SATELLITE SYMPOSIUM EAHP 2015

OPTIMISING BIOLOGIC CARE IN AN EVOLVING LANDSCAPE: REAL WORLD DECISIONS IN RHEUMATOLOGY

25 March 2015
14:00-15:30
Hall 4

SATELLITE SYMPOSIUM EAHP 2015

Dr Christine Clark

WELCOME & INTRODUCTION

Housekeeping

- Please turn your mobile phones off or on silent

- Please do not leave bags unattended

Symposium Objectives

- Discuss how hospital pharmacists can better manage their resources

- Highlight the real cost of biologic drugs in a challenging and changing environment

- Discuss how to optimise treatment with biologics

Agenda

Budgetary challenges in rheumatology	**Michael Sobanja**
Are you getting what you budget for? Biologic costs in the real world	**Professor Robert J Moots**
Real world cost of biologic therapy: A European perspective	**Dr Luca Degli Esposti**
Panel discussion	

Introductions

Dr Christine Clark
Independent Pharmaceutical Consultant, UK

Michael Sobanja
Policy Director, NHS Alliance, UK

Professor Robert J Moots
University of Liverpool, UK

Dr Luca Degli Esposti
DEA Srl and CliCon Srl, Italy

Your questions

- Questions will be taken during the panel discussion at the end of the symposia
- Questions can be submitted at any time using the question cards in your programme book
- Alternatively, you can ask your question using the aisle microphones

There is an evaluation form inside your programme book

Please fill this out at the end before leaving the symposium

SATELLITE SYMPOSIUM EAHP 2015

Michael Sobanja

BUDGETARY CHALLENGES IN RHEUMATOLOGY

Pfizer

Disclosures

- I have received unrestricted research grants or acted as a speaker for a range of pharmaceutical companies and a number of commercial companies that operate in the health and healthcare environment
  - Including but not limited to: Abbvie, Amgen, BMS, Celgene, GSK, Janssen, MSD, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi, Servier, UCB

The budgetary challenge

- There are more beneficial interventions than we can actually finance
- Healthcare resources are limited
- Resources allocated (devoted) to an intervention can not be allocated to another one
- Somebody has to decide which interventions will be financed and what the priorities are

Opportunity cost

- Economists define costs in terms of benefits forgone
- The cost of treating Mr Brown is the benefit forgone for not treating Mr Green with the resources used to treat Mr Brown
- Thus: choices have to be made

The importance of economic evaluations in RA

1. Licensing and reimbursement authorities now require comparative effectiveness and cost-effectiveness data
2. Healthcare payers justify funding (or not funding) therapies and interventions in terms of effectiveness and cost-effectiveness
3. Disability and lost productivity are main determinants of costs; therapies are expected to show economic advantage
4. Choice of long-term therapies may depend on:
   - Comparative effectiveness
   - Costs weighed against societal burden

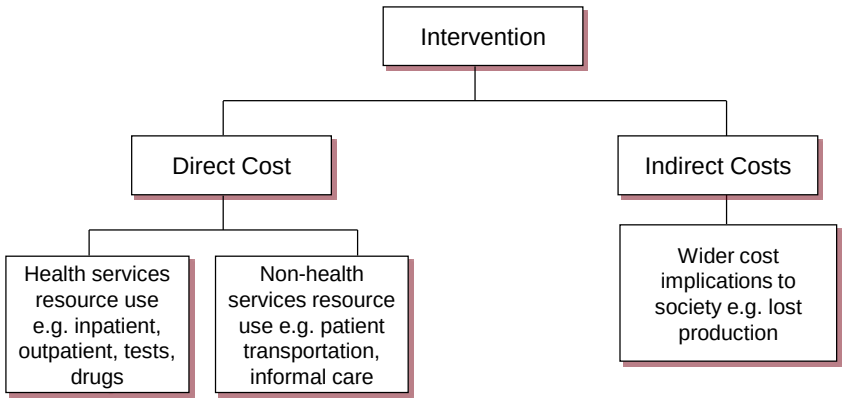
Kremers HM, et al. In: Hochberg MC, Silman AJ, Smolen JS, Weinblatt ME, Weisman MH, eds. *Rheumatology*. 5th ed. Philadelphia, PA: Mosby Elsevier; 2010;3:23–28.

Cost-effectiveness

- Costs
  - Direct medical costs
  - Patient/family costs
  - Offset savings
- Effectiveness
  - Clinical outcomes from clinical trials
  - Quality of life
- Patient preferences

MEASURING COSTS

Identification

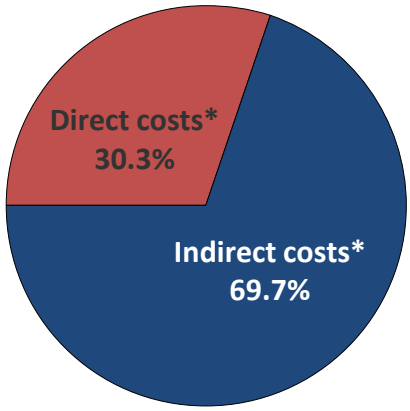


Inclusion criteria: dependent on perspective

Indirect costs comprise the majority of the cost of RA

Direct costs (2002 analysis) include:

- Visits to physician
- Drug costs
- In-patient treatment
- Non-drug treatments
- Surgery
- Imaging



Indirect costs include:

- Sick leave
- Work disability

Direct costs for RA=4,737 Euros, and total RA costs=15,637 Euros.
Direct costs are 30.29% of the total cost with indirect costs therefore being 69.7% of the total costs.

n=4,351
*Mean costs

Huscher D, et al. *Ann Rheum Dis*. 2006;65:1175–1183.

MEASURING VALUE

Type of Analysis determines choice of Outcome Measure

Analysis	Comparing	To
Cost-Benefit	Dollar value of resources used	Dollar value of resources saved or created
Cost-Effectiveness	Dollar value of resources used	Clinical effects produced
Cost-Utility	Dollar value of resources used	Quality of life produced by clincal effects

NLM Health Economics Information Resources: A Self-Study Course: Module 4. 2006.

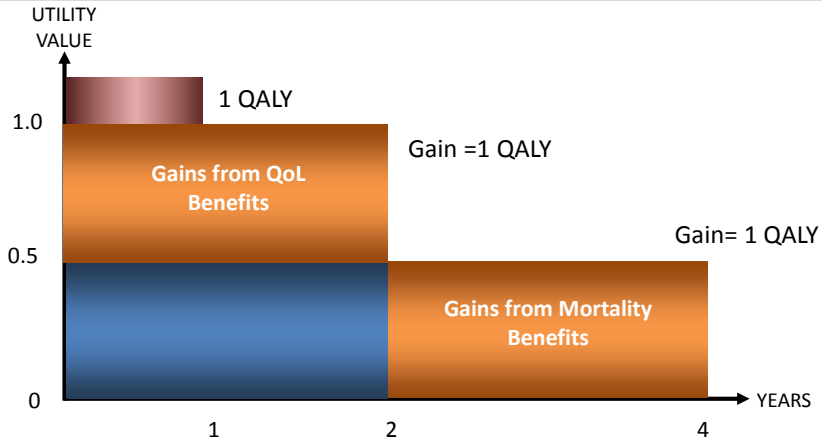
Assessing Value
What is a QALY?

Assessing value using QALYs

- A Quality Adjusted Life Year (QALY) is a composite measure of morbidity and mortality and is one of the commonly used measurements of value
- The health benefit of a health-care intervention can be measured by:
  - Reduced mortality, and/or
  - Improved health
- Economists use QALYs because it allows comparisons across diseases and interventions to support decisions on health-care resources
- The measurement of value using QALYs may indicate the best use of limited resources:
  - Interventions that offer more QALYs for every Dollar/Euro spent are of better value

NICE Guide to the methods of technology appraisal 2013. http://publications.nice.org.uk/pmg9 Accessed March 2015.
Phillips C. Health Economics. What is a QALY? 2009.

Assessing Value
An illustration of QALYs



COST EFFECTIVENESS OF ANTI-TNF TREATMENTS

Treatment Costs for RA

Annual cost per patient treated

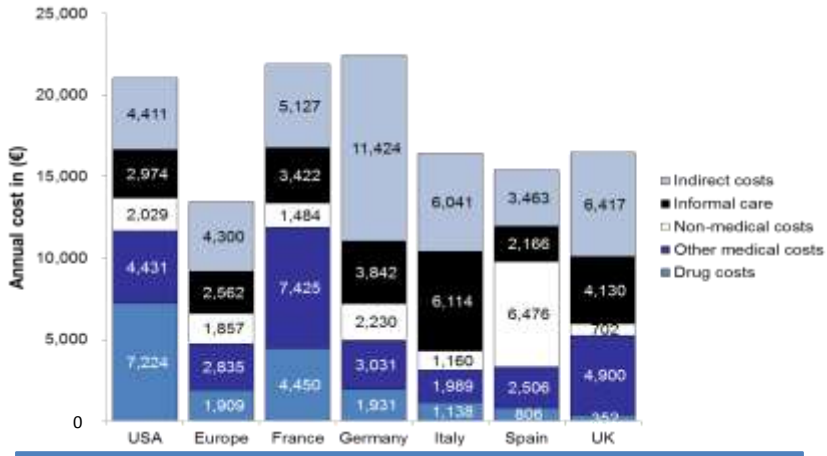
Old drugs

- Methotrexate
  - Introduced 1950s
  - €400
- High value and affordability
- Do not work for all patients

New drugs

- Anti-TNFs
  - €15-20 000
- High value
- Affordability a problem
- Optimal treatment strategies must be designed

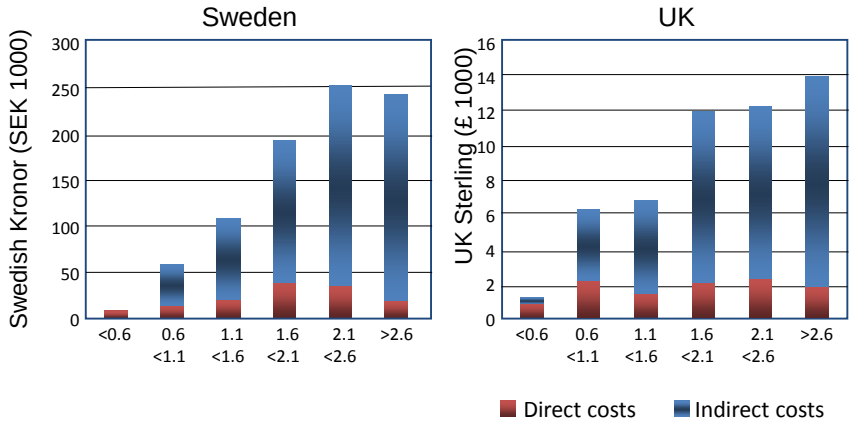
Breakdown of RA costs



There is more to consider than drug acquisition cost

Lundkvist J, et al. Eur J Health Econ 2008; 8 (Suppl. 2): S49-60.

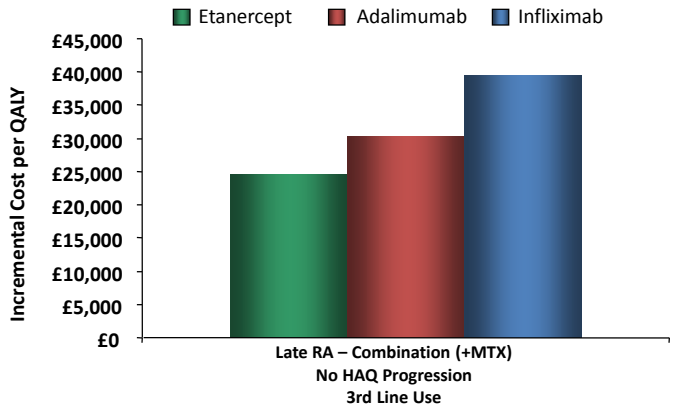
The Cost of RA by Functional Level



Kobelt G *et al*. *Arthritis Rheum*. 2002;46:2310-9.

NICE (UK) review:
Cost effectiveness of anti-TNF therapy

- NICE cost-effectiveness recommendations range from less than £24,000 to nearly £40,000



NICE Technology Appraisal Guidance 130 issued October 2007

Anti-TNF inhibitors are more cost effective in RA?

Systematic literature review on economic implications and pharmacoeconomic issues of rheumatoid arthritis

G. Furneri[1], L.G. Mantovani[2], A. Belisari[1], M. Mosca[3], M. Cristiani[1], S. Bellelli[4], P.A. Cortesi[1,5], G. Turchetti[4]

"Economic evidence suggests that biologic agents generally are cost effective compared to DMARDs for RA in adults in selected populations at a willingness to pay threshold of $50,000 per QALY."

Cost of switching

- There is a cost of switching therapy:
  - Extra physician visits
    - Physician's time
    - Nurses' time
    - Patient's time
  - Extra monitoring
  - Tests
  - etc

Is value based pricing the answer?

- Pharmaceutical manufacturers have voluntary agreement with UK Government to set prices - subject to a cap (Pharmaceutical Price Regulation Scheme, PPRS)
- National Institute for Health & Care Excellence (NICE) examines cost-effectiveness
- Proposed new scheme – drugs to be priced by Government using new definitions of value: 'Value-based pricing'
- Due to start January 2014, now delayed indefinitely

Does health economic assessment make the decision for us?

"...it is better to have an approximate measure of the right factors than a precise measure of the wrong ones."

Drummond, Stoddard, Torrance, 1987

Summary

- Economic evaluation is being increasingly applied to inform resource allocation decisions
- Care needs to be taken in developing or reviewing an economic evaluation
  - Perspective
  - Comparator
  - Presentation of findings
  - Handling of uncertainty
- Affordability may be a separate issue

Are you getting what you budget for? Biologic costs in the real world

Professor Robert Moots
University of Liverpool, Liverpool, United Kingdom

UNIVERSITY OF LIVERPOOL

13.enb.25.2

Disclosures

- I do not receive personal income from this presentation
- Funding for this presentation supports development of Rheumatology in Africa
- I work with a number of pharmaceutical companies
- I believe that choice in biologic therapy is important – with access to a range of biologic drugs

Rheumatoid Arthritis

A prevalent disease

- Affects <1% of the UK population (~387,000 people)
- More common in females

A serious disease

- Pain
- Social effects
- Cost to society
- Not just joints

Severe uncontrolled RA increases mortality

Arthritis Research Campaign (ARC). Arthritis – The Big Picture. Chesterfield, ARC 2002.

Who Chooses Therapy in RA?

- In a cost-constrained healthcare environment choices have to be made
- Evidence of value is required by payors
- Choices are based on comparative value

Payors make choices!

Value required!

Chaudhari P. *Biotechnol Healthc* 2008;5:37–44.

What is Value?

Does a healthcare intervention:

- Save lives or reduce disease?
- Save cost?
- Get people back to normal living or work?

- Do all of these better than the existing therapies?

Value $\propto$ [cost][benefit]

Porter, ME. *N Engl J Med* 2010;363:2477-248.

Biologics in the Balance

Rapid effects

High efficacy

Sustained benefits

Efficacy when DMARDs fail

Halt structural damage

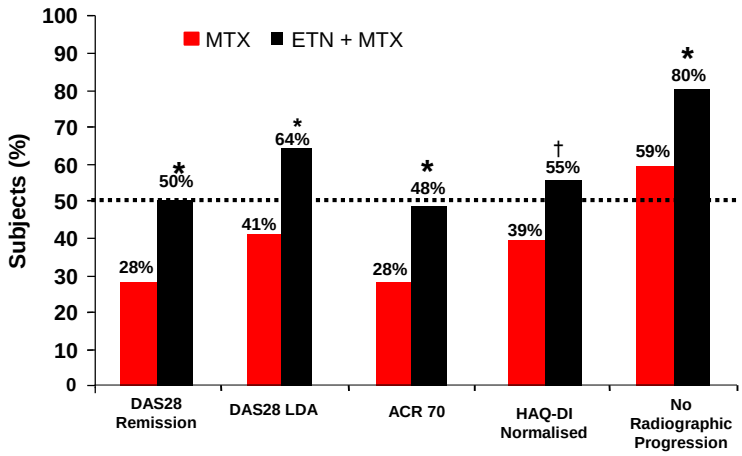
Good safety profile

Not a cure

Lambert CM. *Rheumatol* 2001;40:961-964.

Enbrel (etanercept) Summary of Product Characteristics.

COMET: Clinical outcomes at 1 Year

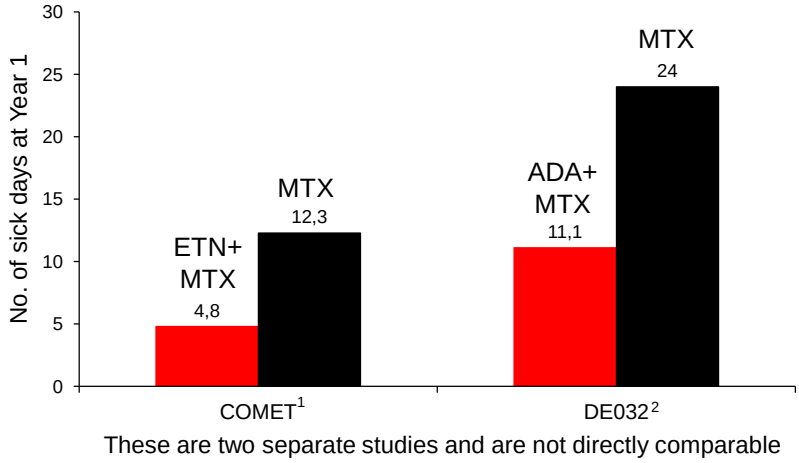


**P*<0.0001

†*P*=0.0004

Emery P et al. *Lancet*. 2008;372:375-382.

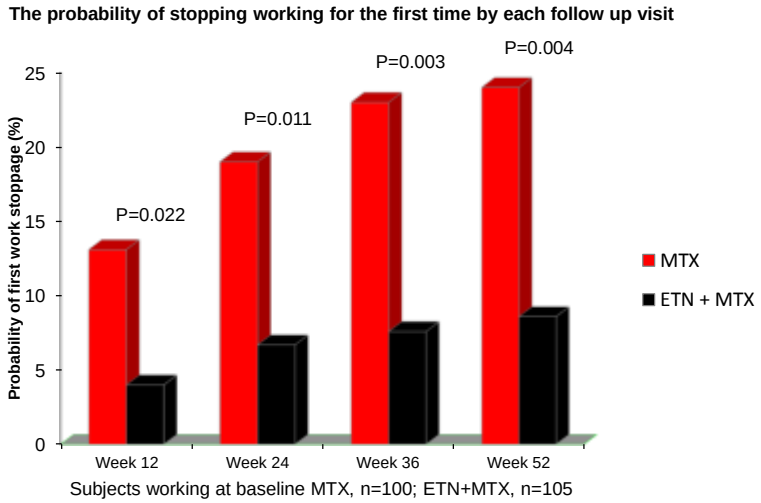
TNFi Trials: Sick Days



These are two separate studies and are not directly comparable

1. Anis A., et al. *Rheumatology* 2009;48:1283–1289;
2. Van Vollenhoven et al. *Ann Rheum Dis* 2007;66 (Suppl 2):192. Abstract THU0216.

COMET Cumulative Percent of Subjects Who Stopped Working



Subjects working at baseline MTX, n=100; ETN+MTX, n=105

Emery P et al. *Lancet*. 2008;372:375-382.
Anis A, et al. *Rheumatology*. 2009;48:1283–1289.

The Importance Of Real-Life Data

"It's time we face reality, my friends… We're not exactly rocket scientists"

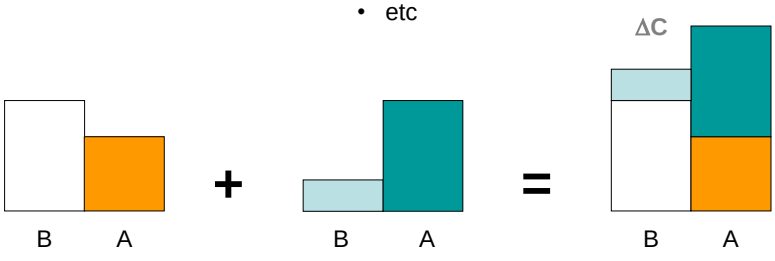
Cartoon by Gary Larson. *The Far Side.*

Treatment Costs: Drug B vs. Alternative A

Average
List price

Average other
treatment costs*
- physicians
- hospital
- surgery
- other drugs
- tests
- increased dosing
- etc

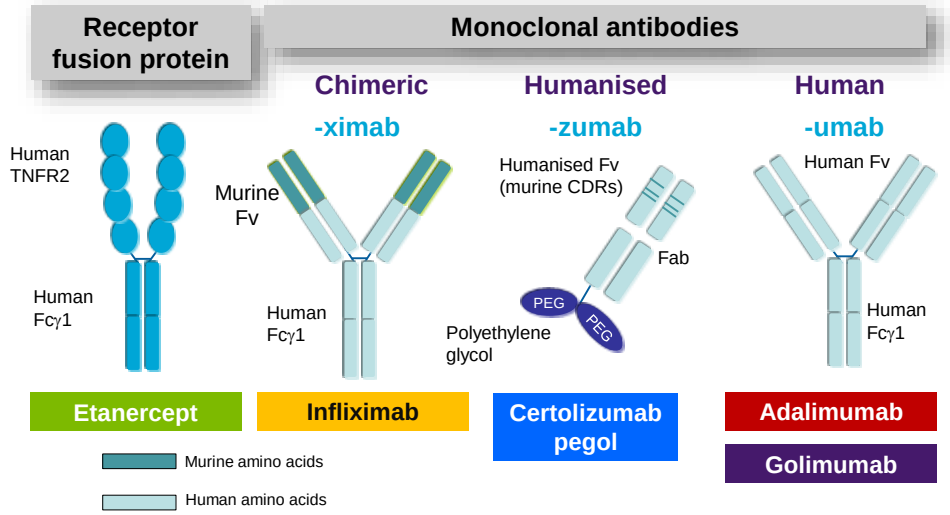
Total treatment cost



**** Disease and treatment related***

Hypothetical example based on: Moots RJ, et al. *Clin Exp Rheumatol* 2011;29:26-34.

Structures of the TNFi treatments used in RA



Anderson PJ. *Semin Arthritis Rheum* 2005;34:19–22; Enbrel EU SmPC; Humira EU SmPC; Remicade EU SmPC; Cimzia EU SmPC; Simponi EU SmPC.

CDR, complementarity determining region; Fab, fragment antigen-binding; Fc, crystalline fragment; Fv, variable fragment; RA, rheumatoid arthritis; TNFi, tumour necrosis factor inhibitor

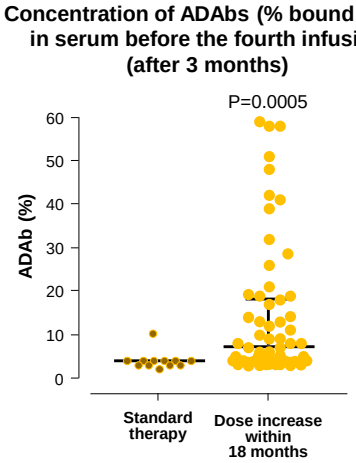
Labelled dose of TNF inhibitors: Guidance on dosing escalation from the SmPC

Therapy	Administration	Labelled dose	Frequency	Guidance on dose escalation?
Infliximab[1]	IV	3 mg/kg	Every 8 weeks	If a patient has an inadequate response or loses response after 12 weeks, consideration may be given to increase the dose step-wise by approximately 1.5 mg/kg, up to a maximum of 7.5 mg/kg every 8 weeks. Alternatively, administration of 3 mg/kg as often as every 4 weeks may be considered.
Etanercept[2]	SC	25 mg/50 mg	Twice weekly/ once weekly	Not recommended
Adalimumab[3]	SC	40 mg†	Every other week	In monotherapy, some patients who experience a decrease in their response may benefit from an increase in dose to 40 mg adalimumab every week
Golimumab[4]	SC	50 mg	Monthly	In patients weighing more than 100 kg who do not achieve an adequate clinical response after 3 or 4 doses, increasing the dose to 100 mg once a month may be considered.
Certolizumab pegol[5]	SC	200 mg	Every other week	Not recommended

1. Remicade (infliximab) Summary of Product Characteristics.
2. Enbrel (etanercept) Summary of Product Characteristics.
3. Humira (adalimumab) Summary of Product Characteristics.
4. Simponi (golimumab) Summary of Product Characteristics.
5. Cimzia (certolizumab pegol) Summary of Product Characteristics.

IV, intravenous; SC, subcutaneous.

Relationship between immunogenicity status and dose escalation in RA



- Elevated ADAb concentrations lead to an increased dose escalation due to decreased clinical response[1]
- The presence of ADAbs at 3 months may predict future dose escalation[1]

Many factors impact the efficacy and safety of biologics or how an individual patient responds to a biologic. The presence or absence of neutralising anti-drug antibodies is one of these factors and does not allow any conclusions about the overall efficacy and safety of a drug. The occurrence of anti-drug antibodies is also influenced by several factors including the co-treatment with immunosuppressive drugs such as MTX

Bendtzen K, et al. *Arthritis Rheum* 2006;54:3782–3789.

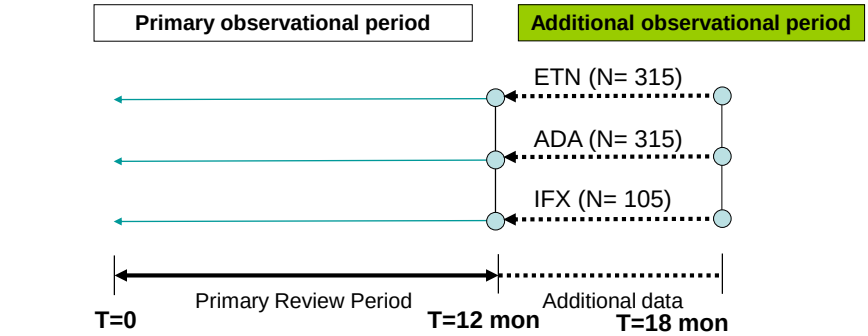
ADAb, anti-drug antibody; RA, rheumatoid arthritis

Real Life Usage of TNFi in Europe: DART Study

Anti-TNF ***D***rug utilization and dosing patterns ***A***ssessment: a ***R***etrospective observational study of subjects ***T***reated for Rheumatoid Arthritis

Moots RJ, et al. *Clin Exp Rheumatol* 2011;29:26-34.

Study design: Patients started first biologic between Jan 2003 and Dec 2004

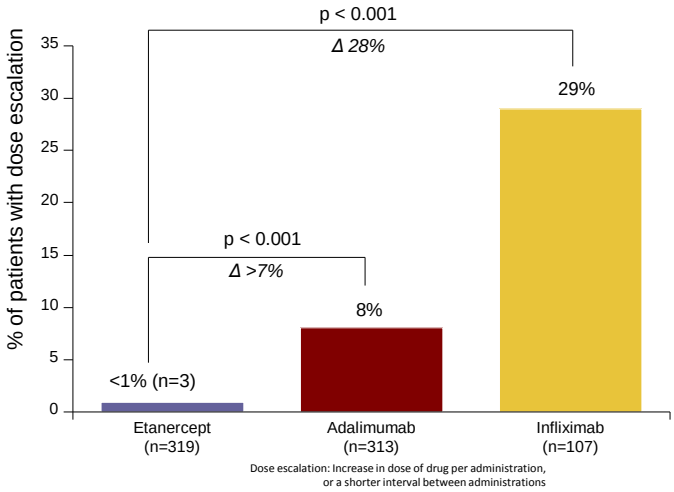


Baseline
- Gender, Weight, Disease Duration
- Signs and symptoms
- Co-morbidities
- Prior DMARDs
- Hospitalization
- Economic
- Starting dose

Periodic
- Dose
- Dosing interval
- Steroid-use
- DMARD dosing
- Reasons for dose adjustments
- Disease severity
- Economic

Moots RJ. BMJ Satellites 2009; 22-5.

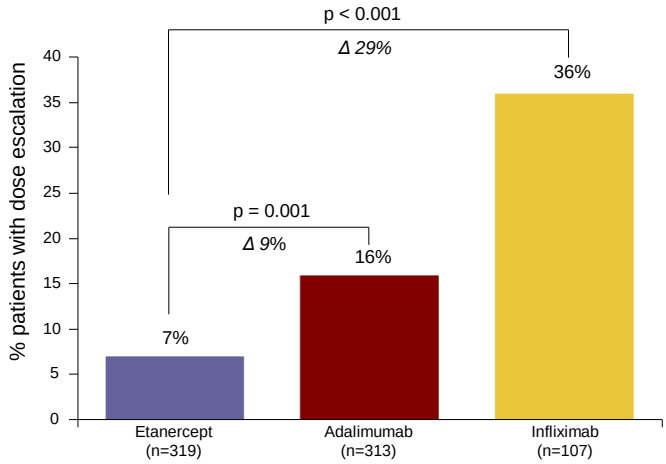
Occurrence of Dose Escalation Is Significantly Greater with anti-TNF mAbs



Moots RJ. BMJ Satellites 2009; 22-5.

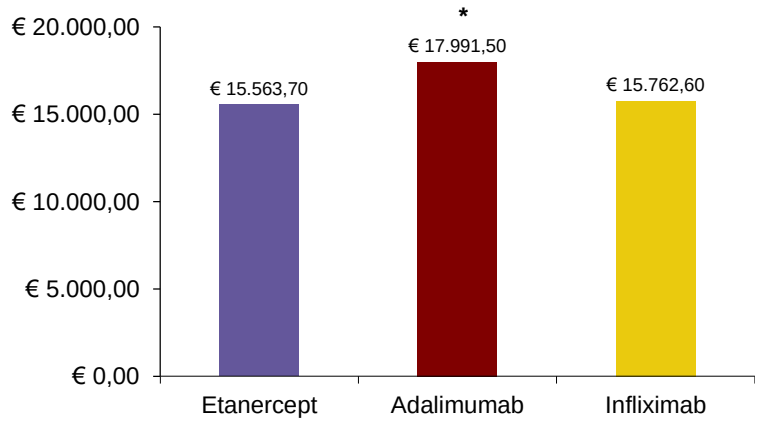
Occurrence of Secondary Escalation is Significantly Greater with Anti-TNF mAbs

Secondary escalation: intensifying the dose of the biologic drug or intensifying the DMARD component of therapy



Moots RJ. BMJ Satellites 2009; 22-5.

Per Patient Estimated Total Annual Cost of Care



*** p-value <0.001**

Per Patient Annual Total Cost of Care

Moots RJ. BMJ Satellites 2009; 22-5.

Dose Escalation in RA and Costs: What is the Evidence Overall?

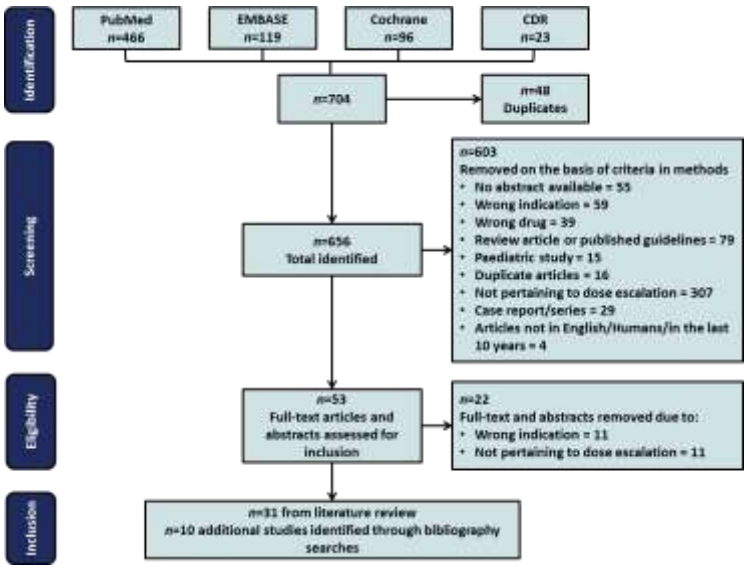
Burden of dose escalation with tumour necrosis factor (TNF) inhibitors in rheumatoid arthritis: a review of frequency and costs

Robert J. Moots[1], Robyn Mays[2], Congyu Li[2], Jennifer Stephens[2] and Miriam Tarallo[3]

[1]Department of Musculoskeletal Biology, University of Liverpool, UK, [2]Pharmerit International, 4350 East-West Highway, Bethesda, Maryland, USA, [3]Pfizer Italia, Via Valbondione, Rome, Italy

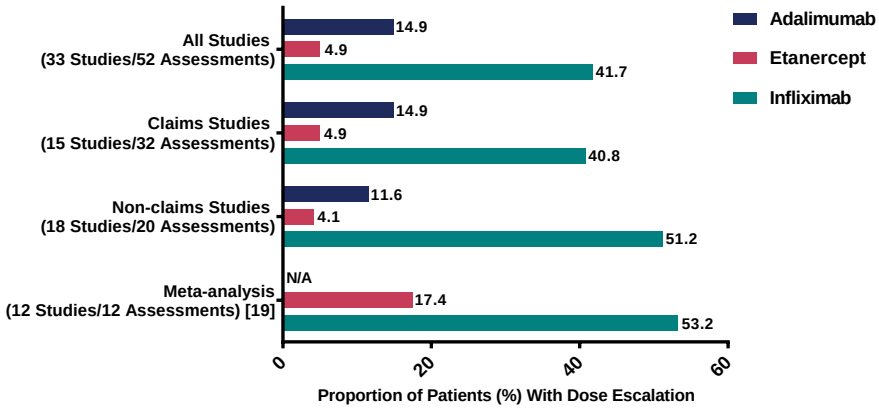
Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

Literature Review Flow Diagram



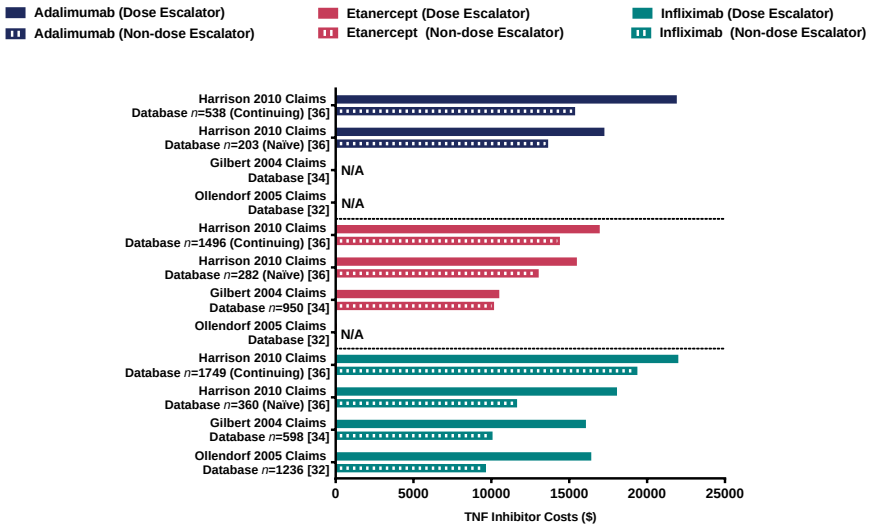
Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

Weighted Proportion of Patients Undergoing Dose Escalation



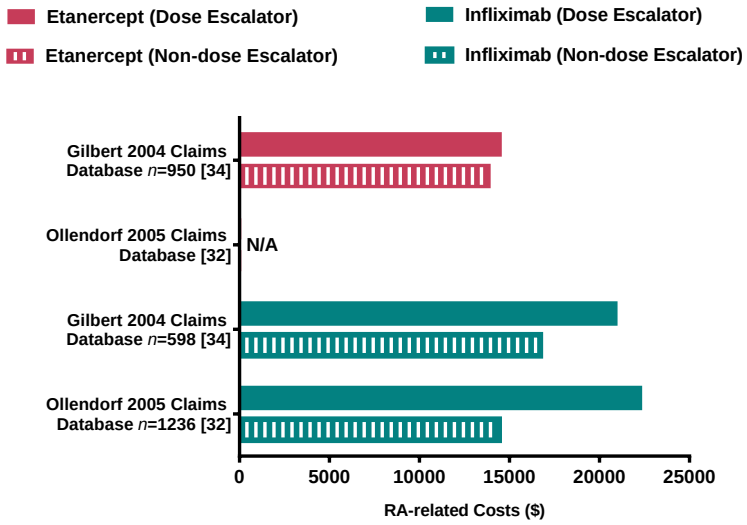
Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

TNF Inhibitor Costs Associated with Dose Escalators & Non-Dose Escalators



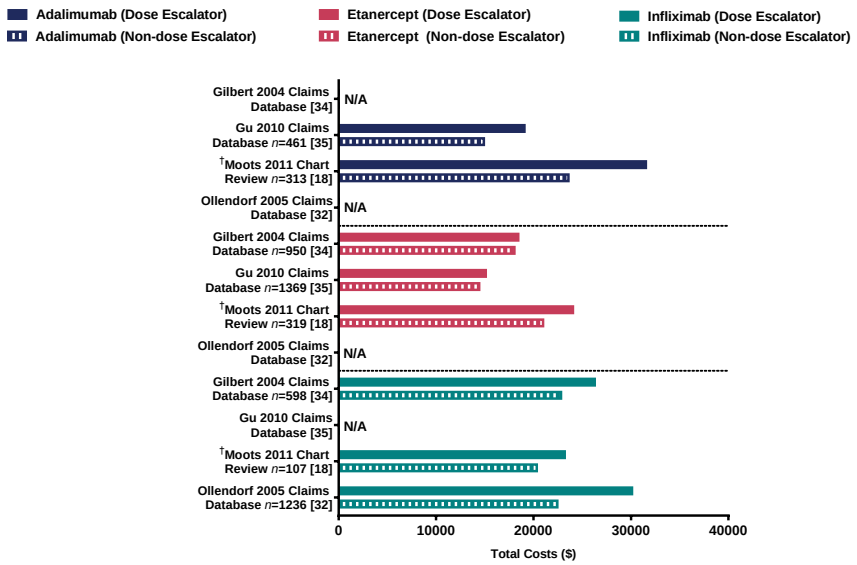
Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

RA-Related Costs Associated with Dose Escalators & Non-Dose Escalators



Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

Total Costs Associated with Dose Escalators & Non-Dose Escalators



Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

Dose Escalation with TNFi in RA: Conclusions

- Pooled results demonstrated that dose escalation occurred most frequently with IFX and least frequently with ETN
  - Results are consistent with individual comparative studies
- In patients with RA undergoing dose escalation, not only were biologic costs increased, but also RA-related and total costs
- ETN was associated with the lowest cost increases compared with ADA and IFX

These are not head-to-head comparisons between the three TNFi. Differences in baseline characteristics may exist in the comparative studies

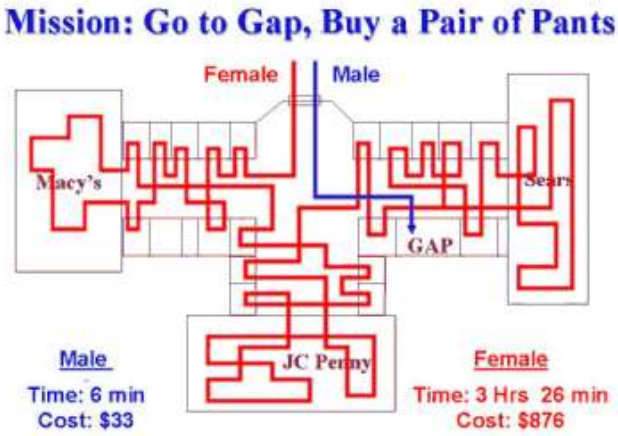
Moots RJ, et al. *Clin Exp Rheumatol* (In Press).

ADA, adalimumab; ETN, etanercept; INF, infliximab; RA, rheumatoid arthritis

Economics and RA: Summary

- Rheumatoid arthritis: high morbidity/mortality and costly for society
- Therapies for RA effective – but some expensive
- Heath economies have limited resource – value for money is important everywhere!
- Data is accruing (e.g. UK NICE) to show that biologics are good value for money
- Sustainable efficacy varies between TNFi's
- The challenge remains to give the right drug to the right person at the right time!

Value – Keep it simple!



Hamburg, 25 marzo 2015

European Association of Hospital Pharmacy 2015

Real world cost of biologic therapy: A European perspective

Optimising biologic care in an evolving landscape: Real world decisions in rheumatology

Degli Esposti, EconD

CliCon S.r.l.
Health, Economics & Outcomes Research

Disclosure

- Speaking and research grants from:
  - Pfizer
  - BMS
  - MSD

Treatment patterns and health resources use in patients affected by Rheumatoid Arthritis (RA) and treated with biologic drugs

Objective: To discuss Italian and European real-world evidence on patients affected by **rheumatoid arthritis** (RA) and treated with **biologic drugs**, in particular tumour necrosis factor alpha (TNF-α) inhibitors, with specific focus on:

- **treatment patterns** in terms of dose escalation, dose de-escalation, treatment switch, and treatment persistence
- **health resources use** (HRU) in terms of drugs, tests, visits, hospitalizations, and other items in charge of public system

CliCon S.r.l. Health, Economics & Outcomes Research

Hamburg, 25 marzo 2015

Definition of Real-world Evidence by the International Society for Pharmacoeconomics & Outcomes Research Task Force

As defined by the ISPOR task force:

"Data used for clinical, coverage and payment decision-making that are not collected in conventional randomized controlled trials (RCTs)"

Real-world data are observations of treatment or procedure effects where the researcher has no control over subsequent medical management of the patient beyond observing the outcomes

Garrison Jr. LP, Neumann PJ, Erickson P, et al. Using real-world data for coverage and payment decisions: The ISPOR real-world data task force report. Value Health 2007;10:326-35.

CliCon S.r.l. Health, Economics & Outcomes Research

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…on patient selection

…on treatment patterns

Garrison Jr. LP, Neumann PJ, Erickson P, et al. Using real-world data for coverage and payment decisions: The ISPOR real-world data task force report. Value Health 2007;10:326-35.

CliCon S.r.l. Health, Economics & Outcomes Research

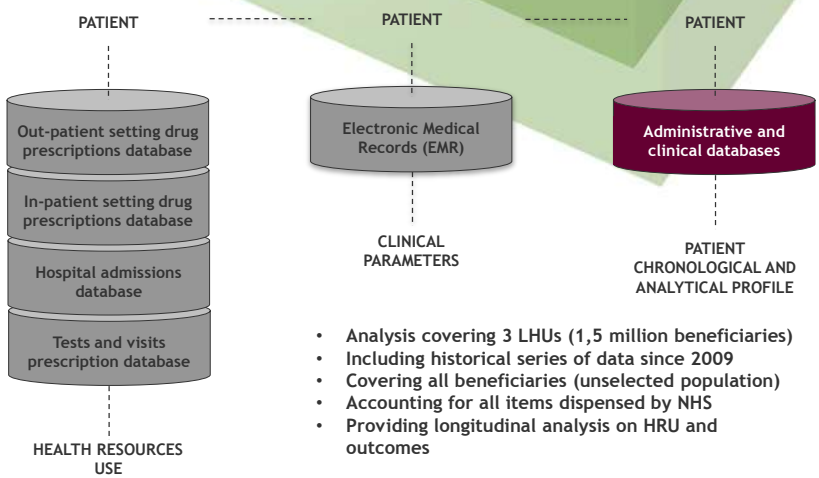
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs (Italian evidence)

- Observational retrospective cohort analysis using the **administrative databases** of three Italian local health units.
- **Rheumatoid arthritis patients filling at least one prescription for anti-TNF** alpha between January 2010 and December 2012 were included into the analysis and followed-up to Dec 2013.
- **564 patients** were included into the analysis with a mean age (standard deviation) equal to 53.8±13.7 and female-male ratio equal to 3:1.
- **Dose escalation** was defined as having two consecutive claims with an average weekly dose 30% greater (lower) than the initial average weekly dose*
- **Dose de-escalation** was defined as having two consecutive claims with an average weekly dose 30% lower than the initial average weekly dose*
- **Anti-TNF treatment persistence** was defined as having the same anti-TNF in the last quarter of the follow-up period
- **Anti-TNF treatment switch** was defined has having an anti-TNF in the last quarter of the follow-up period different form those prescribed at the index date

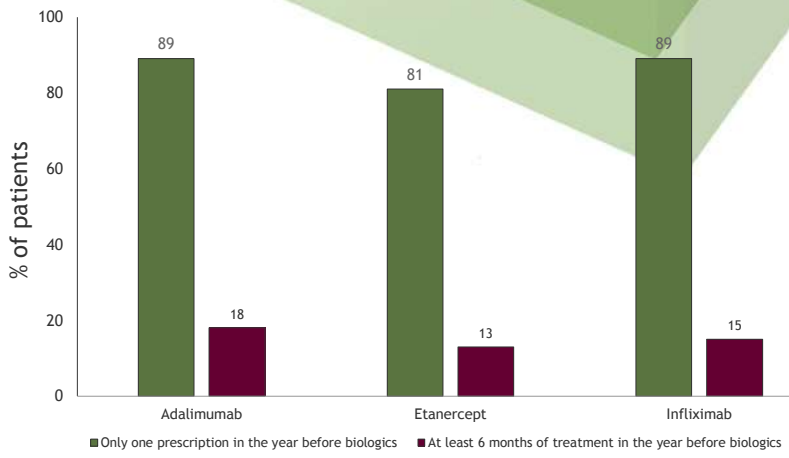
* Bonafede MM et al. Tumor necrosis factor blocker dose escalation among biologic naïve rheumatoid arthritis patients in commercial managed-care plans in the 2 years following therapy initiation. J Med Econ. 2012;15(4):635-43. Darkow et al. Dose Escalation Among Rheumatoid Arthritis Patients Treated with Infliximab or Abatacept: Comparison in Claims Data. Arthritis Rheum 2011; 63(10):1221

An integrated administrative and clinical database to generate real–world evidence across Regional and Local Health Units



- Analysis covering 3 LHUs (1,5 million beneficiaries)
- Including historical series of data since 2009
- Covering all beneficiaries (unselected population)
- Accounting for all items dispensed by NHS
- Providing longitudinal analysis on HRU and outcomes

Use of DMARDS before biologic treatment
(calculated in newly treated patients with biologics)



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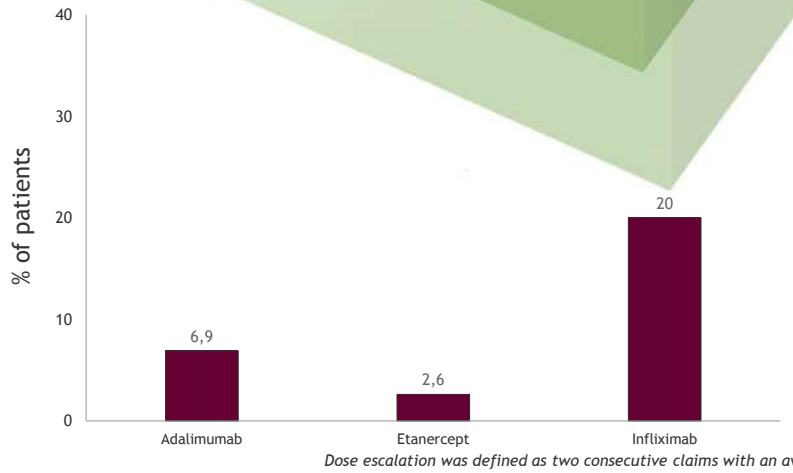
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Dose escalation
(calculated in newly treated patients with biologics and persistent at the index biologic drug during the one year follow-up period)



Dose escalation was defined as two consecutive claims with an average weekly dose 30% greater than the initial average weekly dose.

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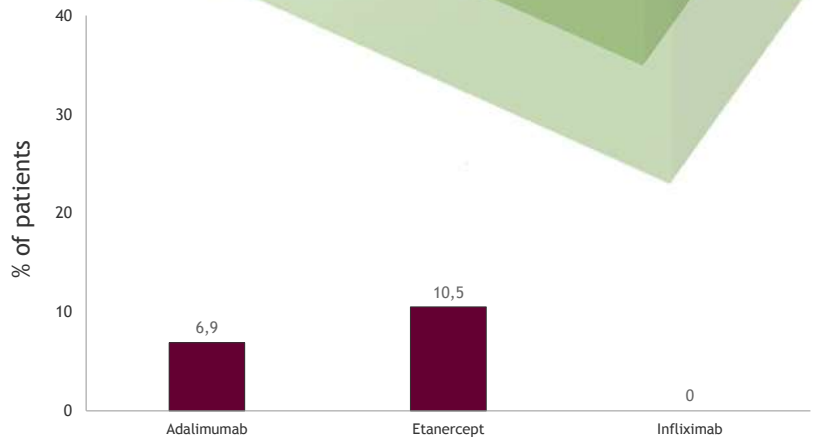
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Dose de-escalation
(calculated in newly treated patients with biologics and persistent at the index biologic drug during the one year follow-up period)



Dose de-escalation was defined as two consecutive claims with an average weekly dose 30% lower than the initial average weekly dose.

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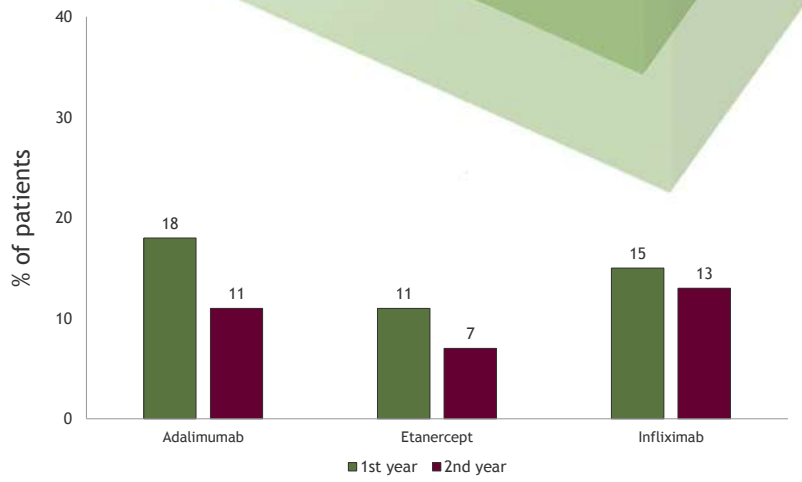
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Treatment switch
(calculated during the first and the second year of the follow-up period)



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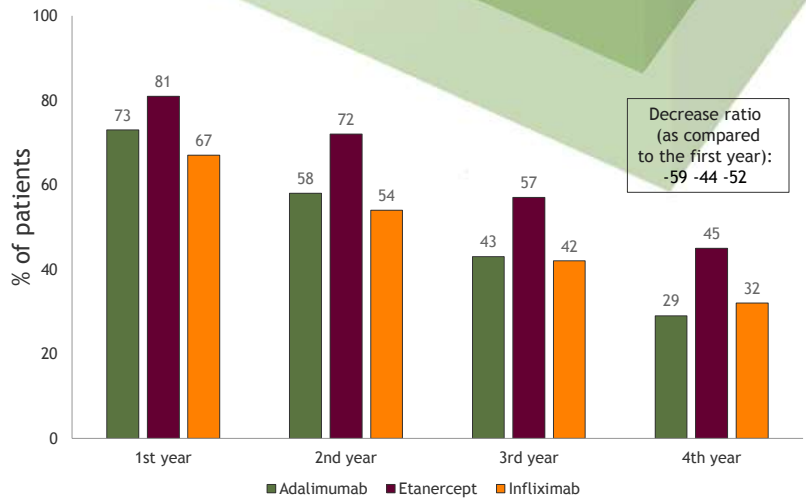
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Persistence with treatment
(calculated during the first, second, third and fourth year of the follow-up period)



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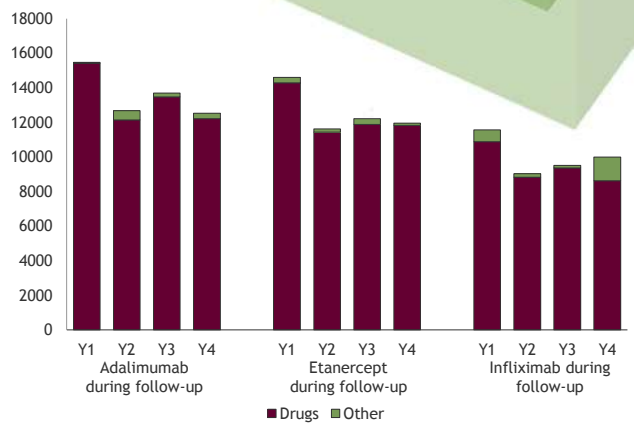
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Average annual cost per patient
(calculated in persistent patients during the first, second, third, and fourth year of the follow-up period)



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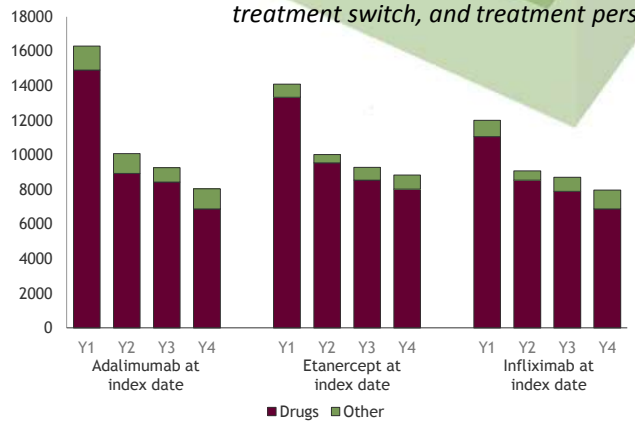
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Average annual cost per patient
(calculated during the first, second, third, and fourth year of the follow-up period)

Cost "mitigation" over years is significantly related to treatment patterns (dose escalation, dose de-escalation, treatment switch, and treatment persistence)



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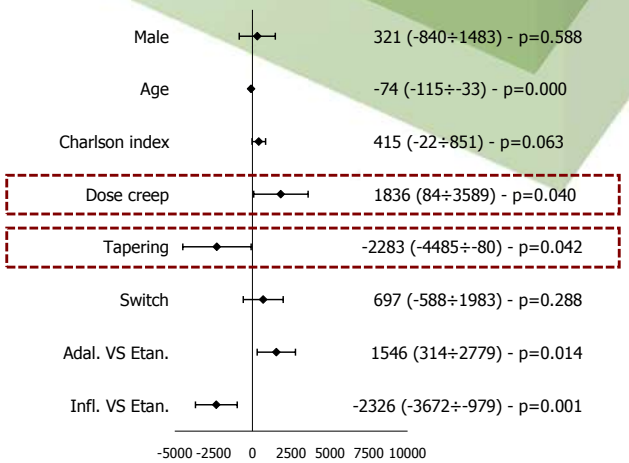
Hamburg, 25 marzo 2015

Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

Average annual patient cost drivers (…)



Baseline cost: €15,127

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Degli Esposti et al. Treatment patterns and health resources use in patients affected by rheumatoid arthritis and treated with biologic drugs. In press.

de la Torre et al. Anti-TNF treatments in rheumatoid arthritis: economic impact of dosage modification (a Spanish case)

Table 2. Distribution of patients according to prescribed anti-TNF treatment regimens.

Anti-TNF	Dose regimen†	n (%)‡	Dose	Dosing frequency (mean§ ± SD)	
ETN (n = 81)	Label	13 (16)	25 mg	Twice weekly	
		46 (56.8)	50 mg	Weekly	
	Reduced	10 (12.3)	25 mg	6.8 ± 1.96 days	
		12 (14.8)	50 mg	10.4 ± 1.44 days	
	Escalated	0			0% of patients escalating dosage
ADA (n = 56)	Label	39 (69.6)	40 mg	Every other week	
	Reduced	14 (25)	40 mg	21.8 ± 3.08 days	
	Escalated	3 (5.4)	40 mg	10.6 ± 3.21 days	5% of patients escalating dosage
IFX (n = 58)	Label	16 (27.6)	3 mg/kg	Every 8 weeks	
	Reduced	2 (3.4)	3 mg/kg	9 ± 0.4 weeks	
	Escalated	40 (69.0)	4 mg/kg	7.8 ± 0.41 weeks	69% of patients escalating dosage

†Label: according to the approved prescribing information: ETN 25 mg every 4 days or 50 mg every 7 days; ADA 40 mg every other week; IFX 3 mg/kg every 8 weeks. Reduced: the time between doses is longer or the dose is lower than the label. Escalated: the time between doses is shorter or the dose is higher than the label.
‡Percentages for the subcategories (label, reduced and escalated) are calculated based on number per each group (ETN, ADA and IFX).
§Mean time between doses.
ADA: Adalimumab; ETN: Etanercept; IFX: Infliximab; SD: Standard deviation.

CliCon S.r.l. Health, Economics & Outcomes Research

de la Torre et al. Anti-TNF treatments in rheumatoid arthritis: economic impact of dosage modification. Expert Rev. Pharmacoecon. Outcomes Res. 13(3), 407–414 (2013).

Hamburg, 25 marzo 2015

de la Torre et al. Anti-TNF treatments in rheumatoid arthritis: economic impact of dosage modification (a Spanish case)

Table 3. Annualized costs associated to label and clinical practice doses.

Annualized costs	ETN (n = 81)	ADA (n = 56)	IFX (n = 58)
Label dose drug costs (€)	11,845.9	12,859.8	7042.05
Infusion cost (€)†			721.0
Total theoretical costs (€)	11,845.9	12,859.8	7763.1
Mean prescribed doses (%)*‡	44.85 mg/every week (89.7)	37.4 mg/every other week (93.5)	3.74 mg/kg/8w (124.5)*
Annual dose per patient (deviation vs theoretical)	2.332 mg (-268 mg)	972 mg (-68 mg)	1.702 mg (+337 mg)
Real-world drug cost (€)	10,622.3	12,020.1	8945.8
Infusion cost (€)			721.0
Total clinical practice costs (€)§	10,622.3	12,020.1	9666.9
Incremental (theoretical vs clinical practice) cost (€)*	-1223.6	-839.7	1903.8*

Costs are expressed as € /patient/year.
* $p < 0.05$ IFX vs ADA and IFX vs ETN.
†Cost derived from intravenous infusion, including day hospital costs.
‡Mean percentage of doses considering the label dose as 100%.
§$p < 0.05$ between all groups.
ADA: Adalimumab; ETN: Etanercept; IFX: Infliximab.

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de la Torre et al. Anti-TNF treatments in rheumatoid arthritis: economic impact of dosage modification. Expert Rev. Pharmacoecon. Outcomes Res. 13(3), 407–414 (2013).

Hamburg, 25 marzo 2015

Ramírez-Herráiz et al. Efficiency of adalimumab, etanercept and infliximab in rheumatoid arthritis patients: dosing patterns and effectiveness in daily clinical practice (a Spanish case)

	ADA	ETN	IFX*
Cases	73	81	61
Recommended dose	40 mg biw	50 mg weekly	3 mg/kg/8 weeks
Patient-year cost (recommended dose)	€12.859.79	€11.845.93	€7.566.27
Average dose (study dose)†	37.21 (9.61) mg/biw	40.5 (13.46) mg weekly	4.07 (1.13) mg/kg/8 weeks
Study dose (% of recommended dose)	93.02%	81.00%	135.73%
Patient-year cost (study dose) ‡	€11.962.58	€9.594.73	€10.094.53
Patient-year costs differences (recommended *vs*. study dose) †	€-897.22	€-2.251.20	€+2.528.26

ADA: adalimumab; biw: twice weekly; ETN: etanercept; IFX: infliximab; DAS28: 28-item Disease Activity Scale; RA: rheumatoid arthritis. Costs are calculated based on ex-factory prices including taxes (2011 €).
*includes indirect costs (€110.93 per infusion) and 0.89% vial wastage; †$p<0.05$ between all groups; ‡ $p<0.05$ ADA *vs*. ETN, ADA *vs*. IFX.

Ramírez-Herráiz et al. Efficiency of adalimumab, etanercept and infliximab in rheumatoid arthritis patients: dosing patterns and effectiveness in daily clinical practice. Clinical and Experimental Rheumatology 2013.

CliCon S.r.l. Health, Economics & Outcomes Research

Hamburg, 25 marzo 2015

Ramírez-Herráiz et al. Efficiency of adalimumab, etanercept and infliximab in rheumatoid arthritis patients: dosing patterns and effectiveness in daily clinical practice (a Spanish case)

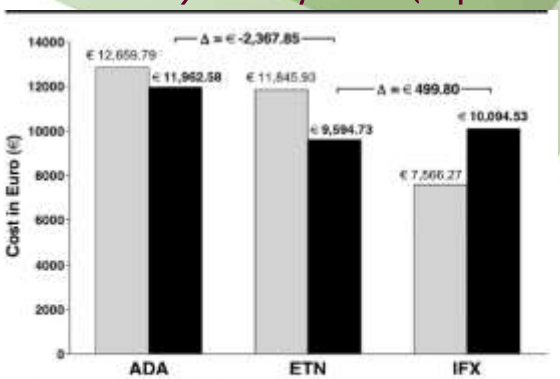

Fig. 2. Annualised cost of each anti-TNF group. Light columns represent patient-year cost based on recommended doses and dark columns account for patient-year cost based on mean doses in study patients. *p*-value was less than 0.05 for all therapies *vs*. theoretical cost. Costs are calculated based on ex-factory prices including taxes (2011 €).
$p<0.05$ adalimumab *vs*. etanercept, and adalimumab *vs*. infliximab according to costs based on study dosing. Infliximab data include indirect costs (€110.93/infusion) and 0.89% vial wastage.
ADA: adalimumab; ETN: etanercept; IFX: infliximab.

Ramírez-Herráiz et al. Efficiency of adalimumab, etanercept and infliximab in rheumatoid arthritis patients: dosing patterns and effectiveness in daily clinical practice. Clinical and Experimental Rheumatology 2013.

CliCon S.r.l. Health, Economics & Outcomes Research

Hamburg, 25 marzo 2015

Sibilia et al. Prescription of anti-TNF in Chronic Inflammatory Rheumatic Diseases in France: dosages observed in clinical practice and impact on cost (a French case)

Freq. Inj. Month*	ETN 25	ETN50	ADA	CZP	GOL
RA	N=378 3.9 [2.8 - 5.1]	N=3207 3.3 [3.2 - 3.4]	N=2715 1.9 [1.8 - 2.0]	N=295 2.1 [1.9 - 2.3]	N=292 1.0 [1.0 - 1.4]
AS	N=138 3.2 [2.4 - 4.0]	N=1392 3.3 [3.1 - 3.5]	N=1484 2.0 [1.8 - 2.1]	N=57 2.3 [1.6 - 2.9]	N=293 1.0 [1.0 - 1.1]
PsA	N=26 2.4 [1.9 - 3.0]	N=202 3.1 [2.8 - 3.4]	N=273 1.0 [1.6 - 2.0]	N=15 2.2 [1.4 - 2.7]	N=36 1.0 [1.0 - 1.0]
Theo. Cost**	10,481	10,481	10,221	9,168	9,936
Mean cost***	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
CIR	8150 [7768 - 8533]		9824 [9343 - 10305]	9829 [8884 - 10774]	10363 [9927 - 10800]
RA	8211 [7783 - 8638]		9748 [9136 - 10360]	9722 [8794 - 10650]	10529 [9724 - 11334]
AS + PsA	8039 [7434 - 8644]		9933 [9325 - 10542]	10346 [7661 - 13031]	10196 [9942 - 10449]

*Mean [95%CI]; **/*** Theoretical/observed cost during the study period (€)

Sibilia et al. Prescription of anti-TNF in Chronic Inflammatory Rheumatic Diseases in France: dosages observed in clinical practice and impact on cost. French Congress of Rheumatology 2014.

CliCon S.r.l. Health, Economics & Outcomes Research

Hamburg, 25 marzo 2015

Berglund et al. Significant differences in dispensed doses were observed between self-administered TNF-inhibitors (a Swedish case)

Table 1. The Ratio between the Observed and the Expected Dispensed Dose by TNF inhibitor among RA patients in Sweden.

	Overall			12-24 months		
TNF inhibitor	**%**	**95% CI**	**p-value**	**%**	**95% CI**	**p-value**
Etanercept	**92**	**91-94**	**ref.**	**86**	**84-87**	**ref.**
Adalimumab	**98**	**94-102**	**<0.001**	**93**	**89-98**	**<0.001**
Golimumab	**105**	**100-109**	**<0.001**	**101**	**96-106**	**<0.001**
Certolizumabpegol	**92**	**88-97**	**0.87**	**94**	**89-99**	**<0.001**

ref. = reference, CI = confidence interval

Berglund et al. Significant differences in dispensed doses were observed between self-administered TNF-inhibitors. Reumadagarna 2014.

CliCon S.r.l. Health, Economics & Outcomes Research

Hamburg, 25 marzo 2015

Fragoulakis et al. Economic evaluation of anti-TNF agents for patients with rheumatoid arthritis in Greece (a Greek case)

Table 3 Average cost per patient per year for the base case scenario (in €)

	New patients		Existing patients**
	Nonresponders	Responders*	Responders
Etanercept	2,276 (NA)	9,845 (NA)	9,840 (NA)
Etanercept + MTX	2,278 (NA)	9,857 (NA)	9,852 (NA)
Infliximab + MTX	3,171 (NA)	11,728 (11,642–11,813)	11,342 (10,471–12,211)
Adalimumab	2,293 (NA)	10,389 (10,289–10,485)	11,163 (10,915–11,404)
Adalimumab + MTX	2,296 (NA)	10,400 (10,300–10,497)	11,175 (10,927–11,417)

Notes: Values are expressed as mean (95% UI), where UI was the lower and upper uncertainty interval from 10,000 Monte Carlo simulations. *Minimum improvement criteria for a responder were the "ACR 20" (the definition requires, among other prerequisites, a 20% improvement in both tender and swollen joint counts);[38] **previously treated patients who were continuing therapy and who achieved an improvement greater than the minimum criteria of ACR 20.
Abbreviations: ACR, American College of Rheumatologists; MTX, methotrexate; NA, not available; UI, uncertainty interval.

Table 4 Average cost per patient per year for two scenario analysis (in €)

	New patients		Existing patients**
	Nonresponders	Responders*	Responders
Scenario 1 Dose escalation: 2.5% (etanercept), 9.6% (adalimumab), and 35% (infliximab) (DART study[37])			
Etanercept	2,276 (NA)	9,938 (9,932–9,944)	10,086 (10,070–10,103)
Etanercept + MTX	2,278 (NA)	9,949 (9,943–9,955)	10,098 (10,082–10,114)
Infliximab + MTX	3,171 (NA)	10,581 (10,496–10,666)	9,133 (8,967 – 9,298)
Adalimumab	2,293 (NA)	10,278 (10,255–10,302)	10,868 (10,807–10,929)
Adalimumab + MTX	2,296 (NA)	10,290 (10,267–10,313)	10,880 (10,819–10,942)
Scenario 2 Dose escalation: 0% (etanercept), 0% (adalimumab), and 55% (infliximab) (Hellenic Registry[46])			
Etanercept	2,276 (NA)	9,845 (NA)	9,840 (NA)
Etanercept + MTX	2,278 (NA)	9,857 (NA)	9,852 (NA)
Infliximab + MTX	3,171 (NA)	11,238 (11,124–11,349)	10,397 (10,147–10,645)
Adalimumab	2,293 (NA)	9,921 (NA)	9,916 (NA)
Adalimumab + MTX	2,296 (NA)	9,932 (NA)	9,927 (NA)

Notes: Values are expressed as mean (95% UI), where UI was the lower and upper uncertainty interval from 10,000 Monte Carlo simulations. *Minimum improvement criteria for a responder were the "ACR 20" (the definition requires, among other prerequisites, a 20% improvement in both tender and swollen joint counts);[38] **previously treated patients who were continuing therapy and who achieved an improvement greater than the minimum criteria of ACR 20.
Abbreviations: ACR, American College of Rheumatologists; MTX, methotrexate; NA, not available; UI, uncertainty interval.

Fragoulakis et al. Economic evaluation of anti-TnF agents for patients with rheumatoid arthritis in greece. ClinicoEconomics and Outcomes Research 2015:7 85–93.

CliCon S.r.l. Health, Economics & Outcomes Research

Treatment patterns and health resources use in patients affected by Rheumatoid Arthritis (RA) and treated with biologic drugs

- In patients affected by RA and treated with biologic drugs, **treatment costs are affected by treatment patterns** (e.g., dose escalation, dose de-escalation, treatment switches, and treatment persistence)
- In clinical practice, **treatment patterns** (e.g., dose escalation, dose de-escalation, treatment switches, and treatment persistence) **differ among TNF-α inhibitors** (adalimumab, etanercept, infliximab)
- Treatment cost evaluation should **consider *real-world cost*** (including dose escalation, dose de-escalation, treatment switches, and treatment persistence) **rather than *theoretical cost*** (based on drug price projection)

CliCon S.r.l. Health, Economics & Outcomes Research

Hamburg, 25 marzo 2015

European Association of Hospital Pharmacy 2015

Real world cost of biologic therapy: A European perspective

Optimising biologic care in an evolving landscape: Real world decisions in rheumatology

Degli Esposti, EconD

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Questions

- Please walk up to one of the aisle microphones to ask a question
- Alternatively, you can still submit a question card

Please remember to fill out your evaluation form

Please leave this on your seat for collection

SATELLITE SYMPOSIUM EAHP 2015

THANK YOU

SATELLITE SYMPOSIUM EAHP 2015

OPTIMISING BIOLOGIC CARE IN AN EVOLVING LANDSCAPE: REAL WORLD DECISIONS IN RHEUMATOLOGY

25 March 2015
14:00-15:30
Hall 4