18th EAHP Congress
Value-based Decision Making in Rheumatic Disease: Considerations for the Pharmacist

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What does it mean for A Pharmacists?

Pr Robert Launois
REES France
28, Rue d'Assas
75016, PARIS

Disclosure

- **Financial interests:** None
- **Durable or permanent links**
  - Expert comittees : Alcon, Alliance-Médica, Aventis, Bayer Diagnotics,Bristol Myers Squibb Company, Eli-Lilly, Pierre Fabre Médicaments, Glaxo-SmithKline, IMS Health, Innothera, MSD, Lundbeck, Medpass International, Pfizer, Roche, Servier, Abbott, Celgene, Les Entreprises du Médicament (LEEM)
  - Occasional interventions : Bayer Diagnotics,Bristol Myers Squibb Company, Eli-Lilly, Pierre Fabre Médicaments, Glaxo-SmithKline, MSD, Lundbeck, Pfizer, Roche, Servier, Abbott, Celgene, Les Entreprises du Médicament (LEEM)
- **Study sponsored by Pfizer**
  - *"Mixed treatment comparison, cost-effectiveness analysis and budget impact model in the treatment of rheumatoid arthritis after failure of conventional DMARD therapy. A comprehensive Bayesian decision analytical modelling"* (To be published)
  - Participation in the protocol design, the statistical analysis and finalization of the manuscript
  - In collaboration with academic researchers Pr MC Boissier MD

Outline

- Background & Objectives
- The Buyer Case
- Methods
- Results
- Discussion

Background

Value-based Decision Making: What Does it Mean?

- Health care professionals are encouraged to consider the value, i.e the balance between costs and benefits in their decisions.
- Value-based decision-making should not be confused with:
  - Value-based purchasing : P4P programs linking payments to specific performance measures.
  - Value-based benefit design : heath plans structuring cost sharing to encourage the use of the most effective services.
  - Value based pricing : payers using the Incremental Cost Effectiveness Ratio (ICER), not as a value criterion in itself, but as a price negotiation tool to be compared to a socially acceptable price.
- The aim of the value-based decision-making approach is to improve the processes by which health-related decisions are made.

Health And Ethics Policies Of The AMA House Of Delegates
H-155.960 Strategies to Address Rising Health Care Costs

What Does it Mean For Pharmacists?

- It encourages pharmacists to achieve better value for healthcare spending.
- Value can be defined as the best balance between benefits and costs.
- Better value can be defined as improved clinical outcomes, quality of life and patient satisfaction per euro spent.
- The goal is not to reduce appropriate utilisation but to find the most valuable use of services : « the bang for the buck »

Aim of the Presentation

The aim of this presentation is to answer the question « What does value-based decision making mean for pharmacists? » by illustrating how to balance the comparative effectiveness, safety and efficiency of anti TNF inhibitors in rheumatoid arthritis in 2nd and 3rd line of treatment.

The Buyer Case

How should pharmacist recommend one out of five TNF α inhibitors in the 2nd and 3rd line of treatment for rheumatoid arthritis?

Launois, R., Le Moine, JG., Huynh MT., Boissier, MC. (To be Published) *"Mixed treatment comparison, cost-effectiveness analysis and budget impact model in the treatment of rheumatoid arthritis after failure of conventional DMARD therapy. A comprehensive Bayesian decision analytical modelling"*

Methods

Alternative Treatment Strategies

- Patients with an inadequate response to MTX are treated with one of the following biotherapies:

  - abatacept (ABA),
  - adalimumab (ADA),
  - etanercept (ETA),
  - infliximab (INF), or
  - certolizumab pegol (CZP)

Target Population

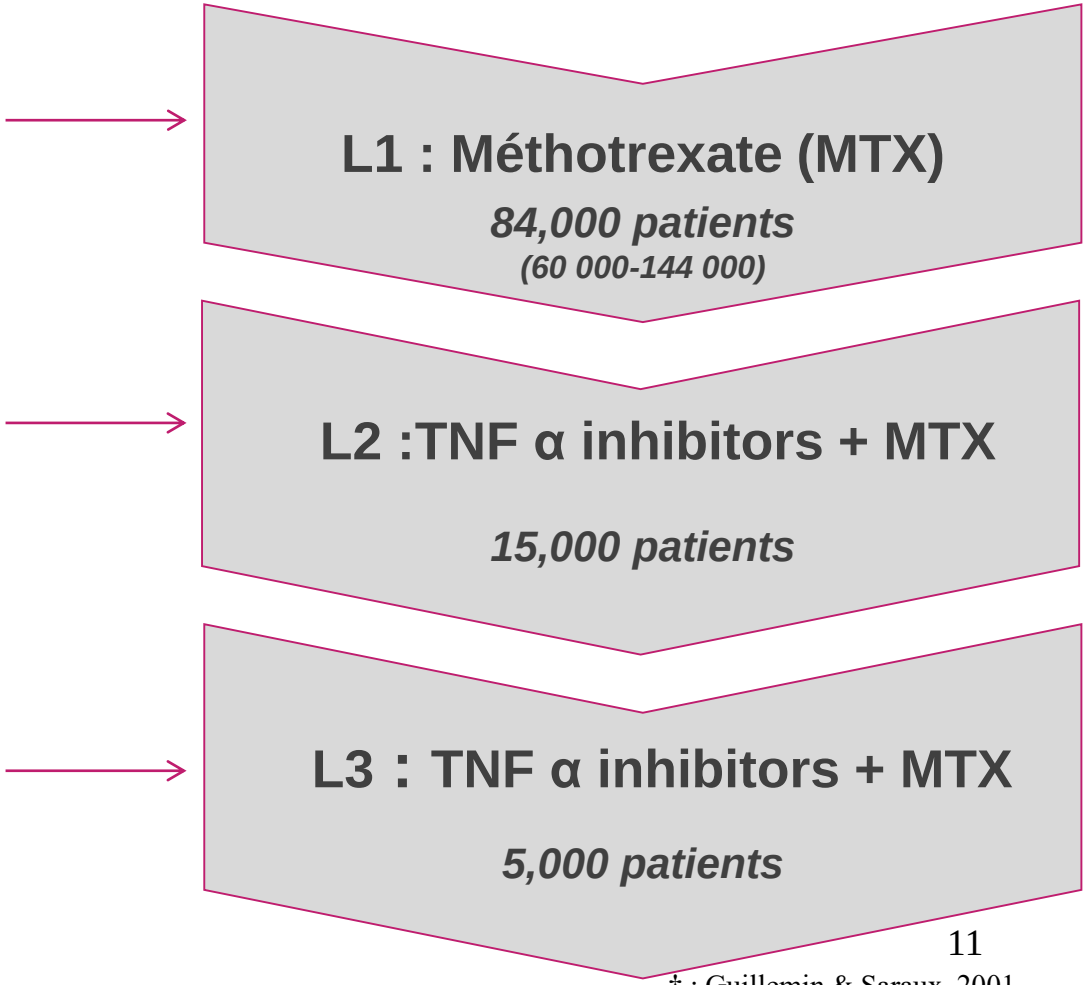
Prevalence estimate: 130,000-240,000 patients

According to expert knowledge†

Median value presented
(45-60% lower & upper bounds estimates treated with MTX)

18% failed treatment with MTX

33% experience an inadequate response to TNF α inhibitors



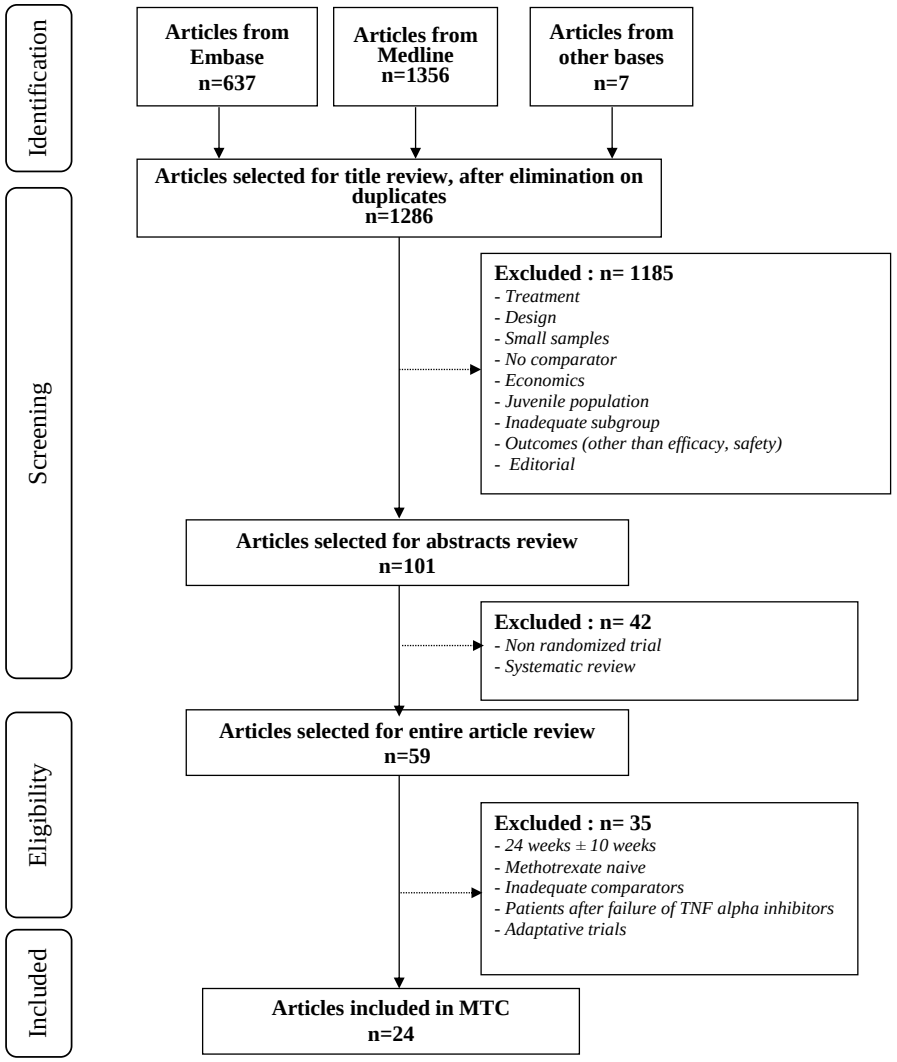
† : Guillemin & Saraux, 2001

Turning Evidence Into Action

- The introduction of TNF alpha inhibitors has provided new treatment options in the therapeutic approach to rheumatoid arthritis.
- Management of the disease is first defined in benefits and harm: will the intervention help or hurt?
- The systematic review is the main instrument for comparing « alternative methods to treat a clinical condition »
- But a second dimension has to be considered : how does the efficiency of a treatment compare with other alternatives?

Systematic Review

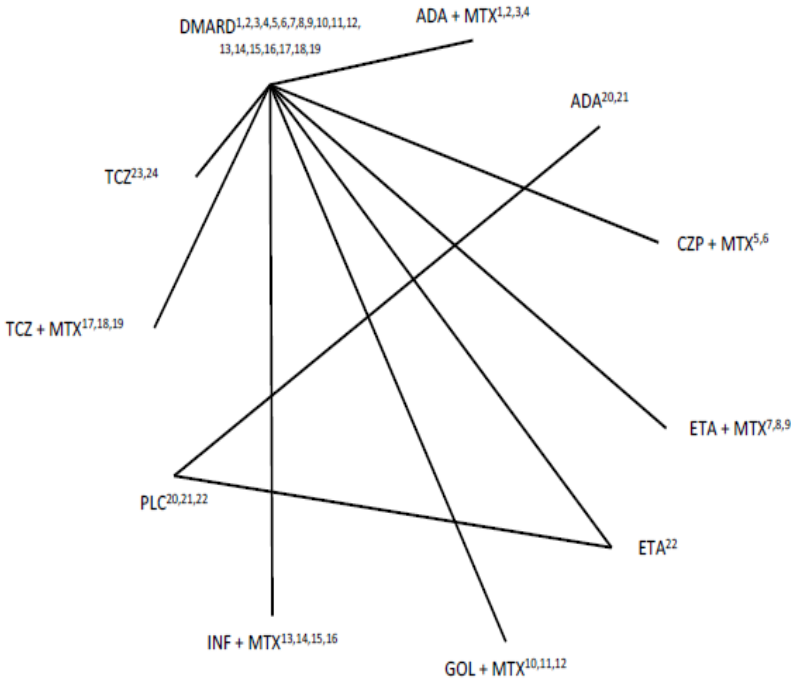
- 2 databases were interrogated between 1999 and 2011.
- There were 2,000 initial hits.
- 714 duplicates identified and eliminated, resulting in 1,300 (approx.) articles for screening, based on title and abstract.
- This resulted in 59 eligible articles for full reading.
- Finally, 24 articles were retained for the meta-analysis.



PRISMA Template, 2009

Bayesian Network Meta Analysis

- 24 trials were included: involving 8,000 (approx.) patients who had an inadequate response to MTX.
- The Network Meta-analysis included 11 protocols, of which 10 were direct comparisons.
- Two studies were excluded to reduce heterogeneity among trials: one on etanercept (ETA) and one on adalimumab (ADA).
- 22 studies were effectively used in the meta analysis.



Value-based Decision Making

- A Markov model was developed to implement:
  - A cost-effectiveness analysis
  - A budget impact analysis

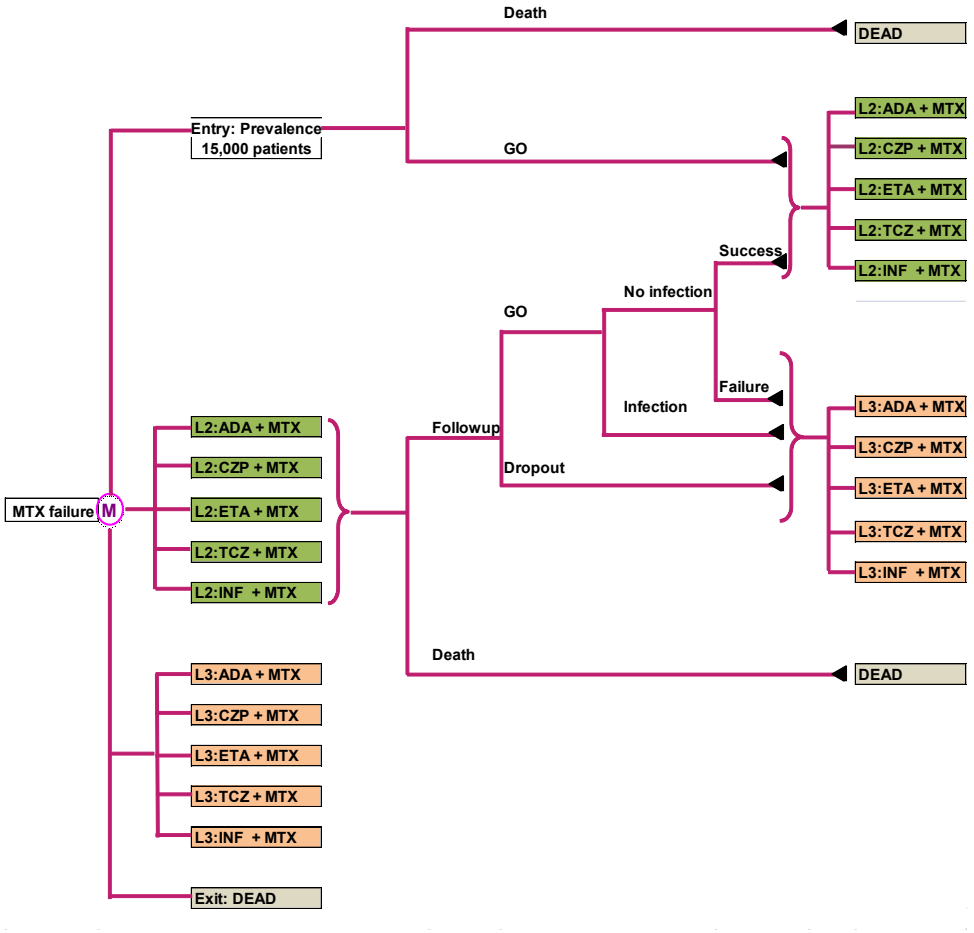
- Both simulations were programmed using Winbugs Software

- The criteria from the American College of Rheumatology (ACR 50†) was used as the effectiveness end-point at week 24 ± 2.

†ACR 50 : ACR 50% improvement incorporates 50% of tender (nombre de synovites) and swollen joints (nombre d'articulations douloureuses) and 3 of the 5 remaining core outcome measures : Pain – (VAS), Patients global assessment -(VAS), Physicians global assessment –(VAS), Function - Health Assessment Questionnaire (HAQ), and biologic Inflammation: CRP or ESR (VS[b] ou Créatinines).

The Engine: A 12 Health-State Markov Model

- Five health states in the 2nd line and 5 in the 3rd line of treatment.
- Two additional health states: one for yearly prevalent cases and another for death.
- In accordance to the patient's clinical pathway: (s)he either stays in the 2nd treatment line or moves to the 3rd.
  - This takes place after either: failure, infection or dropout.
- The fundamental idea: each patient exiting on the right-hand side of the treatment line either
  - (a) loops back to the next cycle on the same treatment or
  - (b) switches to the 3rd line after failure.



Data sources

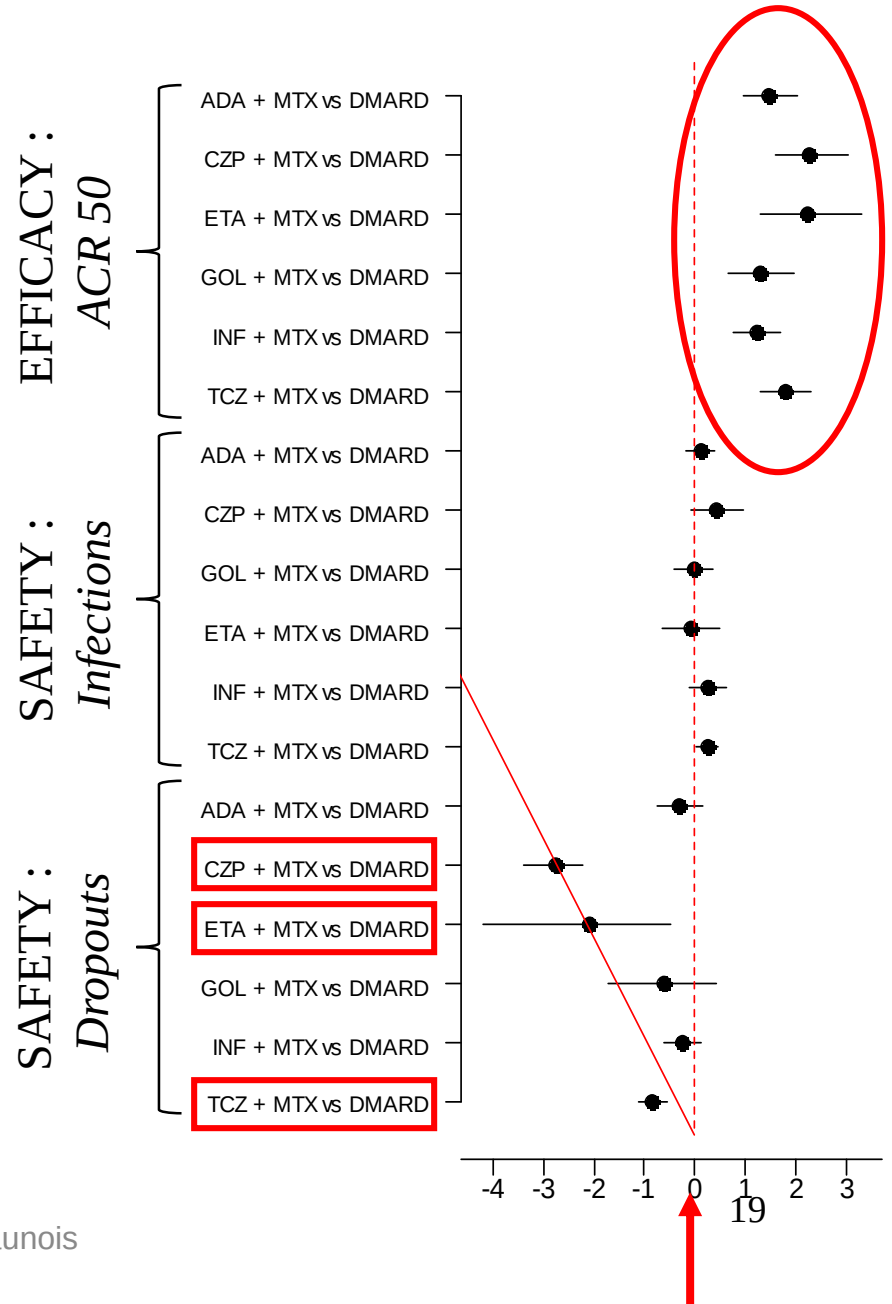
Epidemiological data	Source: French Transparency Commission
Target population size (L2 + L3)	13,500 - 34,000 patients†
Resource utilisation	Ad hoc observational studies
Treatment acquisition costs (per patient for 6 months)	Calculated from: Market Authorization (MA) dosages, Source: Ameli.fr drug database
Treatment administration costs	Extracted from: French National Health Insurance nomenclatures*

† : Guillemin & Saraux, 2001 ; ‡ : Guillemin et al, 1994 ; * : CCAM v32, NABM, v22, DRG v11c, NGAP

Results

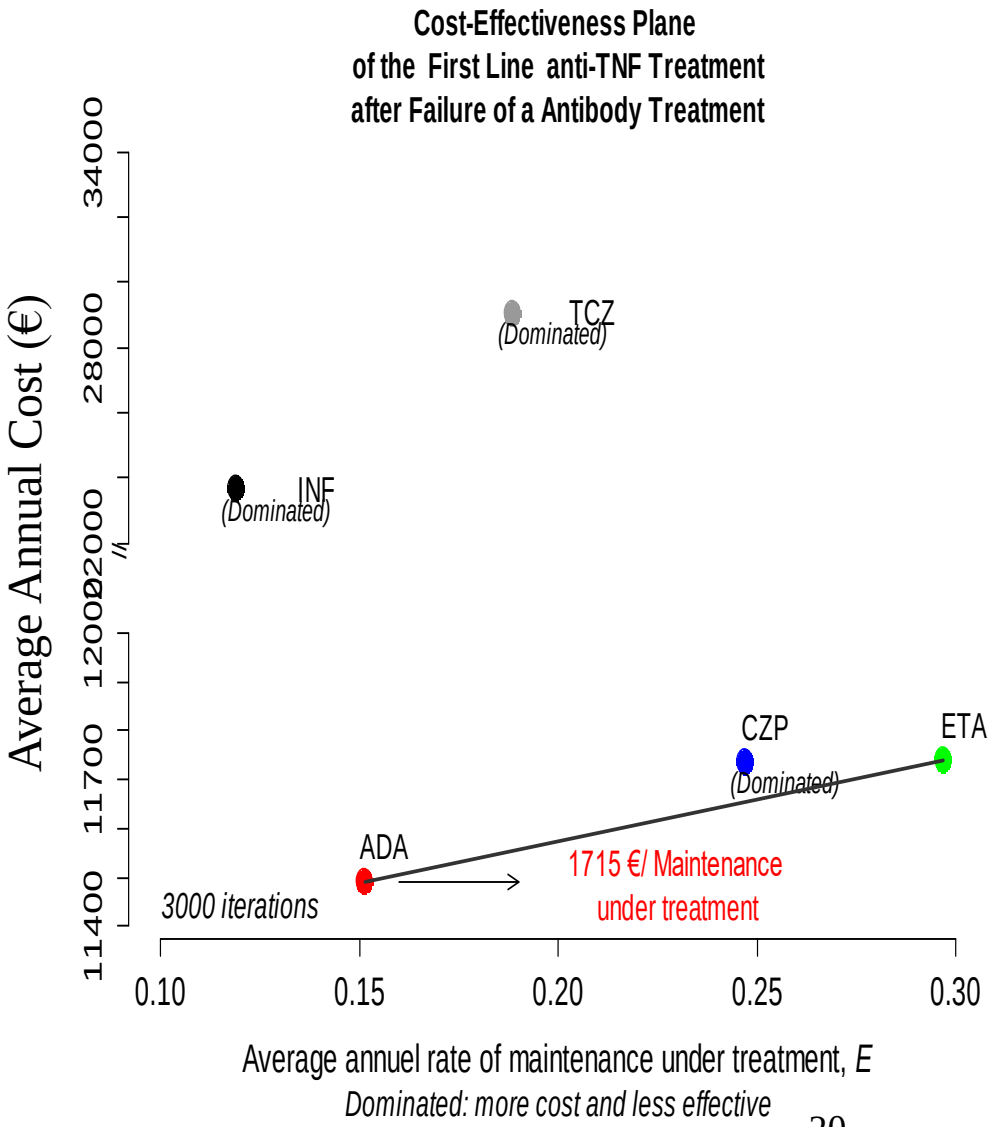
Lessons from the Meta Analysis

- Results reported for the treatment combinations are measured in terms of **log OR**, therefore with respect to zero.
- The line crossing at zero represents equal efficacy/safety with respect to MTX or placebo
- The rates of response are on the right-side and the rates of detrimental side-effects on the left-side.
- ACR 50 response rates for all biotherapies were significantly higher than for the MTX treatment or placebo (circled in red)
- None of the biotherapies could be distinguished from each other because the confidence intervals overlapped.
- No significant difference was found between treatments for infection rates
- Dropout rates were lower for CZP, ETA, and TCZ compared to DMARDs.



Efficiency Frontier

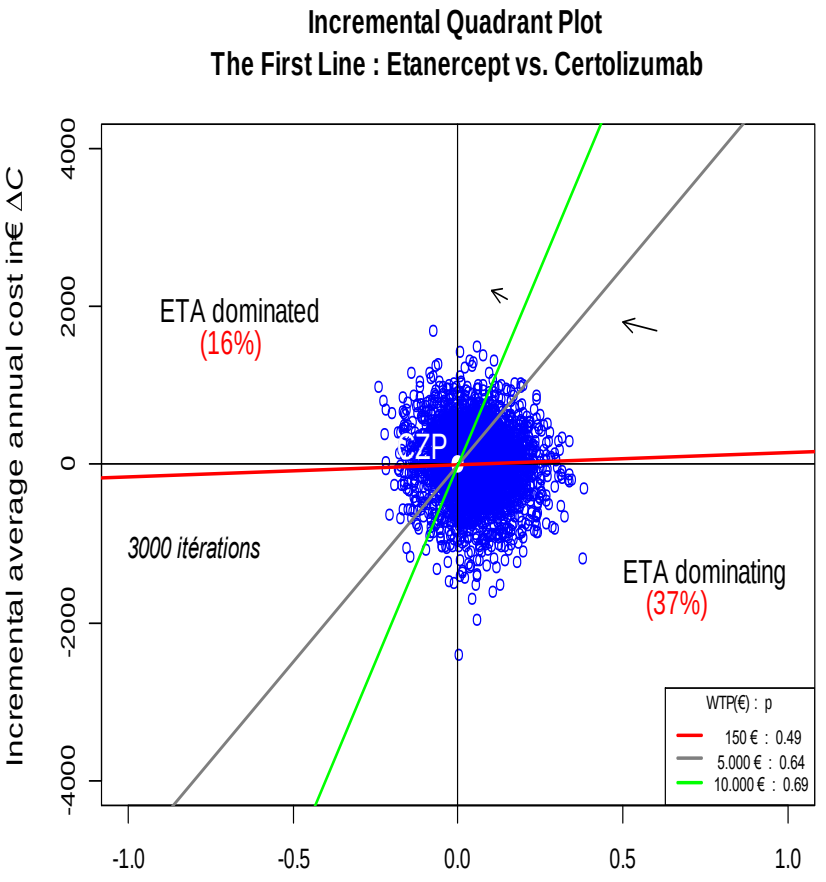
- The Efficiency Frontier was constructed from 3,000 simulations based on:
  - Average annual cost per patient (cost criterion) and,
  - Average annual rate of maintenance on treatment (efficacy endpoint).
- The frontier was defined by the linear combination of ADA and ETA.
- CZP, INF and TCZ combinations are strongly dominated (i.e. more costly for the same effectiveness).
- The positive gradient of the frontier means that remission rate for ETA is greater than that of ADA.
- A longer remission is obtained at an additional cost of 1,715€ p.y.



Cost Effectiveness Plane

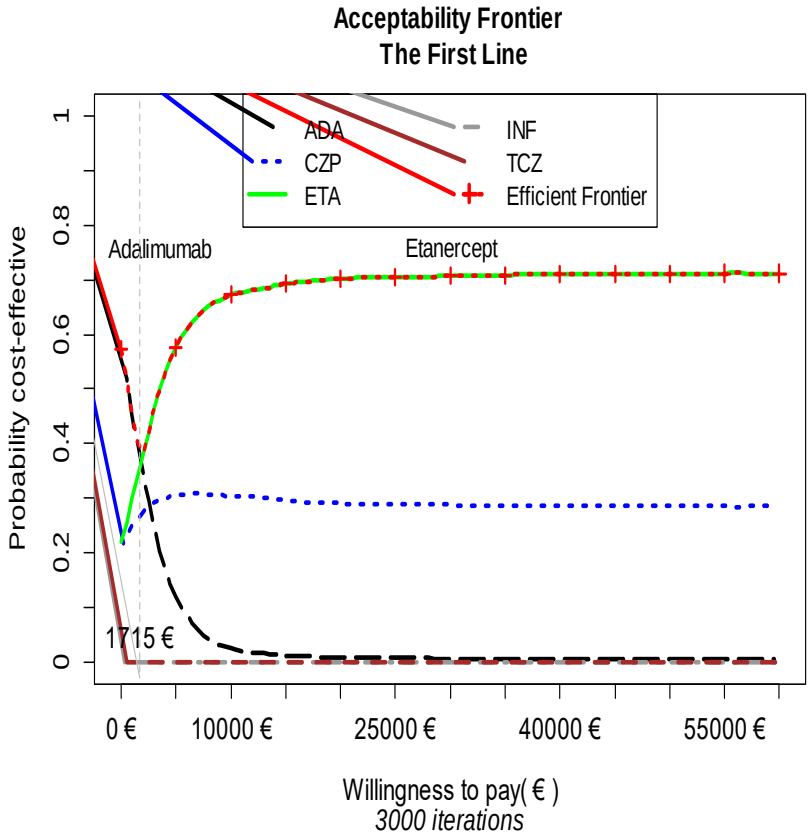
- The value of the societal willingness to pay (WTP) is represented by a line whose slope increases with the amount of money society is willing to allocate
- 3000 simulations of the differences between average cost and effectiveness per patient were implemented.
- **The Incremental Net Health Benefit (INHB)** of an intervention compared to another is equal to the difference between:
  - the value of the additional health benefit **ΔE** valued on the basis of the social WTP and,
  - the amount of the additional expenditure to be incurred in order to fund the project **ΔC**

- **INHB = WTP * ΔE-ΔC .**



Acceptability Frontier

- When several treatments are mutually exclusive; the acceptability frontier, should be used instead of the Cost Effectiveness Acceptality Curve (CEAC)†
- The acceptability frontier envelopes the totality of the Net Health Benefit curves.
- INF, TCZ and CZP being located below the acceptability frontier are dominated and should therefore be considered as inefficient above a WTP of 1,715 € p.y.



† Briggs, 2002 *Medical Desicion Making* 22: 290-308

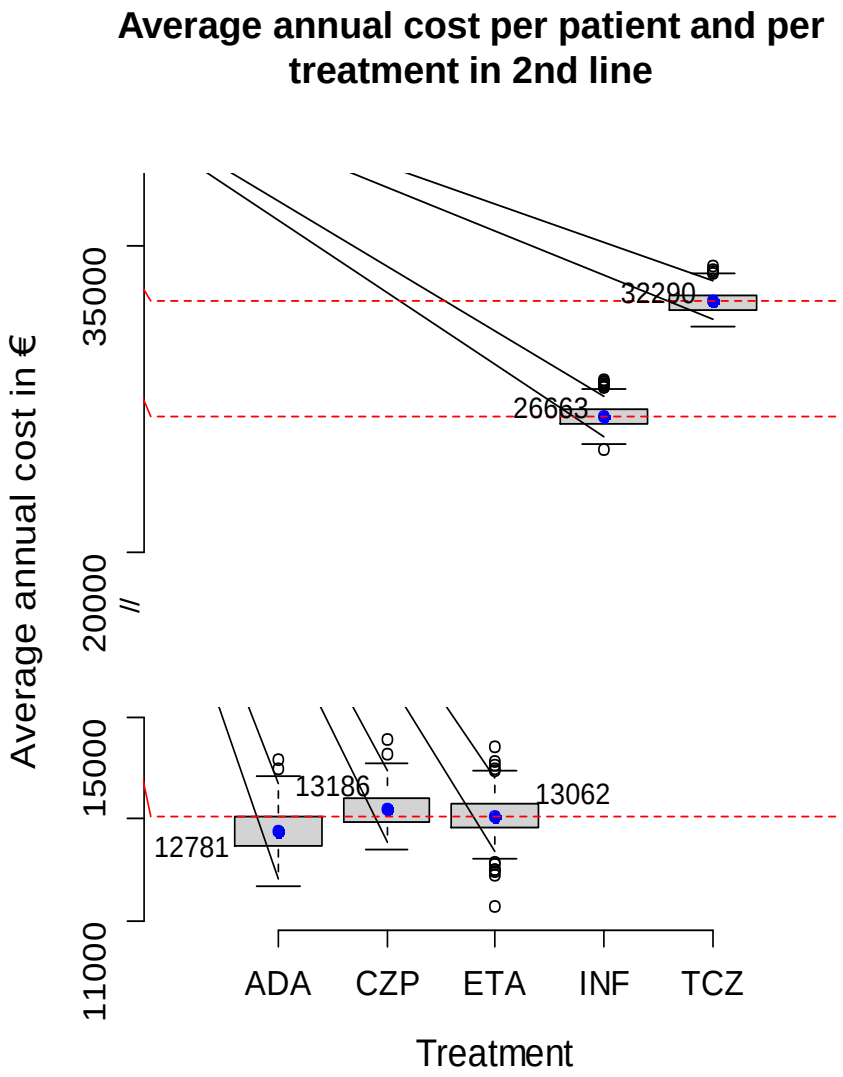
Budget Impact Model

- Average annual costs per patient were estimated assuming a 10% reduction in the market share of eternacept (ETA) in the next 5 years.

- Two distinct groups with significantly different overall annual average expenditures (per patient, per year) were identified :

Group	Components	A. A. C. in €
I	ADA, CZP & ETA	12,000-13,000
II	INF & TCZ	26,000-33,000

- Differences are simply explained by the fact that INF & TCZ are administered intravenously at the hospital.



Discussion

An overly restrictive policy based solely on the daily cost of drug acquisition may mask the positive impact that it could have on the overall cost of the healthcare system.

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Thank you !