Nuovi farmaci in reumatologia

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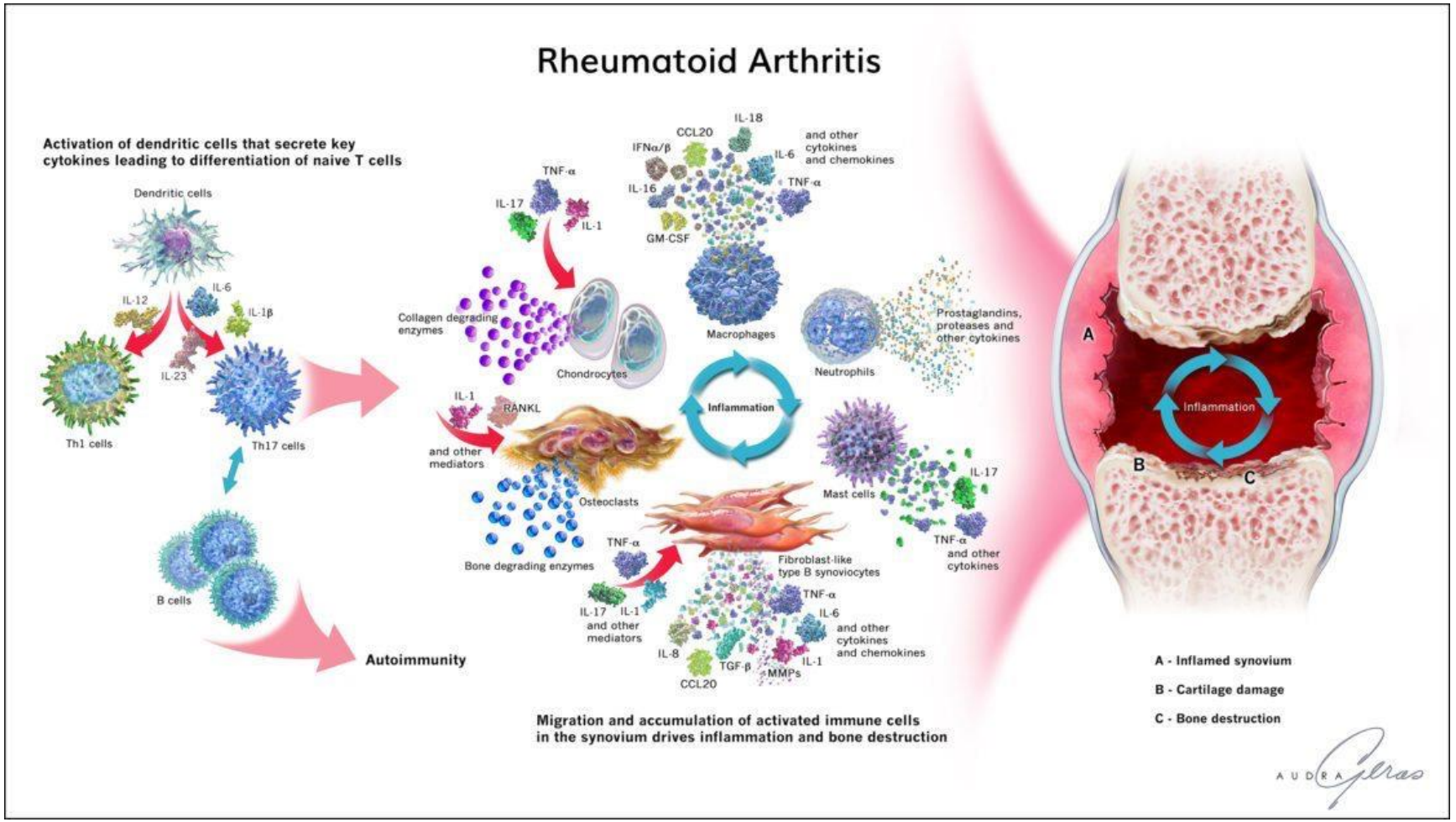
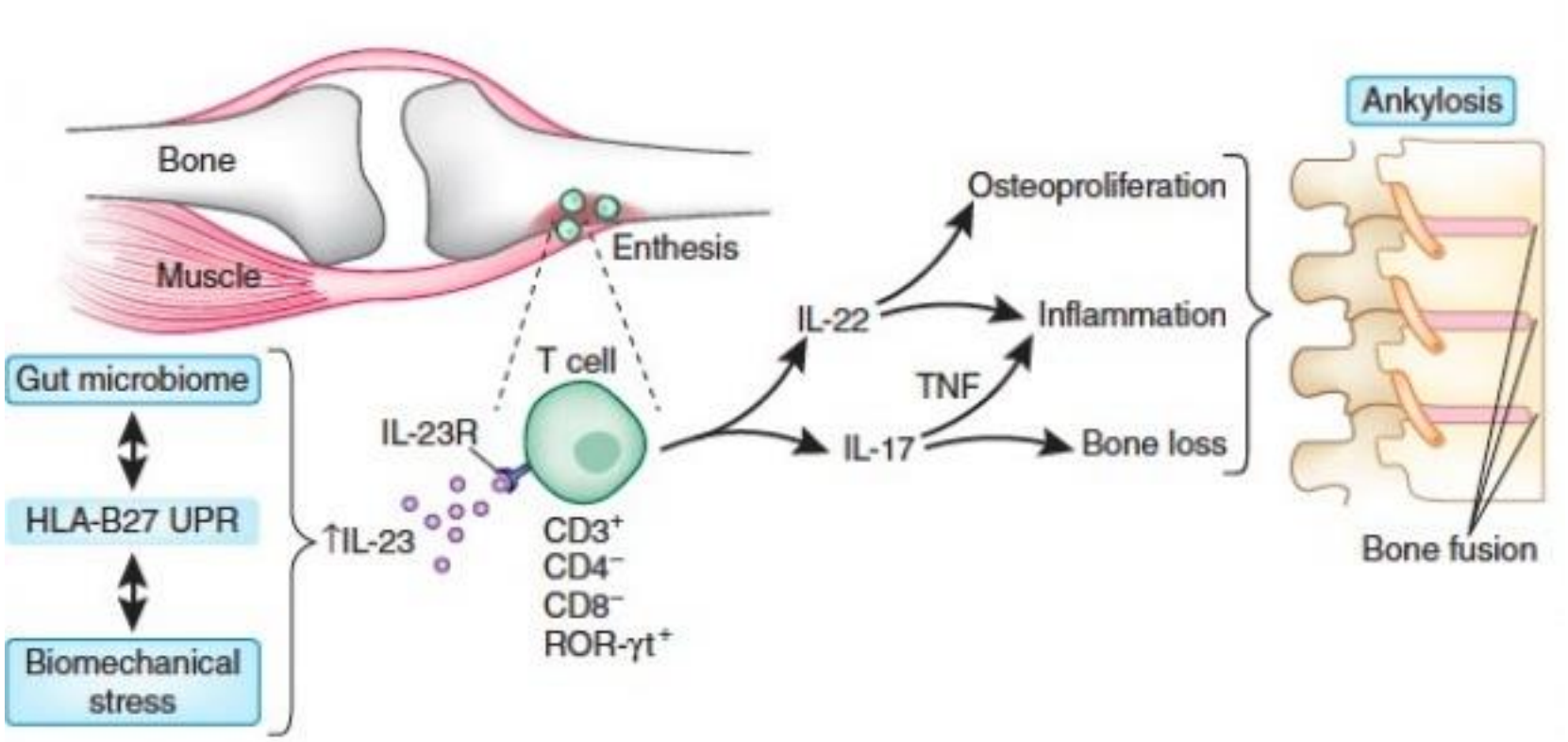
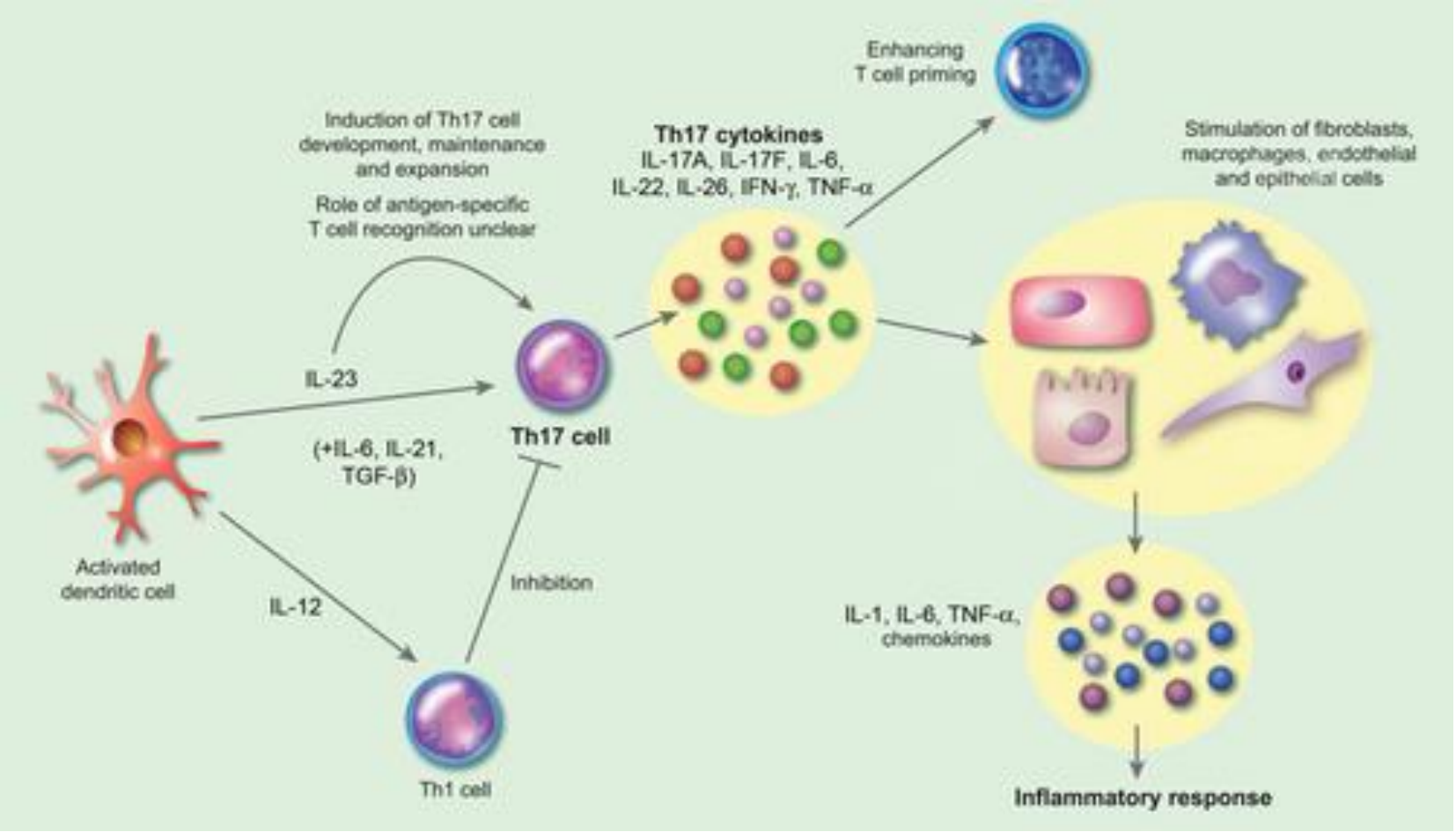
Patogenesi Artrite Reumatoide



Patogenesi Spondilartrite

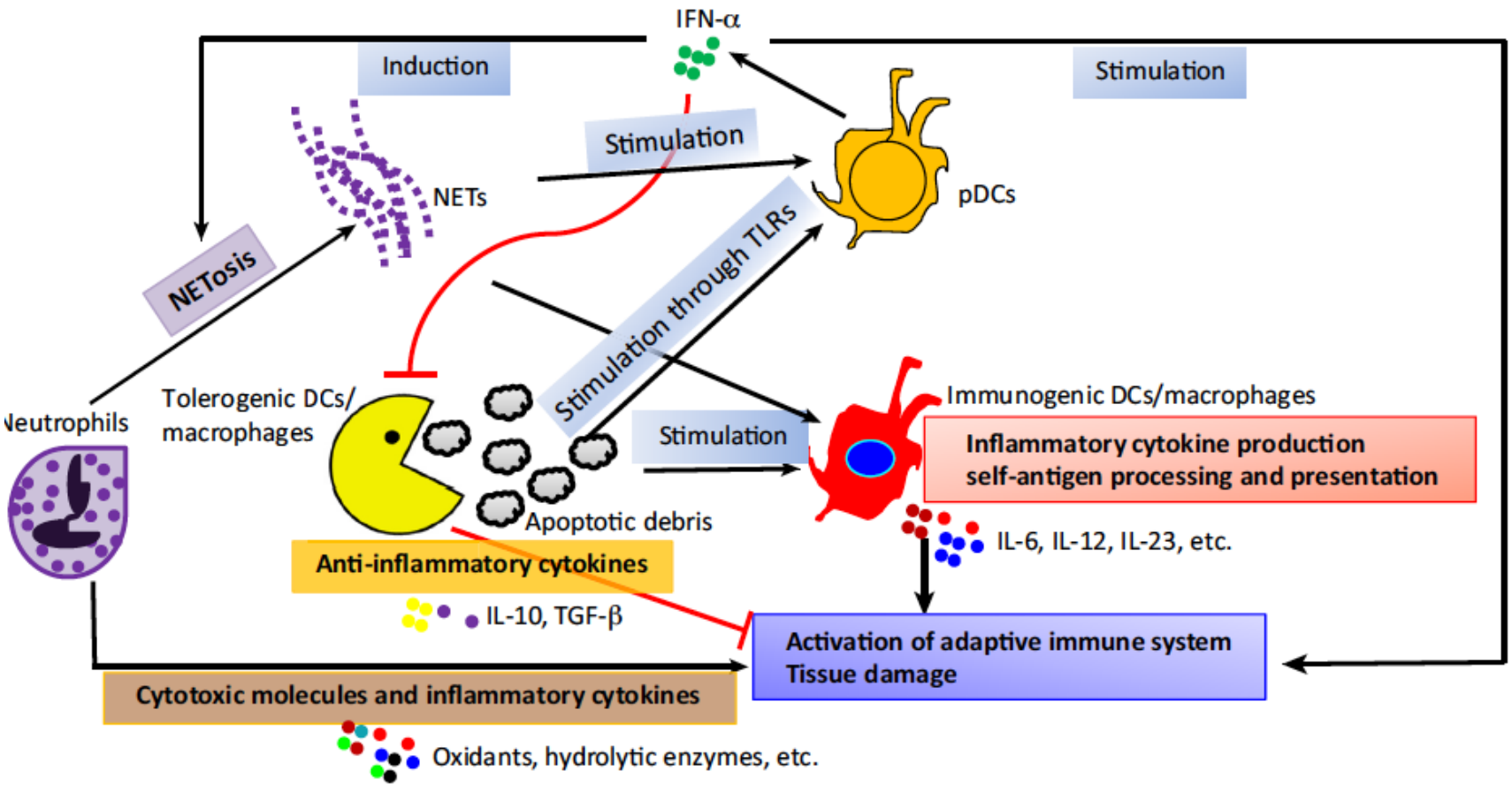


Sherlock JP, Nat. Med 2012
Zhu S et al Nat. Med 2012
O'Connell et al Nat Med 2012



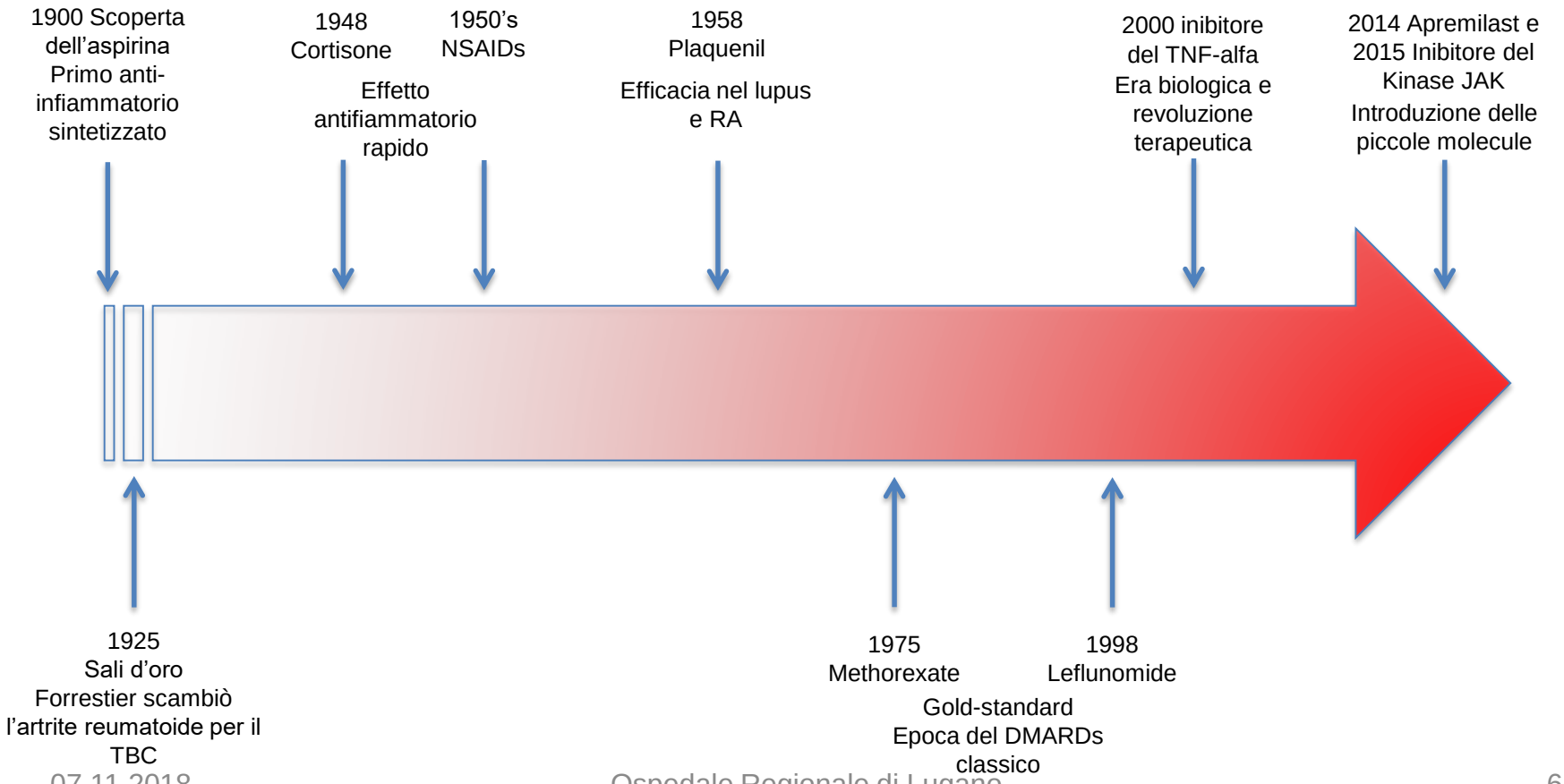
Jethwa, H et al, Clinical and experimental immunology 2015

Patogenesi LES



Moulton V et al., Trends in Molecular Medicine 2017

Evoluzione della terapia



Le malattie reumatiche nell'era di biologici

- Cambiam[illegible] della p[illegible]
- Terapia iniziale con DMARDS classico

- Terapia aggressiva precoce
  - Biologici
  - Terapia combinata

Treat to Target

Cambiamento del paradigma terapeutico

- miglioramento della qualità e aspettativa di vita
  - Miglioramento dei dolori, mantenimento di una buona funzionalità articolare
    - Meno intervento ortopedico

- aumento dei numeri di pazienti con malattie reumatiche attive professionalmente
  - Da 37% (donne) 47% (uomini) a 60% (donne) e 68% (uomini)
  - Riduzione dell'assenteismo per malattia da 88 a 32 giorni

- Prevenzione e riduzione dei danni articolari
  - Riduzione o prevenzione di progressione radiografica
  - Riduzione del numero di interventi ortopedici

Classificazione dei farmaci

Classe di farmaci		esempio
DMARDs classico (syntetico)	cs DMARD	Methotrexat, Leflunomide ecc
Targeted DMARDs	ts DMARD	Apremilast, inibitore del kinase JAK
DMARDs biologico	bo DMARD	Humira®, Simponi®, Actemra®
DMARDs biosimilari	bs DMARD	Inflectra®, Erelzi®

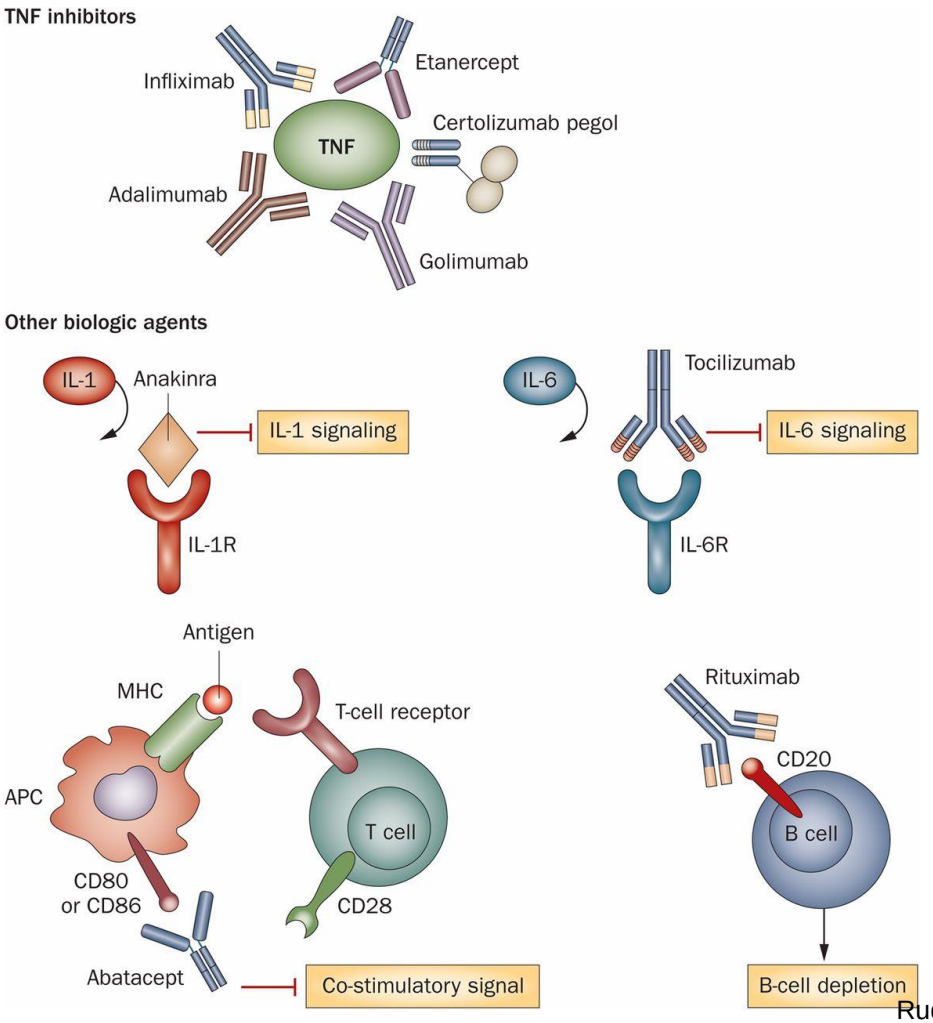
Le famiglie di farmaci biologici utilizzati nelle malattie reumatiche

- Anti-citochine
  - Inibisce l'interazione delle citochine pro-infiammatoria e loro ricettori

- Terapia orientata alle cellule
  - Eliminazione o inibisce l'attivazione oppure della proliferazione cellulare

Anti-citochine	Cell targeted
Inibitore del TNF-alfa Etanercept (Enbrel) Infliximab (Remicade) Adalimumab (Humira) Golimumab (Simponi) Certolizumab (Cimzia)	Anti-CD 20 Rituximab (Mabthera)
Anti-IL 6 Tocilizumab (Actemra) Sarilumab (Kevzara)	CTLA-4 Ig Abatacept (Orencia)
Anti-IL1 Anakinra (Kineret) Canakinumab (Ilaris)	Anti-BLyS/BAFF Belimumab (Benlysta)
Anti-IL 17 Secukinumab (Cosentyx) Ixekizumab (Taltz)	
Anti-p40 (IL12/IL23) Ustekinumab (Stelara)	

Meccanismo d’azione



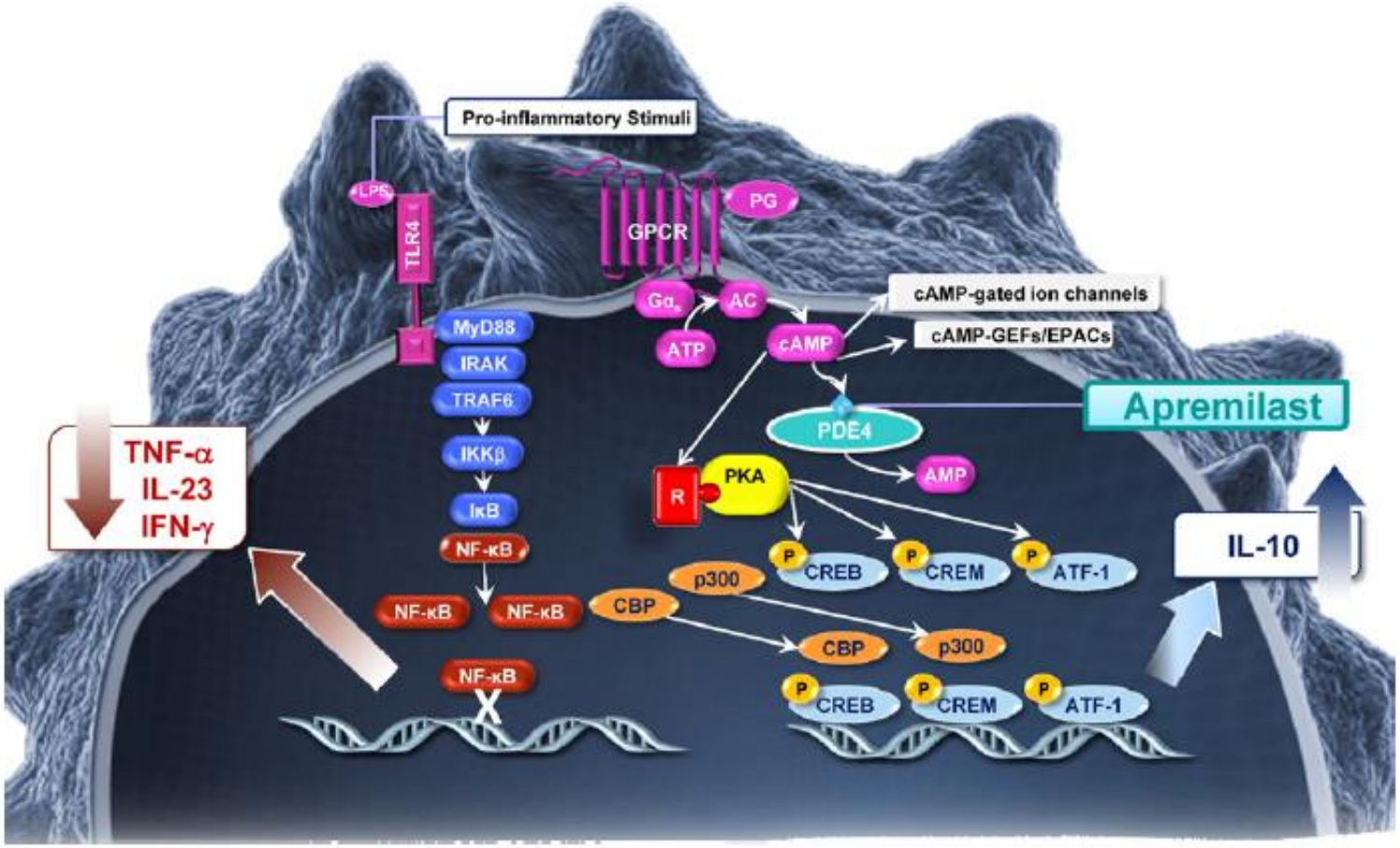
Ruderman E, et al. Nat. Rev Rheu 2011

Small molecules

- Non sono proteina ma piccole molecule
- Agisce a livello intracellulare
- Effetto biologico tramite bloccaggio a valle dei segnali prodotti dall'attivazione dei ricettori di citochine
- Modificano la risposta biologica

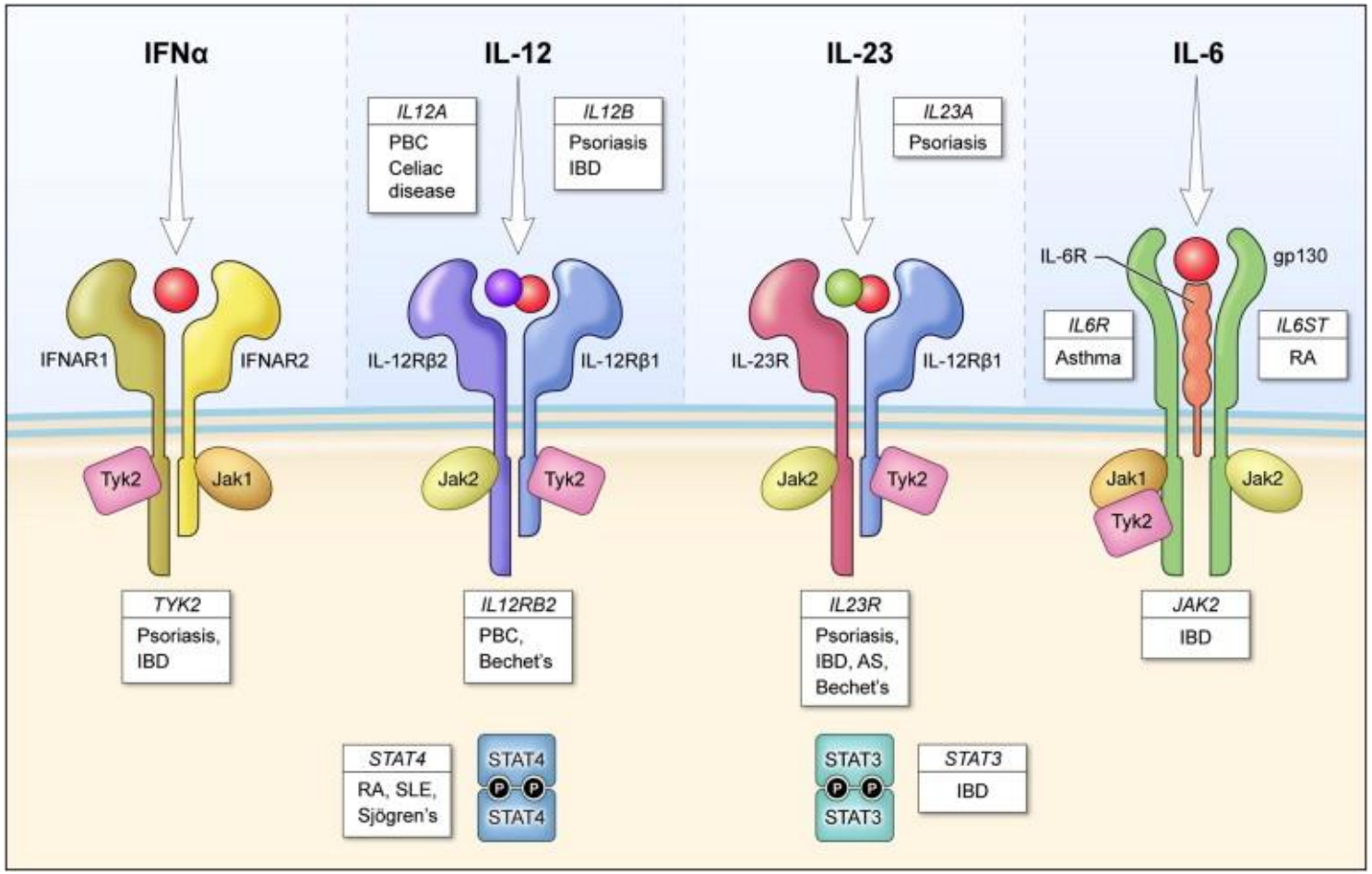
Piccole molecule
Inibitore del PDE 4 Apremilast
Inibitore del Kinase JAK Tofacitinib (Xeljanz) Baricitinib (Olumiant)

Meccanismo d'azione

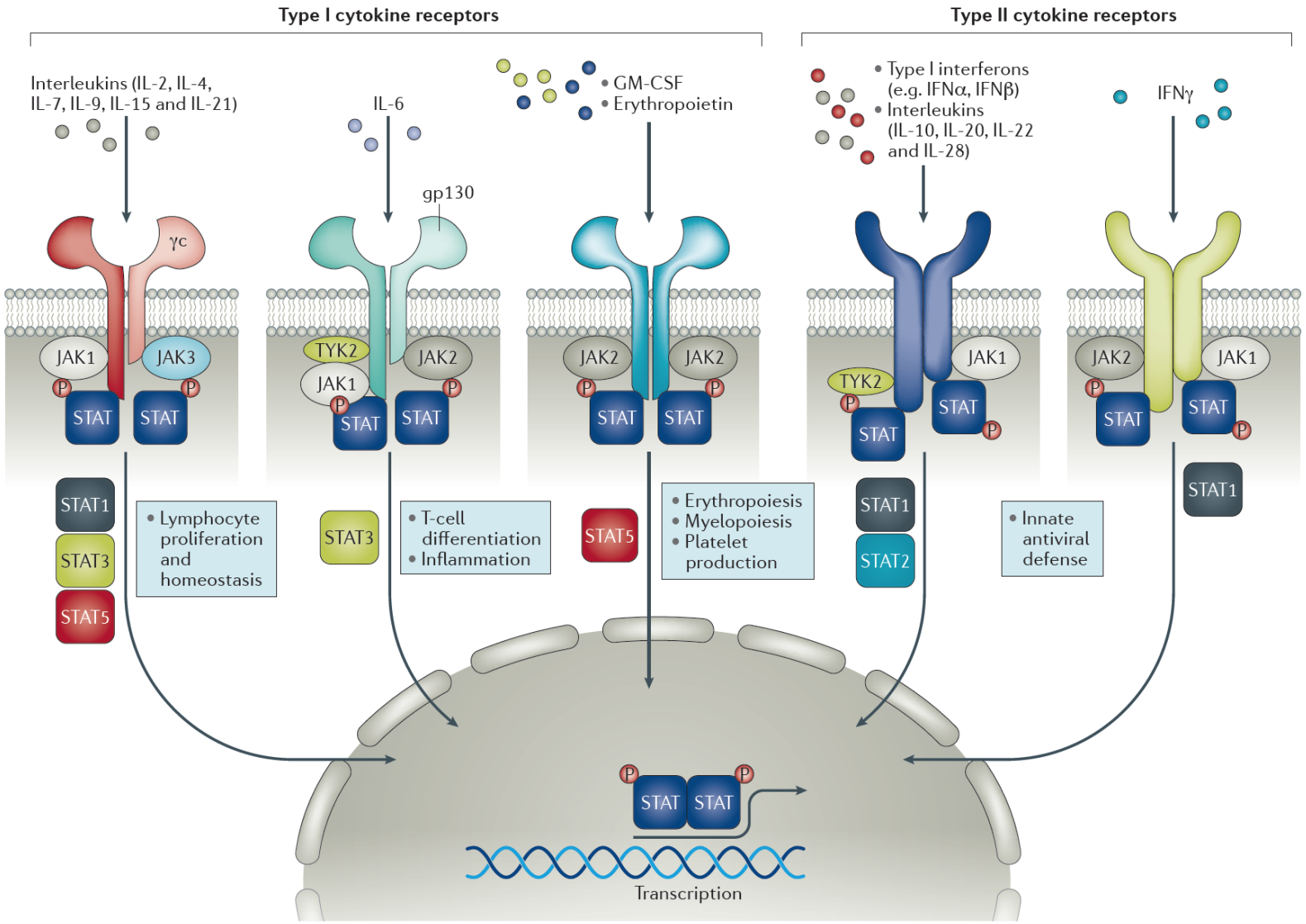


Schafer, P, Biochemical pharmacology 2012

Meccanismo d’azione



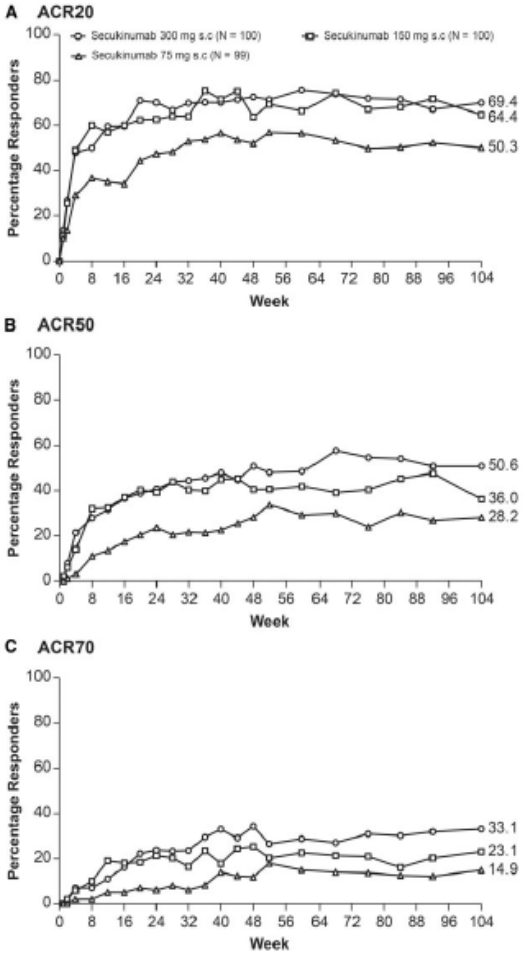
O’Shea,J. et al, Immunity 2012

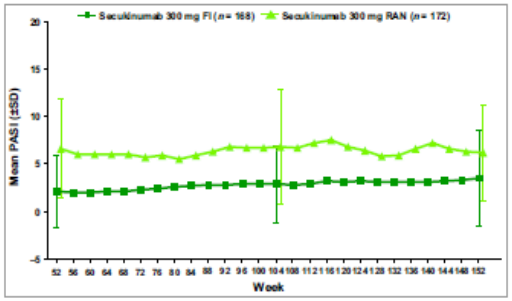


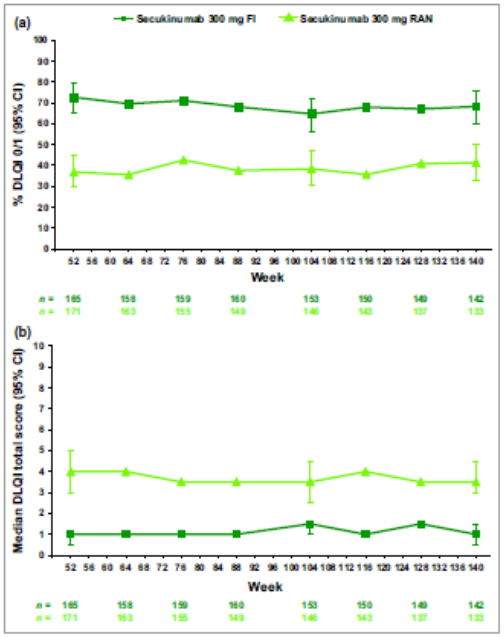
Winthrop, KL. Nat. Rev Rheu 2017

	Secukinumab	Ixekizumab
Inibizione	IL-17A	Il-17A
Biodisponibilità	≈55-77%	50-90%
Concentrazione plasmatica	5-6 giorni	4 giorni
T1/2	27 giorni	13 giorni
Stabilità	24-48 ore	72 ore
Affinità proteica	Non noto	Non noto
Eliminazione	Catabolismo intracellulare	Catabolismo intracellulare

Efficacia del secukinumab sull'artrite psoriatica e psoriasi

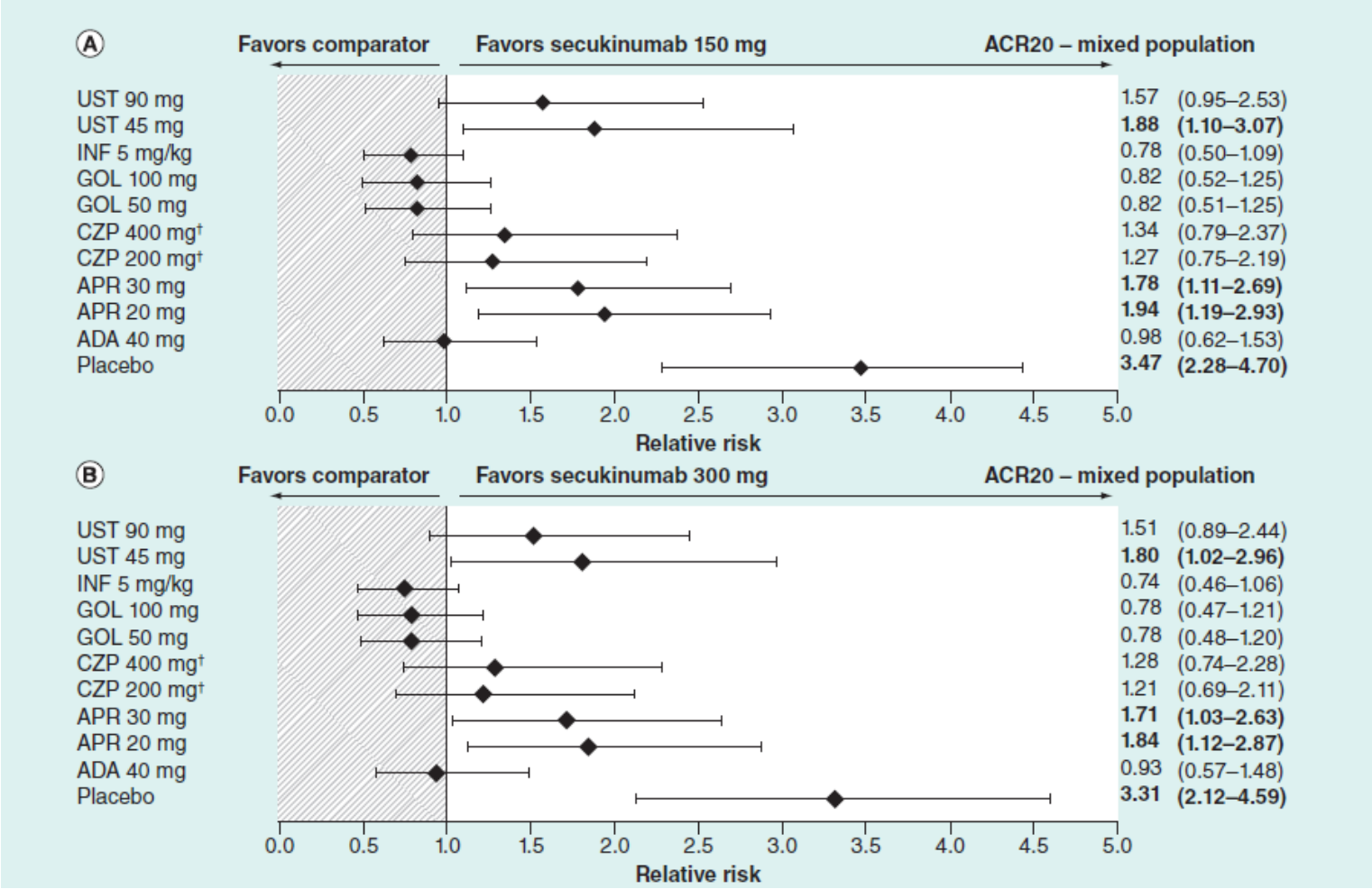






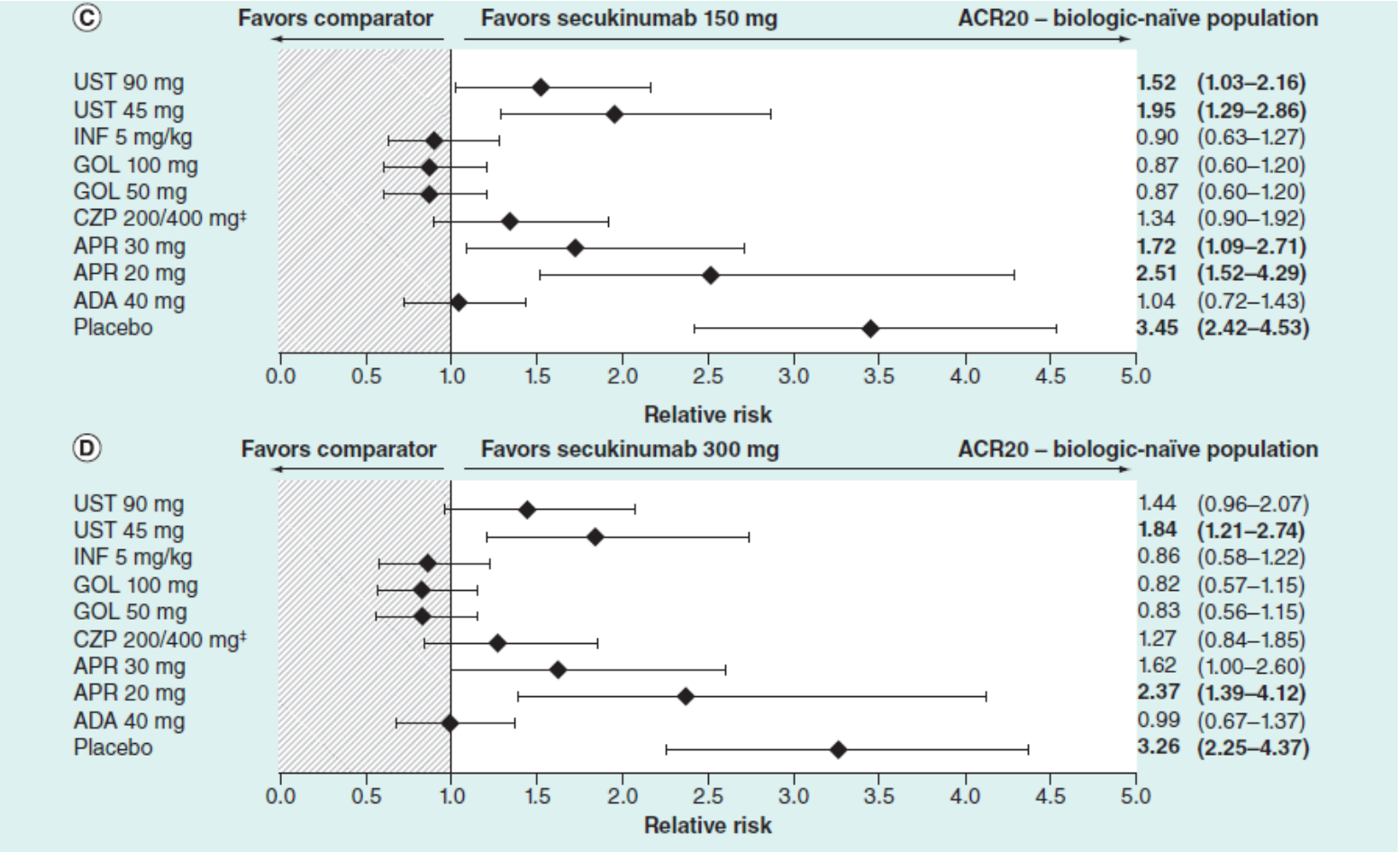
Bissonnette, R et al, Br Journal of Dermatology 2017
McInnes, I et al, Rheumatology (Oxford) 2017

Efficacia del secukinumab sull'artrite psoriatica



McInnes, I et al, J. of comparative effectiveness research 2018

Efficacia del secukinumab sull'artrite psoriatica



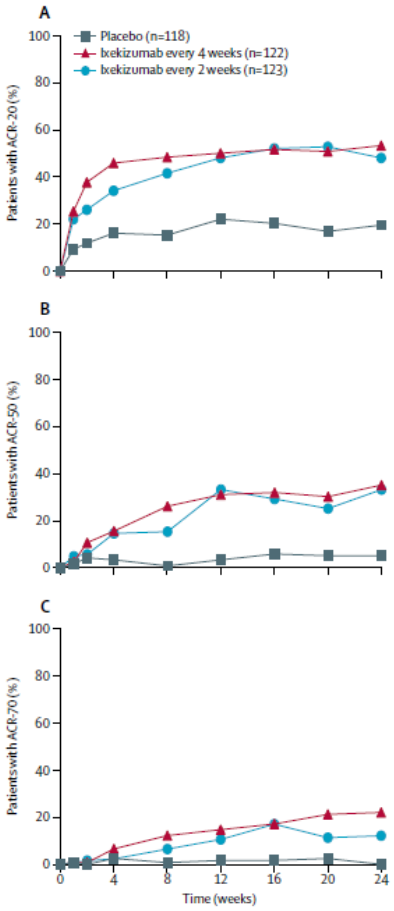
McInnes, I et al, J. of comparative effectiveness research 2018

Profilo di sicurezza secukinumab

Variable	Secukinumab 300 mg (*n* = 145)	Secukinumab 150 mg (*n* = 143)	Secukinumab 75 mg (*n* = 99)	Any secukinumab (*n* = 387)
Duration of exposure, days, mean (S.D.)	726.0 (190.1)	715.5 (196.0)	674.8 (254.8)	709.0 (211.0)
Exposure, patient-years	288.2	280.1	182.9	751.3
EAIR/100 patient-years, *n*				
Any AE	127 (163.3)	126 (181.2)	84 (159.2)	337 (168.5)
Any SAEs	19 (7.0)	15 (5.6)	13 (7.7)	47 (6.6)
Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Discontinuation due to AEs[a]	5 (3.4)	8 (5.6)	5 (5.1)	18 (4.7)
Common AEs, *n* (EAIR/100 patient-years)[b]				
Upper respiratory tract infection	33 (13.4)	30 (12.7)	23 (15.6)	86 (13.6)
Nasopharyngitis	28 (11.3)	33 (13.7)	21 (13.1)	82 (12.6)
Diarrhoea	12 (4.4)	13 (4.9)	11 (6.3)	36 (5.0)
Headache	10 (3.7)	15 (5.7)	5 (2.9)	30 (4.2)
Nausea	9 (3.2)	12 (4.5)	7 (4.0)	28 (3.9)
Urinary tract infection	10 (3.6)	12 (4.5)	6 (3.4)	28 (3.9)
Vomiting	7 (2.5)	7 (2.6)	4 (2.3)	18 (2.5)
AEs of special interest, *n* (EAIR/100 patient-years)				
Serious infections	6 (2.1)	5 (1.8)	1 (0.6)	12 (1.6)
Candida infections	8 (2.9)	8 (2.9)	1 (0.5)	17 (2.3)
Ulcerative colitis	1 (0.3)	1 (0.4)	0 (0.0)	2 (0.3)
Neutropenia	1 (0.3)	0	0	1 (0.1)
Malignancy/unspecified tumour	1 (0.3)	6 (2.2)	3 (1.7)	10 (1.3)
MACE	1 (0.3)	0 (0.0)	1 (0.6)	2 (0.3)

McInnes, I et al, Rheumatology (Oxford) 2017

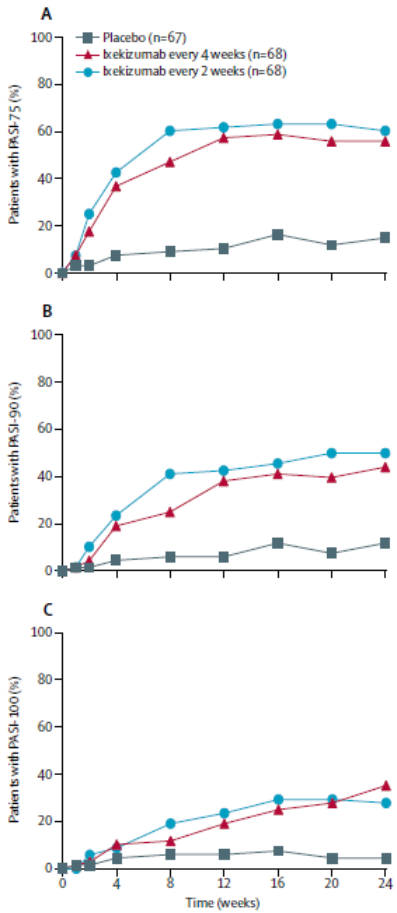
Efficacia dell'ixekizumab sull'artrite psoriatica e psoriasi



Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	0·0012	0·0057
2	<0·0001	0·0055
4	<0·0001	0·0017
8	<0·0001	<0·0001
12	<0·0001	<0·0001
16	<0·0001	<0·0001
20	<0·0001	<0·0001
24	<0·0001	<0·0001

Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0·99	0·28
2	0·06	0·77
4	0·0031	0·0030
8	0·0003	<0·0001
12	<0·0001	<0·0001
16	<0·0001	<0·0001
20	<0·0001	0·0001
24	<0·0001	<0·0001

Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0·99	>0·99
2	>0·99	0·50
4	0·22	>0·99
8	0·0065	0·0360
12	0·0020	0·0059
16	<0·0001	<0·0001
20	0·0002	0·0146
24	<0·0001	<0·0001



Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	0·44	0·44
2	0·0089	0·0017
4	<0·0001	<0·0001
8	<0·0001	<0·0001
12	<0·0001	<0·0001
16	<0·0001	<0·0001
20	<0·0001	<0·0001
24	<0·0001	<0·0001

Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0·99	>0·99
2	0·62	0·06
4	0·0144	0·0022
8	0·0041	<0·0001
12	<0·0001	<0·0001
16	0·0002	<0·0001
20	<0·0001	<0·0001
24	<0·0001	<0·0001

Weeks	Ixekizumab every 4 weeks	Ixekizumab every 2 weeks
1	>0·99	0·50
2	>0·99	0·21
4	0·33	0·49
8	0·37	0·0356
12	0·0356	0·0036
16	0·0092	0·0015
20	0·0003	0·0004
24	0·0001	0·0006

Nash, J et al, Lancet 2017

Profilo di sicurezza dell'ixekizumab

	Placebo (n=118)	Ixekizumab every 4 weeks (n=122)	p value*	Ixekizumab every 2 weeks (n=123)	p value*	Ixekizumab groups combined (n=245)‡
Treatment-emergent adverse events						
Total	76 (64%)	83 (68%)	0·59	90 (73%)	0·17	173 (71%)
Mild	32 (27%)	48 (39%)	..	43 (35%)	..	91 (37%)
Moderate	42 (36%)	31 (25%)	0·68†	38 (31%)	0·06†	69 (28%)
Severe	2 (2%)	4 (3%)	..	9 (7%)	..	13 (5%)
Most frequent treatment-emergent adverse events§						
Injection site reaction	1 (1%)	8 (7%)	0·0358	15 (12%)	0·0004	23 (9%)
Upper respiratory tract infection	9 (8%)	11 (9%)	0·82	12 (10%)	0·65	23 (9%)
Nasopharyngitis	4 (3%)	8 (7%)	0·38	4 (3%)	>0·99	12 (5%)
Sinusitis	2 (2%)	7 (6%)	0·17	5 (4%)	0·45	12 (5%)
Diarrhoea	3 (3%)	5 (4%)	0·72	5 (4%)	0·72	10 (4%)
Urinary tract infection	3 (3%)	6 (5%)	0·50	4 (3%)	>0·99	10 (4%)
Cough	3 (3%)	4 (3%)	>0·99	4 (3%)	>0·99	8 (3%)
Oropharyngeal pain	0	7 (6%)	0·0144	1 (1%)	>0·99	8 (3%)
Headache	3 (3%)	5 (4%)	0·72	2 (2%)	0·68	7 (3%)
Hypertension	3 (3%)	2 (2%)	0·68	5 (4%)	0·72	7 (3%)
Injection-site erythema	0	2 (2%)	0·50	4 (3%)	0·12	6 (2%)
Injection-site hypersensitivity	0	1 (1%)	>0·99	5 (4%)	0·06	6 (2%)
Back pain	2 (2%)	5 (4%)	0·45	1 (1%)	0·62	6 (2%)
Bronchitis	4 (3%)	1 (1%)	0·21	4 (3%)	>0·99	5 (2%)
Psoriatic arthropathy	8 (7%)	2 (2%)	0·06	3 (2%)	0·13	5 (2%)
Adverse events						
Serious adverse events	4 (3%)	3 (2%)	0·72	8 (7%)	0·38	11 (4%)
Serious infection	0	0	NA	3 (2%)	0·25	3 (1%)
Discontinued due to adverse event	6 (5%)	5 (4%)	0·77	8 (7%)	0·79	13 (5%)
Adverse event of special Interest¶						
Infection	35 (30%)	47 (39%)	0·17	47 (38%)	0·18	94 (38%)
Any candida infection	0	2 (2%)	NA	6 (5%)	NA	8 (3%)
Active or reactivated tuberculosis	0	0	NA	0	NA	0
Hepatic events	2 (2%)	2 (2%)	>0·99	5 (4%)	0·48	7 (3%)
Allergic reactions or hypersensitivities	1 (1%)	8 (7%)	0·0358	9 (7%)	0·0192	17 (7%)
Injection-site reactions	5 (4%)	14 (11%)	0·05	29 (24%)	<0·0001	43 (18%)
Cerebrocardiovascular events	2 (2%)	0	0·24	0	0·24	0
Malignancies	0	2 (2%)	0·50	0	NA	2 (1%)
Depression	3 (3%)	2 (2%)	0·68	2 (2%)	0·68	4 (2%)

Nash, J et al, Lancet 2017

	Tofacitinib	Baricitinib
Inibizione	JAK 1/3	JAK 1/2
Biodisponibilità	≈75%	≈80%
Concentrazione plasmatica	30-60 min	30-180 min
T1/2	≈3 ore	≈12 ore
Stabilità	24-48 ore	72 ore
Affinità proteica	≈40%	≈50%
Eliminazione	70% fegato 30% renale	20% GIT 75% renale
Potenziali interazioni	CYP3A4, CYP 2C (Claritromicina, Ketoconazolo)	OAT 3 (Probenecid)
Esame di labor di controllo	Hb, Lc, neutrofili, Transaminasi, lipidi	Hb, Lc,neutrofili, transaminasi, lipidi e creatinina

JAK	Function impaired	Potential adverse effect
JAK1	Severely impaired lymphoid development Defective cytokine signalling	Infection, hyperlipidaemia
JAK2	Impaired erythropoiesis, myelopoiesis	Anaemia, neutropenia
JAK3	Impaired response to gamma chain receptor family of interleukins (*eg* IL-2)	Natural killer cell lymphopenia Diminished function of CD8 T cells Infection, possibly opportunistic infection
TYK2	Impaired helper T cell (Th)1 responses Reduction in pathogenic Th17 cells Blockade of IFN actions	Infection

Kontzias, A. et al, Curr. Op. Pharm 2012

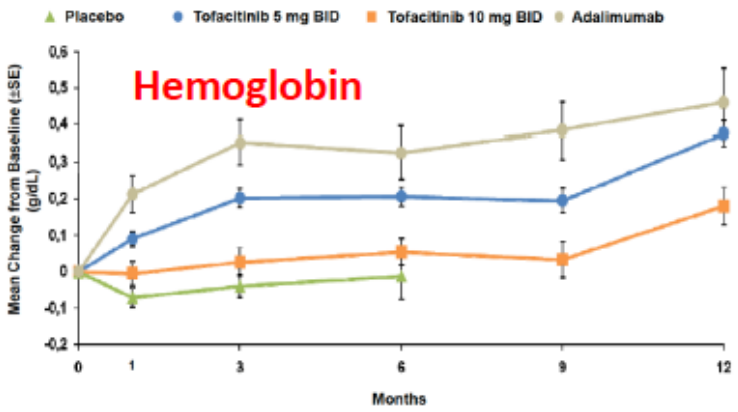
Eventi aversi

Infezione 100p/y	Tofacitinib	Baricitinib
Infezioni gravi	2,7	3,2
HSZ	3,0	3,4
HSZ grave	0,3	0,5

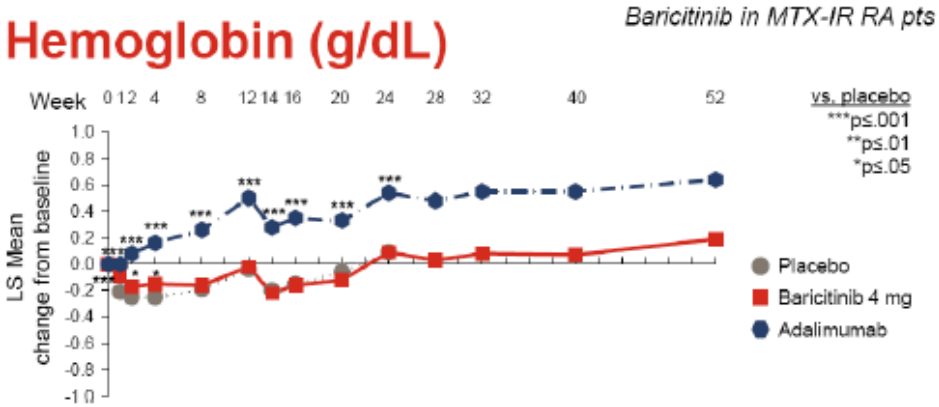
Tumori 100p/y	Tofactinib	Baricitinib
Tutti tipi di tumori esclusi NMSC	0,9	0,8

Cohen et al, ARD 2017
Genovese et al ACR poster 2017

Effetto sull'emoglobina

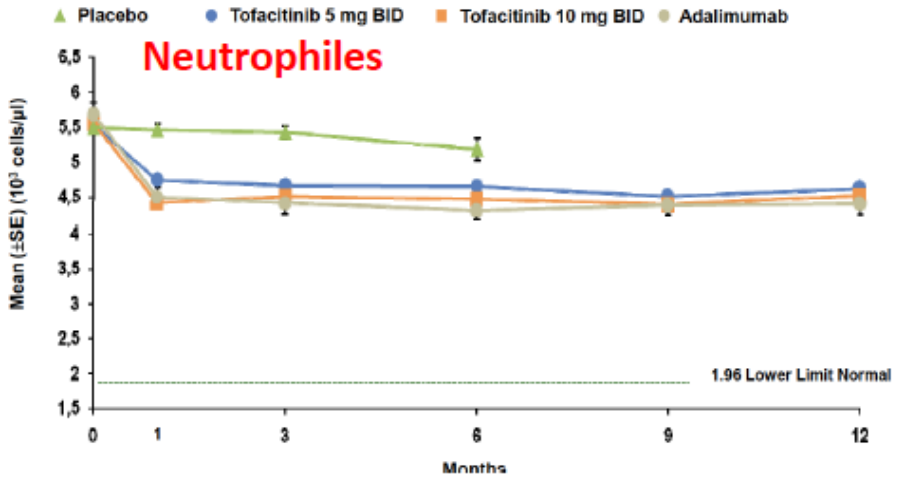


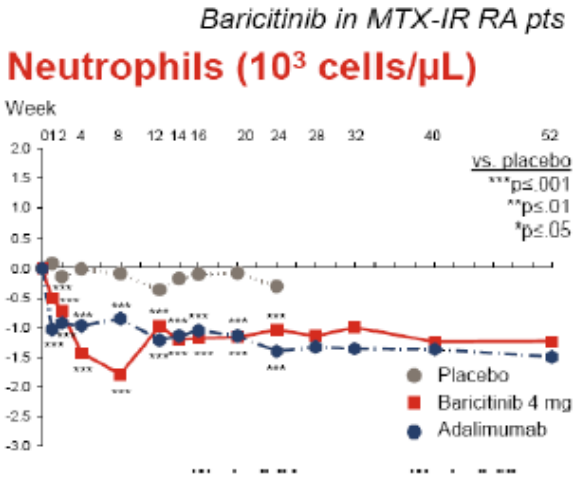
Schulze-Koops H et al.: *Rheumatology; 2017, 56:46-57*

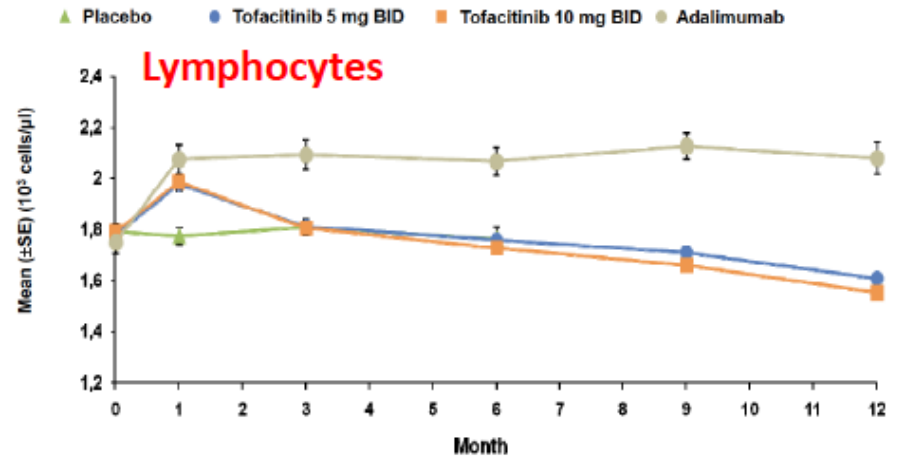


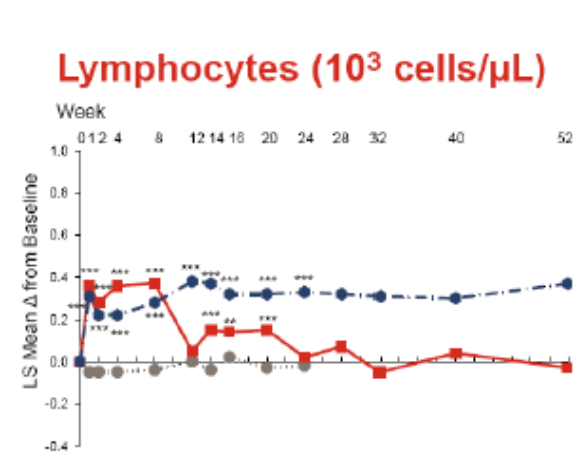
Taylor P et al.: *NEJM; 2017, 376:652-62 (suppl.)*

Effetto sulle leucociti





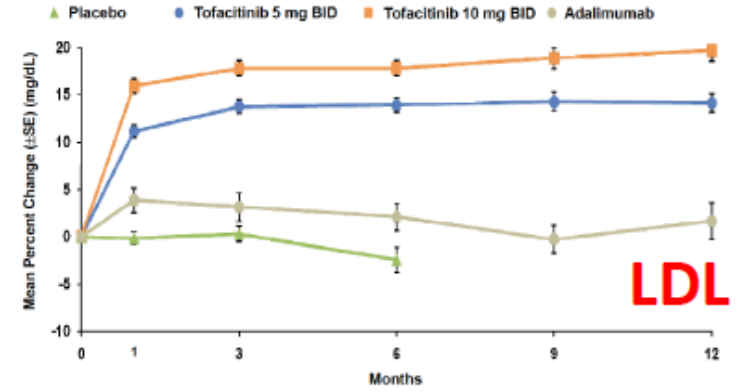


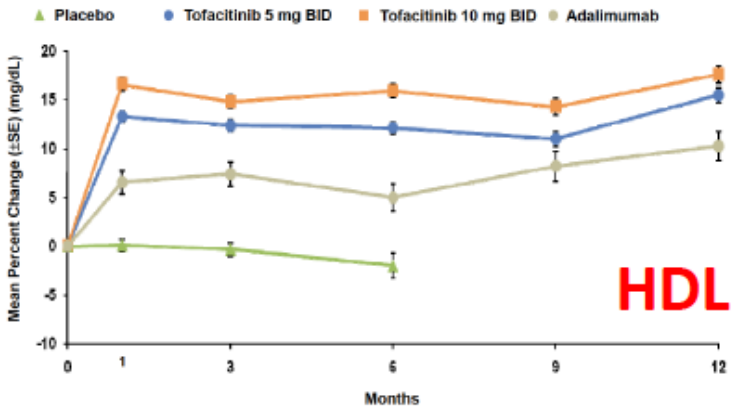


Schulze-Koops H et al.: *Rheumatology; 2017, 56:46-57*

Taylor P et al.: *NEJM; 2017, 376:652-62 (suppl.)*

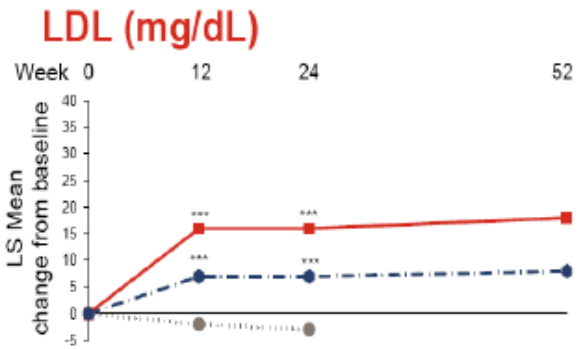
Effetto sui lipidi

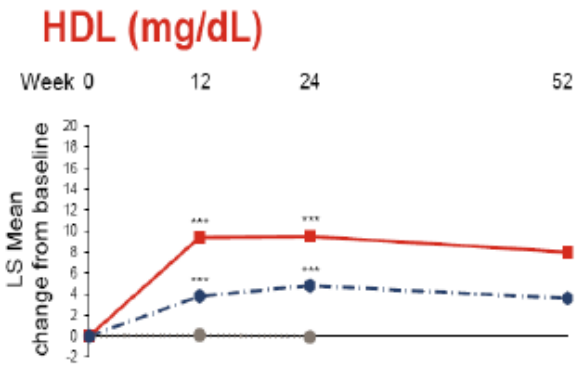




Schulze-Koops H et al.: *Rheumatology; 2017, 56:46-57*

Baricitinib in MTX-IR RA pts





vs. placebo
***p≤.001
**p≤.01
*p≤.05

Placebo
Baricitinib 4 mg
Adalimumab

LDL/HDL ratio (mean)	Placebo (N=487)	Bari (N=484)	ADA (N=330)
Baseline	2.09	2.03	2.03
Week 12	2.04	2.04	2.06
Week 24	2.06	2.07	2.05
Week 52	-	2.12	2.05

Taylor P et al.: *NEJM; 2017, 376:652-62 (suppl.)*

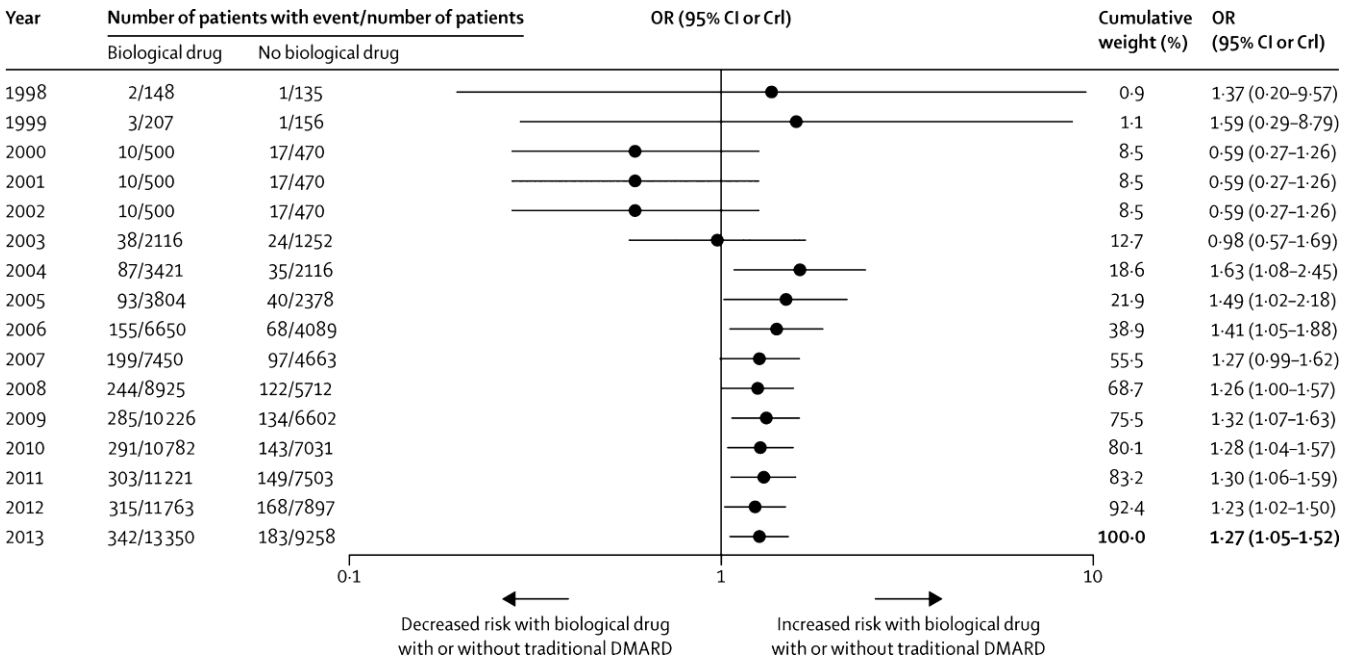
Aspetti clinici relevanti

- Elevato rischio di infezione
  - Tubercolosi (riattivazione o nuova infezione)
  - Leucoenfalopatia progressiva multifocale (PML) infezione da JC virus
  - Candidosi ecc
- Effetti collaterali particolari
  - Rottura di diverticolite (tocilizumab)
  - Psoriasi e Lupus farmaco-indotto (iTNF-alfa)
  - Malattia demielizzante (iTNF-alfa)
  - Ipercolesterolemia (i Kinase JAK)

Fattori di rischio per l’infezione

- Attività della malattia
- Età avanzata
- Co-morbidità (ad esempio DM, insufficienza renale)
- Infezioni gravi in anamnesi
- Concomitante terapia glucocorticoide

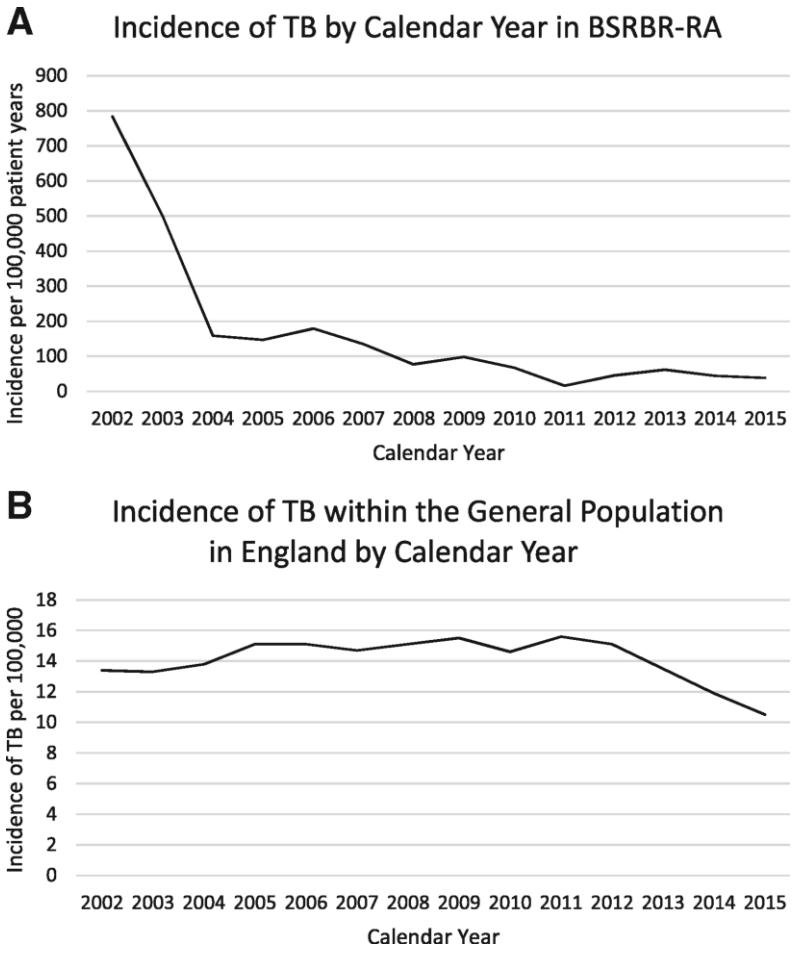
Rischio di Infezione sotto le terapie biologiche



Singh, J et al, Lancet 2015

Misure preventive contro le infezioni sotto le terapia biologiche
Ottimizzare e aggiornare lo stato di vaccinazione dei pazienti
Screening per TBC e le epatiti virali (B e C)
Controllo stretto/osservazioni dei pazienti ad alto rischio di infezione
Riduzione al piu rapido possibile del dosaggio cortisonico
Informazione esauriente ai pazienti e medici curanti sulla gestione delle infezioni (sospensione della terapia durante un infezione o periodo perioperativo)

Prevalenza di Tubercolosi in pazienti sotto terapia con inibitore del TNF-alfa



Rutherford, A et al, Rheumatology 2018

Table 3: Live vaccines during immunosuppressive therapy.

Therapeutic agent	Herpes zoster / varicella vaccination	Mumps, measles, rubella (MMR), yellow fever vaccination
Low-dose systemic or topical corticosteroids: • Short- or long-term daily or alternate-day therapy with <20 mg of prednisone or equivalent • Glucocorticosteroid replacement therapy in adrenal insufficiency / topical steroids (airways, skin, ears, or eyes) • Intra-articular, bursal, or tendon injection of steroids Sulfasalazine Hydroxychloroquine	No restrictions*	No restrictions*
Methotrexate	≤0.4 mg/kg/week (≤20 mg/week): vaccination possible*	≤0.4 mg/kg/week (≤20 mg/week): vaccination possible*†
	>0.4 mg/kg/week (>20 mg/week): contraindication	>0.4 mg/kg/week (>20 mg/week): contraindication
Azathioprine¶	≤3.0 mg/kg/day: vaccination possible*	Contraindication
	>3.0 mg/kg/day: contraindication	
6-Mercaptopurine§	≤1.5 mg/kg day: vaccination possible*	Contraindication
	>1.5 mg/kg/day: contraindication	
Abatacept Adalimumab Anakinra Certolizumab Cyclosporine A Cyclophosphamide Etanercept Golimumab High-dose systemic steroids (≥20 mg per day of prednisone or equivalent for >2 weeks) Infliximab Leflunomide Mycophenolate mofetil Rituximab Tacrolimus Tocilizumab Ustekinumab	Contraindication	Contraindication

Bühler, S et al, Swiss medical Weekly 2015

Table 5: Recommended time period between interruption of immunosuppressive therapy and administration of inactivated vaccines.	
Medication	**Inactivated vaccine**
Corticosteroids Low-dose systemic or topical corticosteroids • Short- or long-term daily or alternate-day therapy with <20 mg of prednisone or equivalent • Glucocorticosteroid replacement therapy in adrenal insufficiency / topical steroids (airways, skin, ears, or eyes) • Intra-articular, bursal, or tendon injection of steroids High-dose systemic steroids (≥20 mg per day of prednisone or equivalent for >2 weeks) Adalimumab Anakinra Azathioprine Certolizumab Ciclosporin Cyclophosphamide Etanercept Golimumab Hydroxychloroquine Infliximab Leflunomide 6-Mercaptopurine Methotrexate Mycophenolate mofetil Sulfasalazine Tacrolimus Tocilizumab Ustekinumab	No time lag necessary
Abatacept	If possible, vaccinate shortly before abatacept administration*
Rituximab	Wait at least 6 months for revaccination and 12 months for primary vaccination, if possible

Bühler, S et al, Swiss medical Weekly 2015

Table 6: Recommended time period between interruption of immunosuppressive therapy and administration of live vaccines.	
Medication	**Mumps, measles, rubella (MMR) vaccine, varicella vaccine, yellow fever vaccine**
Low-dose systemic or topical corticosteroids • Short- or long-term daily or alternate-day therapy with <20 mg of prednisone or equivalent glucocorticosteroid replacement therapy in adrenal insufficiency / topical steroids (airways, skin, ears, or eyes) • Intra-articular, bursal, or tendon injection of steroids Sulfasalazine Hydroxychloroquine	No pausing or time lag necessary
High-dose systemic steroids (≥20 mg per day of prednisone or equivalent for >2 weeks)	Wait at least 1 month
Etanercept	Wait at least 1 month*
Methotrexate	≤0.4 mg/kg/week (≤20 mg/week)†
	>0.4 mg/ kg/ week (>20 mg/ week): Wait at least 1–3 months¶
Abatacept Adalimumab Anakinra§ Azathioprine Certolizumab Cyclosporine Cyclophosphamide Golimumab Infliximab 6-Mercaptopurine Mycophenolate mofetil Tacrolimus Tocilizumab Ustekinumab	Wait at least 3 months*
Rituximab	Wait at least 12 months‡
Leflunomide	Wait at least 2 years**

Bühler, S et al, Swiss medical Weekly 2015

Raccomandazione sulla sospensione terapeutica

- Methotrexate può essere continuata durante il periodo perioperativo.
- I biologici devono essere sospeso prima dell'intervento e riniziato solo dopo una buona e sicura guarigione della ferita.
- L'uso dell'inibitore del IL-6 maschera segni di infezione.

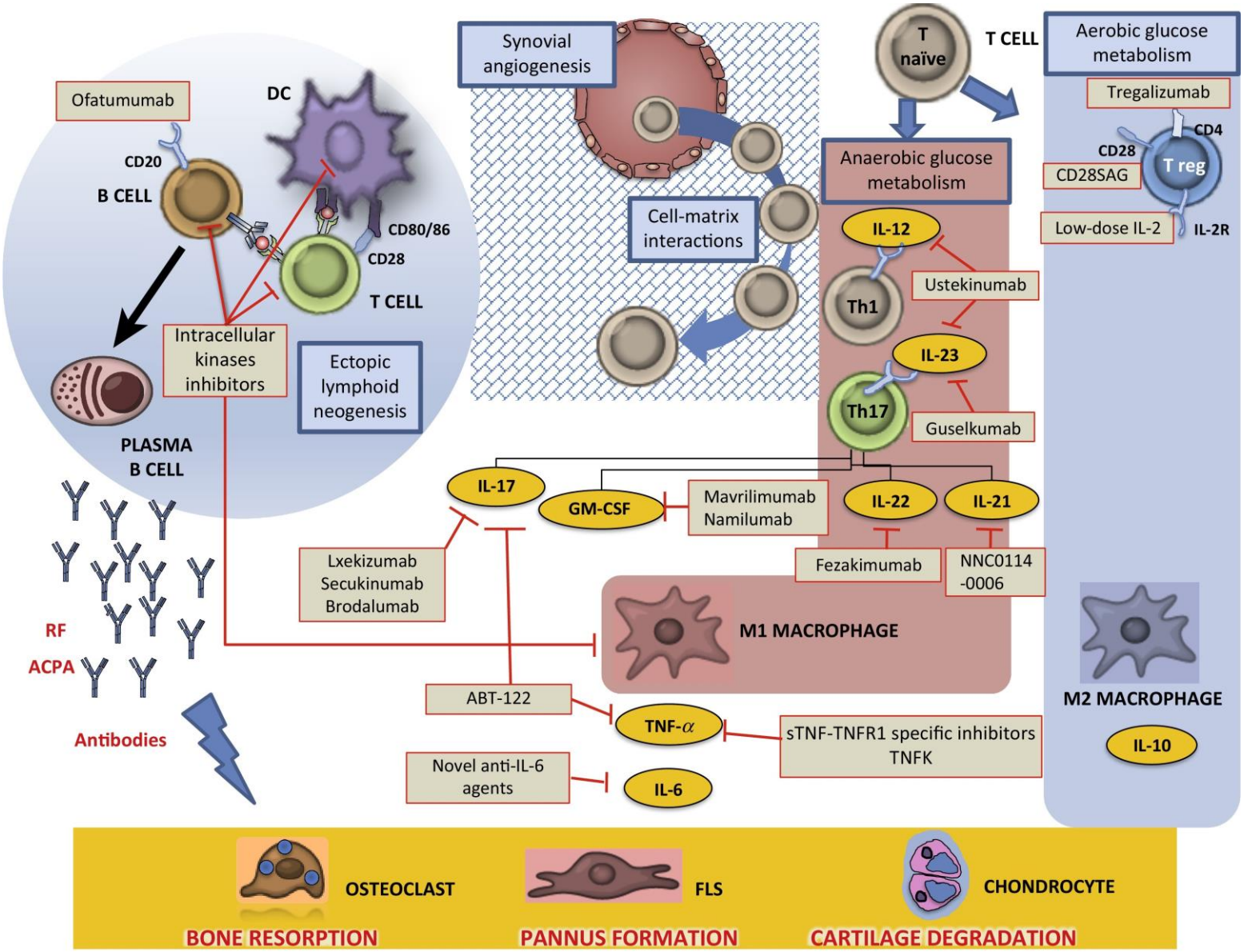
Drugs	Half-life (T1/2)
bDMARDs	
Inibitore del TNF- alfa Infliximab (Remicade) Etanercept (Enbrel) Adalimumab (Humira) Golimumab (Simponi) Certolizumab (Cimzia)	 8-9,5 giorni 70 ore (tra 7-300 ore) 2 settimane 12±3 giorni 14 giorni
Inibitore del IL-6 Tocilizumab (Actemra)	 Tra 6 e 16 giorni
Anti-CD 20 Rituximab (Mabthera)	 22 giorni (tra 6,1-52 giorni)
Anti-p40 (IL12/IL23) Ustekinumab (Stelara)	 Media 3 settimane
IL-1 antagonista Anakinra (Kineret)	 Tra 4-6 ore
csDMARDs Methotrexate Leflunomide	 6-7 ore 1-4 settimane

Medicaments.gouv.fr

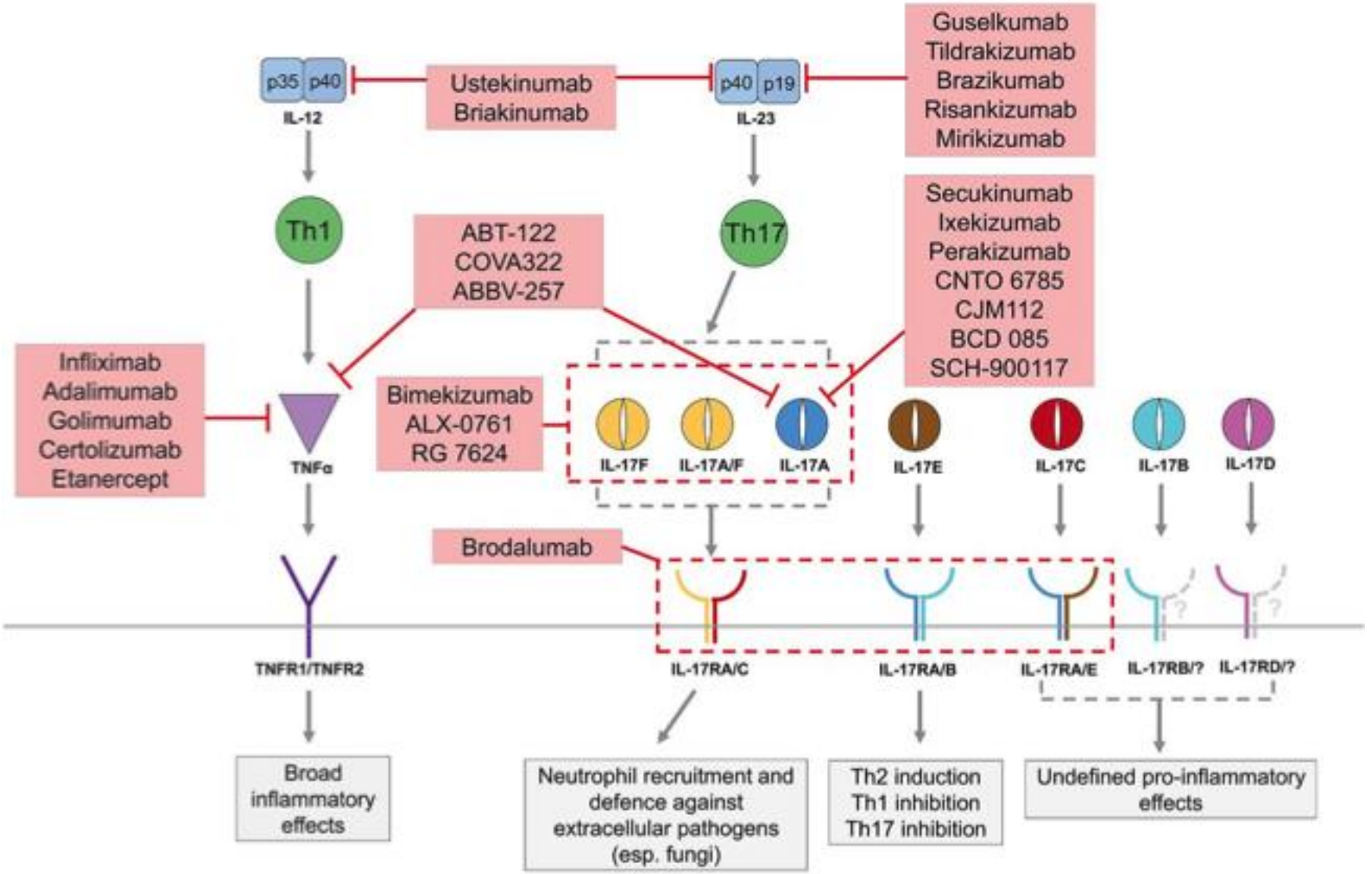
- Il rischio cumulativo d'infezione aumenta con la durata dell'uso del cortisone
  - 5mg di prednisone per
    - 3 mesi = 30%
    - 6 mesi = 46%
    - 3 anni = 100%

Dixon, W et al ARD 2012

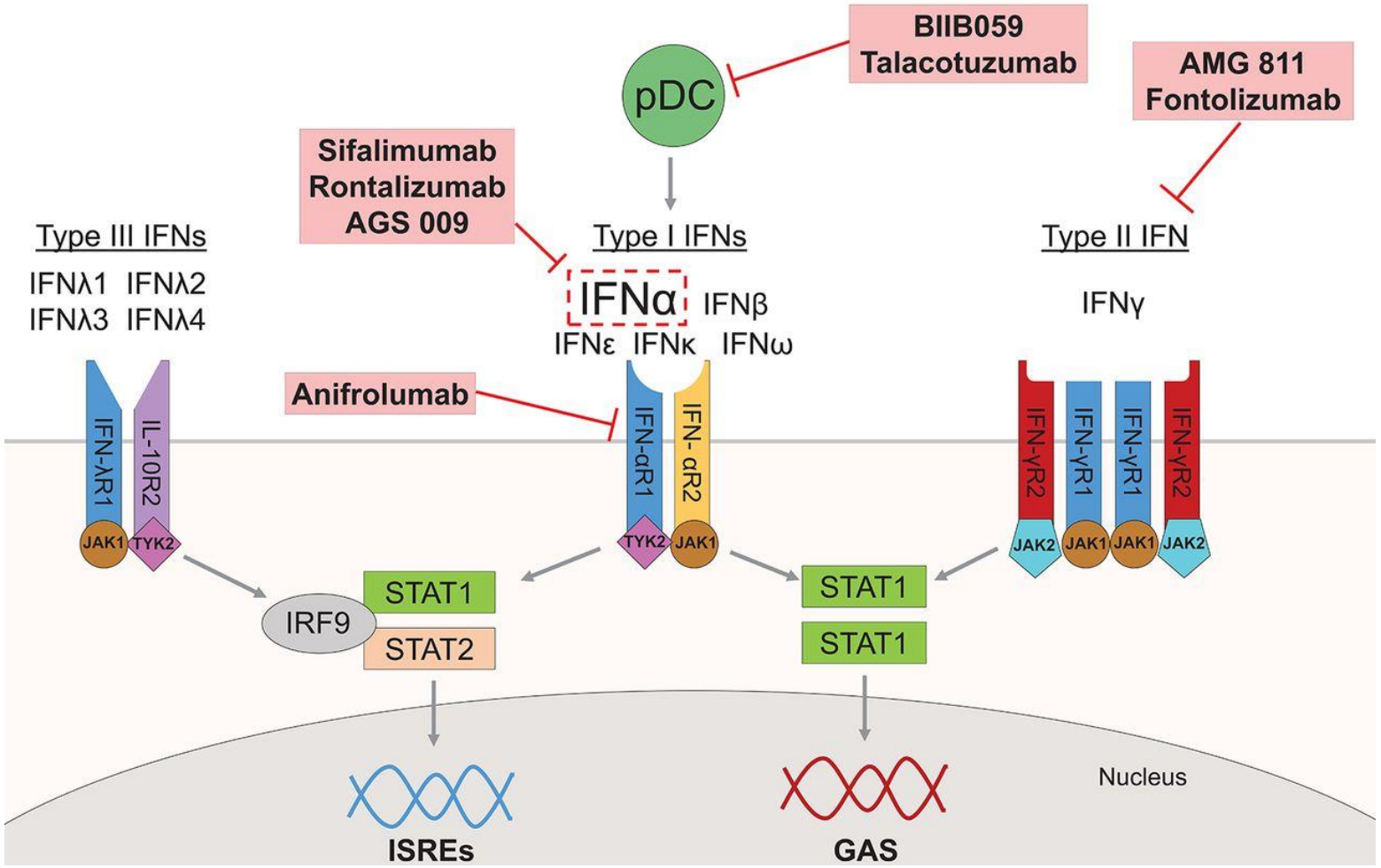
What’s in the pipeline?



Trends in Molecular Medicine



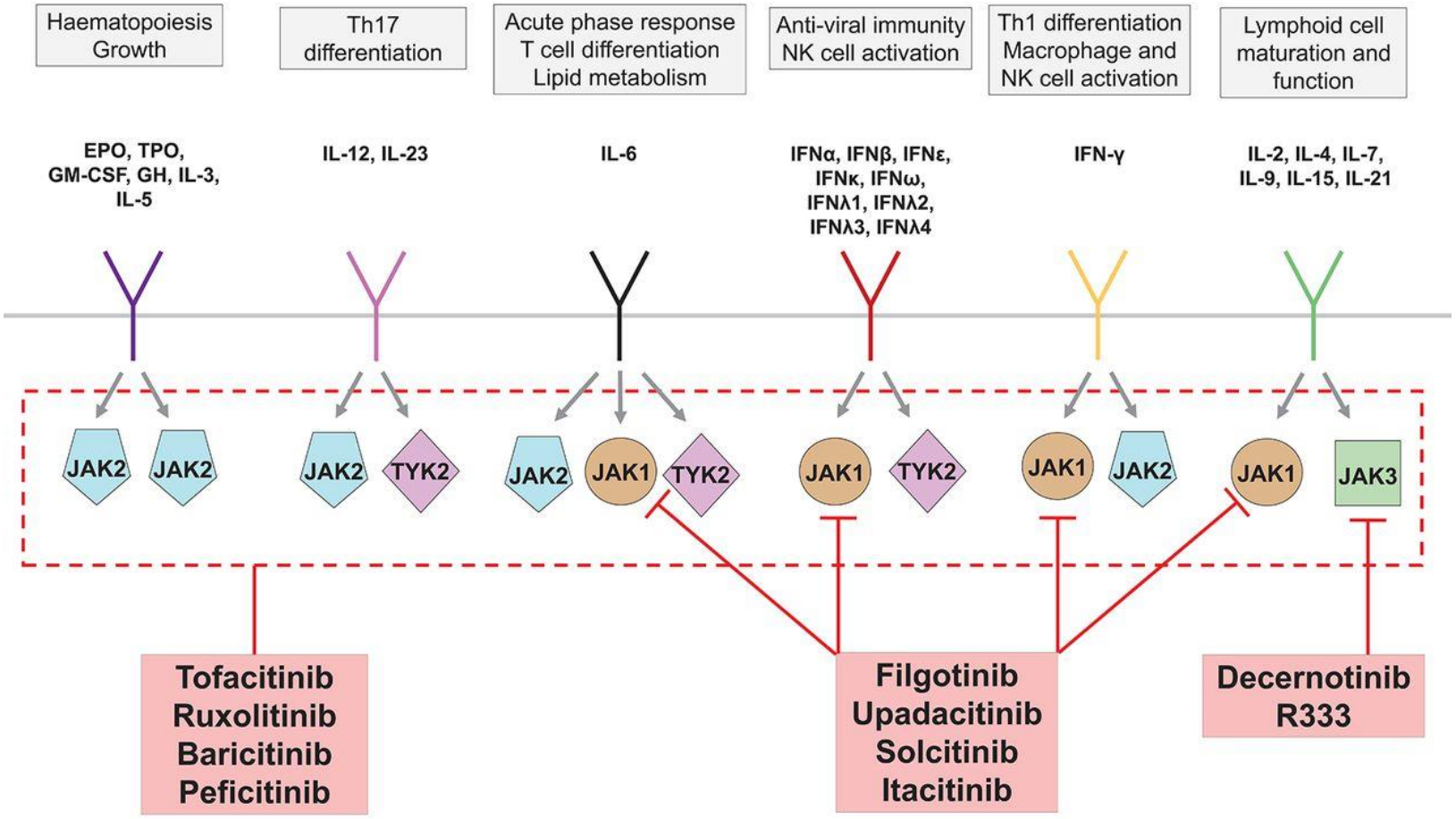
Baker, K et al, ARD 2018



Baker, K et al, ARD 2018

Nuovi farmaci

Biologico	indicazione
Anti-IL6 Olokizumab	RA fase III
Anti-IL23 p19 Guselkumab (Tremfya)	PsA fase III
Anti-IL17 Brodalumab (Kyntheum)	SpA fase III
Anti-IFN ricettore Anifrolumab	LES fase III
Anti-Cellule B Ofatumumab (Arzerra)	RA fase III
Modulatore CD4 Rigerimod	RA fase III
Anti-C5a ricettore Avacopan	Vascolite ANCA associata fase III



Baker, K et al, ARD 2018

	Inibizione JAK	Indicazione
Filgotinib	JAK1	AR, SpA, PsA, Sjögren, Crohn, UC, uveite
Upadacitinib	JAK 1	AR, SpA, PsA, UC, Crohn
Peficitinib	JAK 3	AR
PF-04965842	JAK 1	Dermatite atopica, PsO
Fedratinib	JAK2	Mielofibrosi primaria, Policitemia vera e trombocitemia essenziale

Farmaco	Inibizione	indicazione
Gandotinib	JAK 2	Neoplasia mieloproliferativa
Lestaurtinib	JAK 2	AML
Momelotinib	JAK 1 e JAK 2	Sindrome mielodisplastica, Carcinoma pancreatico metatastatico
Pacricitinib	JAK 2	Linfoma, mielofibrosi,neoplasia mieloproliferativa
Fedratinib	JAK2	Mielofibrosi primaria, Policitemia vera e trombocitemia essenziale

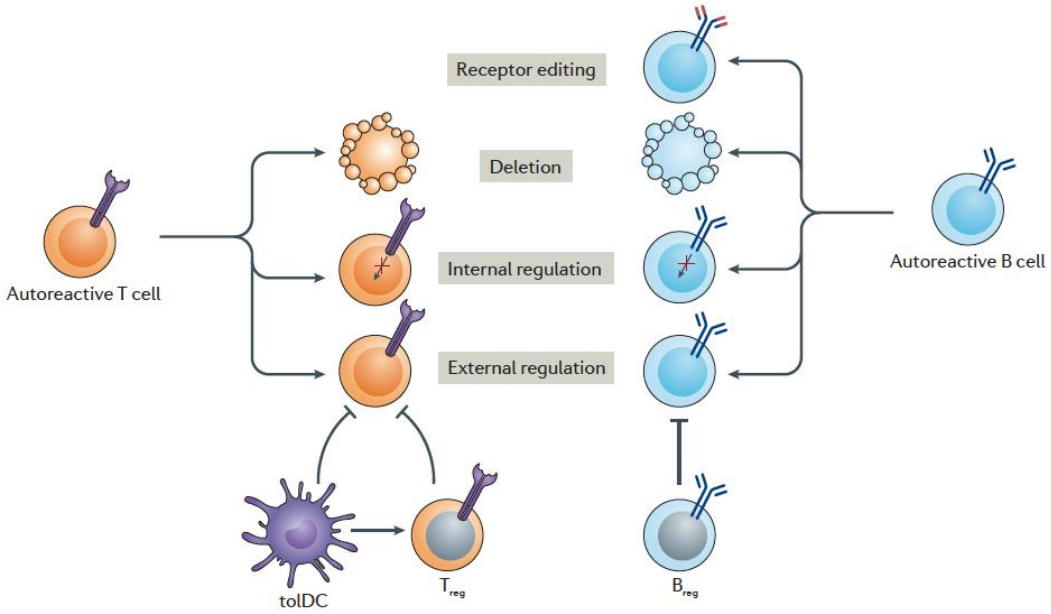

FUTURE

Il futuro

- Trattamento precoce delle malattie reumatiche.
- Definizione della malattia a livello molecolare e classificazione della malattia secondo il patotipo molecolare e non secondo il fenotipo clinico.
- Rivoluzione della medicina di precisione già applicata in oncologia

Terapie nel futuro

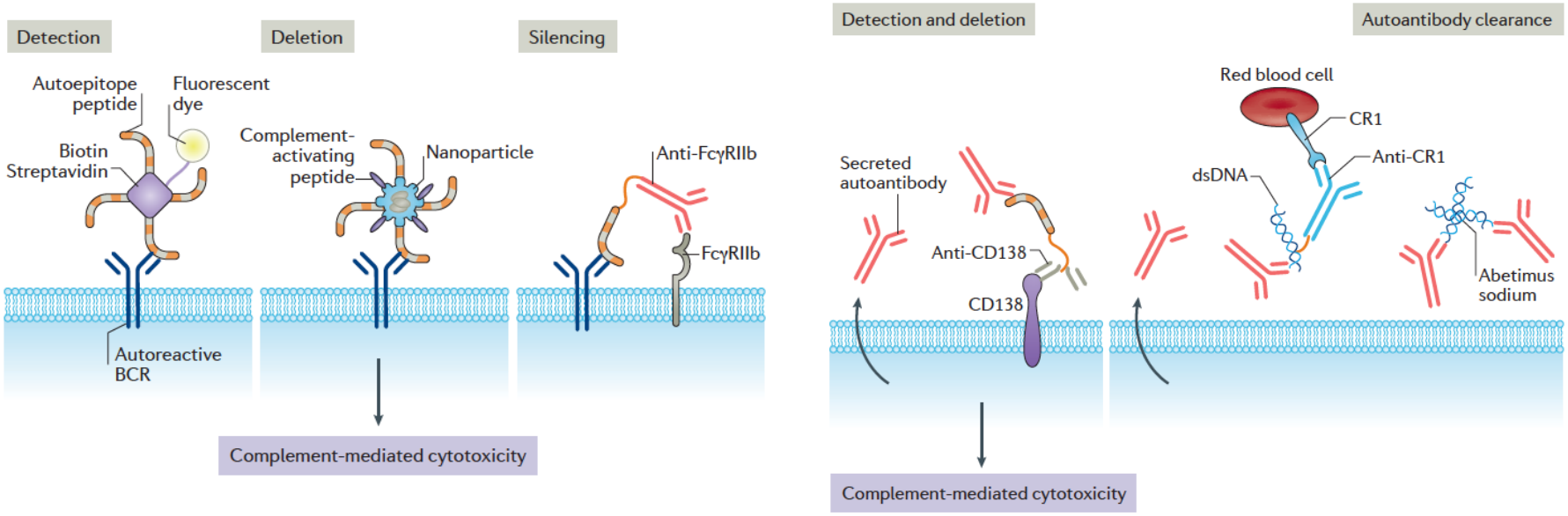
- Immunoterapia antigene specifica
  - Riprogrammare o eliminare cellule autoreattive
  - Indurre una tolleranza immunologica



Induzione dell'immunotolleranza tramite
Eliminazione di cellule T o B autoreattive
Induzione di cellule regolatori (T o B)
Cellule T programmate a eliminare cellule B autoreattive o reindirizzare le cellute T regolari verso le auto-antigene

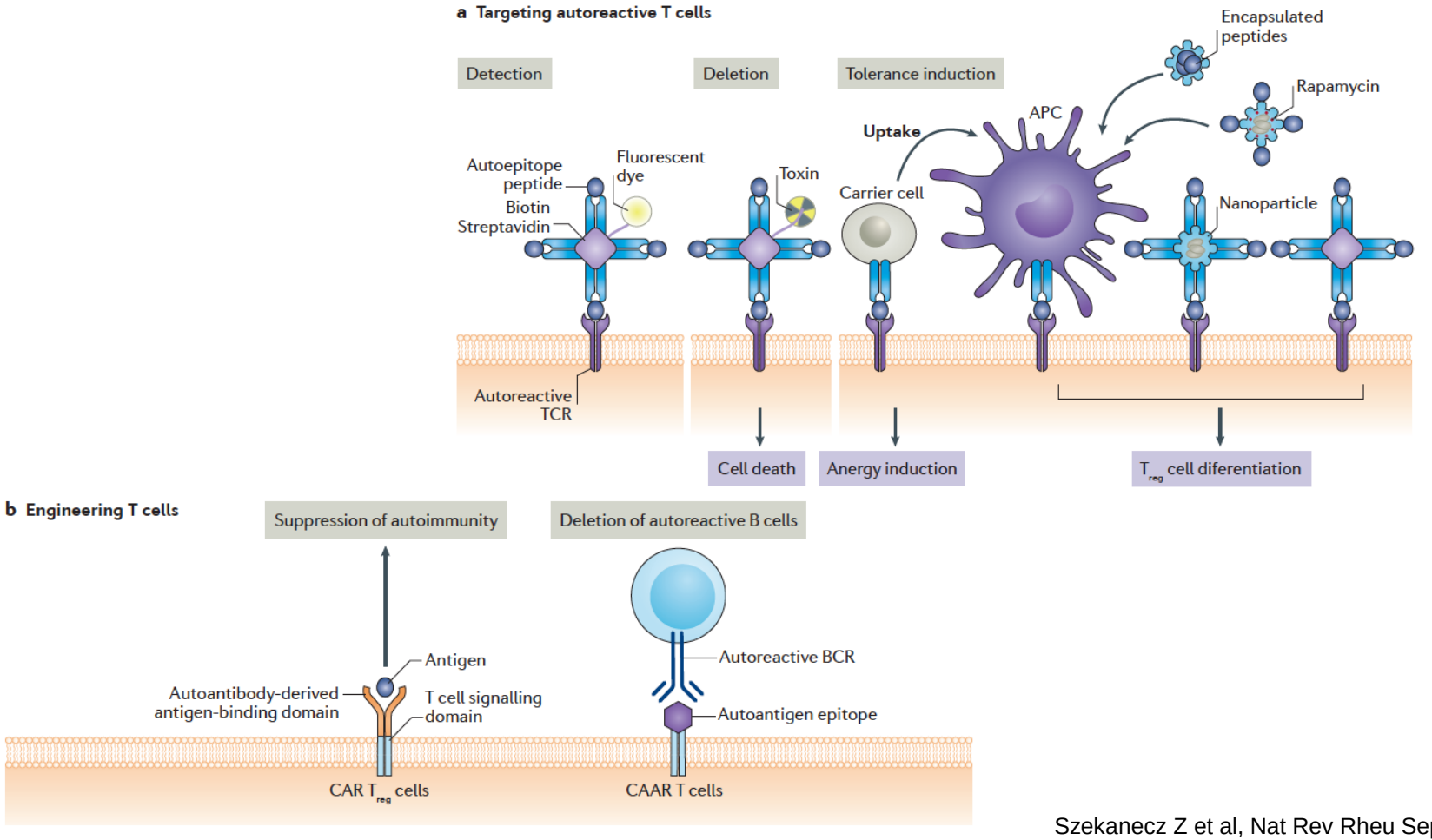
Szekanecz Z et al, Nat Rev Rheu Sept 2017

Strategie di detezione e eliminazione delle cellule B o autoanticorpi



Szekanecz Z et al, Nat Rev Rheu Sept 2017c

Strategie di neutralizzazione o riprogrammazione delle cellule T autoreattive



Szekanecz Z et al, Nat Rev Rheu Sept 2017

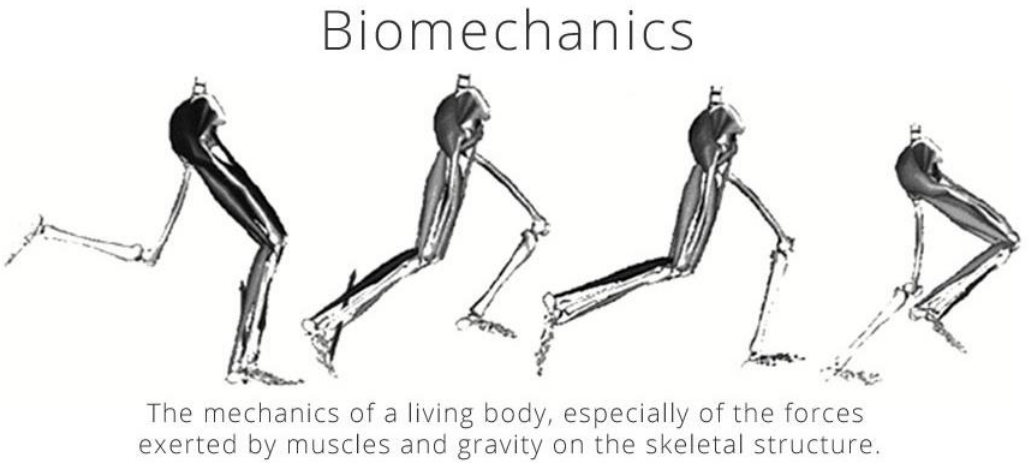
Conclusione

- Ampliamento delle opzione terapeutiche nelle malattie reumatiche
- Strategia di Treat-to-Target
  - Remissione completa o molto bassa attivitità della malattia
- Disponibilità di terapia efficacia con miglioramento della qualità di vita
- Attenzione agli effetti collaterali

Per le ultime raccomandazioni sulle terapie

https://www.rheuma-net.ch/de/fachinformationen/behandlungsempfehlungen

FINE


Biomechanics
The mechanics of a living body, especially of the forces
exerted by muscles and gravity on the skeletal structure.