Medicina off label

Il farmaco “sbagliato”

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Medicina off label

Il farmaco “imputato”

. Uso improprio

. Uso potenzialmente pericoloso

. Costo ingiustificato

Medicina off label

Perché mai il medico dovrebbe prescrivere un farmaco off label ?

- ✓ Malvagità
- ✓ Interesse
- ✓ Sperimentalismo
- ✓ Protagonismo
- ✓ Inconsapevolezza
- ✓ Coraggio
- ✓ Deontologia

Medicina off label e Medicina difensiva

Quando il medico dovrebbe prescrivere un farmaco off label ?

- ✓ **Mai**

- ✓ **Assoluta necessità di trattamento e sufficiente evidenza di efficacia e tollerabilità in caso di**
  - ✓ Inefficacia delle alternative terapeutiche approvate
  - ✓ Intolleranza o controindicazione alle alternative terapeutiche
  - ✓ Mancanza di alternative terapeutiche approvate

  (previo consenso informato)

Medicina off label e malattie rare

- ✓ Malattia rara = casistica insufficiente per RCTs
- ✓ Malattia rara = tutti i trattamenti sono off label

Medicina off label

Il farmaco “imputato”

. Uso improprio

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Medicina off label

Il farmaco “imputato”

- ✓ cortisone
- ✓ colchicina (FMF, vasculiti)
- ✓ aspirina (gravidanza aPL)
- ✓ HD IgIV (miositi)
- ✓ anti-TNF (uveiti, vasculiti)

TNFa blocker indications

	Infliximab	Etanercept	Adalimumab
RA	+	+	+
AS	+	+	+
PsA	+	+	+
Psoriasis	+	+	+
Crohn's	+		+
UC	+		+
JIA		+	

15/1/2008 ***http://www.emea.europa.eu/humandocs/Humans/EPAR***

Anedoctical studies of TNFa blockers

(Furst DE et al. Ann Rheum Dis 2008)

Disease	Author(s)	Medication	No. of patients
Adult Still's disease	Huffstutter and Sienknechet[247]	Infliximab	2
	Kraetsch *et al*[248]	Infliximab	6
	Weinblatt *et al*[149]	Etanercept	12
	Fernandez-Nibro[249]	Etanercept	3
Behçet's disease	Estrach *et al*[260]	Infliximab/ adalimumab	7
	Gulli *et al*[261]	Infliximab	1
	Hassard *et al*[262]	Infliximab	1
	Licata *et al*[263]	Infliximab	1
	Melikoghu *et al*[264]	Etanercept	20
	Morillas *et al*[265]	Adalimumab/ etanercept	
	Rosenbaum *et al*[266]	Anti-TNF	1
	Saulsbury and Mann[267]	Infliximab	1
	Sangle *et al*[268]	Infliximab	1
	Sfikakis *et al*[269]	Infliximab	5
	Sfikakis[270]	Infliximab	11
	Ribi *et al*[271]	Infliximab	1
	Sweiss *et al*[272]	Infliximab	3
	Van Laar et at[273]	Adalimumab	6
Dermatomyositis	Hengstman *et al*[282]	Infliximab	2
	Miller *et al*[283]	Etanercept	10
	Sprott *et al*[284]	Etanercept	1
	Nzeusseu *et al*[285]	Infliximab	1
	Saadeyh[286]	Etanercept	4
	Norman *et al*[287]	Etanercept	2

Adult Still's disease

Behcet's disease

Dermatomyositis

Anedoctical studies of TNFa blockers

(Furst DE et al. Ann Rheum Dis 2008)

Disease	Author(s)	Medication	No. of patients
Uveitis	Estrach *et al*[360]	Infliximab/ adalimumab	7
	Joseph *et al*[369]	Infliximab	5
	Smith *et al*[370]	Etanercept	7
	Braun *et al*[371]	Etanercept/Infliximab	717 (uveitis in AS)
	Foster *et al*[372]	Etanercept	20 (ineffective)
	Biester *et al*[373]	Adalimumab	18
	Foeldvari *et al*[374]	Anti-TNF	47
	Vazquez-Cobain *et al*[375]	Adalimumab	14
	Reiff *et al*[376]	Etanercept	10
	Schmeling and Horneff[377]	Etanercept	20 (ineffective)
	Guignard *et al*[378]	Adalimumab	8
Vasculitis (see also Behcet's, GCA, Takayasu's, Wegener's)	Booth *et al*[379]	Infliximab	32
	Feinstein and Arroyo[380]	Etanercept	1
	Van dan Bijl[381]	Infliximab	11
	Saji *et al*[382]	Infliximab	1 (Kawasaki's)
	Sangle *et al*[268]	Infliximab	1 (Churg-Syrauss)
	Arbach *et al*[383]	Etanercept/infliximab	3
Wegener's granulomatosis	Gause *et al*[384]	Infliximab	10
	Sangle *et al*[268]	Infliximab	3

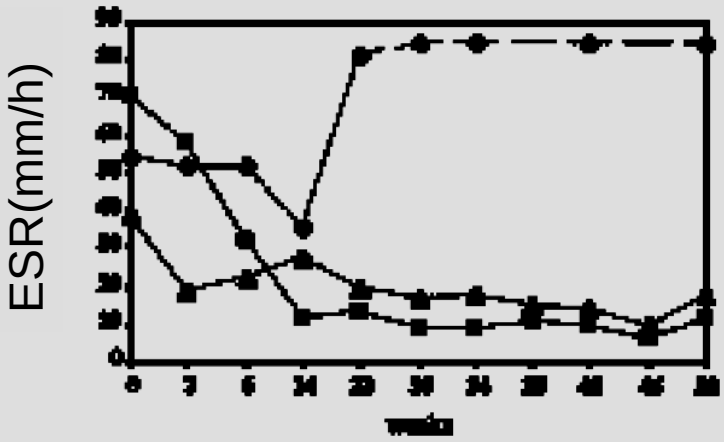
Uveitis

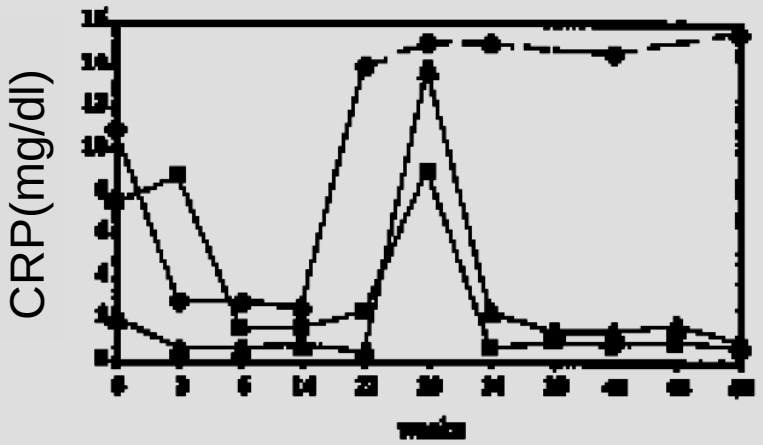
&

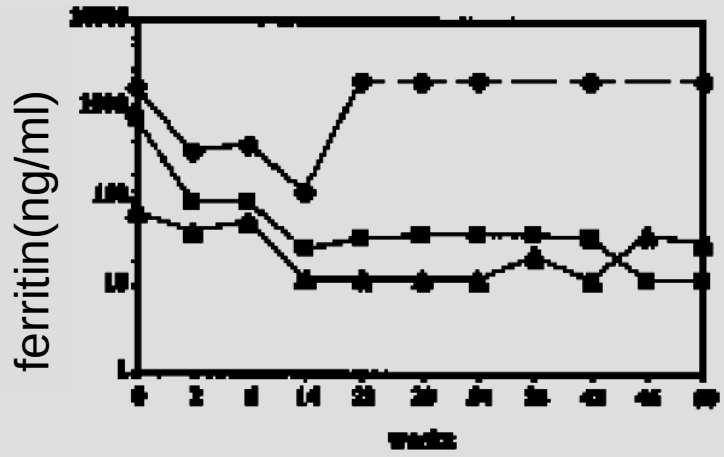
Vasculitis

Infliximab in the treatment of adult Still's disease refractory to conventional therapy

Cavagna L, Caporali R, Epis O, Bobbio-Pallavicini F, Montecucco C.







Clin Exp Rheumatol. 2001

EXTENDED REPORT

Tumour necrosis factor α blocking agents in refractory adult Still's disease: an observational study of 20 cases

B Fautrel, J Sibilia, X Mariette, B Combe, the Club Rhumatismes et Inflammation

Ann Rheum Dis 2005;**64**:262–266. doi: 10.1136/ard.2004.024026

Table 1 Summary of patient characteristics

Characteristic	
Age at ASD diagnosis	
Mean (SD) (range)	32.2 (19) (11 to 72)
Median	28
Childhood onset (no.)	4
Disease free interval between childhood and adult symptoms	1
Disease duration (years)	
Mean (SD) (range)	8.5 (6) (2 to 21)
Median	6.5
Age at anti-TNF start (years)	
Mean (SD) (range)	40.7 (17) (18 to 74)
Median	34.5
Predominant clinical expression	
Chronic arthritis	15
Systemic	5
Symptoms (no.)	
Fever	20
Arthralgia	20
Polyarthritis	18
Sore throat/pharyngitis	14
Rash	16
Seritis	4
Lymphadenopathy	6
Increased leukocyte level	20
Polymorphonuclear level >10 000 mm^3	20
Abnormal liver function test result	6
High serum ferritin level	14
Disseminated intravascular coagulation syndrome	5
Previous treatments	
Prednisone	20
Methotrexate	20
Intravenous polyvalent immunoglobulin	5
Sulfasalazine	2
Hydroxychloroquine	6
Gold salts	2
D-Penicillamin	1
Thalidomide	1
Cyclosporine A	5
Cyclophosphamide	4
Azathioprine	3

Table 3 Treatment response

	All treatments (n = 25)*	Etanercept (n = 10)	Infliximab (n = 15)
Treatment duration (months)			
Mean (SD)	13 (14)	13 (14)	14 (14)
Median	9	9	10
Range	1 to 44	1 to 43	1 to 44
Response to therapy			
Complete remission	5	1	4
Partial response	16	7	9
Failure	4	2	2

*A total of 25 treatments in 20 patients were analysable. 10 patients received etanercept, 15 infliximab, and 5 both drugs.

Fautrel B et al. Ann Rheum Dis 2005

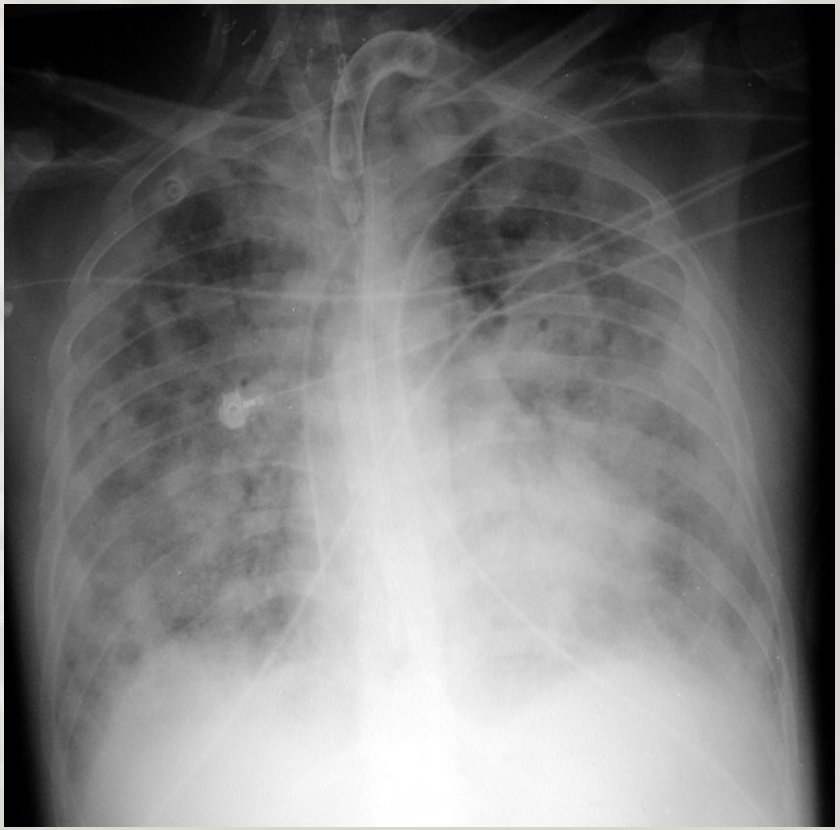
Acute respiratory distress syndrome in adult-onset Still's disease is often fatal

- Manganelli P et al *Clin Exp Rheumatol* 2003
- Mito K. *Nihon Kokyuki Gakkai Zasshi* 2002
- Suleiman M et al *Scand J Rheumatol* 2001
- Iglesias J et al *Chest* 1999
- Pedersen JE et al *Intensive Care Med* 1991

Acute respiratory distress syndrome in adult-onset Still's disease:

Successful treatment with repeated Infliximab infusions in a 41 years old woman

Broggini M, Montecucco C (unpublished)



Anti-TNFa in PAN

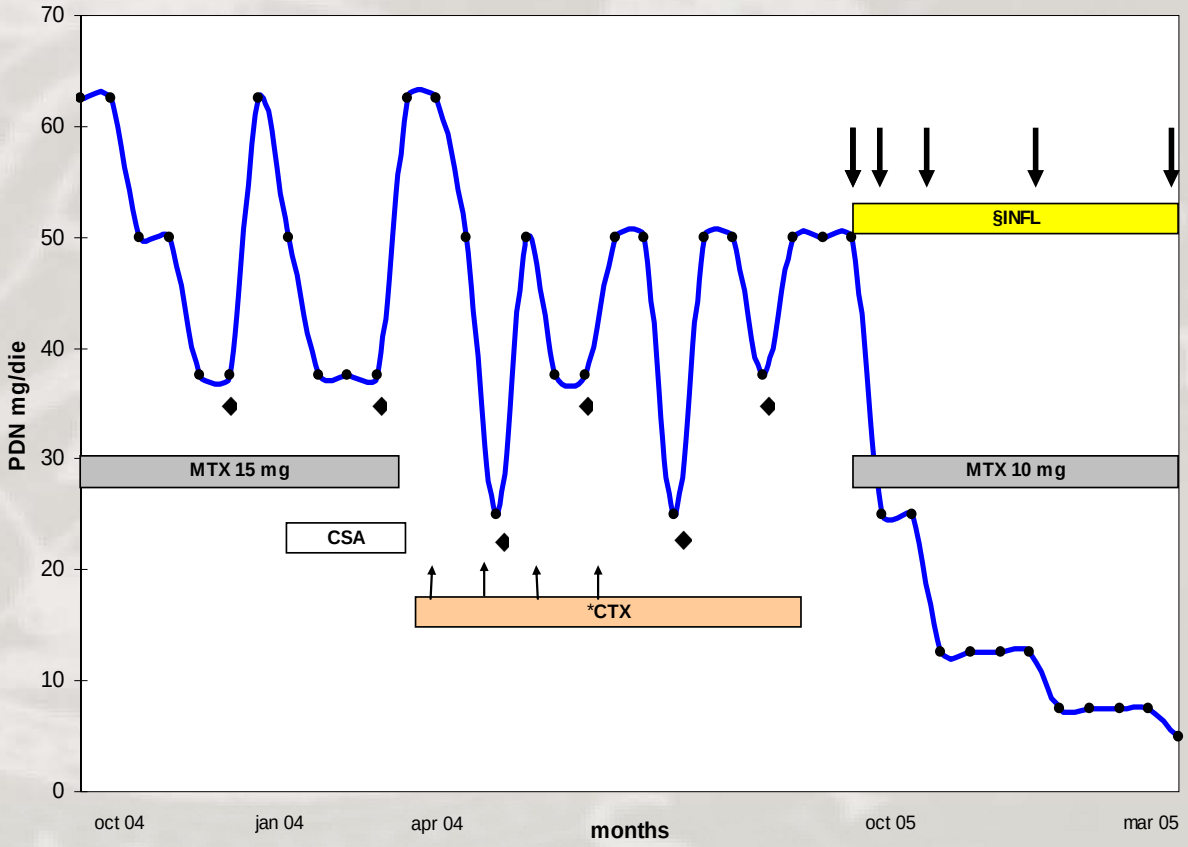
- Vega Gutierrez J et al. Successful treatment of childhood cutaneous polyarteritis nodosa with infliximab. *J Eur Acad Dermatol Venereol* 2007;21(4):570-1
- Brik R et al. Tumor necrosis factor blockade in the management of children with orphan diseases. *Clin Rheumatol* 2007;26(10):1783-5.
- Wu K et al. A new treatment for polyarteritis nodosa. *Nephrol Dial Transplant* 2006;21(6):1710-2
- de Kort SW et. Infliximab in a child with therapy-resistant systemic vasculitis. *Clin Rheumatol* 2006;25(5):769-71.
- Al-Bishri J et al. Refractory polyarteritis nodosa successfully treated with infliximab. *J Rheumatol* 2005;32(7):1371-3

Case report

Male, 40 years

PAN onset:
Oct 2003

Previous therapy:
high-dose steroids



Medicina off label

Il farmaco sbagliato ?

Il farmaco indovinato ?

Società Italiana Reumatologia

Corsi residenziali gratuiti per specializzandi in Reumatologia

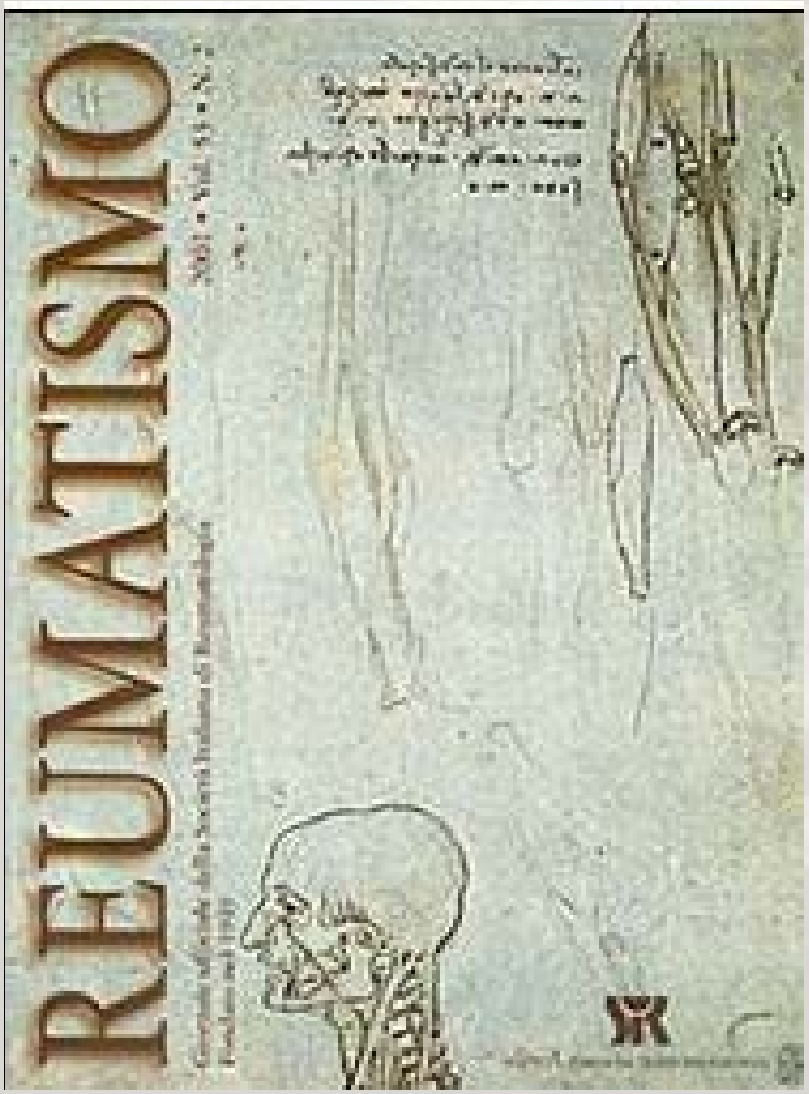
I anno: diagnostica per immagini in Reumatologia

II anno: analisi del lilquido sinoviale

III anno: le misure in reumatologia – laboratorio e clinimetria

IV anno: le malattie rare in Reumatologia

Medicina off label



Numero monografico:
Raccolta della letteratura sui trattamenti off label nelle malattie reumatologiche.

Prima edizione 2007
Aggiornamento previsto per fine 2009

Recepito dalla Regione Toscana
DGR 836/2008

Direttiva alle aziende sanitarie toscane sull'impiego in reumatologia dei farmaci fuori dalle indicazioni di registrazione.

Medicina off label

- ✓Conoscenza
- ✓Prudenza
- ✓Condivisione

Per non sbagliare farmaco