Biothérapies et risque infectieux

Le poumon

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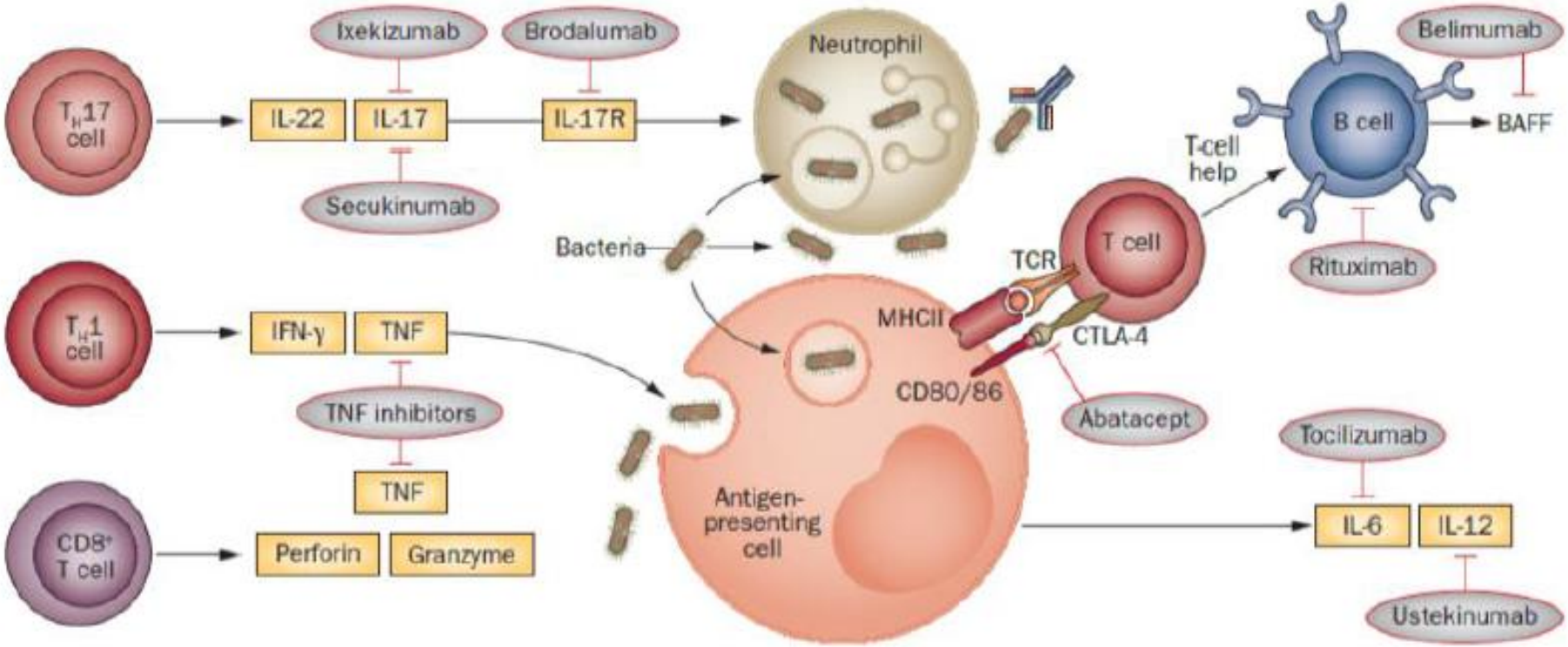
Les biothérapies: une multitude de cibles…
Une multitude d'effets secondaires



Boyman, Nature Review Rheumatol 2014

Anti-TNFα et tuberculose:
Le cas d'école

The New England Journal of Medicine

TUBERCULOSIS ASSOCIATED WITH INFLIXIMAB, A TUMOR NECROSIS FACTOR α–NEUTRALIZING AGENT

JOSEPH KEANE, M.D., SHARON GERSHON, PHARM.D., ROBERT P. WISE, M.D., M.P.H., ELIZABETH MIRABILE-LEVENS, M.D., JOHN KASZNICA, M.D., WILLIAM D. SCHWIETERMAN, M.D., JEFFREY N. SIEGEL, M.D., AND M. MILES BRAUN, M.D., M.P.H.

2001

- 70 cas (USA et Europe)
- Age médian: 53 ans
- délai médian au Dg: 12 sem

- Forme pulmonaire: 31%
- Extra-pulmonaire: 33%
- Disséminée: 42%

- Contage récent: 3%

- Incidence (PR):
- 24,4 cas/100000 sur 1 an
- Vs 6,2 cas/100000/an

- 12 décès (4 imputables)

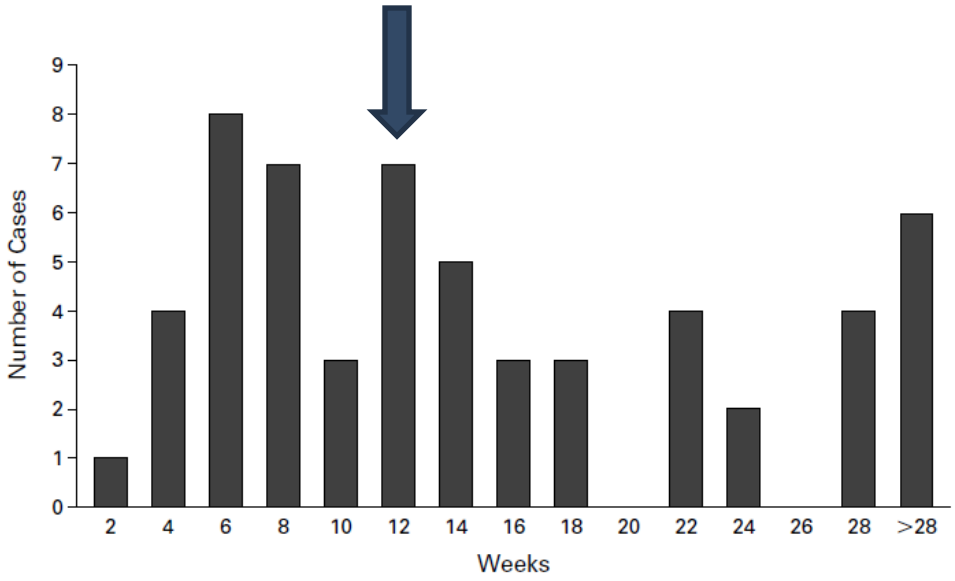
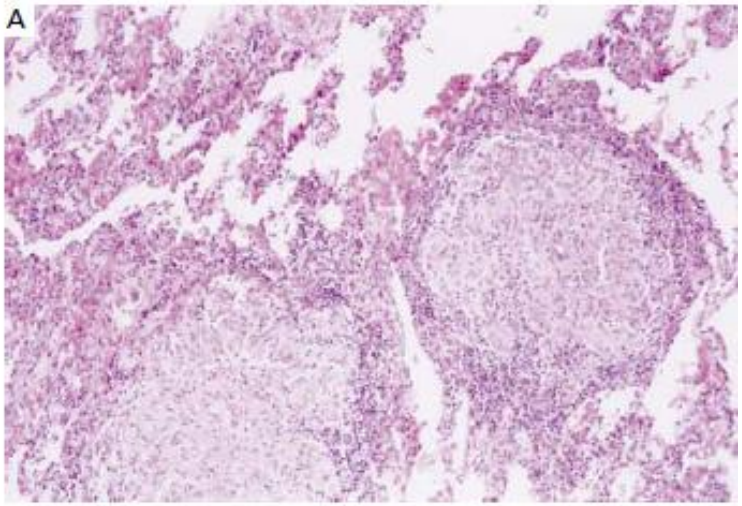
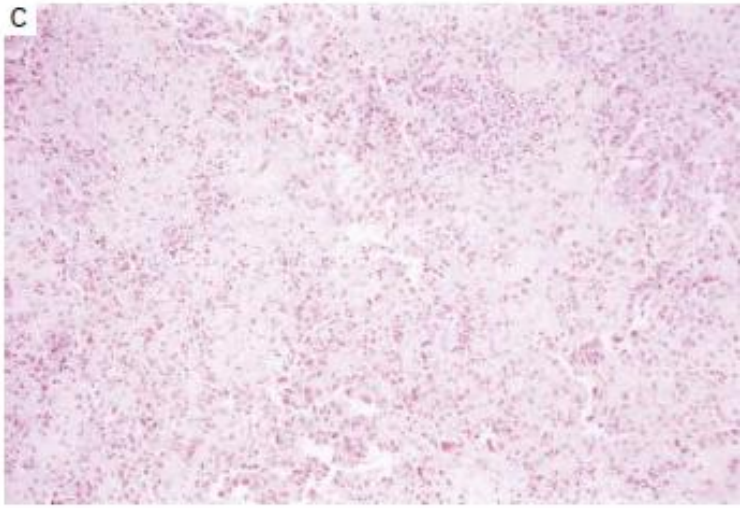


Figure 1. Time from the Initiation of Infliximab Therapy to the Diagnosis of Tuberculosis. Data were available for 57 patients, most of whom had received monthly infusions of infliximab.

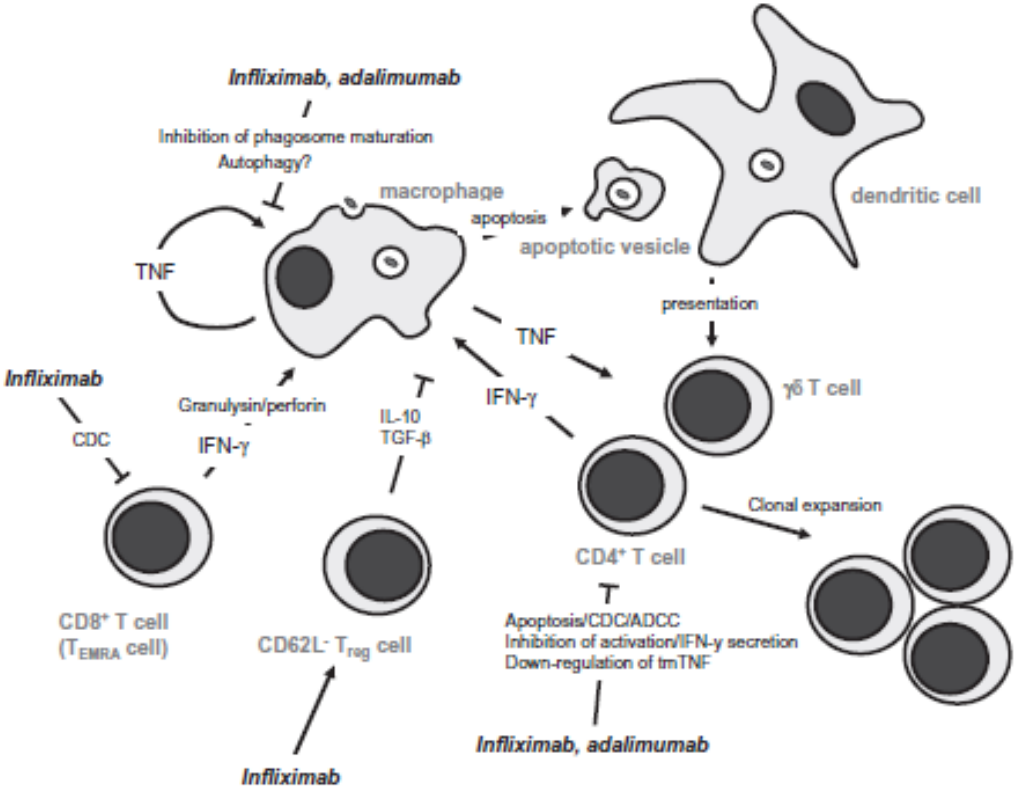
Anti-TNFα et tuberculose



TB + Infliximab -

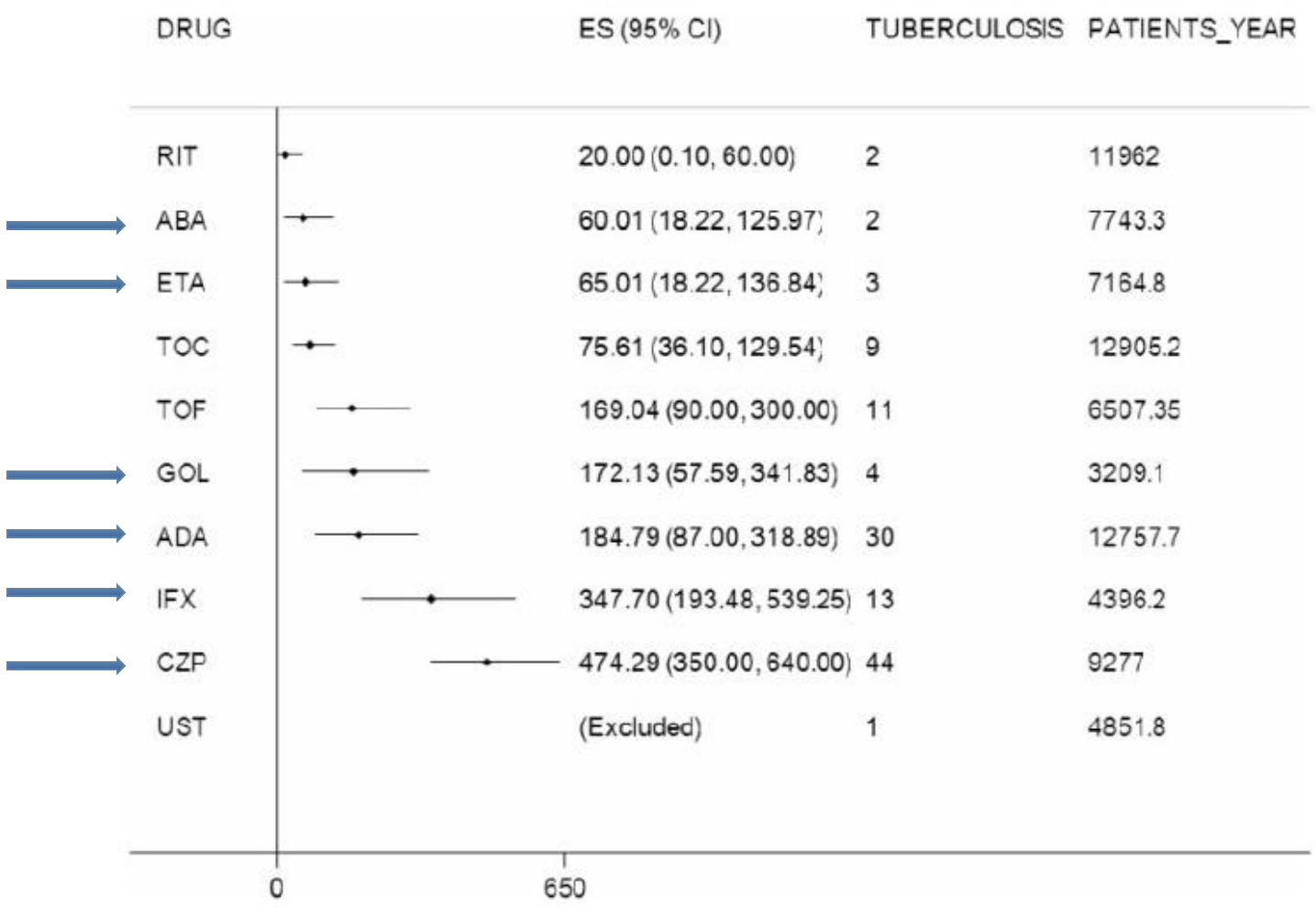


TB + Infliximab +



Anti-TNFα et tuberculose

FIG. 3 Meta-analysis of incidence rates by treatment of long-term extension studies

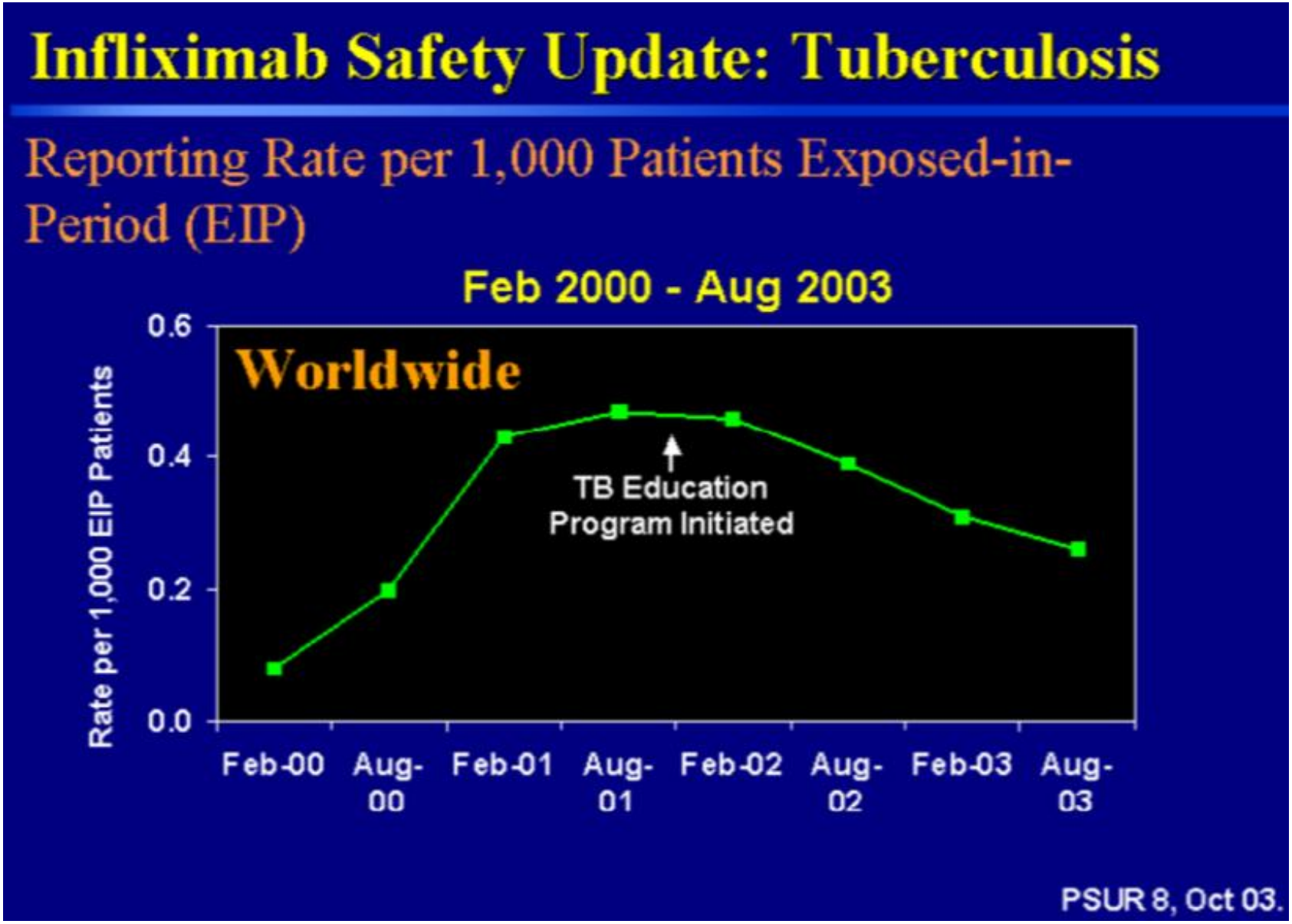


ES: incidence rate per 100 000 patient-years; ABA: abatacept; ETA: etanercept; TOC: tocilizumab; TOF: tofacitinib; GOL: golimumab; ADA: adalimumab; IFX: infliximab; CZP: certolizumab; UST: ustekinumab; RIT: rituximab.

Souto, Rheumatology 2014

Anti-TNFα et tuberculose

Anti-TNFα et tuberculose



Il n’y a pas que la tuberculose…

Il n'y a pas que la tuberculose…

CHEST

Original Research

CHEST INFECTIONS

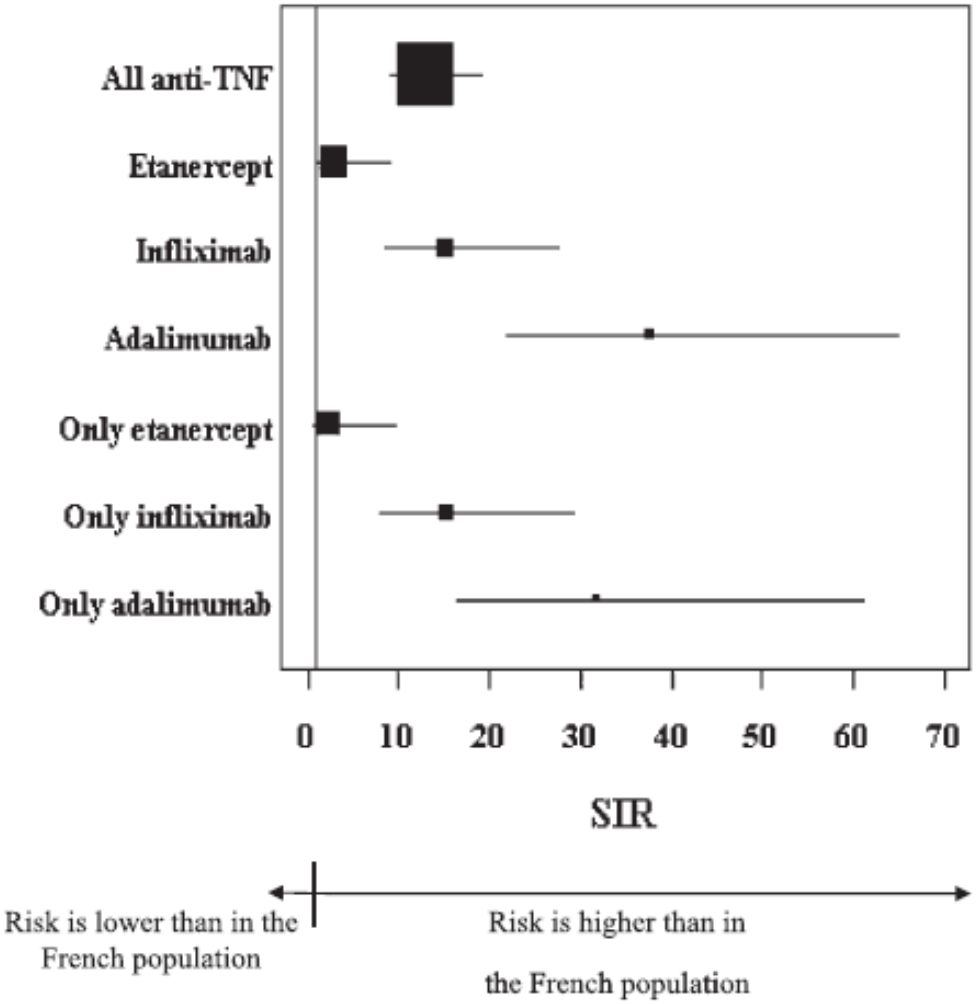
Incidence and Risk Factors of *Legionella pneumophila* Pneumonia During Anti-Tumor Necrosis Factor Therapy

A Prospective French Study

*Fanny Lanternier, MD; Florence Tubach, MD, PhD; Philppe Ravaud, MD, PhD; Dominique Salmon, MD, PhD; Pierre Dellamonica, MD, PhD; Stephane Bretagne, MD, PhD; Marie Couret, MD; Beatrice Bouvard, MD; Michel Debandt, MD; Isabelle Gueit, MD; Jean-Pierre Gendre, MD; Jean Leone, MD; Nathalie Nicolas, MD; Dider Che, PharmD, MPH; Xavier Mariette, MD, PhD; and Olivier Lortholary, MD, PhD; for the Research Axed on Tolerance of Biotherapies Group**

2013

Anti-TNFα et légionelle



SIR=13.1 [16.6-61.2] p<0.0001 n=27

SIR=3.0 [1.0-9.2] p=0.0599 n=3

SIR=15.3 [8.5-27.6] p<0.0001 n=11

SIR=37.7 [21.9-64.9] p<0.0001 n=13

SIR=2.4 [0.6-9.6] p=0.2130 n=2

SIR=15.3 [7.9-29.3] p<0.0001 n=9

SIR=31.8 [16.6-61.2] p<0.0001 n=9

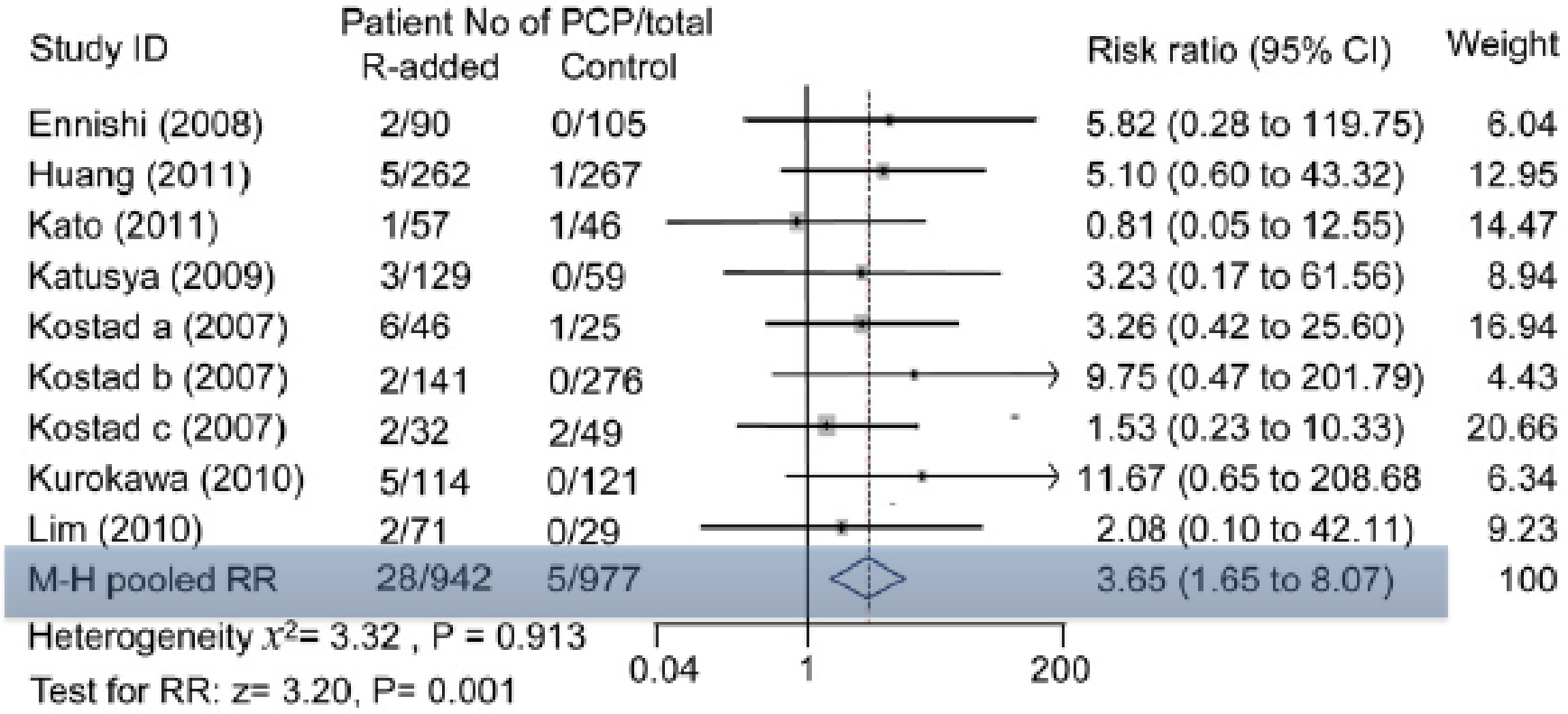
27 cas entre 2004 et 2007

Lanternier, Chest 2013

Il n’y a pas que les anti-TNFα…

Rituximab et pneumocystose

Risque de pneumocystose chez des patients atteints de lymphome



Jiang, Plos One 2015

Rituximab et pneumocystose

Rituximab versus Azathioprine for Maintenance in ANCA-Associated Vasculitis

Guillevin, NEJM 2014

Table 2. Severe Adverse Events According to Treatment Group.*

Severe Adverse Event	Azathioprine Group (N=58)	Rituximab Group (N=57)
	no. of events	
Infection	8	11
Bronchitis	0	3
Tuberculosis	0	1
Pneumonia with respiratory distress	1	2
Pneumocystis jiroveci pneumonia	0	1
Bacterial endocarditis	1	0
Atypical mycobacterial infection	1	0
Prostatitis	1	0
Herpes zoster infection	1	1
Cholecystitis	1†	0
Septicemia	1‡	0
Esophageal candidiasis	0	1
Infectious diarrhea	1§	2¶
Cancer	2	1
Pancreas	1‡	0
Prostate	0	1
Basocellular carcinoma	1	0
Hematologic event	9	1
Anemia	1	0
Leukopenia	6	0
Lymphopenia	1	1
Thrombocytopenia	1	0
Other	25	26

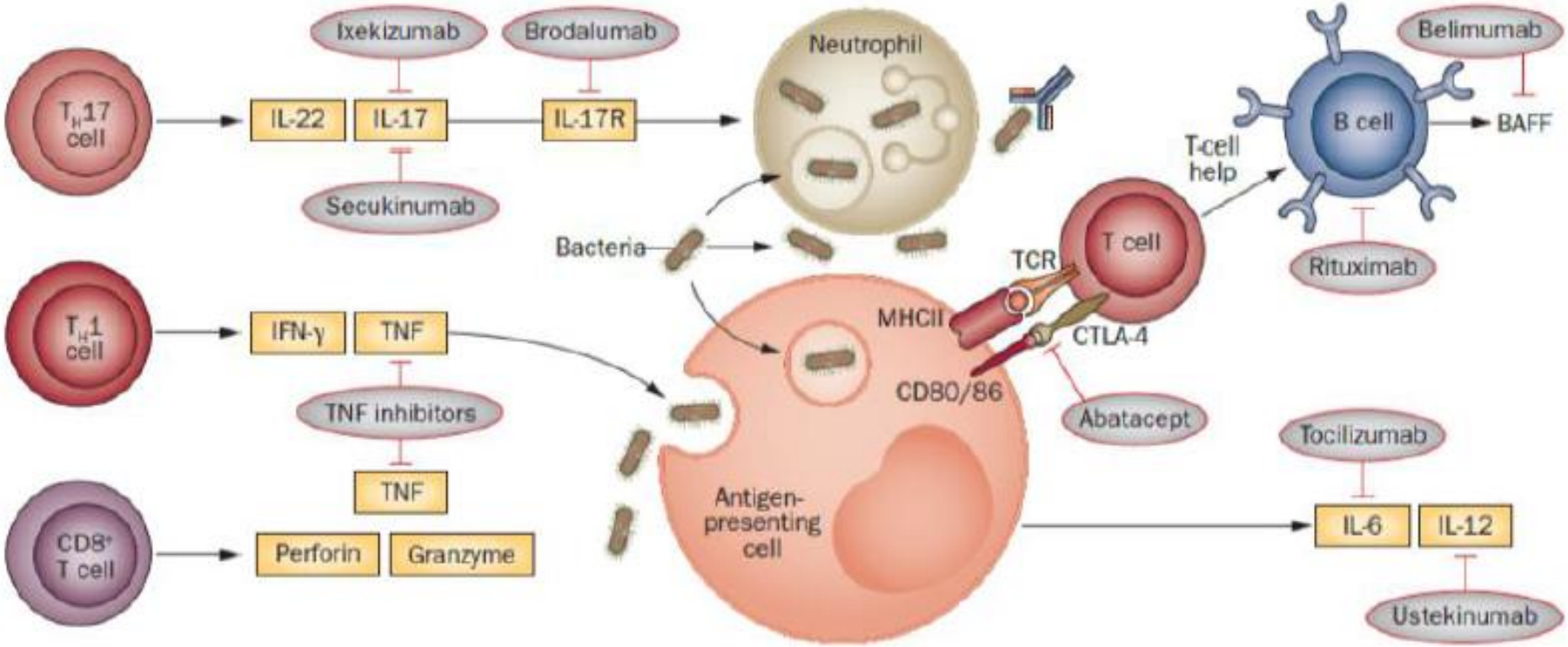
Rituximab et pneumocystose

Clin Rheumatol. 2013 Nov;32(11):1677-81. doi: 10.1007/s10067-013-2293-4. Epub 2013 Jun 11.

Should Pneumocystis jiroveci prophylaxis be recommended with Rituximab treatment in ANCA-associated vasculitis?

Besada E[1], Nossent JC.

Il n'y a pas que l'infectieux…



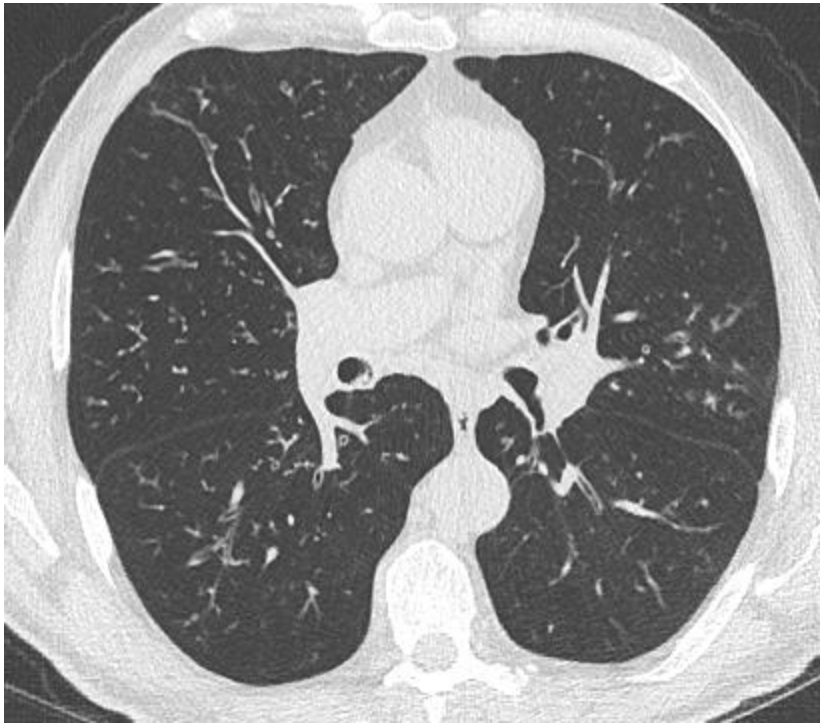
Boyman, Nature Review Rheumatol 2014

PID médicamenteuse

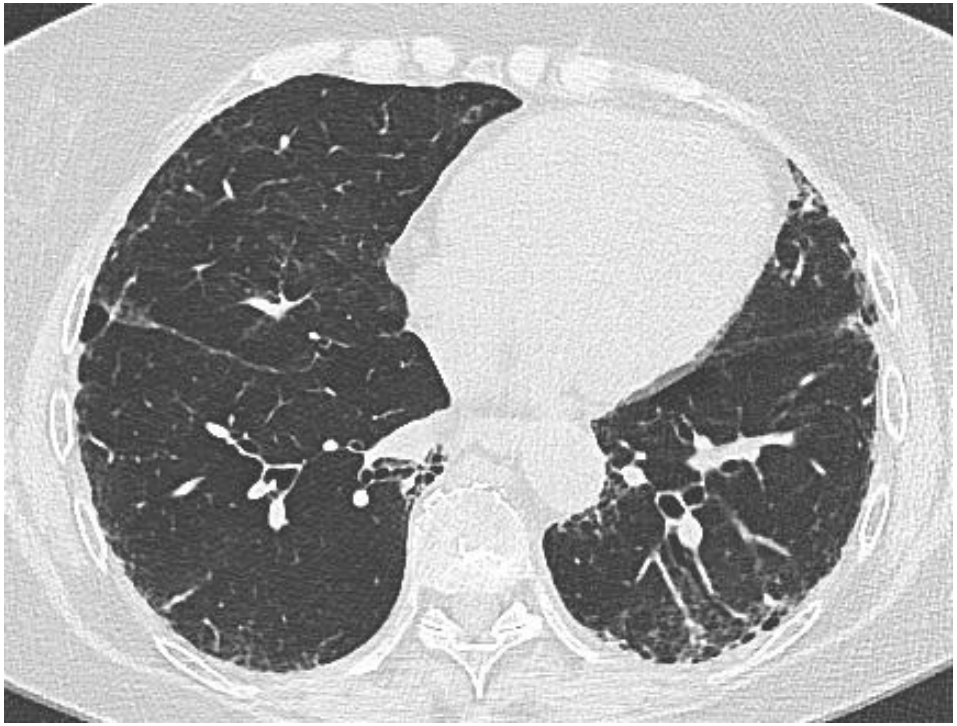
PO au pembrolizumab

www.Pneumotox.fr

PID liée à la maladie causale



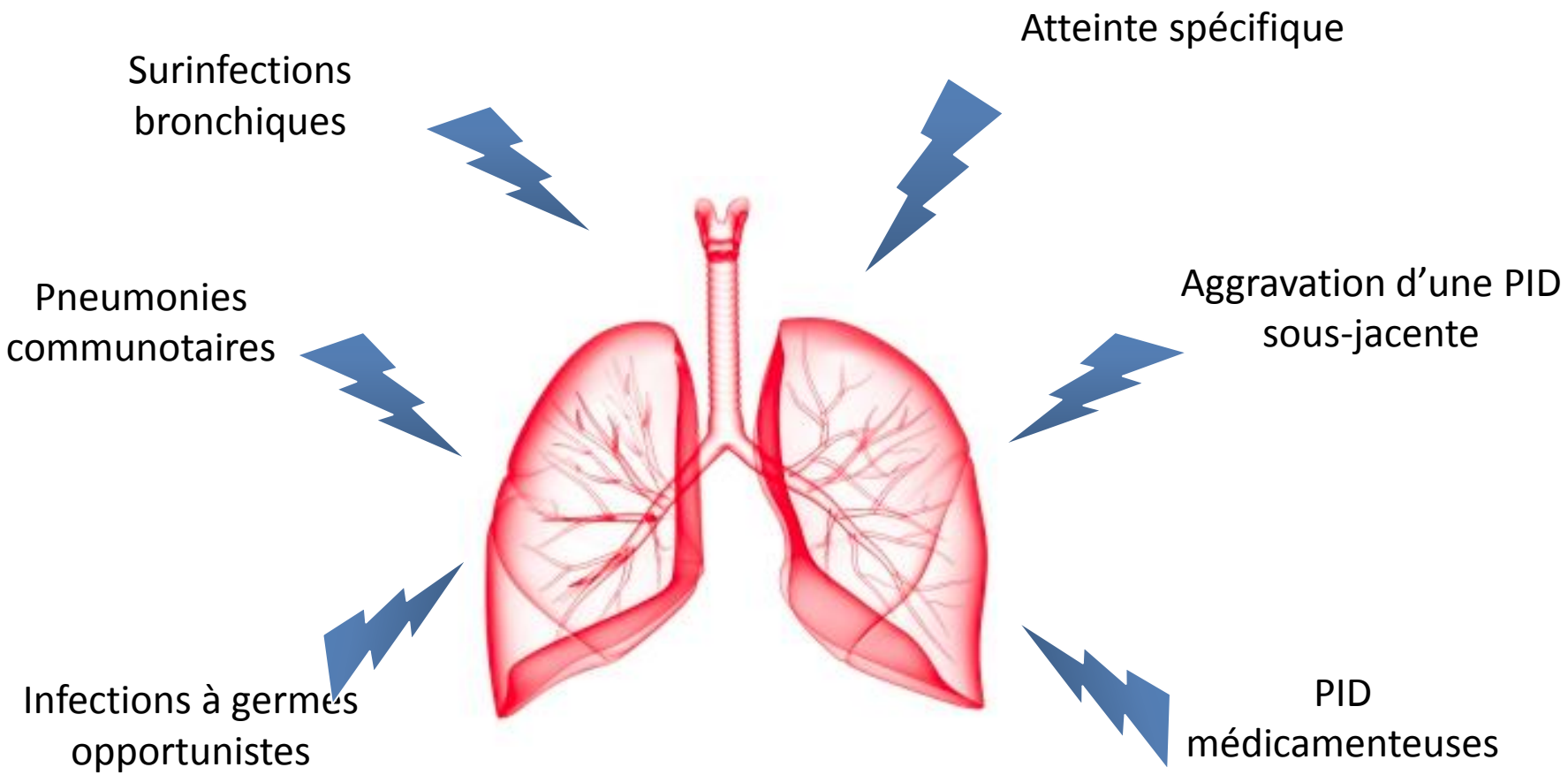
Bronchiolite sur LLC



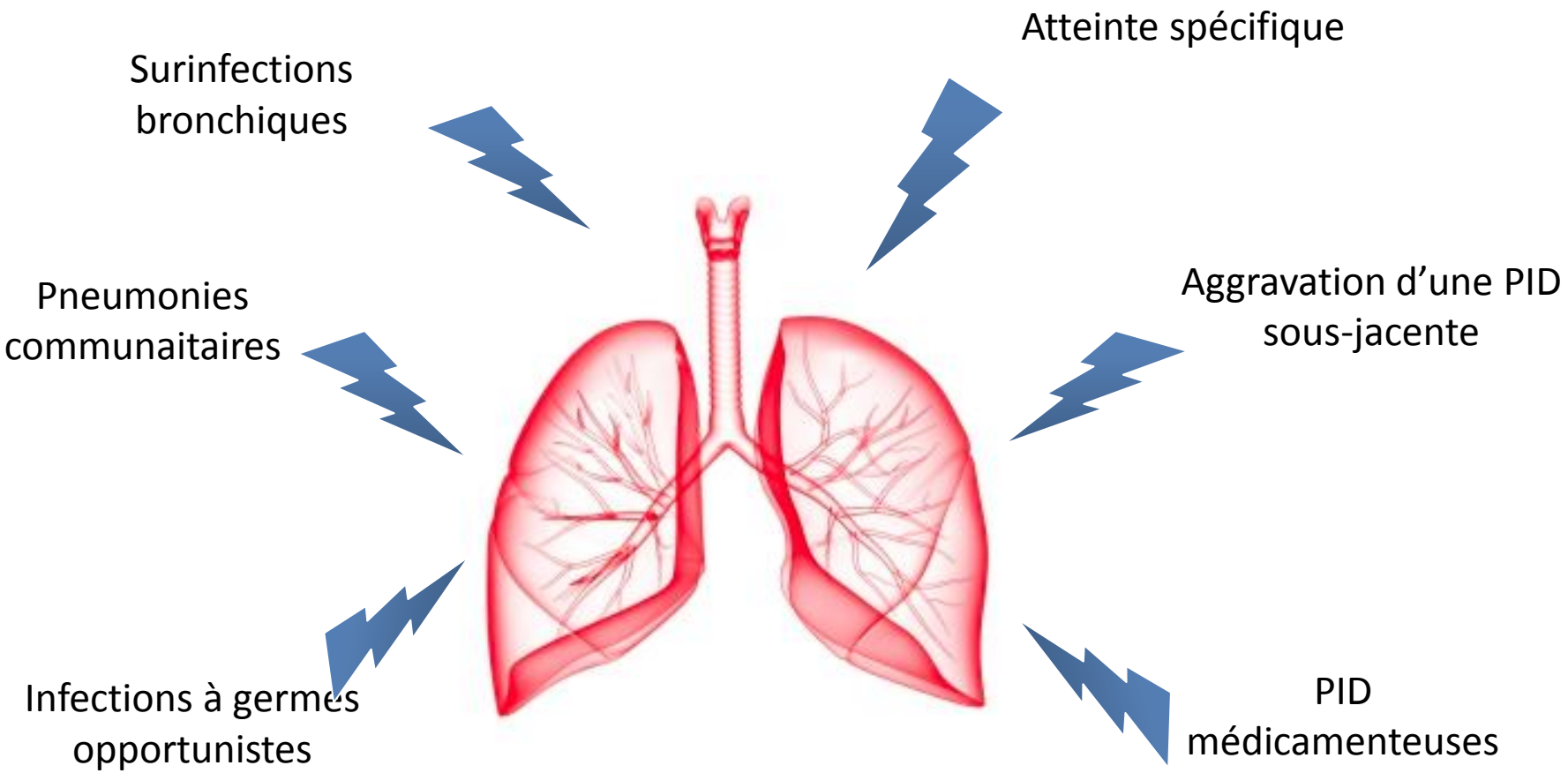
PINS sur PR

En conclusion

En conclusion



En conclusion



La pneumologie à de beaux jours devant elle!

Mod Rheumatol. 2012 Feb;22(1):122-7. doi: 10.1007/s10165-011-0488-6. Epub 2011 Jul 8.

Incidence of serious respiratory infections in patients with rheumatoid arthritis treated with tocilizumab.

Hoshi D[1], Nakajima A, Inoue E, Shidara K, Sato E, Kitahama M, Seto Y, Tanaka E, Urano W, Ichikawa N, Koseki Y, Momohara S, Taniguchi A, Nishimoto N, Yamanaka H.

Author information

Abstract

We aimed to demonstrate the incidence of serious respiratory infections in patients with rheumatoid arthritis (RA) treated with tocilizumab (TCZ) monotherapy. We analyzed the incidence of serious respiratory infections in 601 RA patients enrolled in TCZ clinical trials and their extension studies (TCZ cohort) and in 601 age- and sex-standardized RA patients treated in daily clinical practice at Tokyo Women's Medical University (IORRA subsample cohort). The rates of serious respiratory infections were 1.77 per 100 patient-years from 1999 to 2008 in the TCZ cohort and 0.53 per 100 patient-years from 2000 to 2009 in the IORRA subsample cohort. With the IORRA subsample cohort regarded as a standard population, the standardized incidence ratio (SIR) of serious respiratory infection in the TCZ cohort was 3.64 [95% confidence interval (CI) 2.56-5.01], standardized for age and sex; 2.35 (95% CI 1.66-3.24), standardized for age sex, and corticosteroid use; 1.85 (95% CI 1.30-2.55), standardized for age sex, and pre-existing pulmonary involvement; and 2.41 (95% CI 1.68-3.34) standardized for age sex, and disease activity. The risk of serious respiratory infection in the TCZ cohort was approximately double that in the IORRA subsample cohort after standardizing for corticosteroid use, pre-existing pulmonary involvement, or disease activity. This is comparable to the risk reported when tumor necrosis factor (TNF) inhibitors are used

+ PO 1 cas (Internal Medecine 2011)
+ progression d'une PID pre-existante 2 cas
(Rheumatol Intern 2012)
+ granulomatose sarcoidose like (J Rheumatol 2013)

Clin Rheumatol. 2013 Nov;32(11):1677-81. doi: 10.1007/s10067-013-2293-4. Epub 2013 Jun 11.

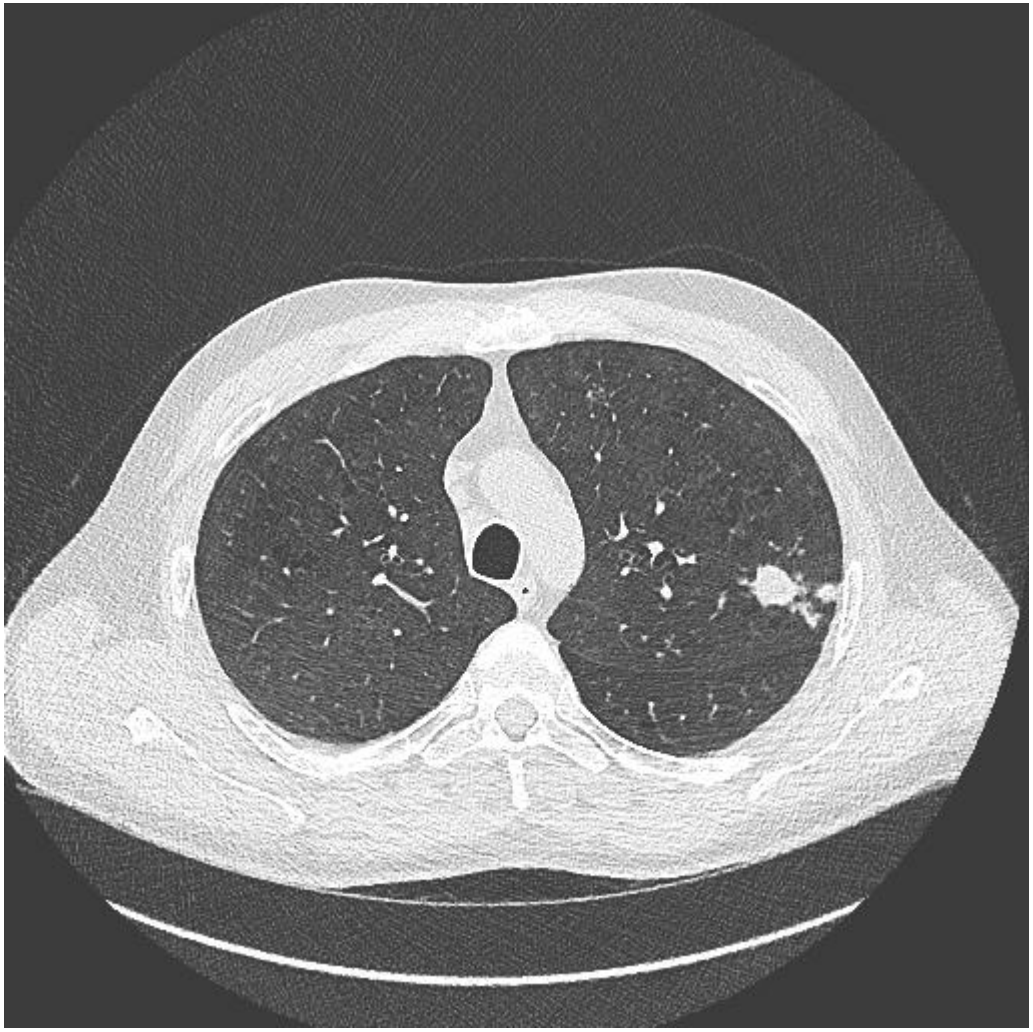
Should Pneumocystis jiroveci prophylaxis be recommended with Rituximab treatment in ANCA-associated vasculitis?

Besada E[1], Nossent JC.

Author information

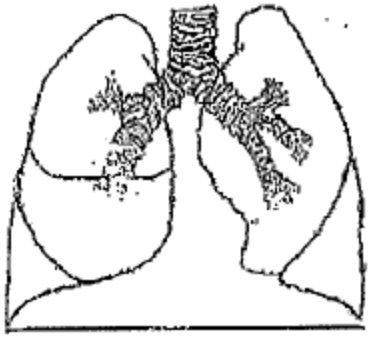
Abstract

Reports in haematology, transplantation medicine and rheumatology indicate that Rituximab, a B cell depleting therapy, increases the risk for Pneumocystis jiroveci pneumopathy. Patients with antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitis have an increased incidence of P. jiroveci pneumopathy compared to other autoimmune diseases and Rituximab is often used to induce and maintain remission. Herein, we present a case of a patient with granulomatosis with polyangiitis treated with Rituximab for relapse that developed P. jiroveci pneumopathy 3 months after and we review the relevant literature to assess P. jiroveci pneumopathy incidence and risks factors under Rituximab. We also discuss whether P. jiroveci screening before Rituximab and P. jiroveci pneumopathy prophylaxis under Rituximab are indicated. P. jiroveci colonisation is found in 25 % of patients with autoimmune diseases. However, the association between colonisation and P. jiroveci pneumopathy development is not very strong. P. jiroveci pneumopathy incidence in ANCA-associated vasculitis patients treated with Rituximab is found to be 1.2 %. Therefore, evidence and practice do not support the use of P. jiroveci pneumopathy chemoprophylaxis in all ANCA-associated vasculitis patients receiving Rituximab. CD4 cell count cut-off does not work well in patients treated with Rituximab as it does not reflect T cell impairment following B cell depletion. To help stratify the risk of both colonisation and P. jiroveci pneumopathy development, assessment of the patient's net state of immunodeficiency before administering Rituximab-including age, renal or lunginvolvement, previous infections due to T cell dysfunction, blood tests (lymphocytopenia, low CD4 cell count) and concomitant therapy-is warranted



UF 1440 Poste 30152

- ☐ Autofluorescence patient à risque
- ☐ Recherche de tumeur bronchique
- ☐ Surveillance post-chimio-radiothérapie
- ☐ Surveillance post-chir
  - → intervention chirurgicale réalisée :



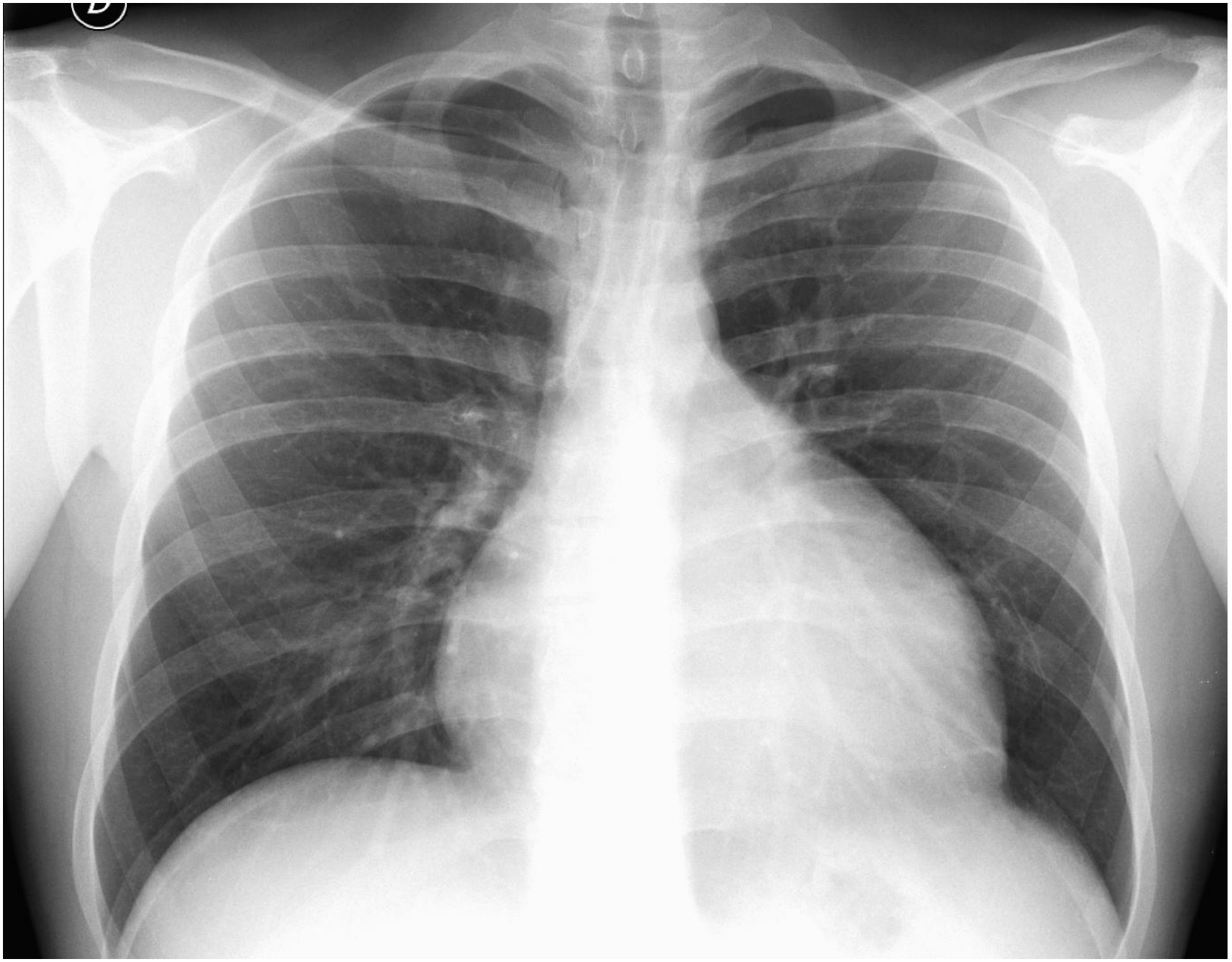
- ☑ Prélèvements Fibro - LBA
- ☐ Thérapeutique

DETAIL DU MOTIF

- Tôx depuis 3 semaines +/- grave : suspicion BK
- Patient suivi pour RCH sous immunomodulateurs (Vedo/HUREL)
- déjà eu 2 lignes d'ABT par son MT (échec)
- RXT ⊥ : ∅ foyer.

→ vedolizumab

J-Integ

FACTEURS DE RISQUE :

- ☐ IRC – dyspnée - Asthme – BPCO : Joindre spirométrie
- ☐ Antécédents cardiaques et/ou coronarite connue :
- ☐ Traitement anticoagulant (pas de biopsies)
- ☐ Plavix – Ticlid (pas de biopsies sauf si arrêt depuis 10 jours)
- ☐ Aspirine
- ☐ anti-arythmiques/ β-bloquants :