Tumor Necrosis Factor Agents Infliximab and Etanercept

J. Braun,[1] X. Baraliakos,[1] J. Listing,[2] and J. Sieper[3]

Objective. To estimate the incidence of anterior uveitis in patients with ankylosing spondylitis (AS) who underwent anti–tumor necrosis factor (anti-TNF) therapy, using data from recently performed trials.

Methods. Data from 4 placebo-controlled studies with anti-TNF agents in AS (2 with etanercept and 2 with infliximab) and 3 open-label studies were analyzed for the prestudy prevalence and the incidence of reported flares of anterior uveitis.

Results. A total of 717 patients who received treatment for anterior uveitis during the course of published clinical studies were identified by a systematic literature search using Medline. Followup information on the course of anterior uveitis was available for 397 patients. Of these, 297 were exposed to etanercept and 90 were exposed to infliximab for a total of 430 and 146.4 years, respectively. Among 190 patients who received placebo, the overall exposure was 70.5 years. The frequency of flares of anterior uveitis in the placebo group was 15.6 per 100 patient-years (95% confidence interval 7.8–27.9), while the patients treated with anti-TNF agents had a mean of only 6.8 anterior uveitis flares per 100 patient-years ($P = 0.01$). Flares of anterior uveitis occurred less frequently (although not significantly) in patients treated with infliximab than in patients treated with etanercept (3.4 per 100 patient-years and 7.9 per 100 patient-years, respectively).

Conclusion. Treatment of AS patients with biologic agents directed against TNFα is associated with a significant decrease in the number of anterior uveitis flares. This reduction was slightly more marked among patients treated with infliximab, but the difference was not significant.

EXTENDED REPORT

Efficacy of tumour necrosis factor blockers in reducing uveitis flares in patients with spondylarthropathy: a retrospective study

S Guignard, L Gossec, C Salliot, A Ruyssen-Witrand, M Luc, M Duclos, M Dougados

Ann Rheum Dis 2006;**65**:1631–1634. doi: 10.1136/ard.2006.052092

Objective: To evaluate the efficacy of anti-tumour necrosis factor (TNF) treatments (given for rheumatological manifestations) in reducing uveitis flares in patients with spondylarthropathy in daily practice.

Methods: A retrospective observational study of all patients with spondylarthropathy with at least one uveitis flare treated with anti-TNF in one centre (December 1997–December 2004). The number of uveitis flares per 100 patient-years was compared before and during anti-TNF treatment; each patient was his or her own control. The relative risk (RR) and the number needed to treat (NNT) were calculated.

Results: 46 patients with spondylarthropathy treated with anti-TNF drugs had at least one uveitis flare (33 treated with anti-TNF antibodies, infliximab or adalimumab, and 13 with soluble TNF receptor, etanercept). The mean age at first symptoms was 26 years, 71% were men. Patients were followed for 15.2 years (mean) before anti-TNF versus 1.2 years during anti-TNF treatment. The number of uveitis flares per 100 patient-years before and during anti-TNF were, respectively: for all anti-TNF treatments,—51.8 *v* 21.4 (p = 0.03), RR = 2.4, NNT = 3 (95% confidence interval (CI) 2 to 5); for soluble TNF receptor—54.6 *v* 58.5 (p = 0.92), RR = 0.9; and for anti-TNF antibodies—50.6 *v* 6.8 (p = 0.001), RR = 7.4, NNT = 2 (95% CI 2 to 5).

Conclusion: Anti-TNF treatments were efficacious in decreasing the number of uveitis flares in patients with spondylarthropathy. Anti-TNF antibodies decreased the rate of uveitis flares, whereas soluble TNF receptor did not seem to decrease this rate. These results could have consequences for the choice of anti-TNF treatment in certain patients.

See end of article for authors' affiliations

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Differential Effectiveness of Etanercept and Infliximab in the Treatment of Ocular Inflammation

Anat Galor, MD,[1] Victor L. Perez, MD,[2,3] Jeffrey P. Hammel, MS,[4] Careen Y. Lowder, MD, PhD[3]

Purpose: Anti–tumor necrosis factor α (anti–TNF-α) agents are being used increasingly in refractory inflammatory eye diseases. We reviewed our patients on etanercept and infliximab to determine whether these medications are equally efficacious in controlling ocular inflammation.

Design: Exploratory retrospective analysis.

Participants: Patients with ocular inflammatory disease on an anti–TNF-α agent (etanercept, infliximab).

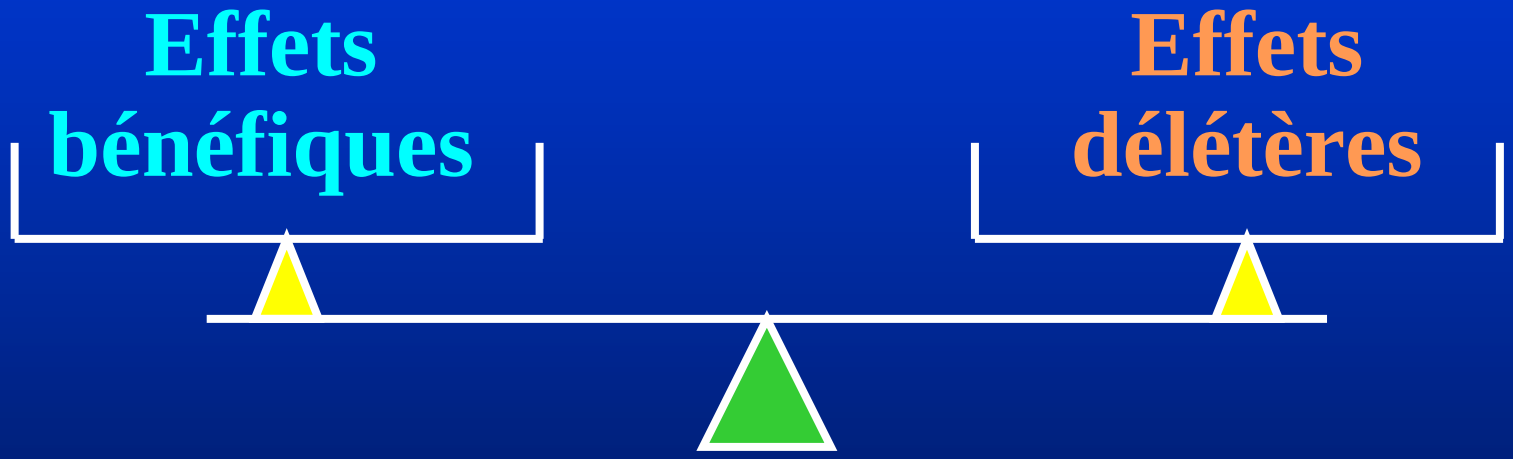
Methods: Case records of 22 patients treated with anti–TNF-α therapy were reviewed for demographic information, ocular and systemic diagnosis, duration and dose of anti–TNF-α treatment, concomitant ocular and systemic immunosuppressive medications, and treatment response.

Main Outcome Measures: Uveitis recurrence rate, initial treatment response, treatment response, and medication use at 6 months, 1 year, and last visit.

Results: Patients treated with infliximab had a significant decrease in uveitis recurrences after starting therapy compared with those treated with etanercept (59% vs. 0%, $P = 0.004$). One year after treatment initiation and at final visit, more infliximab-treated patients had an improvement in their ocular inflammation (100% vs. 33%, $P = 0.002$, and 94% vs. 0%, $P<0.001$, respectively) and a decreased requirement for topical prednisolone acetate 1% (94% vs. 33%, $P = 0.009$, and 89% vs. 29%, $P = 0.007$, respectively) compared with those treated with etanercept. No significant differences in the use of oral corticosteroids and immunosuppressive agents were noted between the 2 groups at 6 months, 1 year, and final visit.

Conclusions: Infliximab was more effective than etanercept in the treatment of recalcitrant uveitis and decreased the use of topical steroids. *Ophthalmology 2006;113:2317–2323 © 2006 by the American Academy of Ophthalmology.*

TNFα :



ANTI TNFα

- **Infection**
- **Lymphome**
- **Allergie (Anticorps anti anti-TNF)**
- **Autoimmunisation**
- **Syndrome lupique induit**
- **Vascularite**

ANTI TNFα

- La **tuberculose**
  - » **ETA: 21 cas/ 100 000 vs. IFLX: 48 cas/ 100 000**
  - » **Mais mis sur marché + tard (plus de précautions)**
  - » **Mais plus prescrit USA (faible incidence BK)**

ANTI TNFα

- Infection
- Lymphome
- Allergie
- Anticorps anti anti-TNF
- Autoimmunisation
- Syndrome lupique induit
- Vascularite

ANTI TNFα

Immunisation

- **Etanercept < 5%**
- **Adalimumab : 1-12%**
- **Infliximab : 10-15%**

→ **Rôle des anticorps anti-infliximab ?**

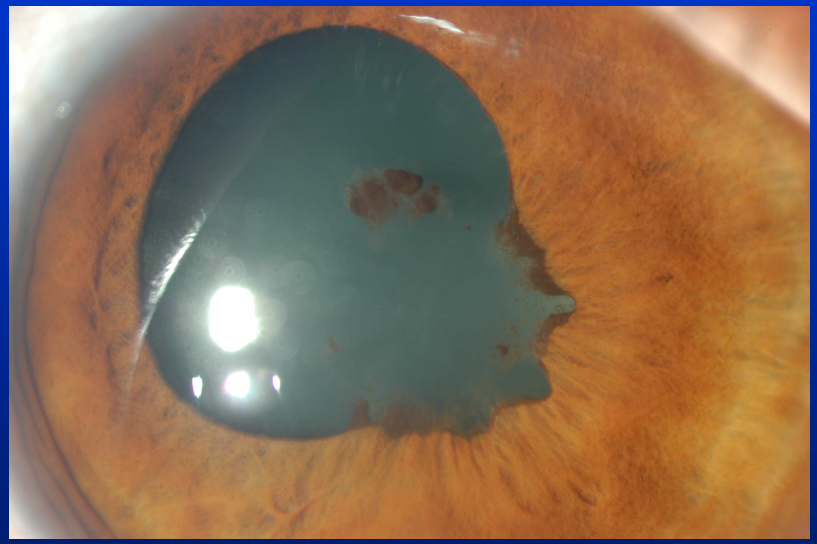
Carte de surveillance

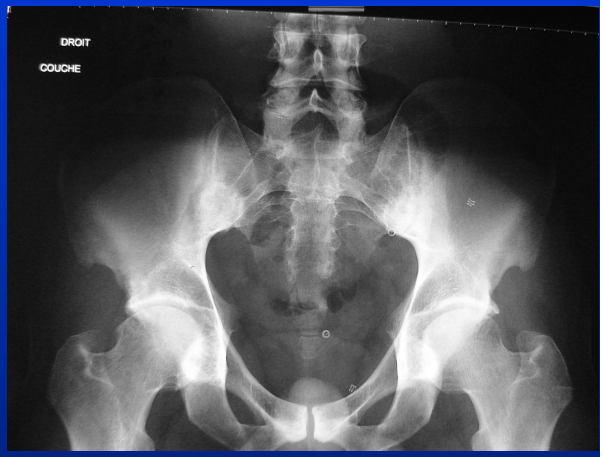
- **Cette carte de surveillance contient des informations importantes de sécurité d'emploi que le patient doit connaître avant la mise sous traitement par HUMIRA® et pendant le traitement.**
- **Le médecin prescripteur ou le patient doivent notamment y faire figurer les dates de réalisation des tests tuberculiniques et de la radiographie pulmonaire, la date d'initiation du traitement et les dates des injections.**
- **Cette carte doit être conservée par le patient pendant le traitement et pendant les 5 mois suivant la dernière injection.**
- **Cette carte doit être montrée par le patient à tout médecin intervenant dans le traitement.**

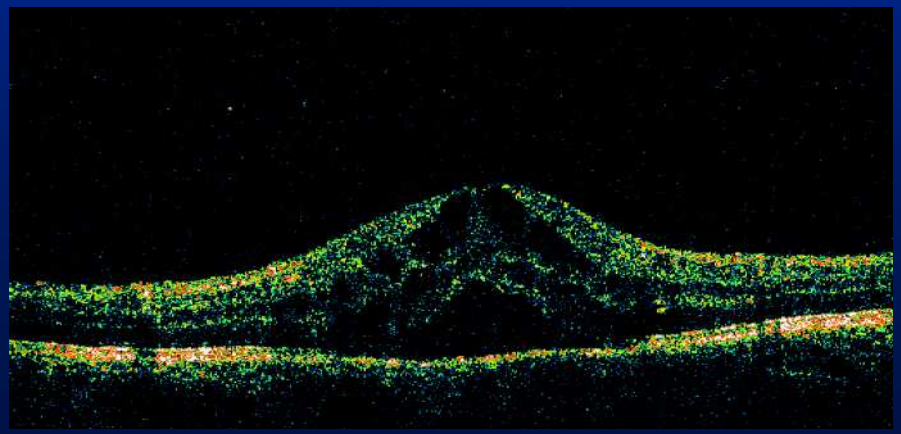
www.nature.com/clinicalpractice/rheum

Severe uveitis in an HLA-B27-positive patient with ankylosing spondylitis

Dominique Monnet, Laurence Moachon, Maxime Dougados and Antoine P Brézin*

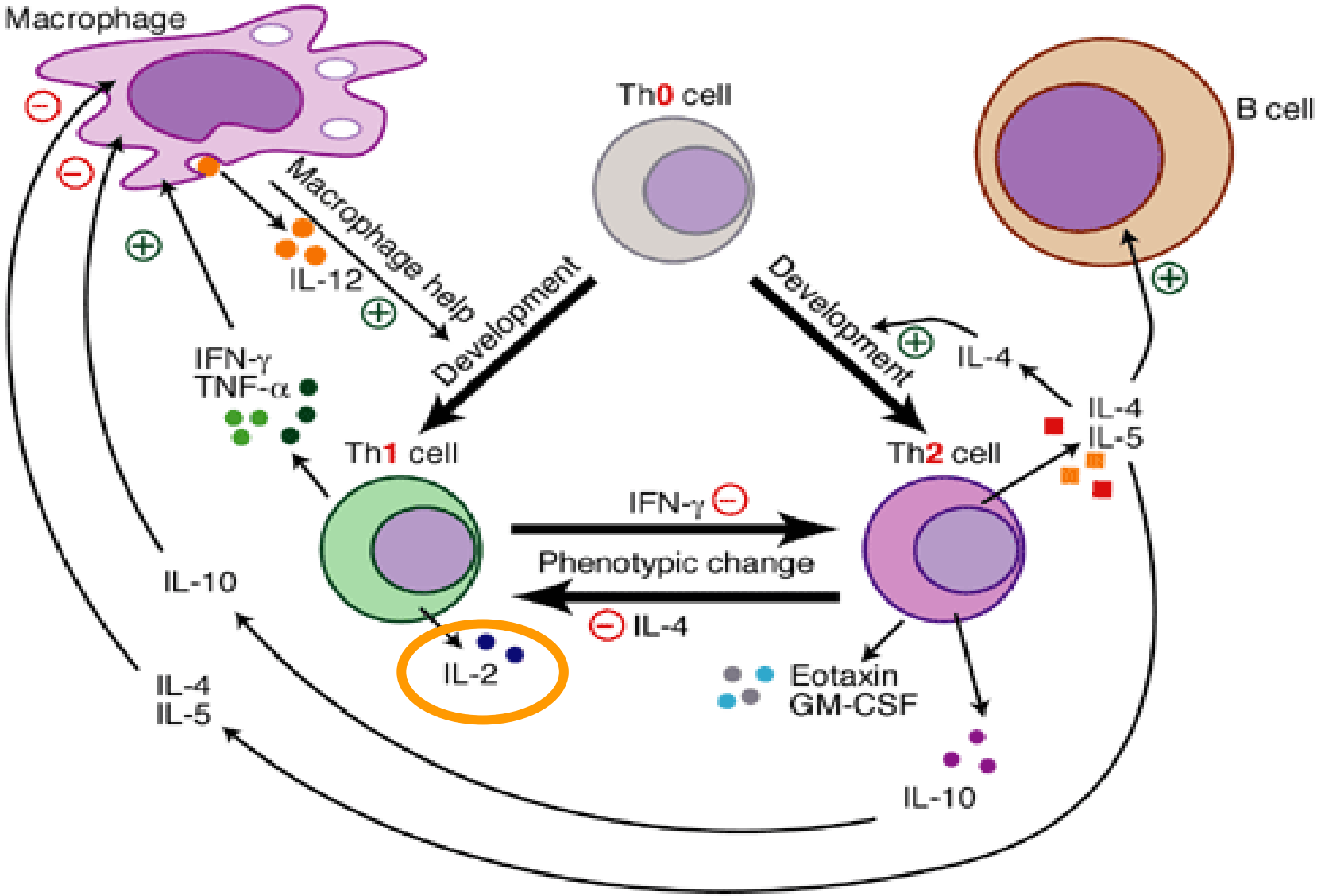






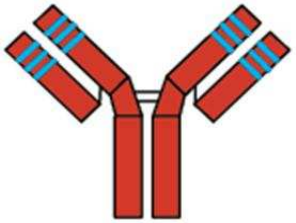
Autres agents biologiques

- Anti CD52 campath
- Anti IL1(IL1-RA) anakinra
- Anti CD20 rituximab
- Anti CD25 (IL2-Rα) daclizumab



A simplified model of the possible interactions between polarised T helper 1 (Th1) and Th2 responses

Daclizumab



- **Anti-IL2Rα humanisé recombinant (IgG1 humaine et CDR murin), dirigé contre le récepteur de type alpha de l'IL2 (p55, CD25, Tac)**

- **Blocage de l'interaction IL2 – T activés**
- **Induction de $CD56^{bright}$ NK régulateurs**

Nussenblatt, PNAS, 1999

Summary

Background Recombinant interferons have been approved by many national regulatory agencies for treatment of relapsing remitting multiple sclerosis, but widespread discussion continues about their true effectiveness, benefits, side-effects, and costs.

Methods With the Cochrane Collaboration methodology, we reviewed all published, randomised, placebo-controlled trials of recombinant interferons undertaken in patients with relapsing remitting multiple sclerosis between 1993 and 2002. Our primary aim was to find out whether recombinant interferons reduced the number of patients who had clinical exacerbations and disease progression, compared with placebo.

Findings The seven trials that met our criteria included 1215 randomised patients: data from 667 (55%) were available for analysis at 1 year's and from 919 (76%) at 2 years' follow-up. Interferon seemed to reduce the number of patients who had exacerbations during the first year of treatment (relative risk 0·73, 95% CI 0·54–0·99), but results at 2 years' follow-up were not robust and were difficult to interpret because of the many dropouts. Although the number of patients who had exacerbations (0·81, 0·74–0·89) or progressed (0·70, 0·55–0·88) during the first 2 years fell significantly in the protocol analysis, results were inconclusive after sensitivity analyses for exacerbations (1·11, 0·73–1·68) and disease progression (1·31, 0·60–2·89). Data were insufficient to establish whether steroid use and admissions to hospital were reduced in the interferon group. Similarly, MRI outcome data could not be analysed quantitatively. Side-effects were common, and acute toxic effects adversely affected quality of life.

Interpretation Recombinant interferons slightly reduce the number of patients who have exacerbations during first year of treatment. Their clinical effect beyond 1 year is uncertain and new trials are needed to assess their long-term effectiveness and side-effects.

Lancet 2003; **361:** 545–52

Articles

Interferons in relapsing remitting multiple sclerosis: a systematic review

Graziella Filippini, Luca Munari, Barbara Incorvaia, George C Ebers, Chris Polman, Roberto D'Amico, George P A Rice

- Discrète diminution du nombre de patients présentant des poussées pendant la première année de traitement.

- Au delà d'un an : effet incertain

- Effets secondaires +

CONCLUSIONS

- L'embarras du choix…
- Peu d'études randomisées et contrôlées
- Coopération avec l'interniste/rhumatologue
- Suivre les recommandations validées par des essais :
  - Azathioprine
  - Infliximab (adalimumab)
- Mais aussi rester innovants…