



Esperienze ed evidenze in Reumatologia



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Milan

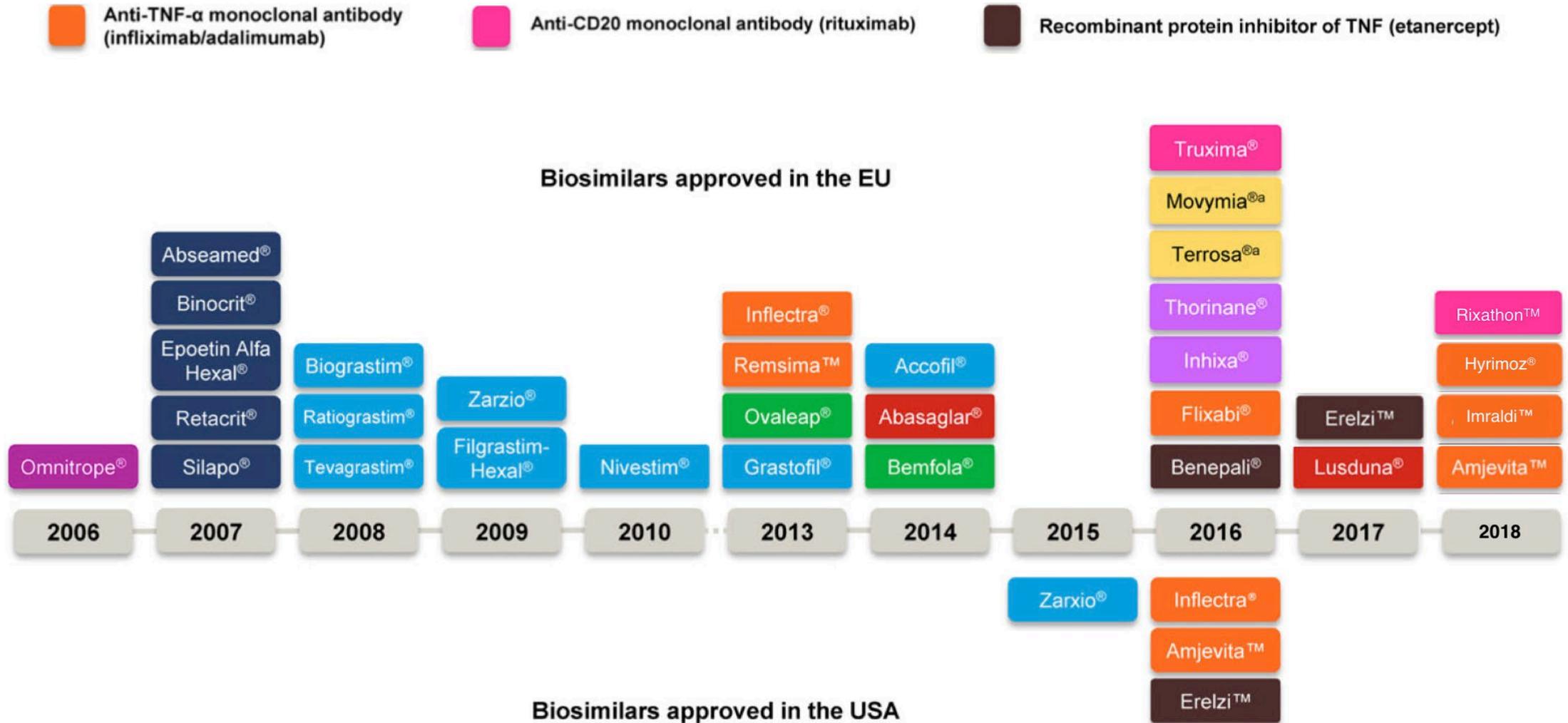


Financial disclosure

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- ◆ *AbbVie*
- ◆ *Abiogen*
- ◆ *Alfa-Sigma*
- ◆ *Bristol-Myers-Squibb*
- ◆ *Celgene*
- ◆ *Eli-Lilly*
- ◆ *Hoffmann-La Roche*
- ◆ *Janssen*
- ◆ *Merck-Sharp & Dohme*
- ◆ *Mundipharma*
- ◆ *Novartis*
- ◆ *Pfizer*
- ◆ *Samsung-Biogen*
- ◆ *Sandoz*
- ◆ *Sanofi-Genzyme*
- ◆ *UCB Pharma*

The approval of biosimilar drugs



Talk composition

- ☑ Rheumatic diseases: overview
- ☑ Treatment strategies in rheumatology
- ☑ Biosimilar drugs for rheumatology
- ☑ What concerns?
- ☑ Role and positioning



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Rheumatic diseases: classification and prevalence

Arthritis

- Rheumatoid Arthritis
- Ankylosing spondylitis
- Psoriatic Arthritis
- Osteoarthritis
- Gout
- Infective arthritis
- Polimyalgia Rheumatica

Miscellaneous

- Fibromyalgia



Connective tissue disease

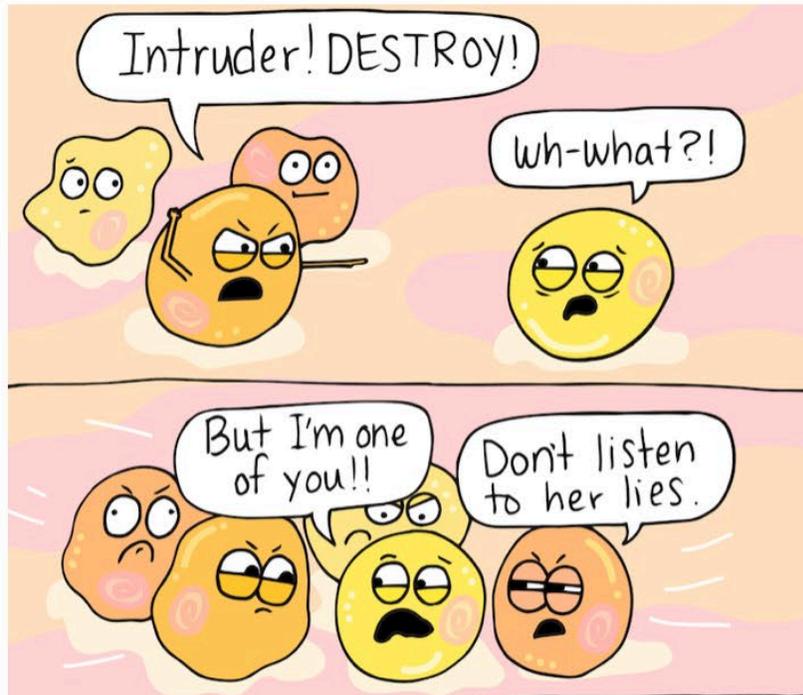
- Systemic Lupus Erythematosus
- Systemic Sclerosis
- Sjögren's Syndrome

Bone diseases

- Osteoporosis
- Paget's Disease
- Bone edema syndromes

Vasculitis

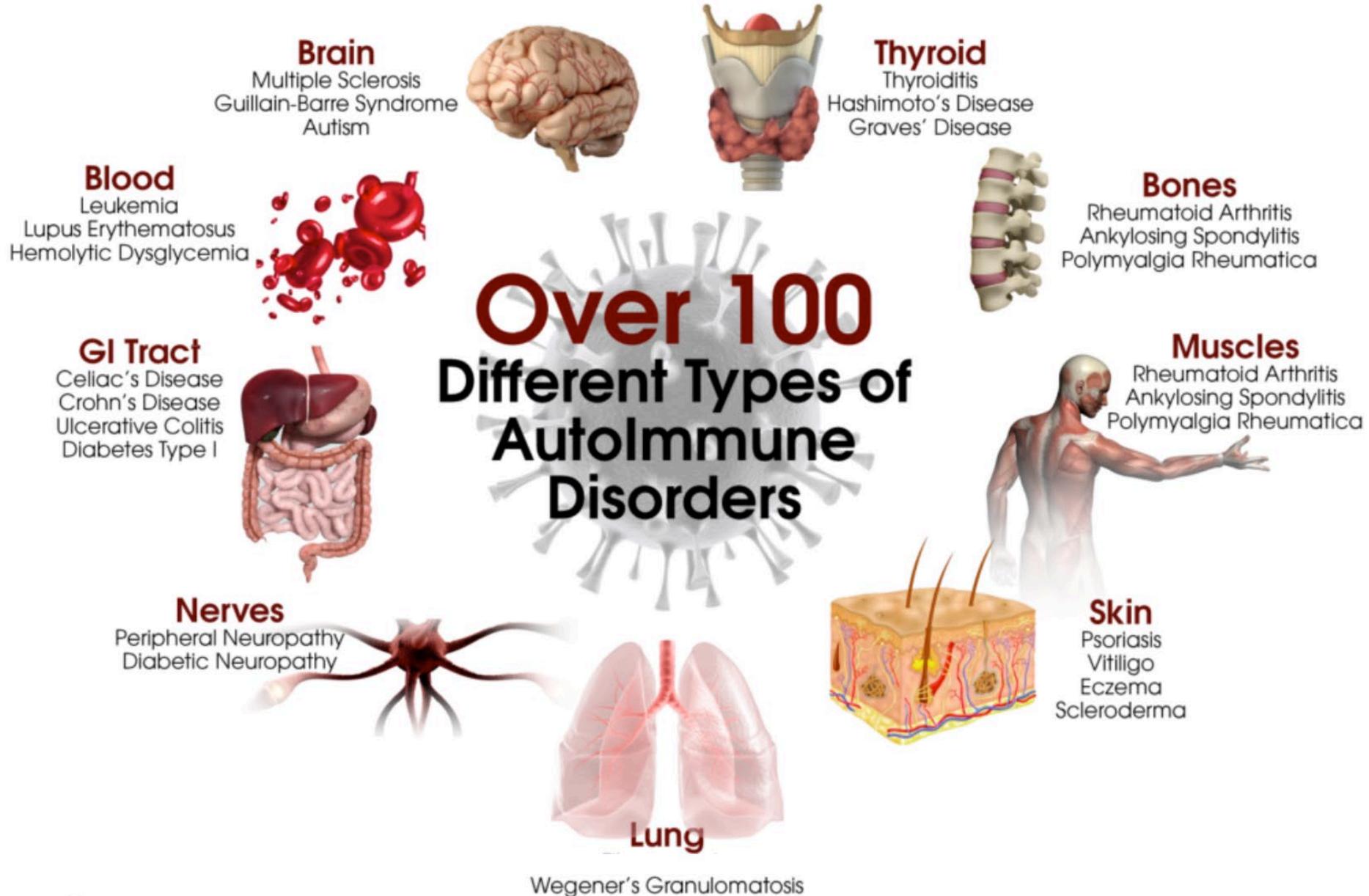
Autoimmunity is the system of immune responses of an organism against its own healthy cells and tissues.



Autoimmune disorders in a nutshell.



AUTOIMMUNE DISEASES



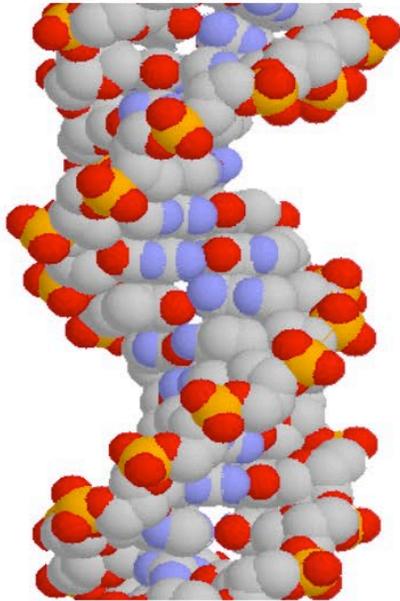
Inflammatory arthritis: a common paradigm



Autoimmunity

The development of autoimmunity

Genetic
predisposition



Smoke



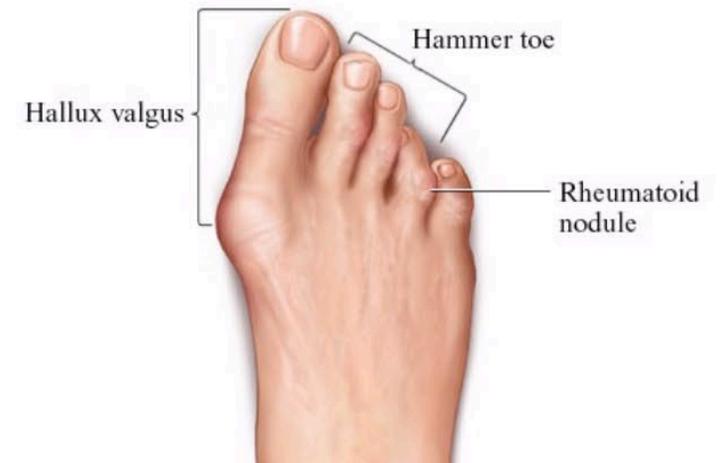
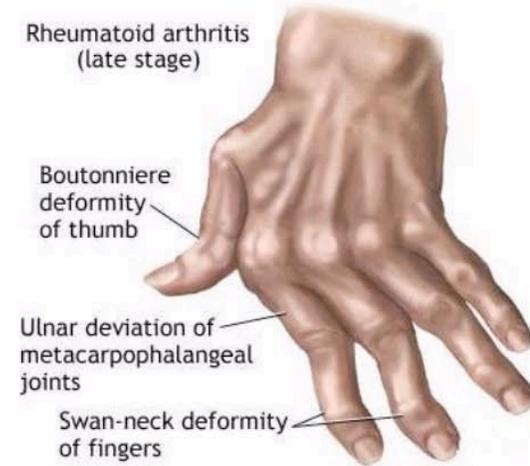
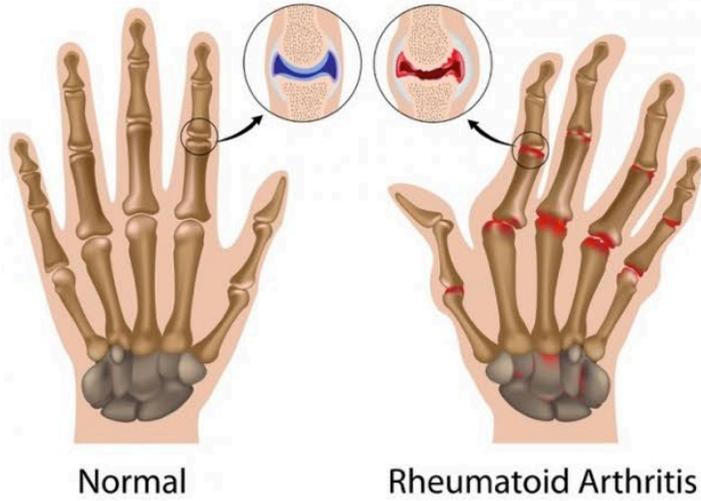
Infections/Microbiome

Inflammatory arthritis: a common paradigm

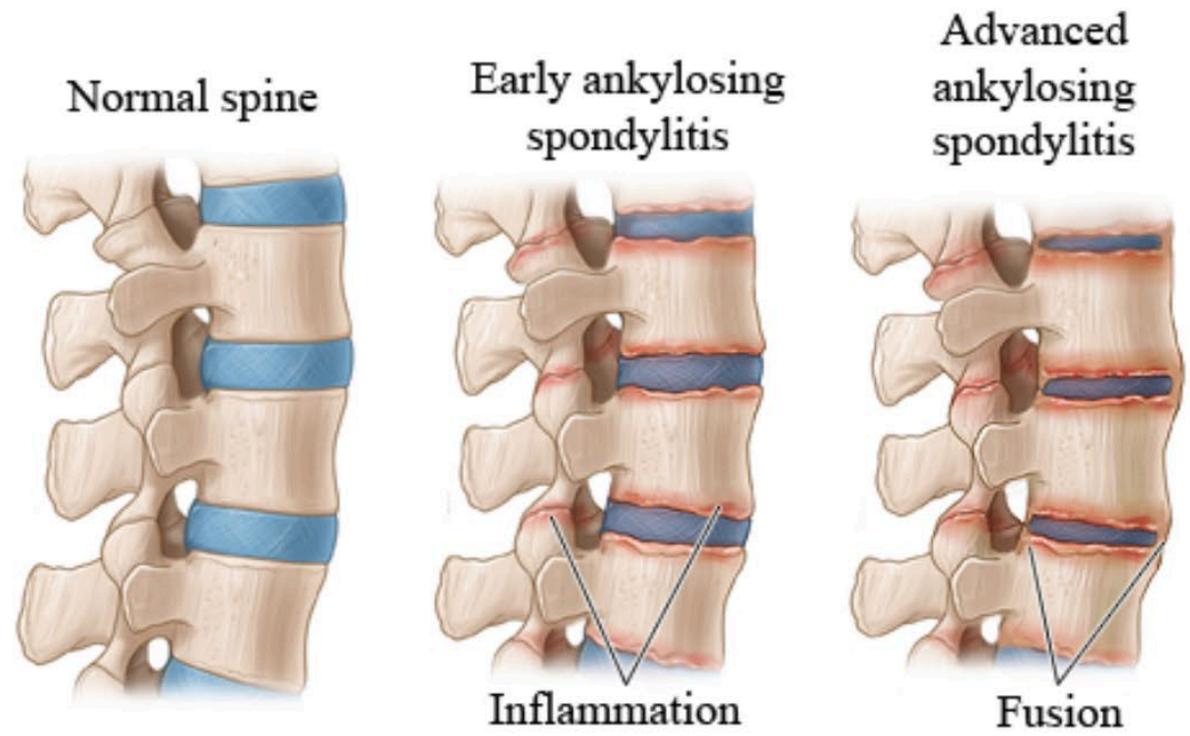
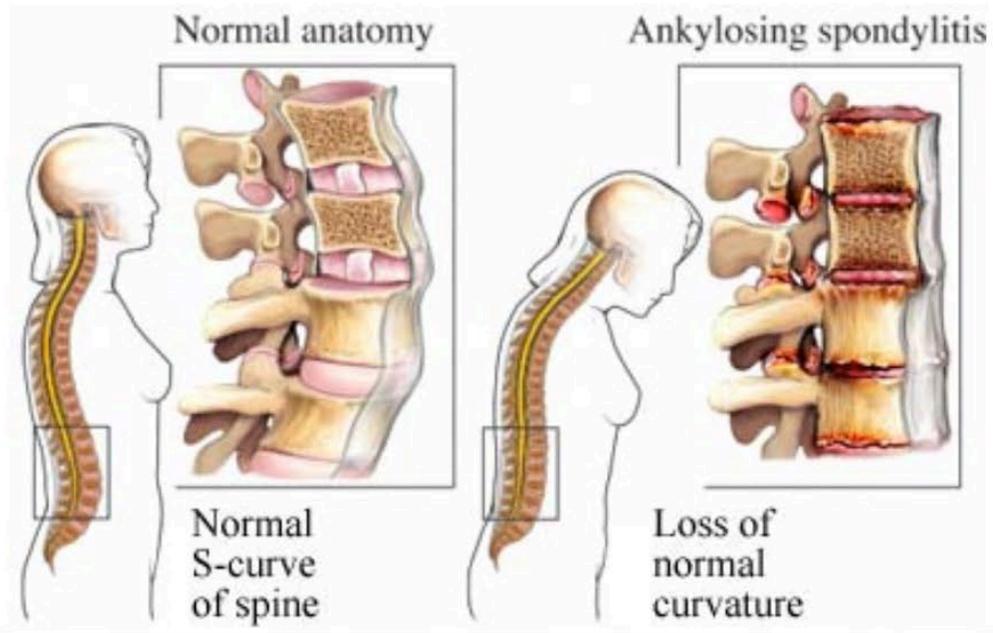


Autoimmunity

Rheumatoid arthritis



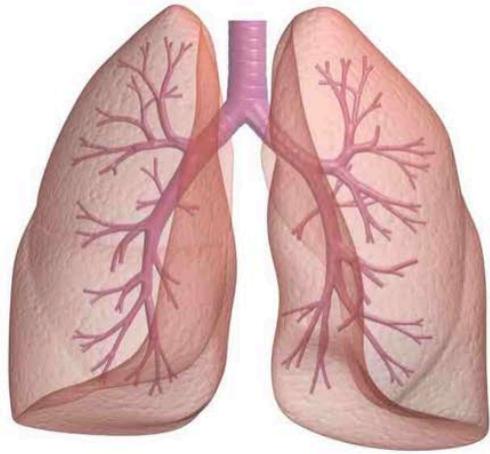
Ankylosing spondylitis



Psoriatic arthritis



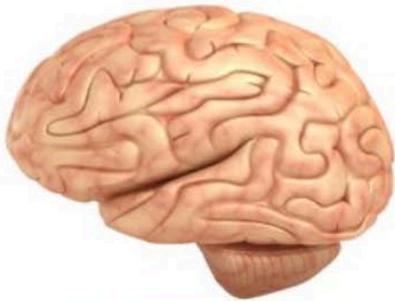
Arthritis as a systemic syndrome



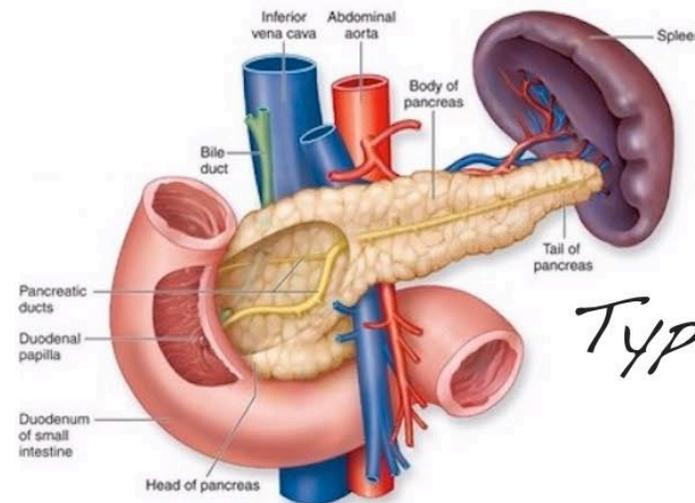
Chronic obstructive pulmonary disease



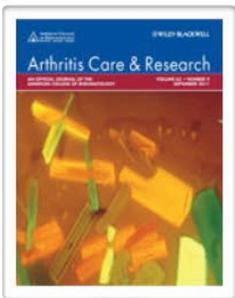
Cardiovascular diseases



Mood disorders



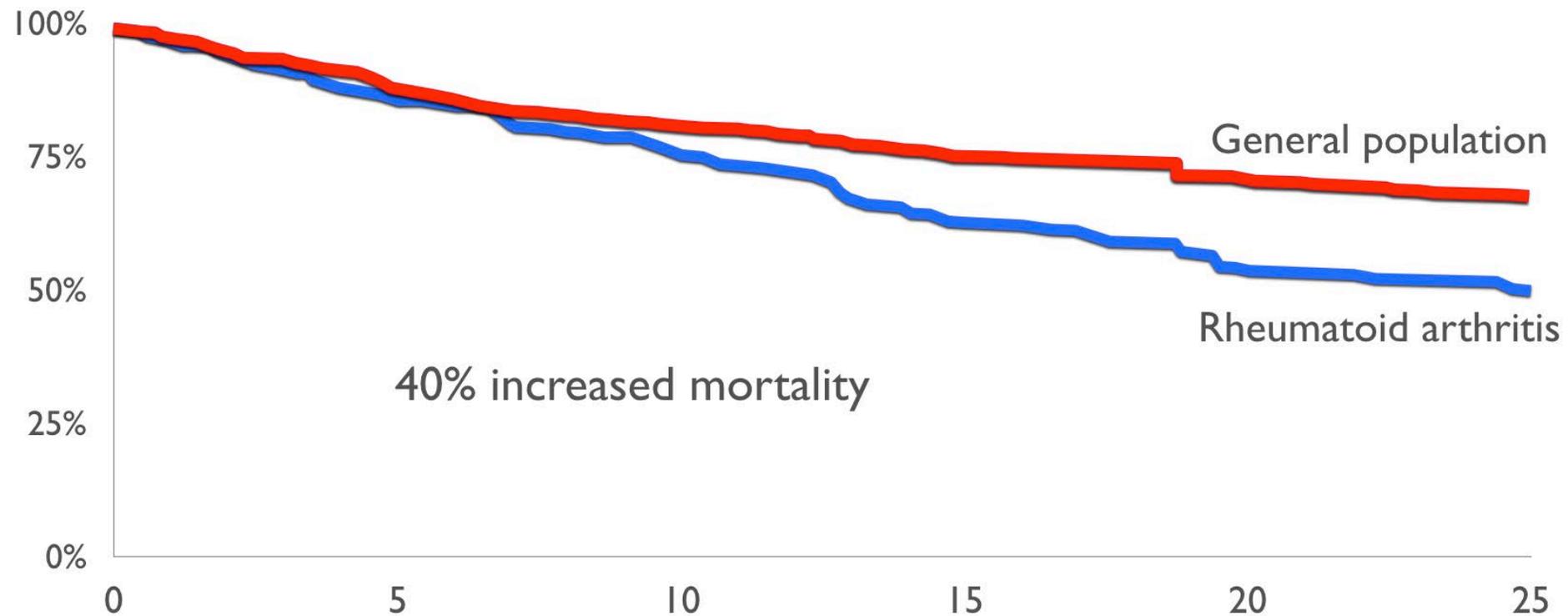
Type-2 diabetes mellitus



Excess Mortality Emerges After 10 Years in an Inception Cohort of Early Rheumatoid Arthritis

B. J. RADOVITS,¹ J. FRANSEN,¹ S. AL SHAMMA,¹ A. M. EIJSBOUTS,² P. L. C. M. VAN RIEL,¹ AND R. F. J. M. LAAN¹

Arthritis Care Res 2010

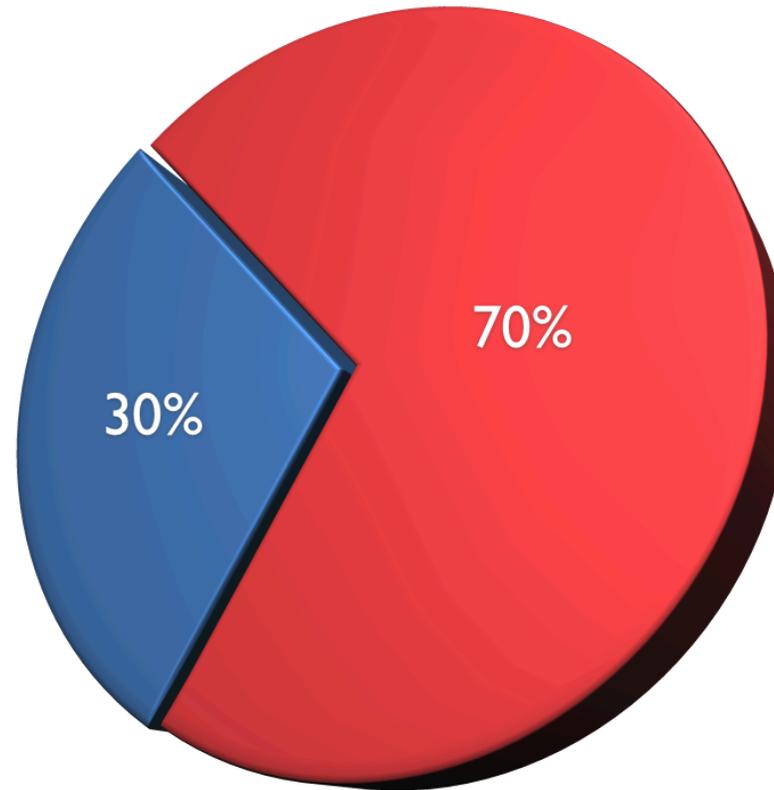


Costs of illness of arthritis

Direct costs

Healthcare costs for:
diagnosis
treatment
rehabilitation

Non-healthcare costs for:
transportation
household expenditures
relocating
property losses
informal cares of any kinds



Indirect costs

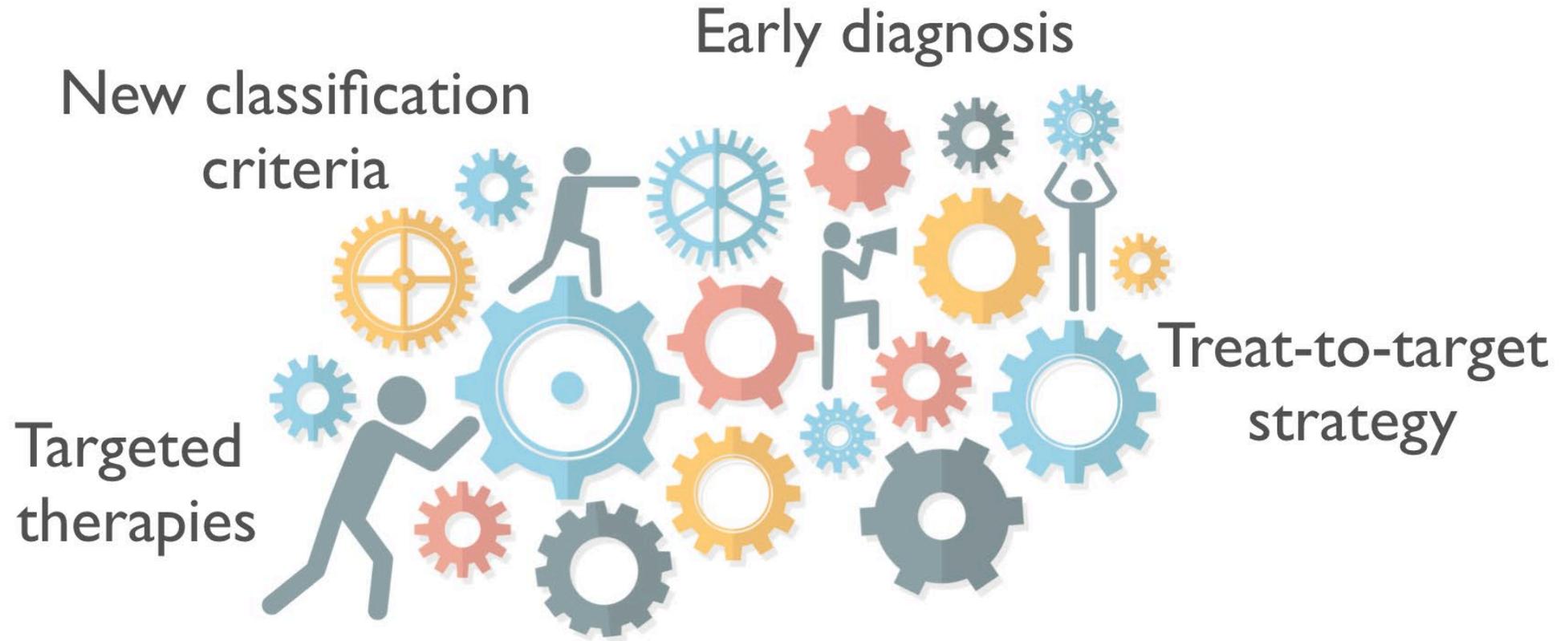
Expenses incurred from the cessation or reduction of work productivity as a result of the morbidity and mortality associated with a given disease

Talk composition

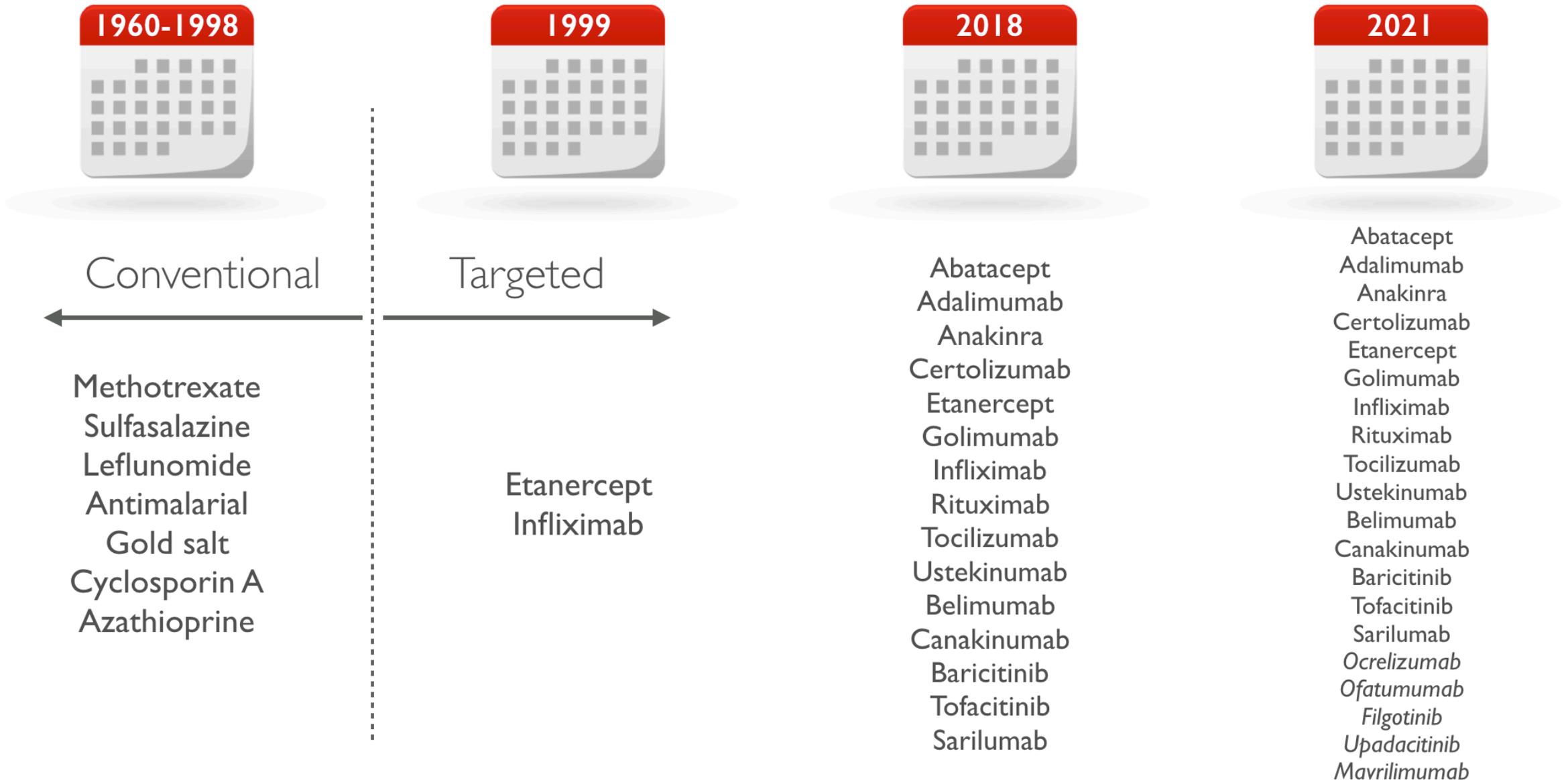
- ☑ Rheumatic diseases: overview
- ☑ **Treatment strategies in rheumatology**
- ☑ Biosimilar drugs for rheumatology
- ☑ What concerns?
- ☑ Role and positioning



The revolution of new millennium in rheumatology



The revolution of treatments in rheumatology



Conventional synthetic versus biotechnological drugs



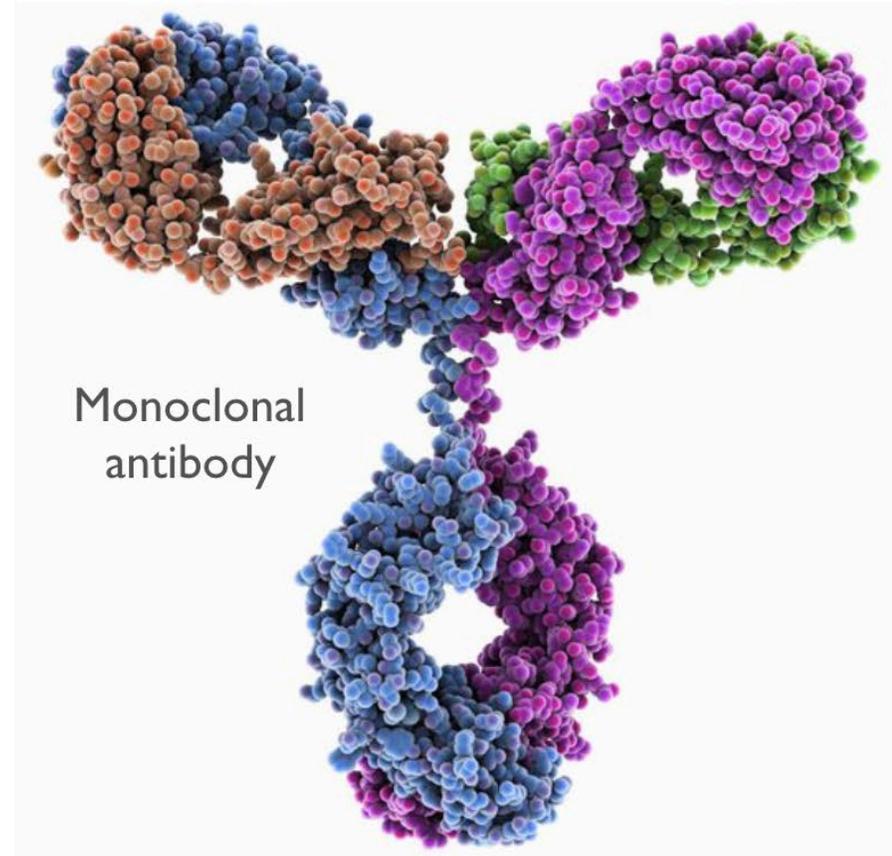
Methotrexate

Conventional synthetic molecules

- Chemical nature
- Small-medium size (100-1000 Dalt)

Targeted biological drugs

- Structure similar to autologous proteins
- Larger size (200.000 Dalton)



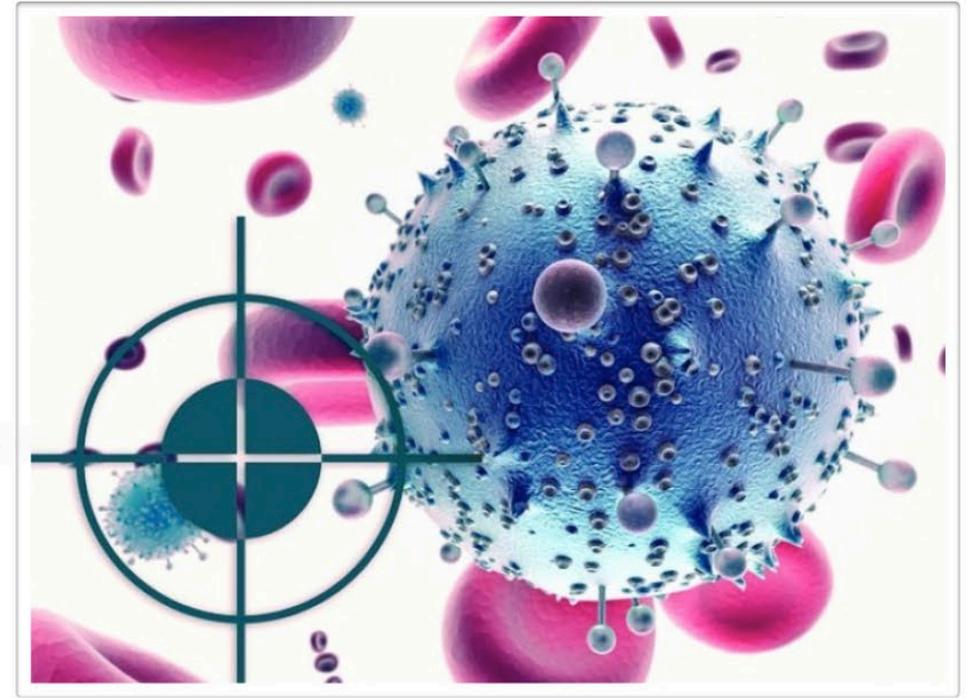
Monoclonal antibody

Conventional synthetic versus biotechnological drugs

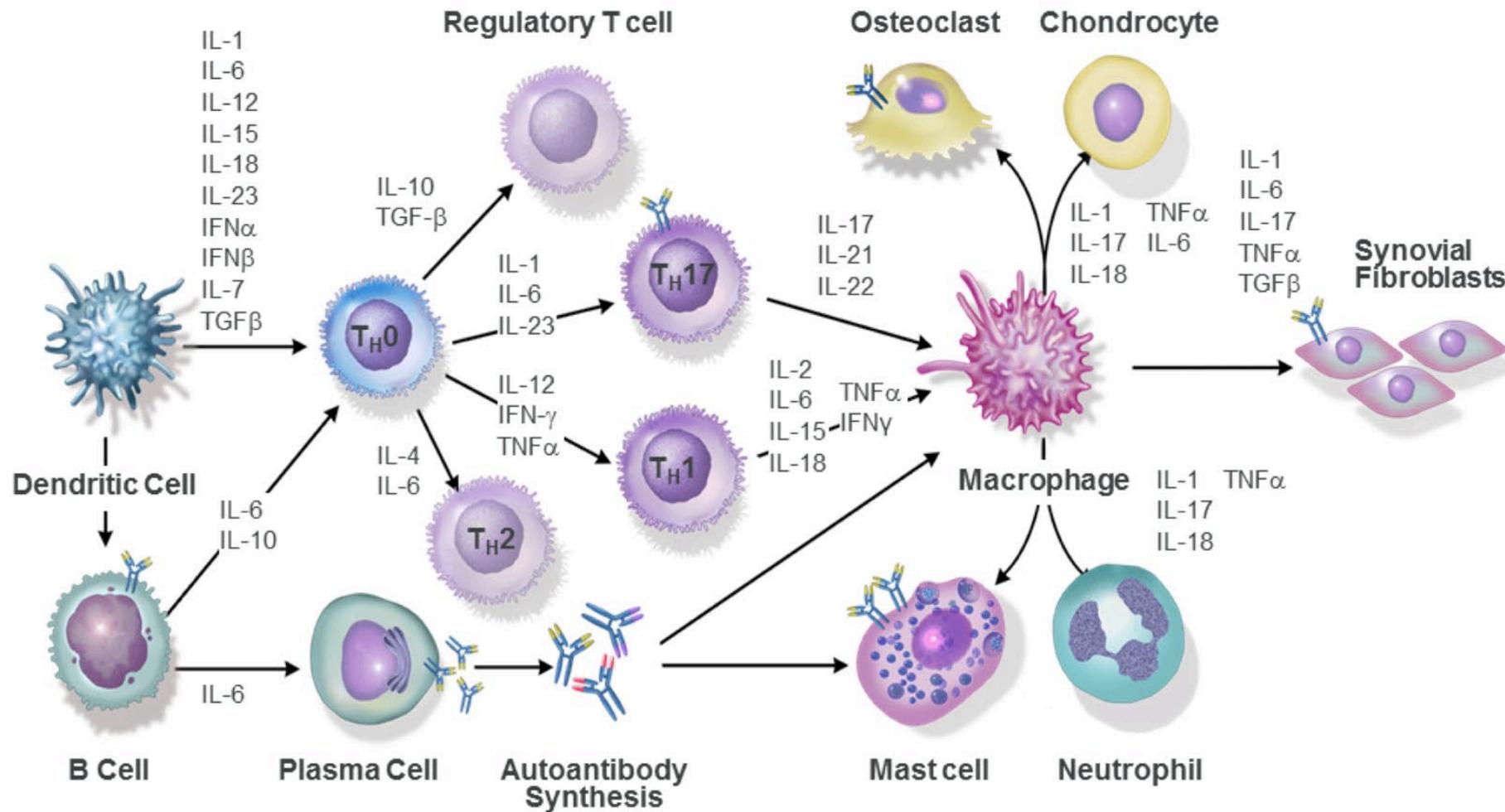
Conventional immunosuppressants



Targeted biotechnological drugs

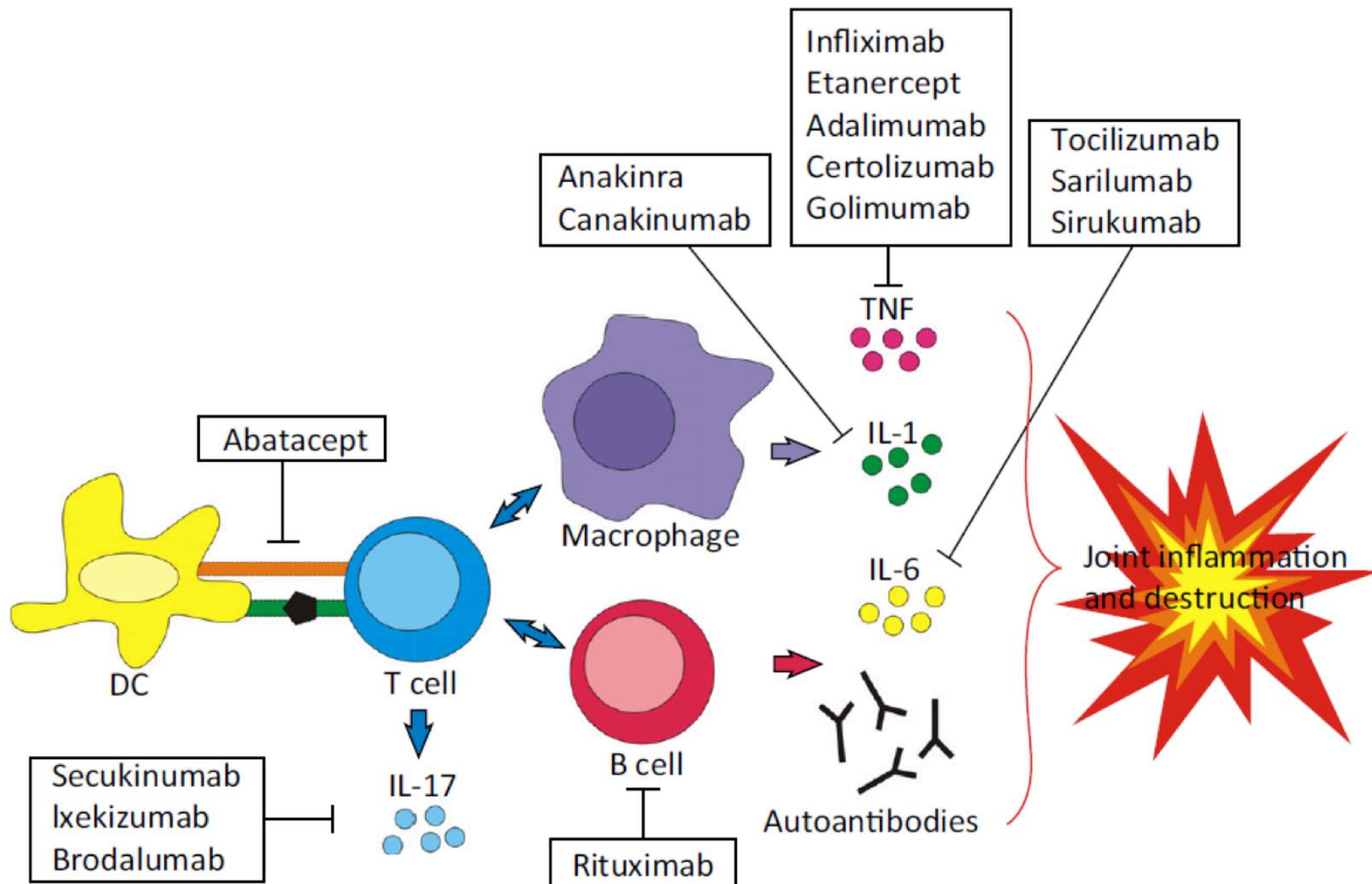


Actors involved in arthritis pathogenesis



McInnes IB et al. Nat Rev Immunol. 2007
 Smolen JS et al. Nat Rev Rheumatol. 2012
 McInnes IB et al. N Engl J Med. 2011

Available targeted therapies for the treatment of arthritis

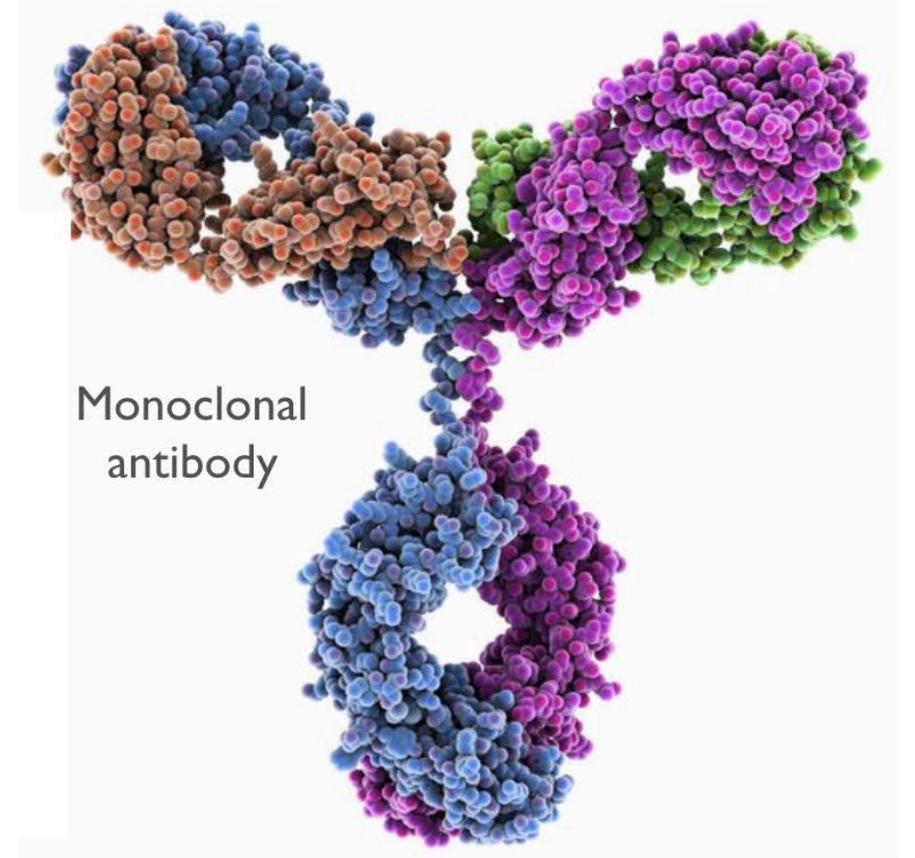


Different annual cost of drug class for arthritis



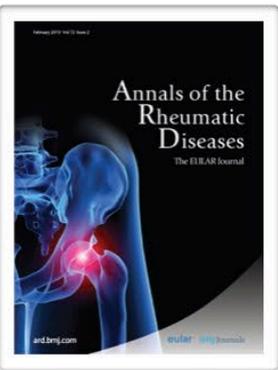
Methotrexate

500 €



Monoclonal antibody

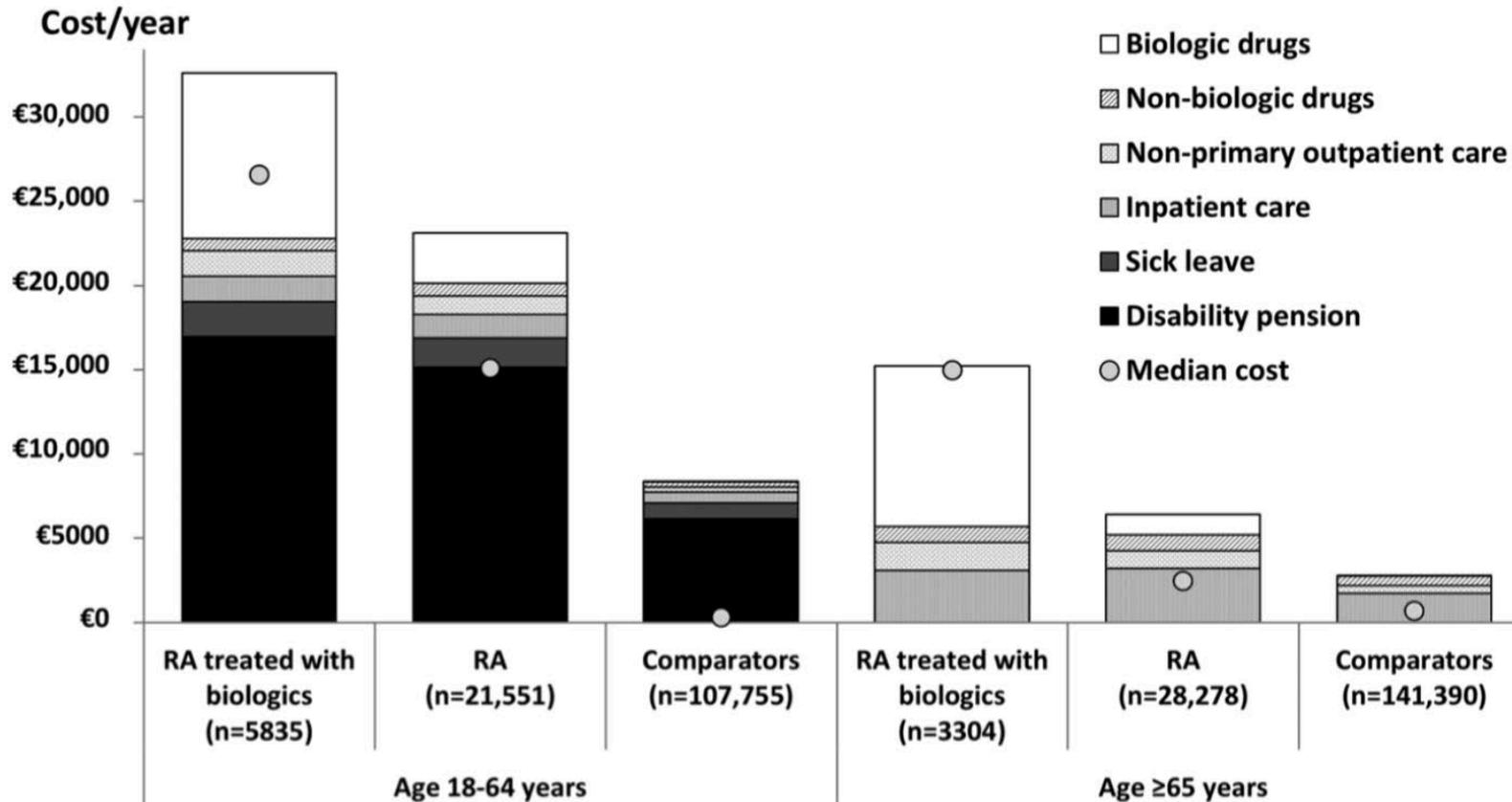
8,000-11,000 €

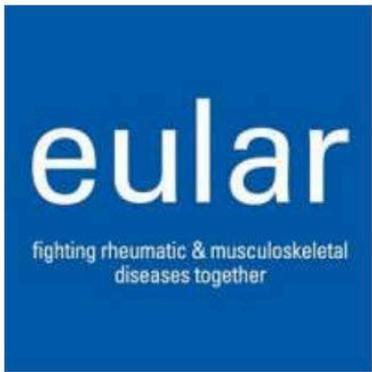


Costs for hospital care, drugs and lost work days in incident and prevalent rheumatoid arthritis: how large, and how are they distributed?

Jonas K Eriksson,¹ Kari Johansson,¹ Johan Askling,^{1,2} Martin Neovius¹

Ann Rheum Dis 2013





Recommended algorithm for the management of arthritis

1st line

Conventional drug
(mainly methotrexate)



2nd line

1st targeted drug

Based on
patient/disease
features

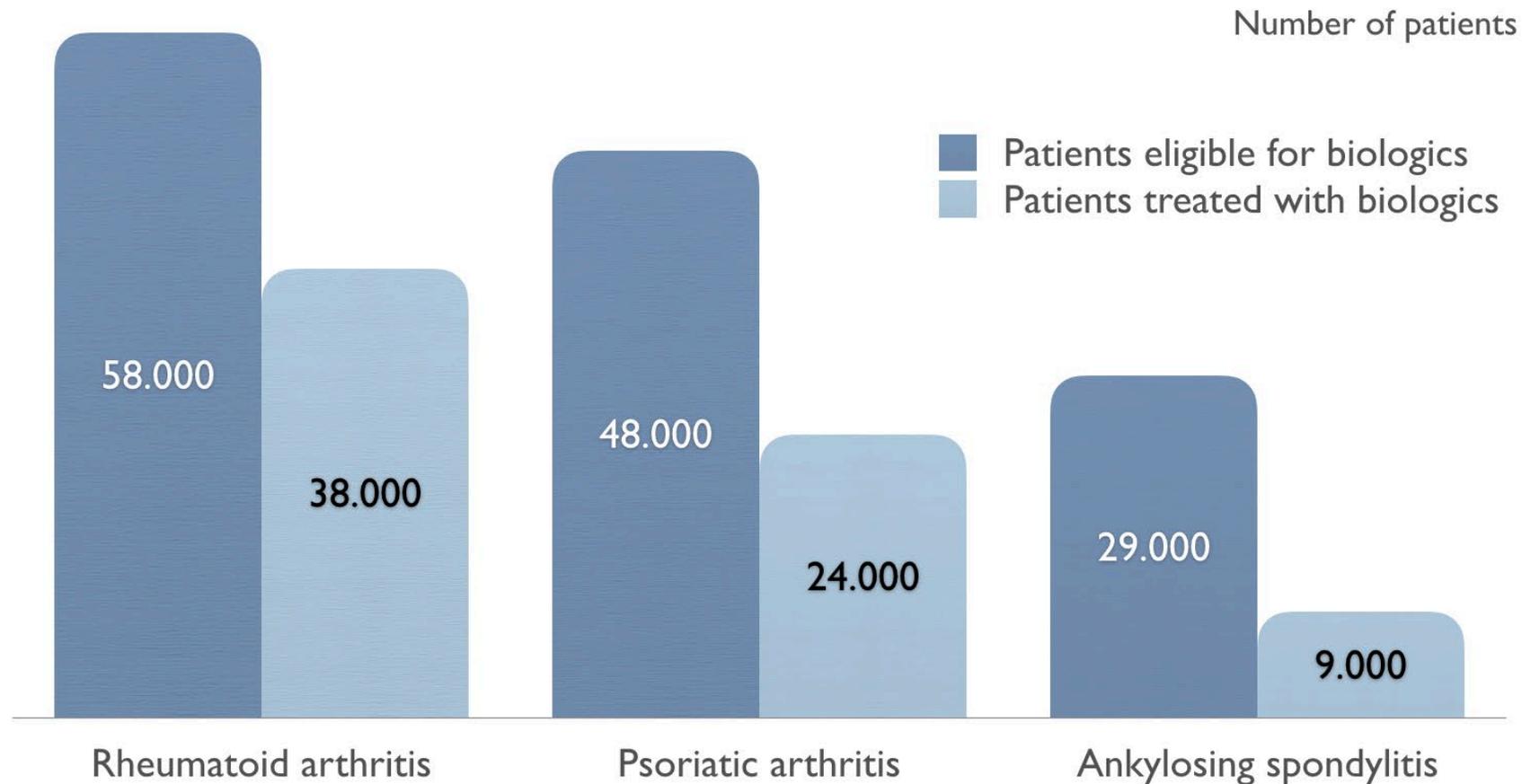


3rd line

2nd targeted drug

Based on
patient/disease
features

A significant proportion of Italian patients with arthritis are undertreated

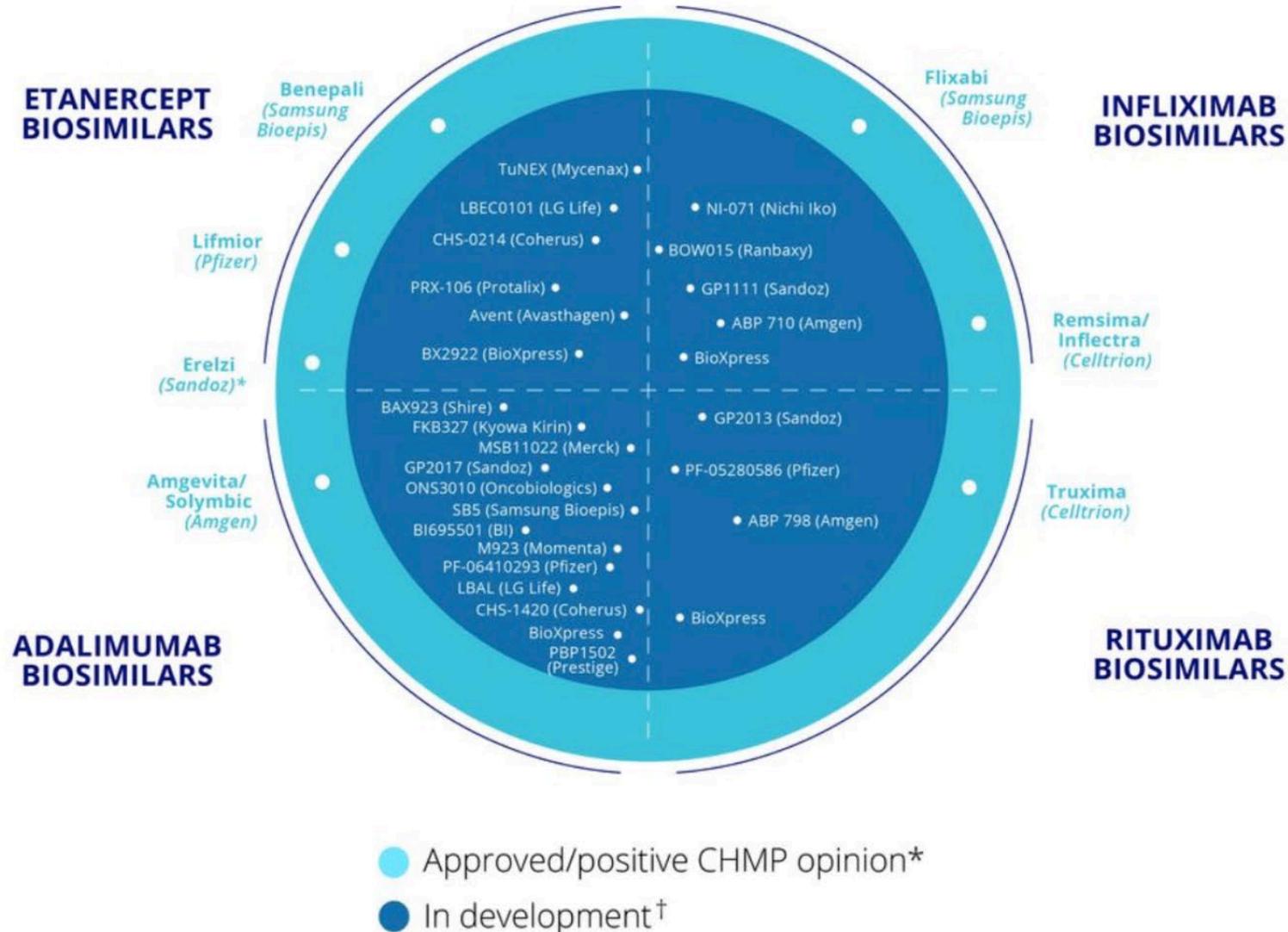


Talk composition

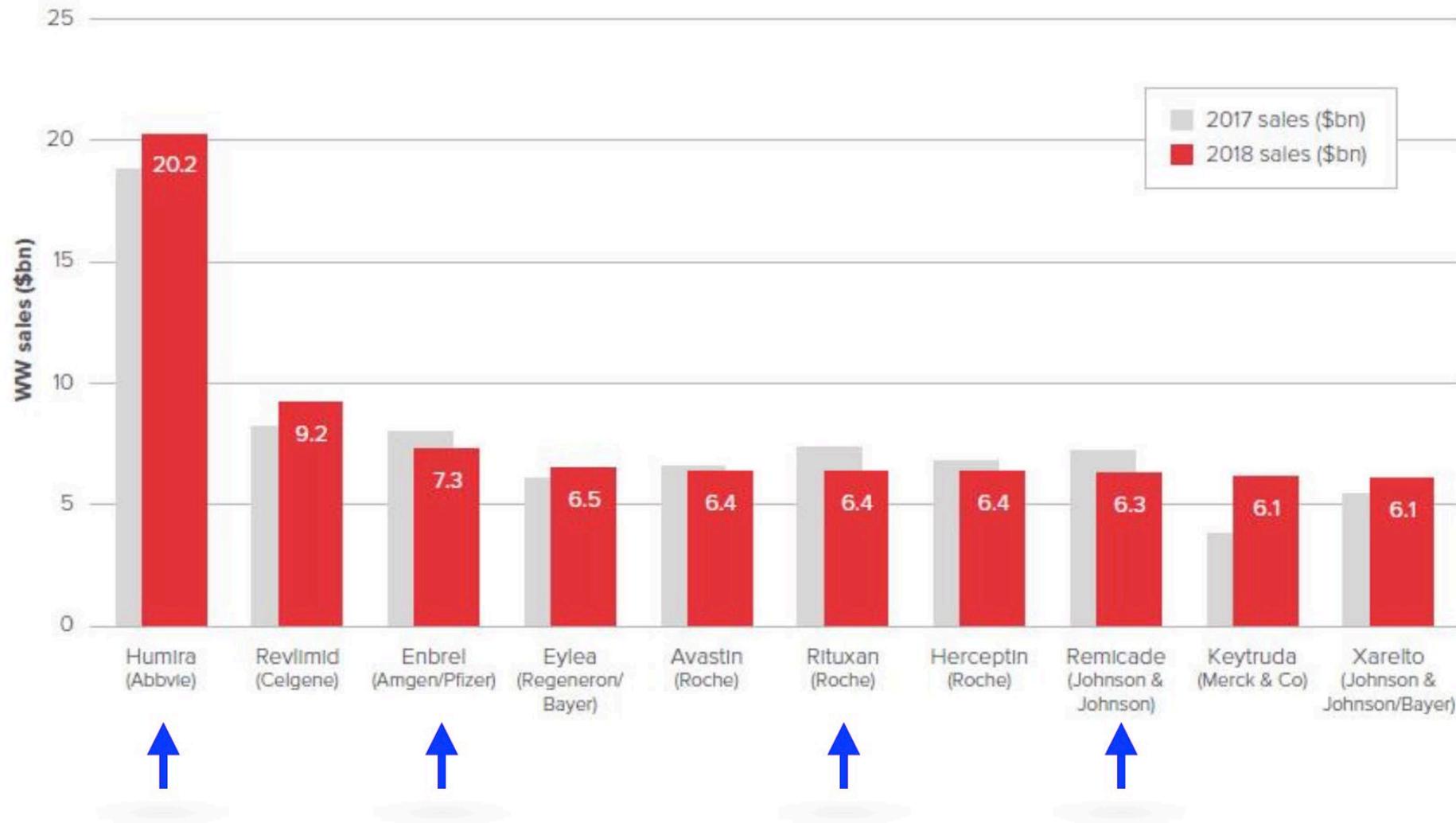
- Rheumatic diseases: overview
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The galaxy of biosimilar drugs approved or in the pipeline



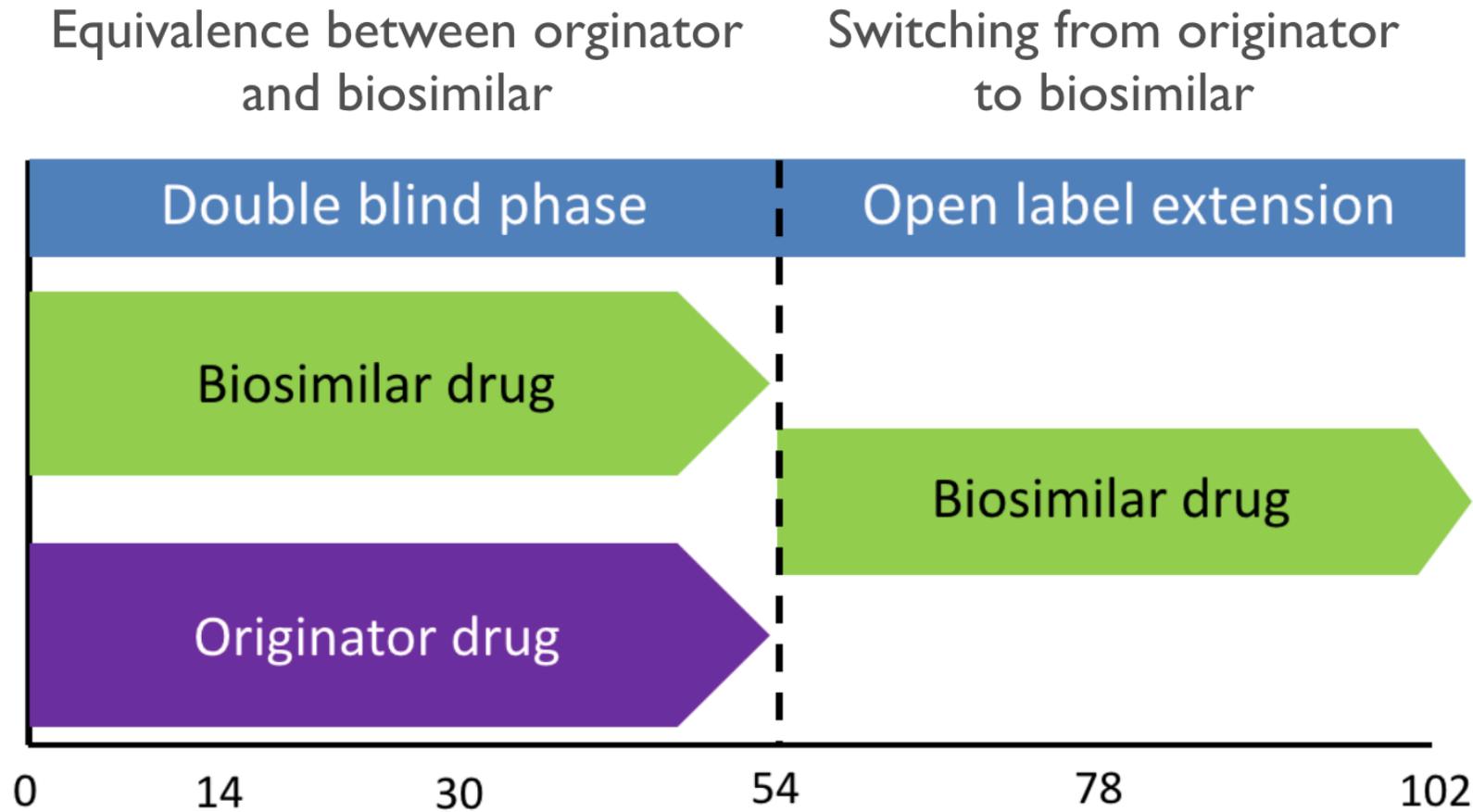
Top 10 drugs by 2018 sales

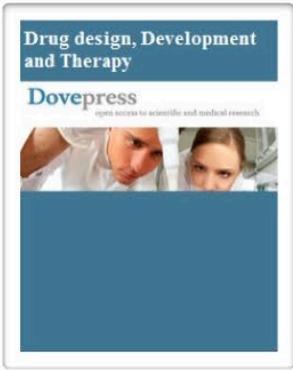


Requirements for monoclonal antibodies approval

		New biologic drugs	Biosimilars
■ Quality studies		✓	✓
■ Non-clinical studies	<i>In vitro studies</i>	✓	✓
	<i>In vivo studies</i>	✓	✓
■ Clinical studies	<i>Phase I</i>	Pharmacokinetics	✓
		Pharmacodynamics	✓
	<i>Phase II</i>	✓	
	<i>Phase III</i>	Clinical efficacy	✓
Safety profile		✓	✓
■ Pharmacovigilance		✓	✓

Comparability phase-III trials: study design





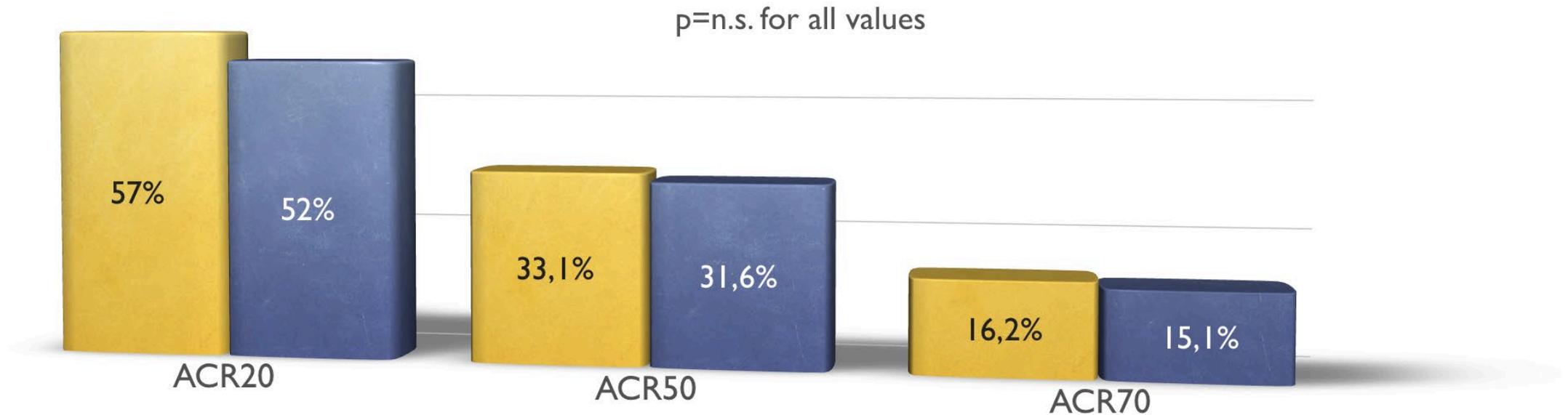
A review of the literature analyzing benefits and concerns of infliximab biosimilar CT-P13 for the treatment of rheumatologic diseases: focus on interchangeability

Andrea Becciolini,¹ Maria Gabriella Raimondo,² Chiara Crotti,² Elena Agape,² Martina Biggioggero,² Ennio Giulio Favalli¹

Drug Des Develop Ther 2017

% of pts achieving ACR response

Infliximab biosimilar (n=125)
Infliximab originator (n=125)



Biosimilar drugs approved by EMA for rheumatology

 **INFLECTRA**[®]
INFLIXIMAB

 **Benepali**[®]
Etanercept

 **Truxima**[®]
Rituximab

 **Imraldi**[®]
Adalimumab

 **Remsima**[®]
infliximab

 **Erelzi**[™]
etanercept

 **Rixathon**[™]
rituximab

 **AMJEVITA**[™]
(adalimumab-atto) injection
40mg/0.8ml
20mg/0.4ml

 **Flixabi**[®]
Infliximab

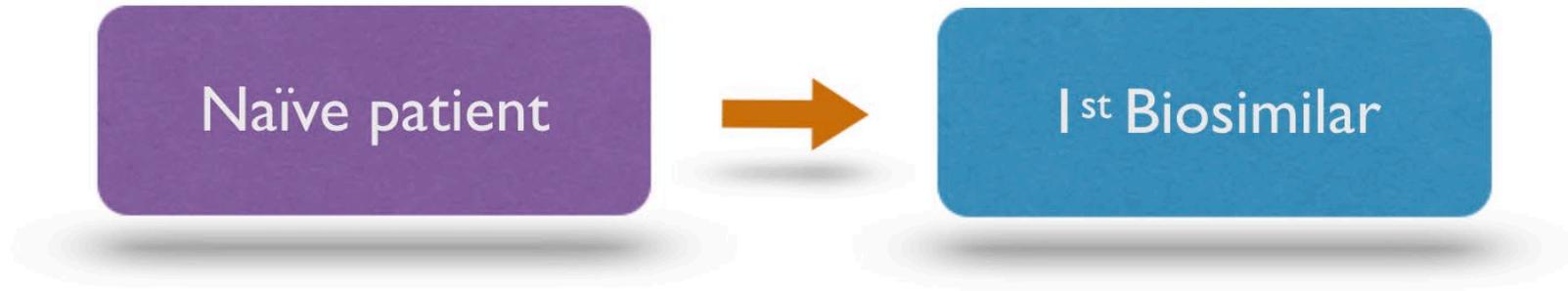
 **CYLTEZO**[™]
(adalimumab-adbm)
Injection

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Originator or biosimilar?



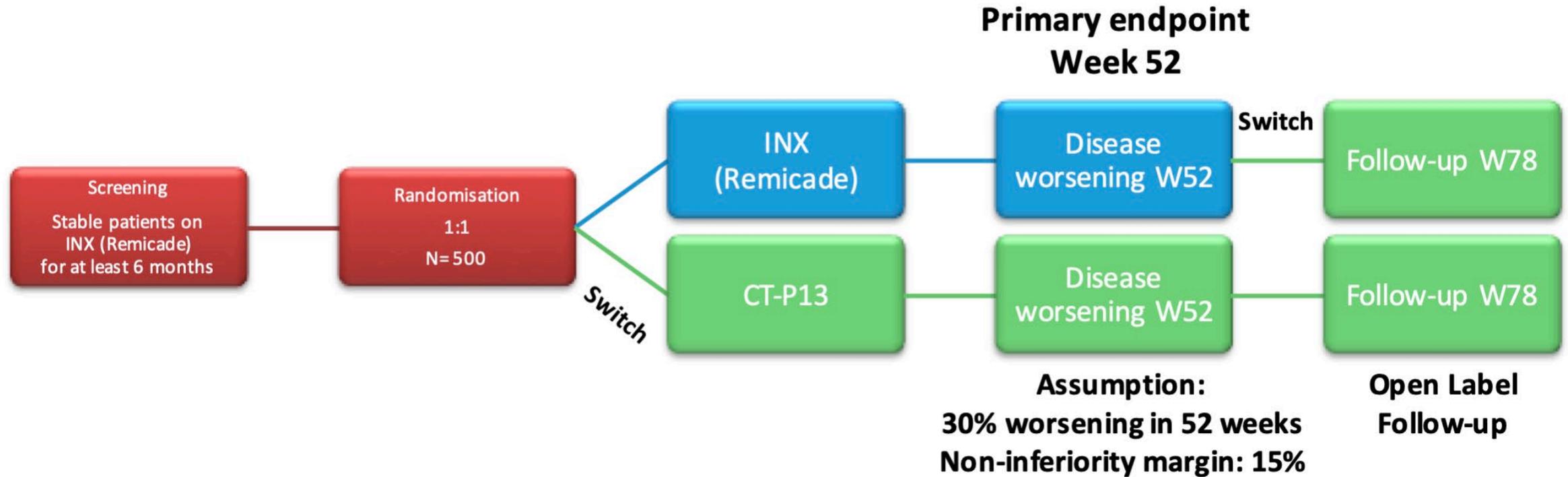


Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial

Kristin K Jørgensen, Inge C Olsen*, Guro L Goll*, Merete Lorentzen*, Nils Bolstad, Espen A Haavardsholm, Knut E A Lundin, Cato Mørkt†, Jørgen Jahnsen†, Tore K Kvient†, on behalf of the NOR-SWITCH study group*



Lancet, 2017



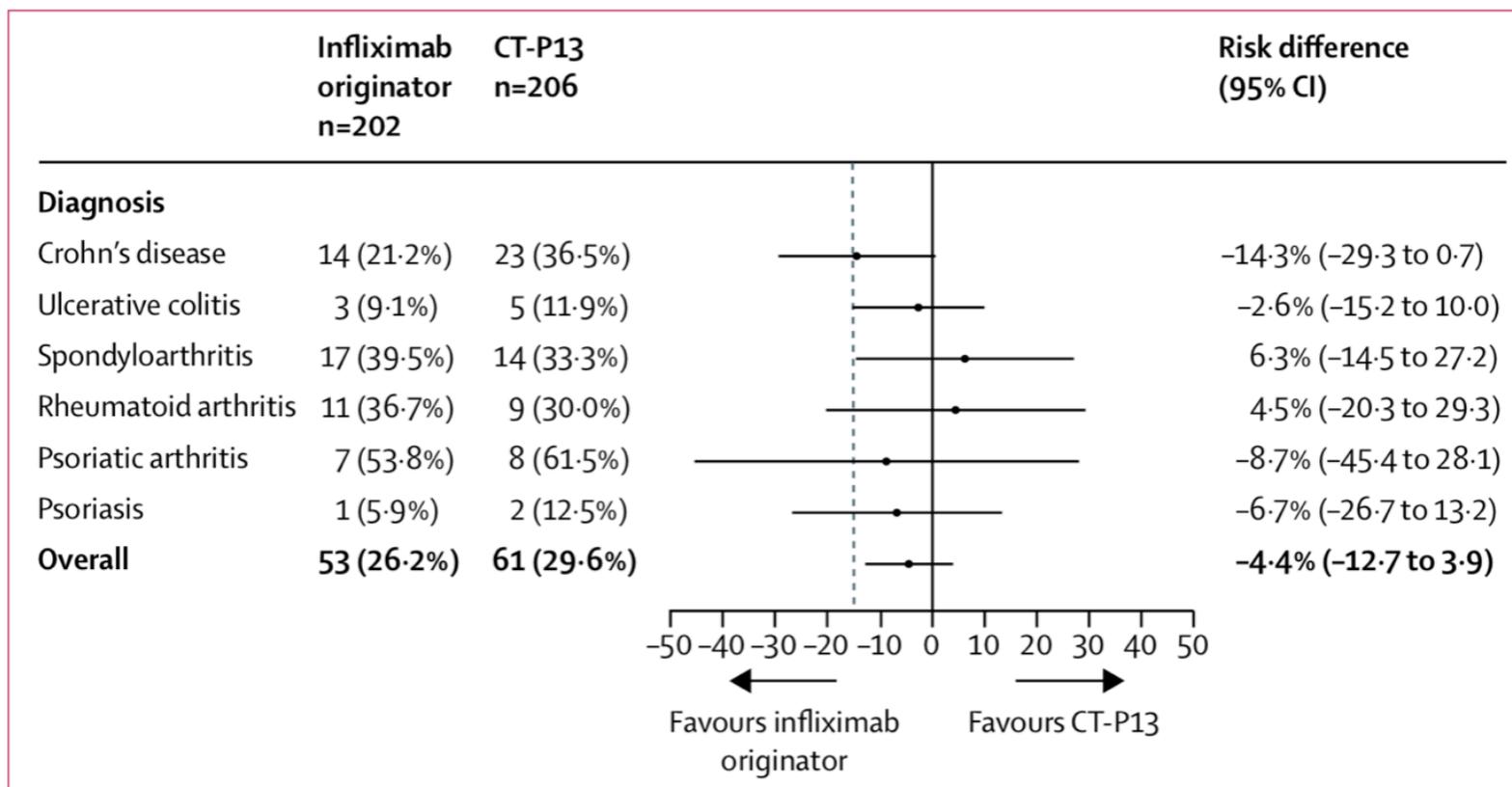


Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial



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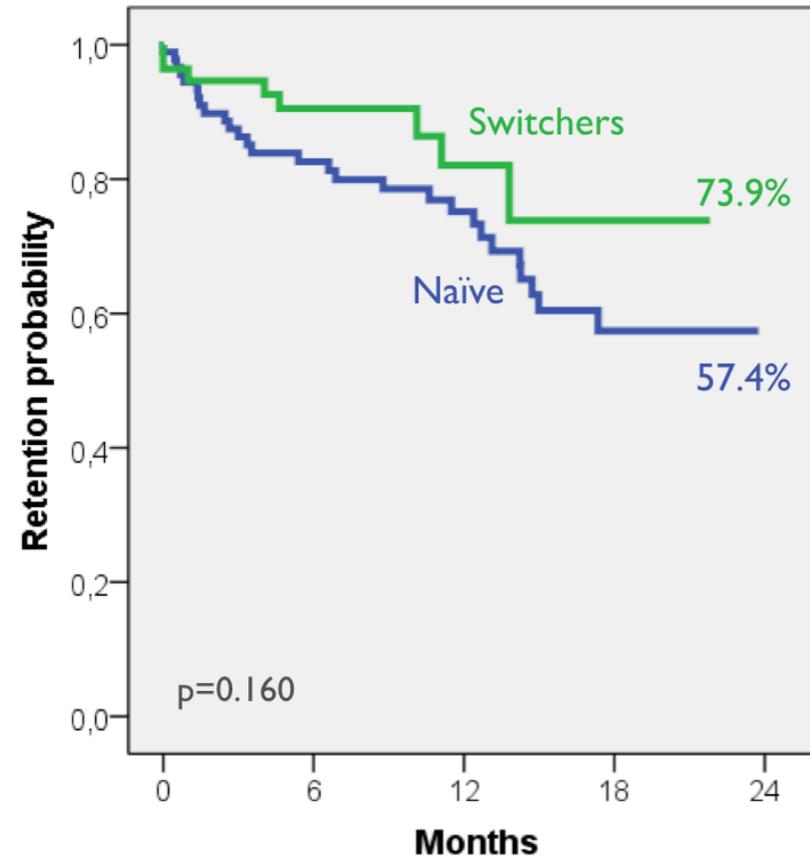
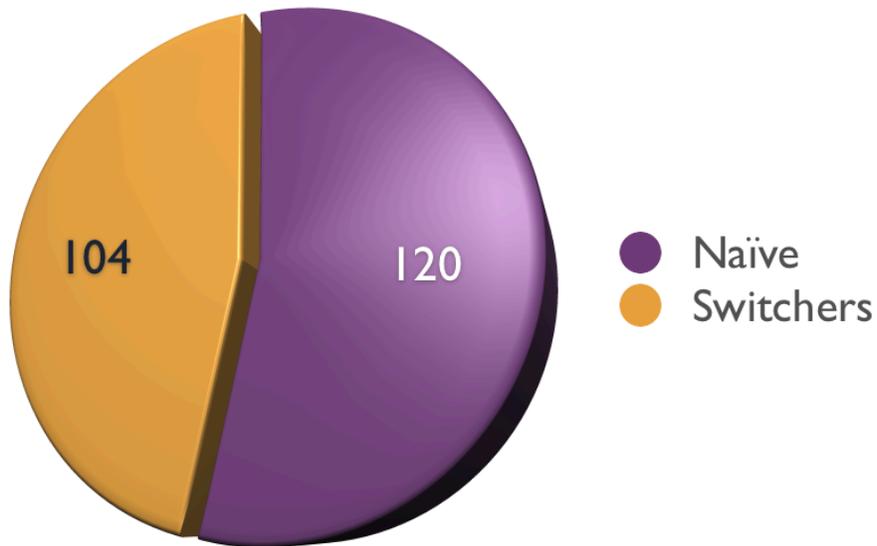


L'impiego di Infliximab biosimilare nella pratica clinica: analisi retrospettiva di una casistica multicentrica italiana



A. Becciolini, E.G. Favalli, F. Iannone, M. Sebastiani, P. Sarzi Puttini, M. Galeazzi, C. Realmuto,
E. Fusaro, R. Ramonda, M. Facchinetti, P. Ostuni, F. Salaffi, E. Silvagni, M. Govoni, R. Caporali,
G.F. Bagnato, F. Dascanio, G. Lapadula

SIR Congress, 2017



I malati reumatici denunciano: «Non si possono imporre cambi di cura ai malati solo per risparmiare»

«Non si può risparmiare sulla salute dei pazienti. La scelta del farmaco va sempre svolta in accordo con il malato e non può essere dettata solo da questioni di budget». È questo il principale messaggio contenuto in una lettera che l'Associazione Nazionale Malati Reumatici Onlus (ANMAR) ha inviato al Presidente della Repubblica Sergio Mattarella.

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Biosimilars offer a significant relief of strained healthcare budgets

20%-30%

Assumed Discount of Biosimilar to Originators

15%

Average Biosimilar Penetration (€ volume)

€12-33 Billion

2007-2020 Estimated Savings Potential from 16 Marketed Biosimilars in the EU

**FUTURE
POTENTIAL**

20

Biosimilars Marketed Today

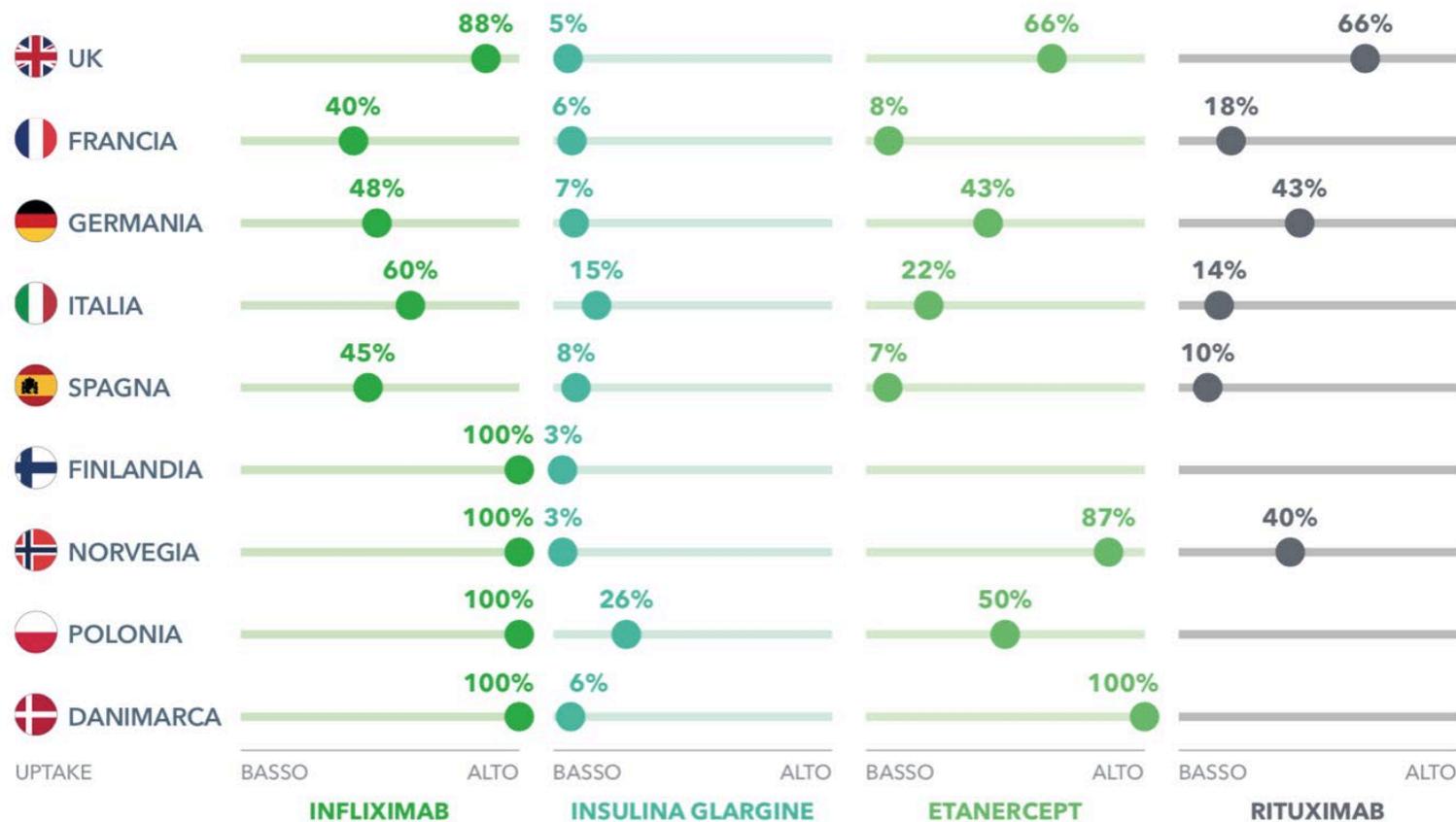
109

Biosimilars in European Clinical Pipelines

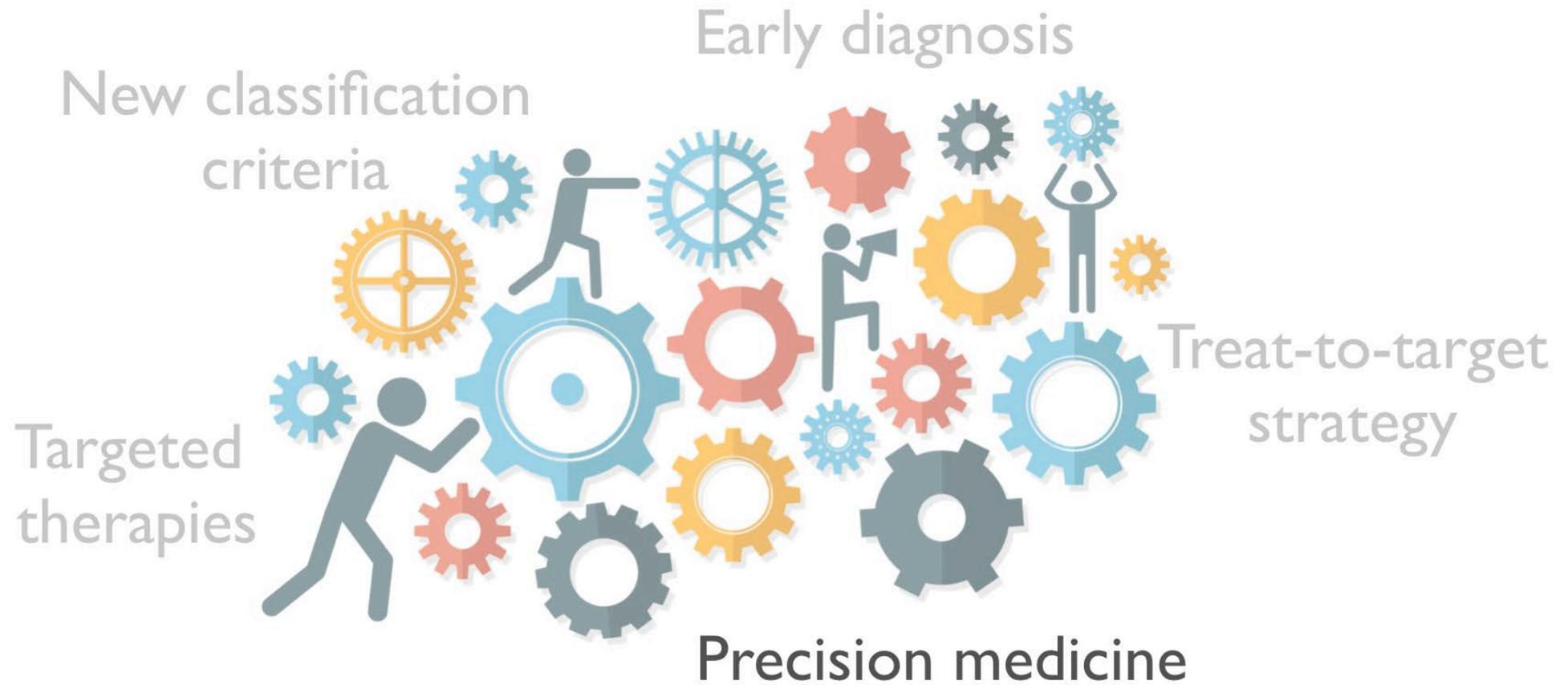


FARMACI BIOLOGICI E BIOSIMILARI

Penetrazione dei biosimilari per paese: giorni di trattamento per biosimilare.



The revolution of new millennium in rheumatology



All of UsSM Research Program



WHAT IS IT?

Precision medicine is a groundbreaking approach to disease prevention and treatment based on people's individual differences in environment, genes and lifestyle.

The *All of Us* Research Program will lay the foundation for using this approach in **clinical practice**.

WHAT ARE THE GOALS?

Engage a group of **1 million or more U.S. research participants** who will share biological samples, genetic data and diet/lifestyle information, all linked to their electronic health records. This data will allow researchers to develop more precise treatments for **many diseases and conditions**.

Pioneer a new model of research that emphasizes **engaged research participants, responsible data sharing and privacy protection**.

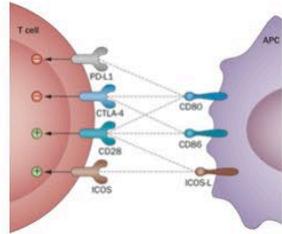


Research based on the cohort data will:

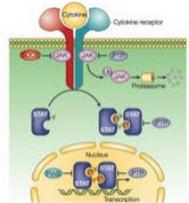
- Lay **scientific foundation** for precision medicine
- Help identify new ways to **treat and prevent disease**
- Test whether **mobile devices**, such as phones and tablets, can encourage healthy behaviors
- Help develop the **right drug** for the **right person** at the **right dose**

The best targeted agent for the right patient

Co-stimulation



Abatacept

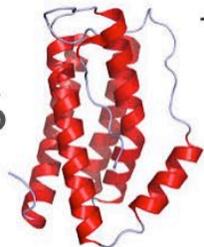


Baricitinib

Tofacitinib

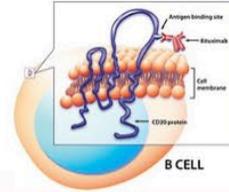
JAK

IL-6



Tocilizumab

Sarilumab

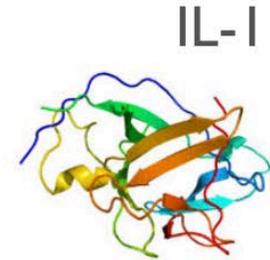


B-cell depletion

Rituximab(*)



Anakinra

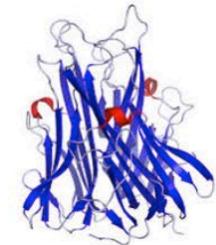


Infliximab

Adalimumab

Etanercept

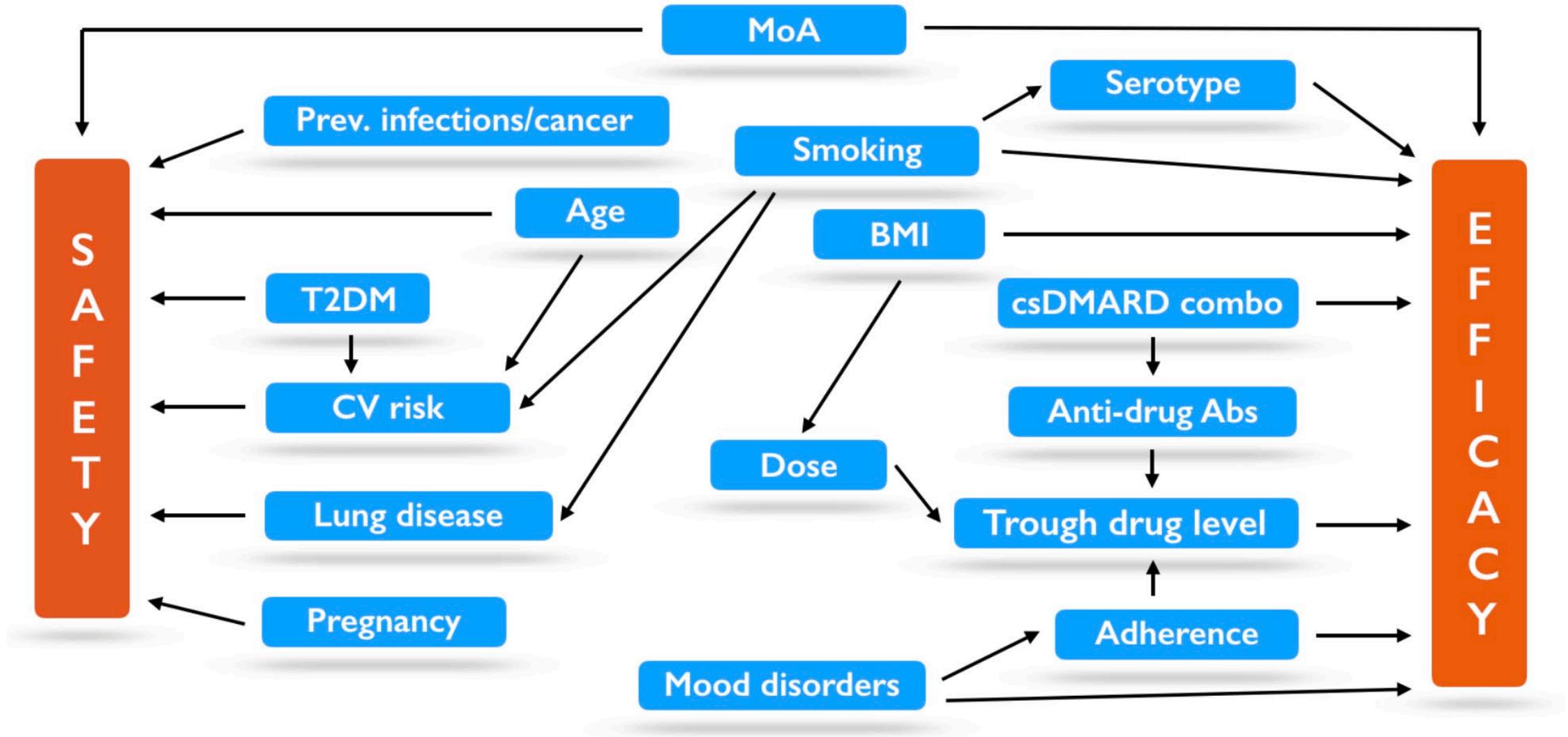
Golimumab



TNFα

Certolizumab pegol

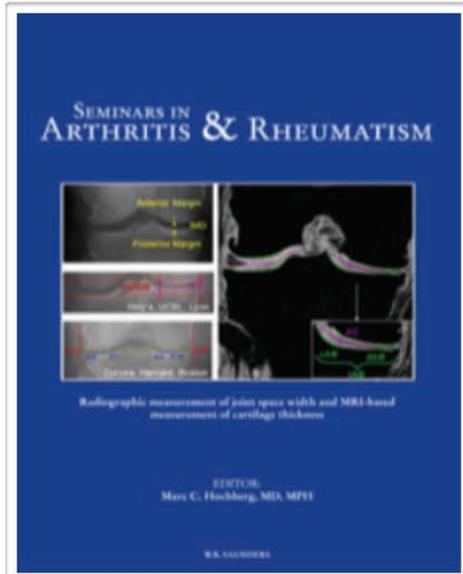
Drivers for the personalized choice of biologic drugs



Tailored first-line biologic therapy in patients with rheumatoid arthritis, spondyloarthritis, and psoriatic arthritis

Fabrizio Cantini^{a,*}, Laura Niccoli^a, Carlotta Nannini^a, Emanuele Cassarà^a, Olga Kaloudi^a, Ennio Giulio Favalli^b, Andrea Becciolini^b, Martina Biggioggero^b, Maurizio Benucci^c, Francesca Li Gobbi^c, Valentina Grossi^d, Maria Infantino^d, Francesca Meacci^d, Mariangela Manfredi^d, Serena Guiducci^e, Silvia Bellando-Randone^e, Marco Matucci-Cerinic^e, Rosario Foti^f, Marcella Di Gangi^f, Marta Mosca^g, Chiara Tani^g, Fabrizio Palmieri^h, Delia Golettiⁱ, On behalf of the Italian board for the Tailored Biologic therapy (ITABIO)¹

Semin Arthritis Rheum 2016

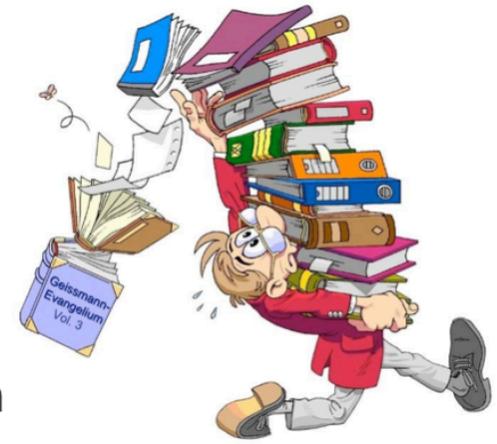


Second-line biologic therapy optimization in rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis

Fabrizio Cantini, MD^{a,*1}, Laura Niccoli, MD^{a,1}, Carlotta Nannini, MD^{a,1}, Emanuele Cassarà, MD^{a,1}, Olga Kaloudi, MD^a, Ennio Giulio Favalli, MD^{b,2}, Andrea Becciolini, MD^b, Maurizio Benucci, MD^{c,3}, Francesca Li Gobbi, MD^c, Serena Guiducci, MD^{d,4}, Rosario Foti, MD^{e,5}, Marta Mosca, MD^{f,6}, Delia Goletti, MD^{g,7}

Semin Arthritis Rheum 2017

Take home messages



- Le **malattie reumatologiche** colpiscono un **numero elevato di persone** e, se non adeguatamente trattate, possono comportare gravi conseguenze in termini di **disabilità**
- L'introduzione dei **farmaci targeted (biologici e non)** ha sensibilmente migliorato l'**outcome a breve e lungo termine** dei pazienti reumatici, riducendo notevolmente il peso dei **costi indiretti di malattia**
- I **farmaci biosimilari** rappresentano un'opportunità per abbattere i **costi di gestione** dei pazienti con malattie reumatologiche
- L'esistenza di farmaci simili a basso costo non deve essere lesiva della **libertà prescrittiva** del reumatologo di scegliere la **miglior terapia** per il singolo individuo, secondo il concetto di **precision medicine**