

# Mixed treatment comparisons : an evidence-based budget impact model of Rituximab (Mabthera®) after failure of one or more TNF inhibitor therapies in the treatment of rheumatoid arthritis

Launois R<sup>1</sup>, Riou-Franca L<sup>1</sup>, Maunoury F<sup>3</sup>, Boissier MC<sup>2</sup>, Florentin V<sup>4</sup>

1: REES France, Paris, France  
 2 : Université Paris Nord, Hôpital Avicenne, AP-HP, Paris, France  
 3 : Satesia, Le Mans, France  
 4 : Roche, Neuilly sur Seine, France

REES France

28, rue d'Assas 75006 Paris – France  
 Tel . 01 44 39 16 90 – Fax 01 44 39 16 92  
 Web : [www.rees-france.com](http://www.rees-france.com)



## Background

Rituximab (RTX) is approved in Europe since July 2006 for its use in adult patients with severe active rheumatoid arthritis (RA) who have had an inadequate response or intolerance to other disease modifying anti-rheumatic drugs including one or more TNF $\alpha$  inhibitor (anti-TNF $\alpha$ ). Compared to anti-TNF $\alpha$  (Adalimumab (ADA), Etanercept (ETA), Infliximab (INF)), RTX has an original administration scheme (2 infusions every 6 to 12 months).

## Objective

The aim of the study was to estimate the budget impact of the introduction of RTX after failure of one or more TNF  $\alpha$  therapies for the French health care system.

## Methods

### Markov model

- Cycle length: 6 months
- Follow-up period: 4 years (2006-2009)
- Patients either in 2<sup>nd</sup> line or in subsequent lines of treatment
- 4 treatment states corresponding to the 3 anti-TNF $\alpha$  (ETA, ADA, INF) + RTX
- 1 additional state to allow treatment switches and to model a dynamic population (entry/exit state)
- Target population and anti-TNF $\alpha$  market shares defined from market studies

### Model resources

- TNF  $\alpha$  inhibitors treatment consumptions : TC2 observational study for patients in 2<sup>nd</sup>-line anti-TNF $\alpha$  treatment gathered inpatient and outpatient consumptions (*EULAR 2007 - poster THU0190*)
- Anti-TNF $\alpha$  treatment efficacy and safety : issued from literature:
  - ✓ Success rate measured by ACR20
  - ✓ Evidence synthesis using bayesian Mixed Treatment Comparisons model on 16 published trials.

### Rituximab costs

- Administration scheme : every 9 months
- Hospital costs : identical to INF costs
- Other hospitalisation costs : average anti-TNF $\alpha$  costs
- Outpatient costs and medical visits : average anti-TNF $\alpha$  costs except for nurses visits for which INF costs were applied

### Hypothesis:

- H<sub>1</sub> : RTX is not used
- H<sub>2</sub> : RTX is used progressively (new 2<sup>nd</sup> line patients are treated with RTX and every switch is in favour of RTX)
- H<sub>3</sub> : RTX is the only treatment used

### Sensitivity analysis

- TC2 study only documented costs for patients in 2<sup>nd</sup> line TNF $\alpha$ . Patients in subsequent lines are expected to require increased resources. Two coefficients were applied:
- Coeff1: to TNF $\alpha$  acquisition costs (patients receive a reinforced treatment)
  - Coeff2: to other costs for each strategy; from 5% to 20%.

## Results

### Base-case analysis

- Target population: 5 700 patients
- Market shares : - ADA : 46%  
 - ETA: 38%  
 - INF: 16%

#### Annual costs per patient

	TNF $\alpha$ only H1 (€)	Rituximab only H3 (€)
<b>Hospitalisation cost</b>		
Administration cost	915	1 577
Other hospitalisations	987	992
Outpatient visits - tests	176	175
<b>Ambulatory cost</b>		
Consultations	136	136
Others	1 135	1 095
<b>Treatment cost</b>	13 206	7 469
<b>TOTAL</b>	<b>16 555</b>	<b>11 444</b>

- Mean annual cost of RTX is 11 444 € per patient versus 16 555 € for anti-TNF $\alpha$  therapies (-31% in favour of RTX).

### Sensitivity analysis

- H<sub>2</sub> versus H<sub>2</sub>' = H<sub>2</sub> + coeff<sub>1</sub> + coeff<sub>2</sub>(20%)
- At the beginning of the simulation, the difference between H<sub>2</sub> and H<sub>2</sub>' reaches 5 400 000€ on the total direct costs.
- However, while RTX enters the market, this difference decreases, reaching only 2 400 000€ at the end of the simulation (-63%).
- The more RTX is used, the less is the impact of the coefficients, because RTX acquisition costs are independent from the treatment line.

#### Cumulated costs over 4 years

	Anti-TNF $\alpha$ only H1 (€)	Anti-TNF $\alpha$ and RTX H2 (€)	RTX only H3 (€)	$\Delta$ H3-H1 (€)
<b>Hospitalisation cost</b>				
Administration cost	21 229 782	30 927 500	35 918 183	14 688 401
Other hospitalisations	22 694 003	22 915 328	22 874 045	180 042
Outpatient visits - tests	4 010 283	3 974 787	3 979 668	-30 615
<b>Ambulatory cost</b>				
Consultations	3 102 241	3 100 885	3 102 100	-141
Others	25 832 513	25 202 024	24 946 058	-886 455
<b>Treatment cost</b>	301 644 646	204 412 229	170 062 585	-131 582 061
<b>TOTAL</b>	<b>378 513 468</b>	<b>290 532 754</b>	<b>260 882 640</b>	<b>-117 630 828</b>

- Mean annual cost of RTX is 11 444 € per patient versus 16 555 € for anti-TNF $\alpha$  therapies (-31% in favour of RTX).
- The decrease of 43% in the drug cost between H<sub>1</sub> and H<sub>3</sub> over 4 years overcompensate the cost increase due to hospital administration costs of RTX. The overall savings with RTX is equal to 31% of the medical expenses observed when its comparators were the only one in use.

## Conclusion

RTX is expected to produce important savings if used after failure of one or more anti-TNF $\alpha$  therapies : -31%. This is mainly due to its lower drug cost with 11 444 € per year. These savings could increase with the development of RTX in earlier stages of treatment (future marketing authorisations).