Innovatività e appropriatezza : criteri di valutazione dei farmaci

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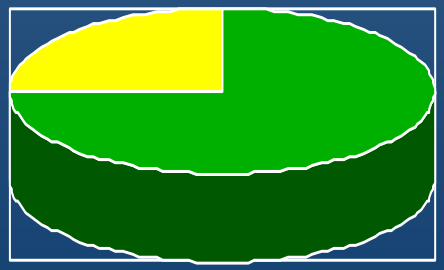
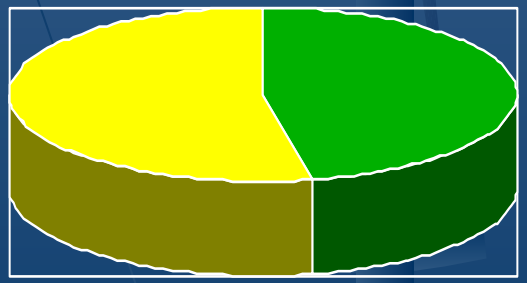
L'innovazione nella terapia biologica dell'Artrite Reumatoide: vantaggi clinici e farmacoeconomici
XXIX Congresso Nazionale SIFO - Napoli 14 ottobre 2008

SPESA FARMACEUTICA EUROPA

1999



2007



FARMACI NUOVI

FARMACI INNOVATIVI

FARMACI BIOLOGICI

FARMACI INNOVATIVI

INNOVATIVITA’

CLINICA

REGISTRAZIONE FARMACI INNOVATIVI BIO

PROCEDURA CENTRALIZZATA (EMEA)

INTRODOTTA NEL 1993

REGOLAMENTATA DAL REGOLAMENTO CE 726/04

VALUTAZIONE SCIENTIFICA DEL DOSSIER

MISURARE L'INNOVAZIONE

1. **TERAPEUTICA**
   - NEC malattie senza trattamento;
   - NEC nuova classe farmacologica;
   - Farmaco già noto con nuova indicazione
2. **COMUNE**
   - NEC in classe farmacologica già nota per indicazioni simili;
   - Farmaco già noto ma ottenuto con tecnologie innovative
3. **INDUSTRIALE**
   - Farmaco già noto con differente grado di innovazione della forma farmaceutica e/o modalità somministrazione

FARMACI INNOVATIVI EMEA

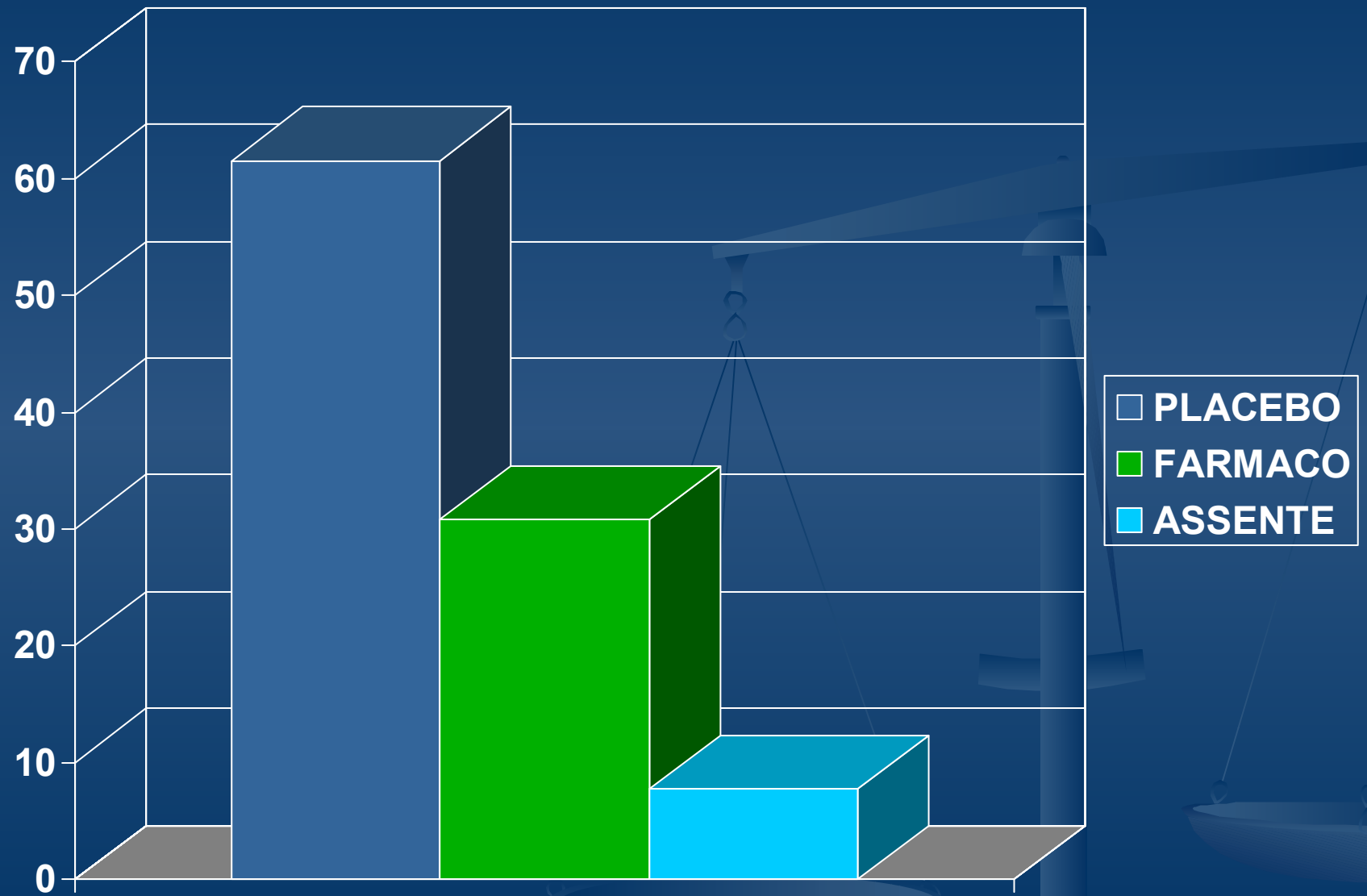
L'innovatività legata al processo produttivo è cosa ben diversa dall'innovatività clinica e terapeutica

Le registrazioni centralizzate avvengono secondo il regolamento approvato del CPMP, sulla base della sicurezza e dell'efficacia (*safe and effective*) e

NON

necessariamente a seguito di studi comparativi che dimostrino un profilo di efficacia e/o tossicità *superiore* rispetto a quello delle alternative terapeutiche disponibili.

COMPARATORI UTILIZZATI NEI PRINCIPALI TRIAL PRE-REGISTRATIVI

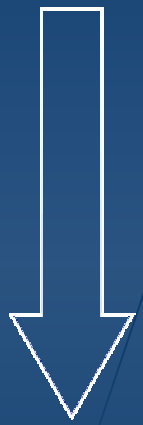


Russo P, "La valutazione farmacoeconomica nel processo regolatorio: criticità e linee di sviluppo" Economia e politica del farmaco – Anno 4, numero 10, luglio 2007

Artrite reumatoide:
COMPARATORI UTILIZZATI NEI PRINCIPALI TRIAL PRE-REGISTRATIVI

Infliximab (REMICADE)	**PLACEBO/MTX**
Etanercept (ENBREL)	**PLACEBO/MTX**
Anakinra (KINERET)	**PLACEBO/MTX**
Adalimumab (HUMIRA)	**PLACEBO/MTX**
Rituximab (MABTHERA)	**PLACEBO/MTX**
Abatacept (ORENCIA)	**PLACEBO/MTX** **(pz resistenti TNF)**

FARMACI INNOVATIVI EMEA



LA REGISTRAZIONE EMEA NON GARANTISCE DI

PER SE' UN MARCHIO E UN CARATTERE DI

INNOVATIVITA' CLINICO-TERAPEUTICA

Agenzia Italiana Farmaco

Nessuna discrezionalità su valutazione scientifica EMEA

- **AIC**
- **CLASSE RIMBORSABILITA'**
- **PREZZO AMMINISTRATO**

VALUTAZIONE EFFICACIA/SICUREZZA

EX ANTE

- **TRIAL CLINICI**
  EFFICACY

REGISTRAZIONE DEL FARMACO

EX POST

- **PRATICA CLINICA**
  EFFECTIVENESS

REGIONE LOMBARDIA

16.11.2004 DG Sanità

"Ruolo del Servizio Farmaceutico ospedaliero nella verifica di appropriatezza d'uso del File F"

COMPITI DEL FARMACISTA

1. ***Aderenza a indicazioni ministeriali e regionali sull'uso dei farmaci a carico del SSN***
2. ***Interpretazione e valutazione dei dati prodotti***
3. ***Fornire alla DS gli elementi utili al governo del file F, in relazione anche al budget assegnato.***

REGIONE LOMBARDIA

SERVIZIO FARMACEUTICO OSPEDALIERO

GARANTE APPROPRIATEZZA

APPROPRIATEZZA

"Distanza che intercorre tra un comportamento osservato ed un comportamento atteso in base a conoscenze scientifiche e/o ad aspetti normativi"

A Federici, Care 1: 1999

APPROPRIATEZZA
LE EVIDENZE

CONOSCENZE SCIENTIFICHE

ASPETTI NORMATIVI

Issue date: October 2007
Review date: September 2010

Quick reference guide

NHS
National Institute for Health and Clinical Excellence

Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis

NOTE: This guidance replaces 'NICE technology appraisal guidance 36' issued in March 2002.

The Institute reviews each piece of guidance it issues.

This review and re-appraisal has additionally included adalimumab for the treatment of rheumatoid arthritis, and has taken into account changes in the marketing authorisations for infliximab and etanercept.

Guidance

1 The tumour necrosis factor alpha (TNF-α) inhibitors adalimumab, etanercept and infliximab are recommended as options for the treatment of adults who have both of the following characteristics.

- Active rheumatoid arthritis as measured by disease activity score (DAS28) greater than 5.1 confirmed on at least two occasions, 1 month apart.
- Have undergone trials of two disease-modifying anti-rheumatic drugs (DMARDs), including methotrexate (unless contraindicated). A trial of a DMARD is defined as being normally of 6 months, with 2 months at standard dose, unless significant toxicity has limited the dose or duration of treatment.

2 TNF-α inhibitors should normally be used in combination with methotrexate. Where a patient is intolerant of methotrexate or where methotrexate treatment is considered to be inappropriate, adalimumab and etanercept may be given as monotherapy.

3 Treatment with TNF-α inhibitors should be continued only if there is an adequate response at 6 months following initiation of therapy. An adequate response is defined as an improvement in DAS28 of 1.2 points or more.

4 After initial response, treatment should be monitored no less frequently than 6-monthly intervals with assessment of DAS28. Treatment should be withdrawn if an adequate response (as defined in 1.3) is not maintained.

5 An alternative TNF-α inhibitor may be considered for patients in whom treatment is withdrawn due to an adverse event before the initial 6-month assessment of efficacy, provided the risks and benefits have been fully discussed with the patient and documented.

6 Escalation of dose of the TNF-α inhibitors above their licensed starting dose is not recommended.

7 Treatment should normally be initiated with the least expensive drug (taking into account administration costs, required dose and product price per dose). This may need to be varied in individual cases due to differences in the mode of administration and treatment schedules.

NICE technology appraisal guidance 130

This guidance represents the view of the Institute, which was arrived at after careful consideration of the available evidence. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. This guidance does not, however, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

NICE technology appraisal guidance is about the use of new and existing medicines and treatments in the NHS in England and Wales.

Adulti (≥ 18 anni)

Artrite reumatoide

Pazienti non trattati in precedenza con Remicade: Una infusione endovenosa di 3 mg/kg, della durata di 2 ore, seguita da infusioni supplementari di 3 mg/kg alle settimane 2 e 6 dalla prima infusione, quindi ogni 8 settimane.

In pazienti con artrite reumatoide attentamente selezionati che hanno tollerato 3 infusioni iniziali di Remicade della durata di 2 ore, si può prendere in considerazione la somministrazione di infusioni successive in un arco di tempo non inferiore a 1 ora. Non sono state studiate infusioni abbreviate con dosi > 6 mg/kg.

Remicade deve essere somministrato in concomitanza con metotrexato.

I dati disponibili suggeriscono che la risposta clinica viene raggiunta solitamente entro 12 settimane dall'inizio del trattamento. Se un paziente ha una risposta inadeguata o perde la risposta dopo questo periodo, potrebbe essere preso in considerazione un aumento graduale del dosaggio di 1,5 mg/kg, fino ad un massimo di 7,5 mg/kg, ogni 8 settimane. In alternativa, si potrebbe prendere in considerazione la somministrazione di 3 mg/kg ogni 4 settimane. Se si raggiunge una risposta adeguata, si devono continuare a trattare i pazienti con il dosaggio o la frequenza scelti. E' necessario valutare attentamente se continuare la terapia nei pazienti che non mostrano evidenza di beneficio terapeutico entro le prime 12 settimane di trattamento o dopo l'adattamento del dosaggio.

Issue date: April 2008

NHS
National Institute for
Health and Clinical Excellence

Quick reference guide

Abatacept for the treatment of rheumatoid arthritis

Guidance

1 Abatacept is not recommended (within its marketing authorisation) for the treatment of people with rheumatoid arthritis.

2 Patients currently receiving abatacept for the treatment of rheumatoid arthritis should have the option to continue therapy until they and their clinicians consider it appropriate to stop.

Implementation tools

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/TA141).

- Audit support for monitoring local practice.
- A costing statement explaining the resource impact of this guidance.

Further information

Ordering information

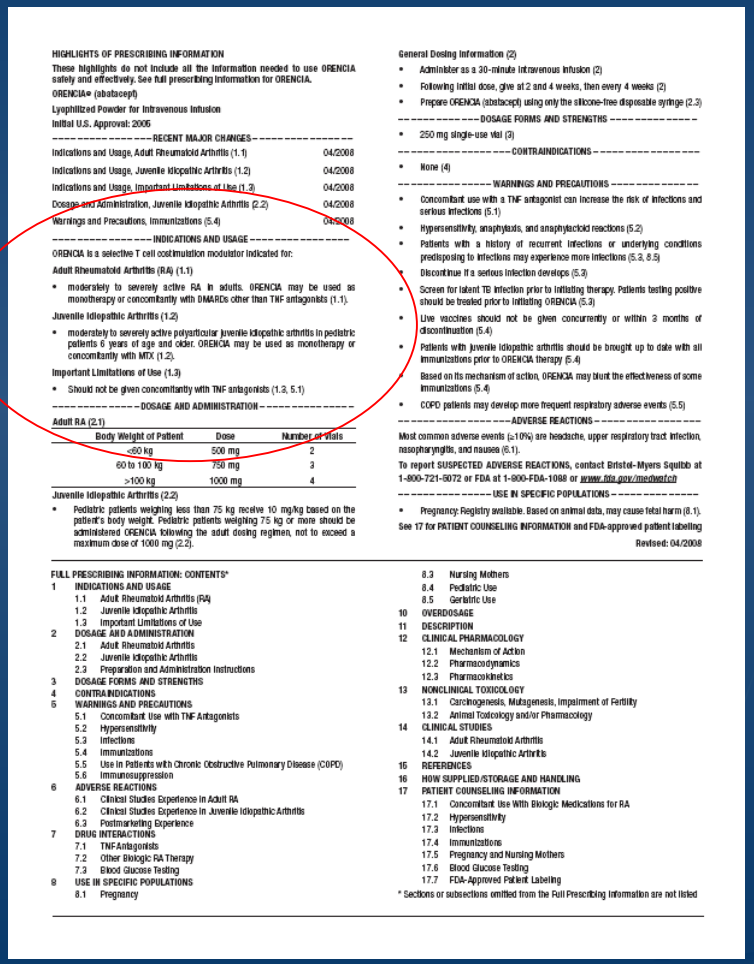
You can download the following documents from www.nice.org.uk/TA141

- A quick reference guide (this document) – a summary of recommendations for healthcare professionals.
- 'Understanding NICE guidance' – information for patients and carers.
- The full guidance.
- Details of all the evidence that was looked at and other background information.

For printed copies of the quick reference guide or 'Understanding NICE guidance', phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and quote:

- N1561 (quick reference guide)
- N1562 ('Understanding NICE guidance').

NICE technology appraisal guidance 141
The guidance was developed using the NICE single technology appraisal process.
NICE technology appraisal guidance is about the use of new and existing medicines and treatments in the NHS in England and Wales.



HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ORENCIA safely and effectively. See full prescribing information for ORENCIA.

ORENCIA® (abatacept)

Lyophilized Powder for Intravenous Infusion

Initial U.S. Approval: 2005

RECENT MAJOR CHANGES

Indications and Usage, Adult Rheumatoid Arthritis (1.1)	04/2008
Indications and Usage, Juvenile Idiopathic Arthritis (1.2)	04/2008
Indications and Usage, Important Limitations of Use (1.3)	04/2008
Dosage and Administration, Juvenile Idiopathic Arthritis (2.2)	04/2008
Warnings and Precautions, Immunizations (5.4)	04/2008

INDICATIONS AND USAGE

ORENCIA is a selective T cell costimulation modulator indicated for:

Adult Rheumatoid Arthritis (RA) (1.1)

- moderately to severely active RA in adults. ORENCIA may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists (1.1).

Juvenile Idiopathic Arthritis (1.2)

- moderately to severely active polyarticular juvenile idiopathic arthritis in pediatric patients 6 years of age and older. ORENCIA may be used as monotherapy or concomitantly with MTX (1.2).

Important Limitations of Use (1.3)

- Should not be given concomitantly with TNF antagonists (1.3, 5.1)

DOSAGE AND ADMINISTRATION

Adult RA (2.1)

Body Weight of Patient	Dose	Number of vials
<60 kg	500 mg	2
60 to 100 kg	750 mg	3
>100 kg	1000 mg	4

Juvenile Idiopathic Arthritis (2.2)

- Pediatric patients weighing less than 75 kg receive 10 mg/kg based on the patient's body weight. Pediatric patients weighing 75 kg or more should be administered ORENCIA following the adult dosing regimen, not to exceed a maximum dose of 1000 mg (2.2).

General Dosing Information (2)

- Administer as a 30-minute intravenous infusion (2)
- Following initial dose, give at 2 and 4 weeks, then every 4 weeks (2)
- Prepare ORENCIA (abatacept) using only the silicone-free disposable syringe (2.3)

DOSAGE FORMS AND STRENGTHS

- 250 mg single-use vial (3)

CONTRAINDICATIONS

- None (4)

WARNINGS AND PRECAUTIONS

- Concomitant use with a TNF antagonist can increase the risk of infections and serious infections (5.1)
- Hypersensitivity, anaphylaxis, and anaphylactoid reactions (5.2)
- Patients with a history of recurrent infections or underlying conditions predisposing to infections may experience more infections (5.3, 8.5)
- Discontinue if a serious infection develops (5.3)
- Screen for latent TB infection prior to initiating therapy. Patients testing positive should be treated prior to initiating ORENCIA (5.3)
- Live vaccines should not be given concurrently or within 3 months of discontinuation (5.4)
- Patients with juvenile idiopathic arthritis should be brought up to date with all immunizations prior to ORENCIA therapy (5.4)
- Based on its mechanism of action, ORENCIA may blunt the effectiveness of some immunizations (5.4)
- COPD patients may develop more frequent respiratory adverse events (5.5)

ADVERSE REACTIONS

Most common adverse events (≥10%) are headache, upper respiratory tract infection, nasopharyngitis, and nausea (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

USE IN SPECIFIC POPULATIONS

- Pregnancy: Registry available. Based on animal data, may cause fetal harm (8.1).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

Revised: 04/2008

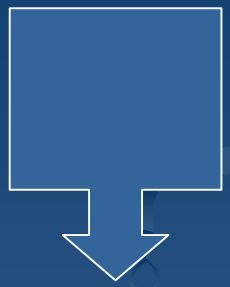
FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the Full Prescribing Information are not listed

INDICATIONS AND USAGE

ORENCIA is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDs, such as methotrexate or TNF antagonists. ORENCIA may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists.

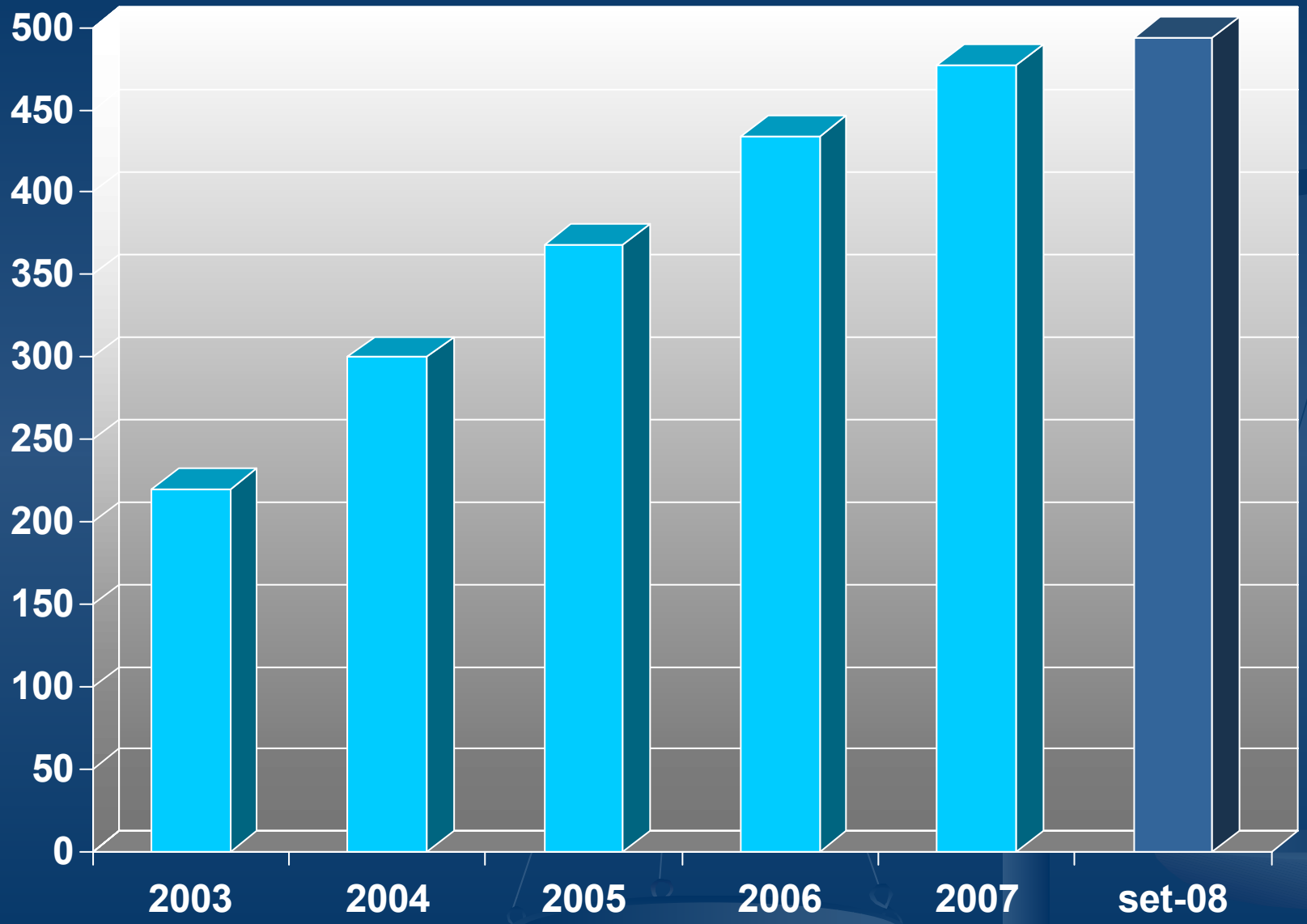
FARMACISTA

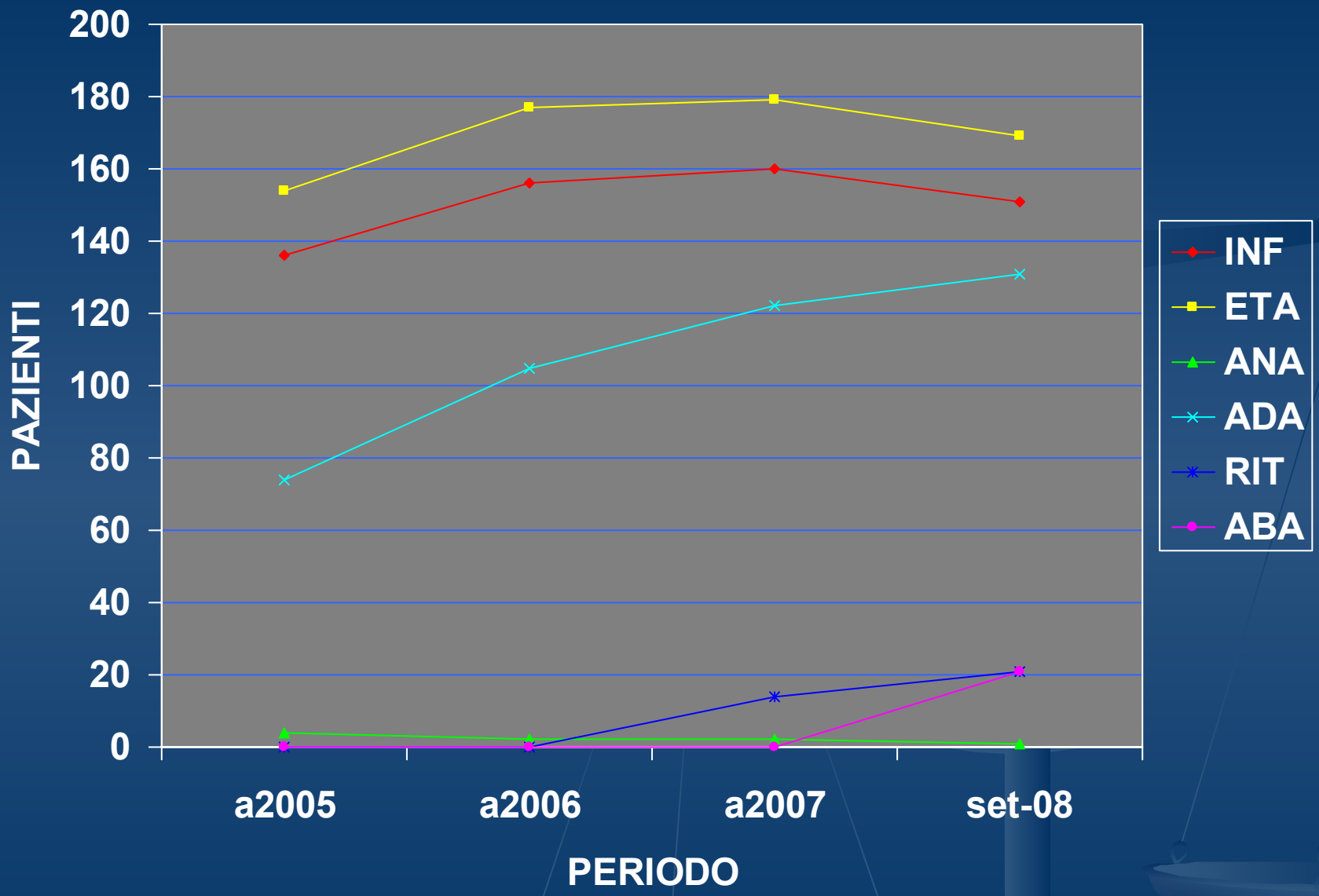


- **Farmacoepidemiologia**
- **Farmacoutilizzazione**

Utilizzo farmaci vs Linee Guida

PAZIENTI TRATTATI CON FARMACI BIOLOGICI IN AMBITO REUMATOLOGICO – H SACCO

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160
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120
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a2006
a2007
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ETA
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ABA

APPROPRIATEZZA FARMACO 2° LINEA

- RITUXIMAB 100%
- ABATACEPT 100%

SWITCH

GENNAIO 2005 – SETTEMBRE 2008		
Pazienti	680	
Nr pazienti c/switch	77	11,3%
Nr paz. c/switch	2 (2008)	25 (2005-7)

SWITCH PIU' FREQUENTI

Tipologia switch	24	
Switch "semplici"	14/24	67/680
Switch "doppi"	5/24	5/680
Switch "tripli"	5/24	5/680

FARMACI BIOLOGICI NECESSITA' DI

- STUDI SUL LUNGO PERIODO
- STUDI COMPARATIVI EFFICACIA E SICUREZZA
- VALUTAZIONI ECONOMICHE

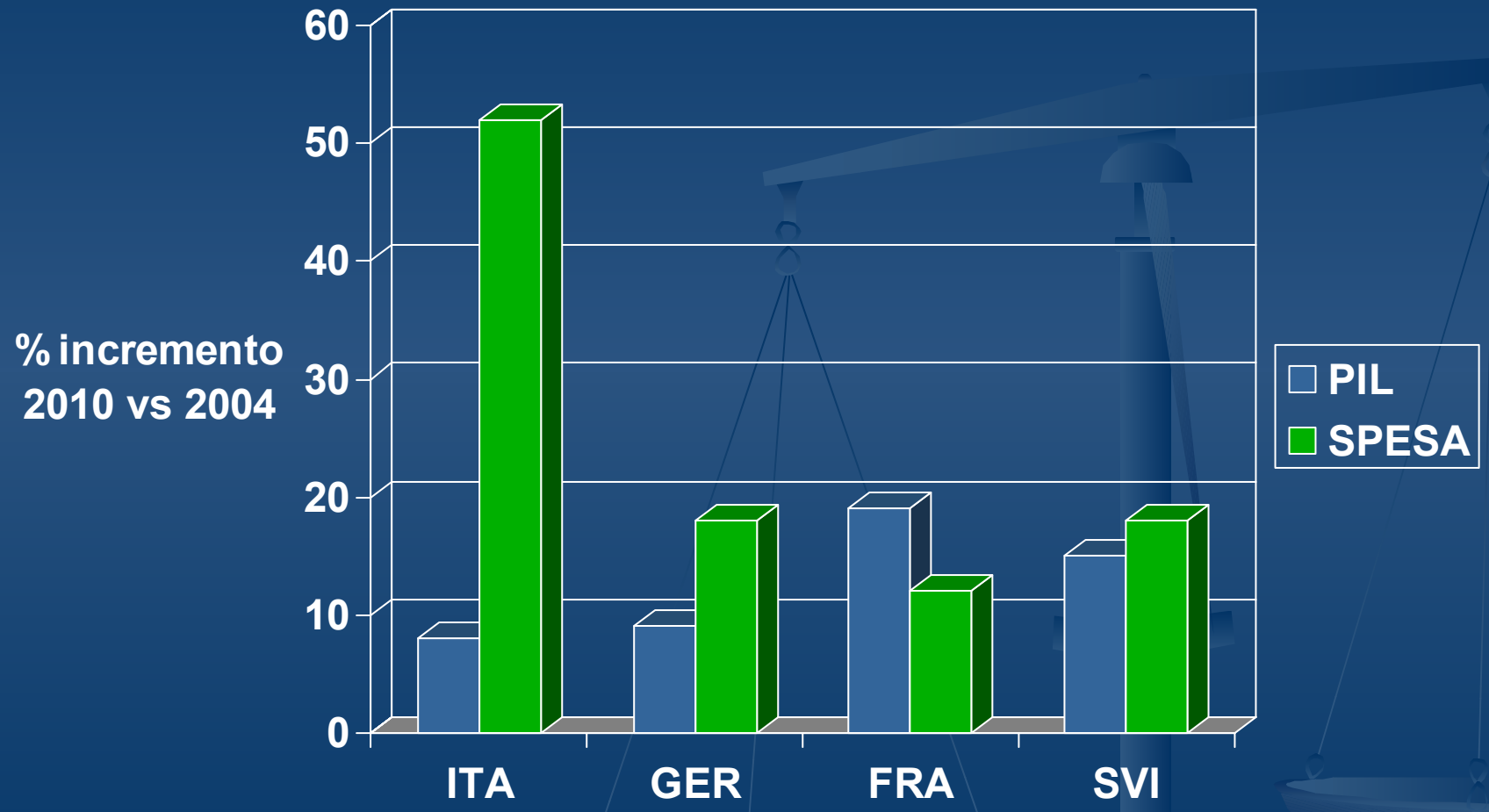
L'OBIETTIVO E' DUPLICE

CONSENTIRE

1. **L'ACCESSO DEI PAZIENTI ALLE TERAPIE NECESSARIE ED EFFETTIVAMENTE INNOVATIVE**

2. **L'UTILIZZO APPROPRIATO DELLE RISORSE DISPONIBILI**

PREVISIONI DI VARIAZIONE
PRODOTTO INTERNO LORDO vs SPESA SANITARIA



Business Monitor International, 2006

IPOTESI FUTURE

MAGGIORE RESTRITTIVITA' REGISTRATIVA EMEA

LIMITAZIONI AIFA / REGIONI

- PTOReg FARMACI INNOVATIVI ?
- ISTITUZIONE DI REGISTRI ?
- SCHEDE DI MONITORAGGIO ?
- GRUPPI INTERDISCIPLINARI PER LA VALUTAZIONE DEGLI ESITI ?

REGIONE LOMBARDIA
Health Technology Assessment

Determinazione della Giunta Regionale 7856/2008

"Determinazione in merito alla valutazione dell'appropriatezza d'uso dei farmaci, dispositivi bio-medici e tecnologie diagnostico terapeutiche al fine del loro impiego nell'ambito del servizio sanitario regionale"

Obiettivo generale

Facilitare la diffusione nella pratica clinica delle tecnologie più sicure, efficaci ed efficienti in sostituzione/alternativa di tecnologie meno efficaci, sicure ed efficienti, secondo modalità condivise, trasparenti, monitorabili e verificabili, che attribuiscano chiare responsabilità ai soggetti coinvolti…….. ……..all'interno di un processo decisionale orientato alla sostenibilità economica ed all'appropriatezza specifica.

ISTITUZIONI NAZIONALI e/o REGIONALI

GARANZIA

EFFICACIA

EQUITA’

RUOLO DEL PROFESSIONISTA SANITARIO

NON

risolvere il problema dell'esiguità delle risorse disponibili

MA

assicurare l'appropiatezza delle prestazioni erogate