Use of Biological Agents in Rheumatoid Arthritis

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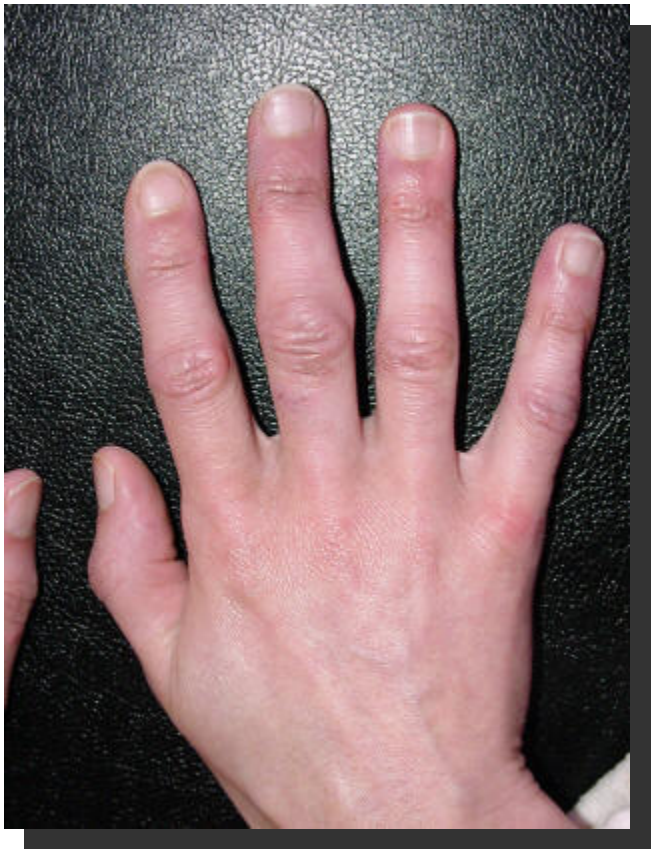
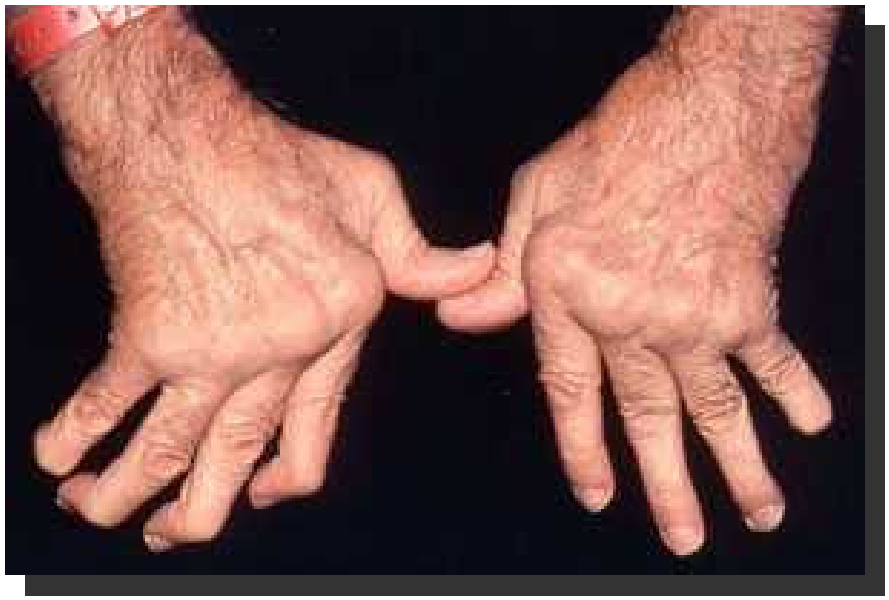
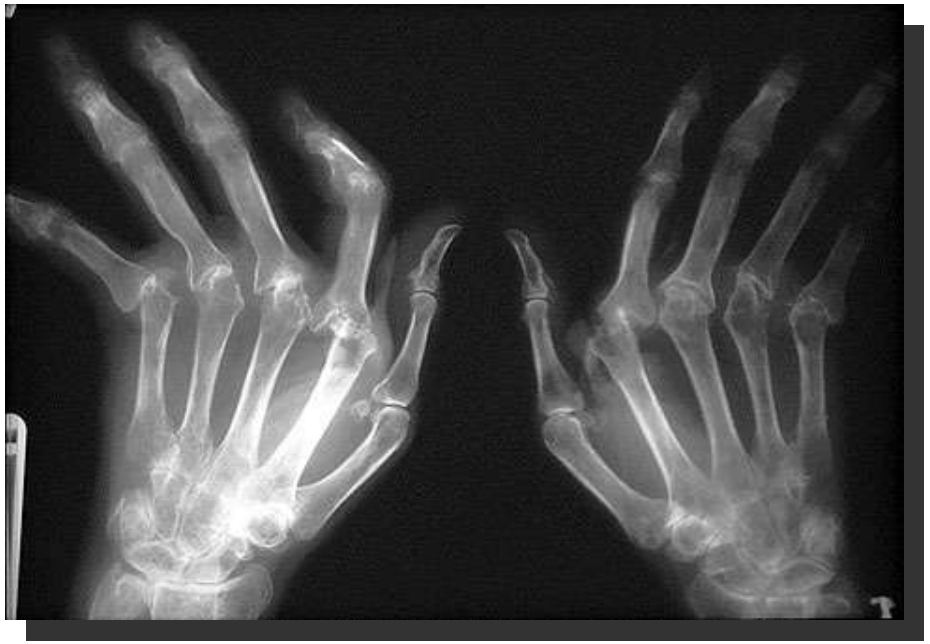
Early rheumatoid arthritis

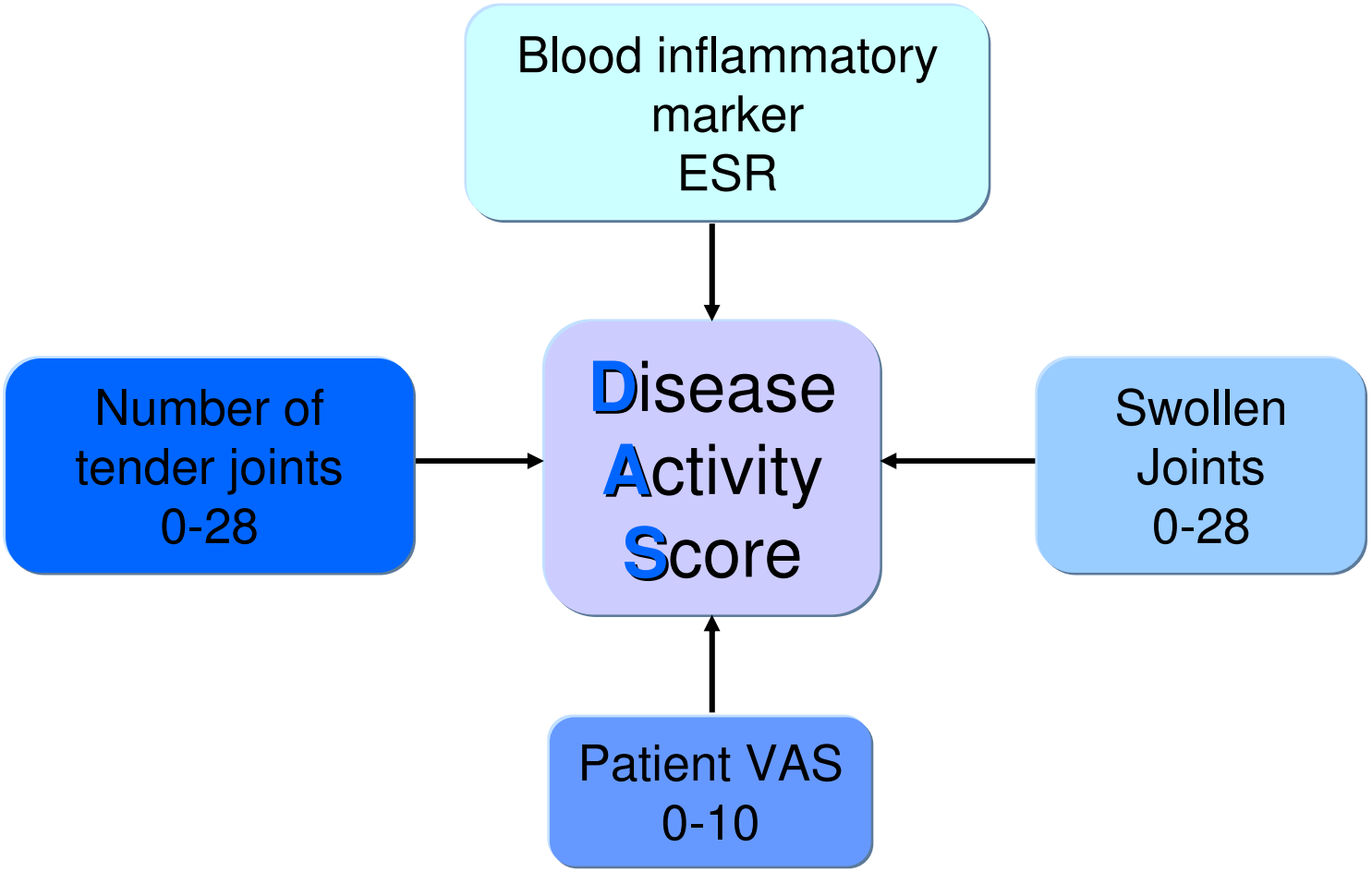


Severe rheumatoid arthritis





Outcome assessment: DAS



DAS formula

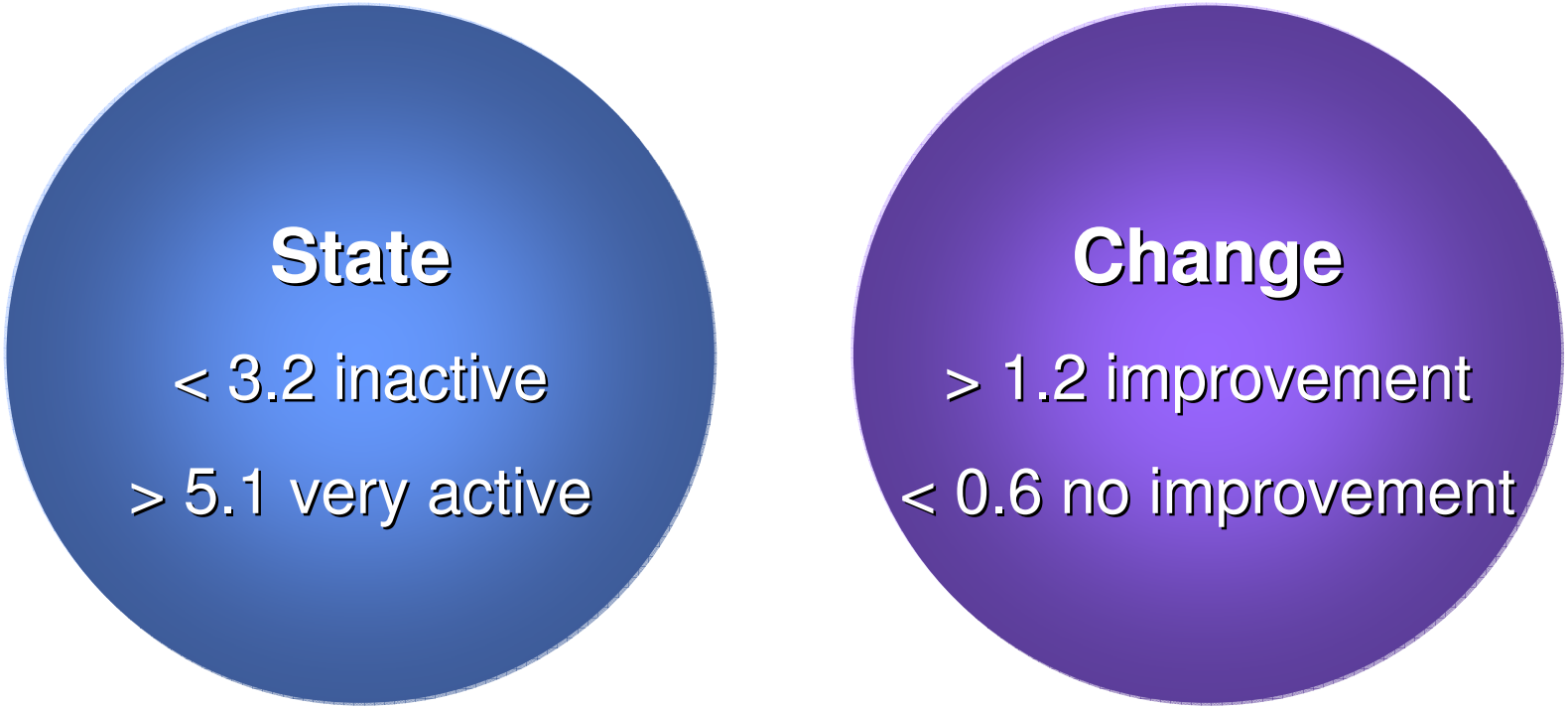
DAS = $0.56\sqrt{\text{Tender}}$

$+ 0.28\sqrt{\text{Swollen}}$

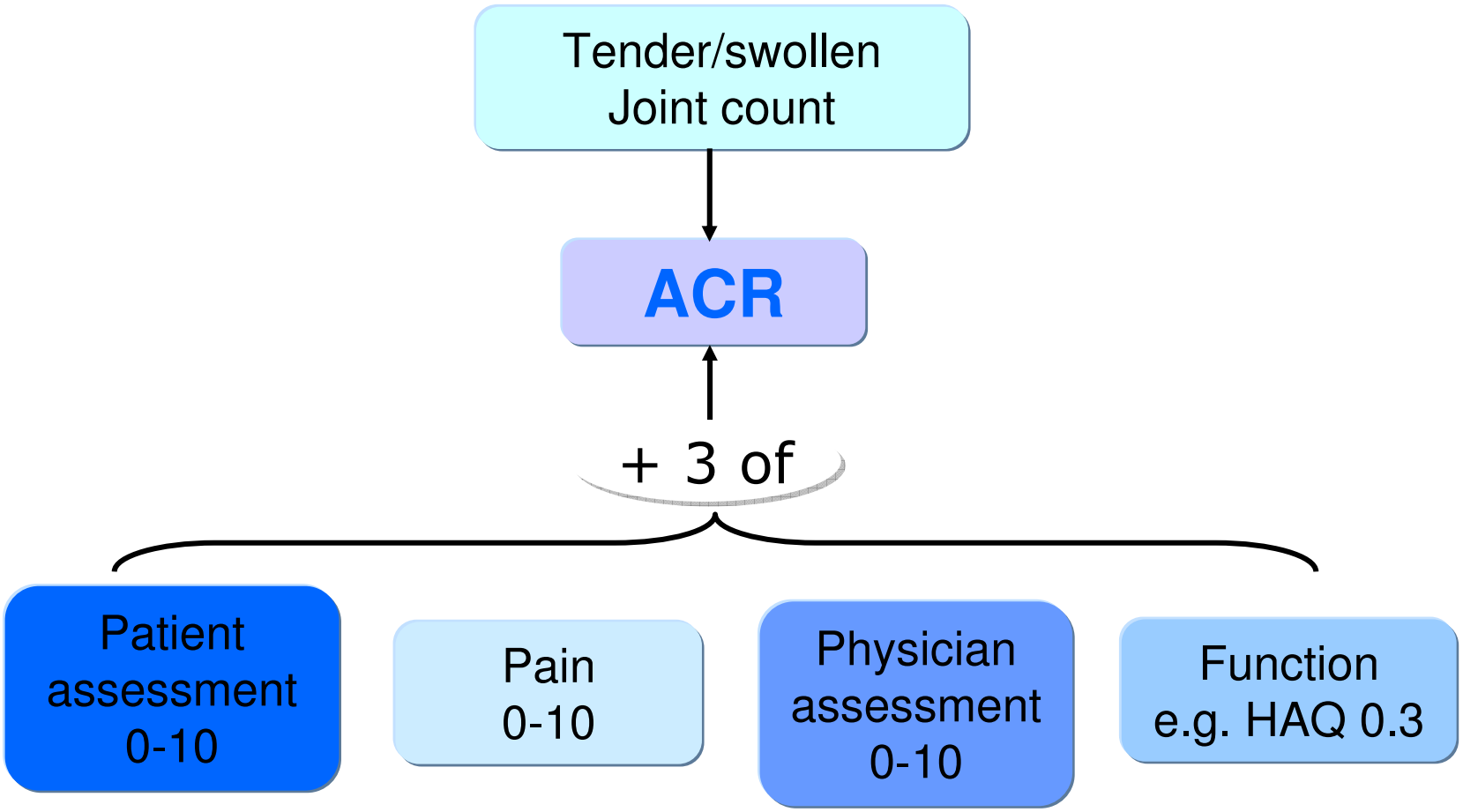
$+ 0.70 \log_n \text{ESR}$

$+ 0.14$ patient VAS

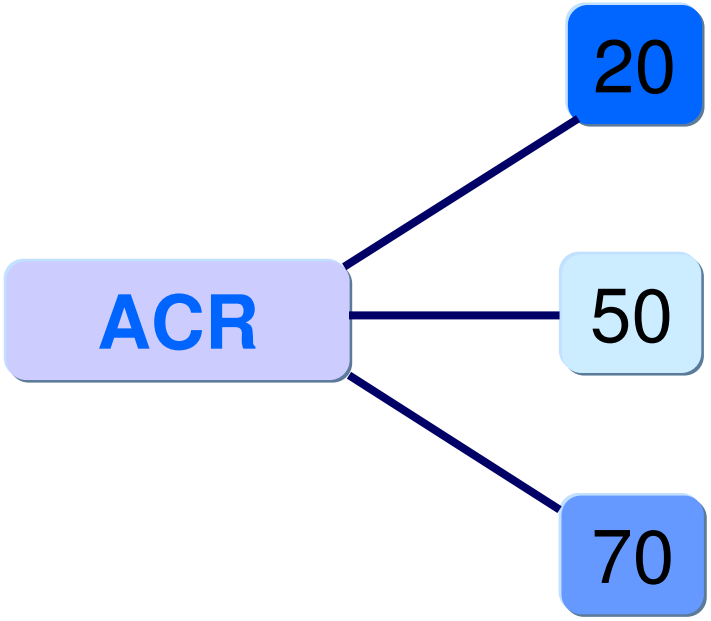
Interpretation of DAS



American College of Rheumatology Criteria



ACR Criteria



At least %

response in 1+3

outcomes

m1

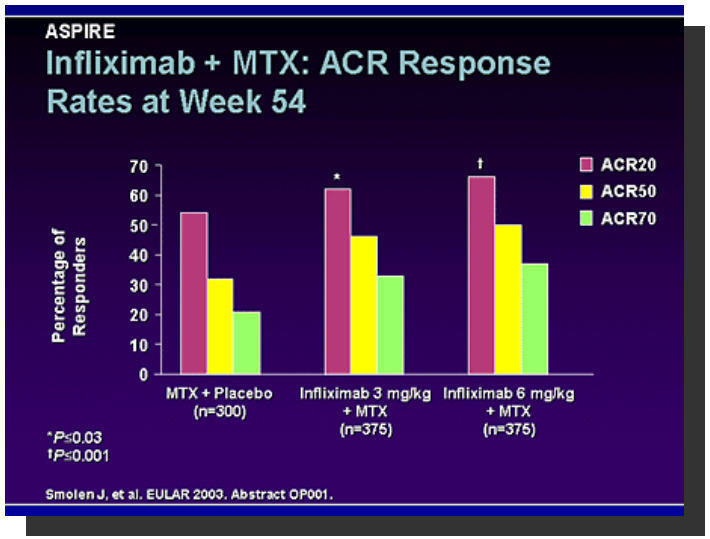
Typical recent RA trial

	Test	Standard
ACR 20	60%	45%
ACR 50	35%	22%
ACR 70	20%	8%

Slide 9

m1 Not sure if you want to keep this slide or not?
mdeasjep, 10/08/2010

Which response?

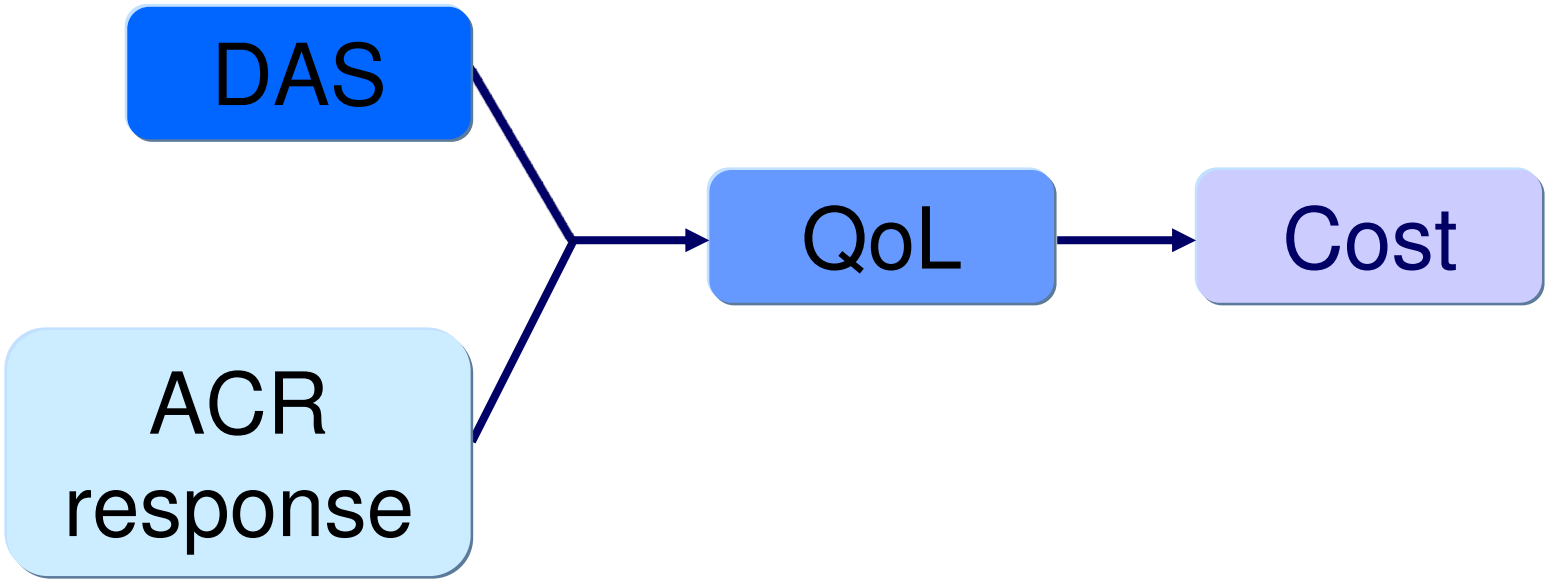


- Trials report ACR response

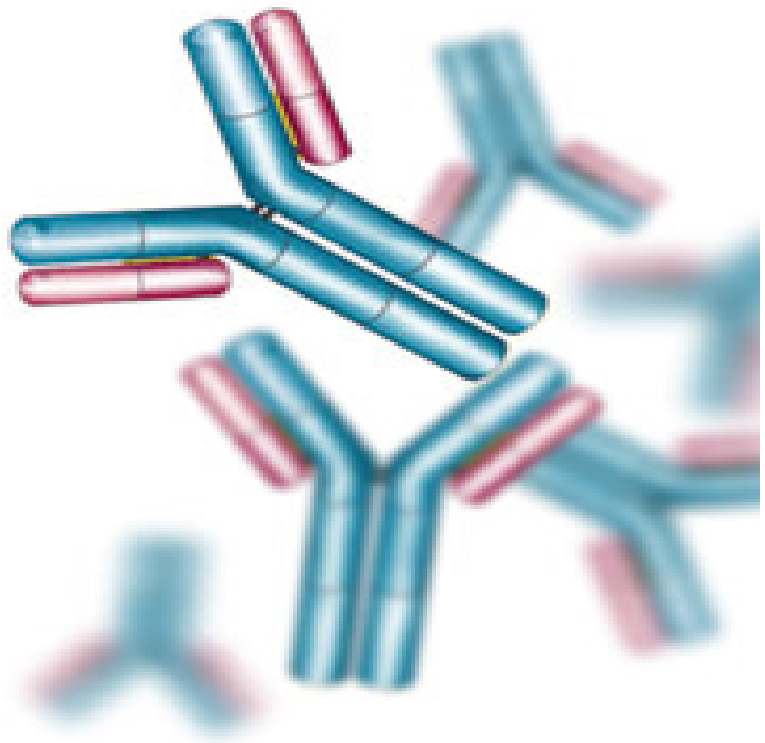
NHS
National Institute for Health and Clinical Excellence

- NICE advice on DAS response

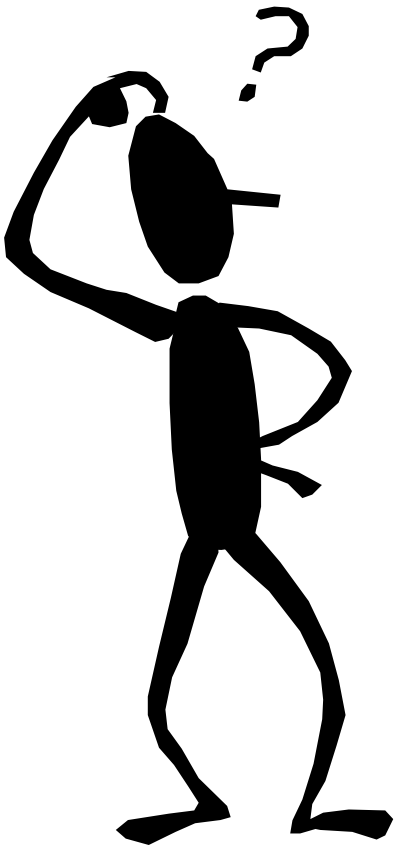
How do they fit together?



Biologics and RA

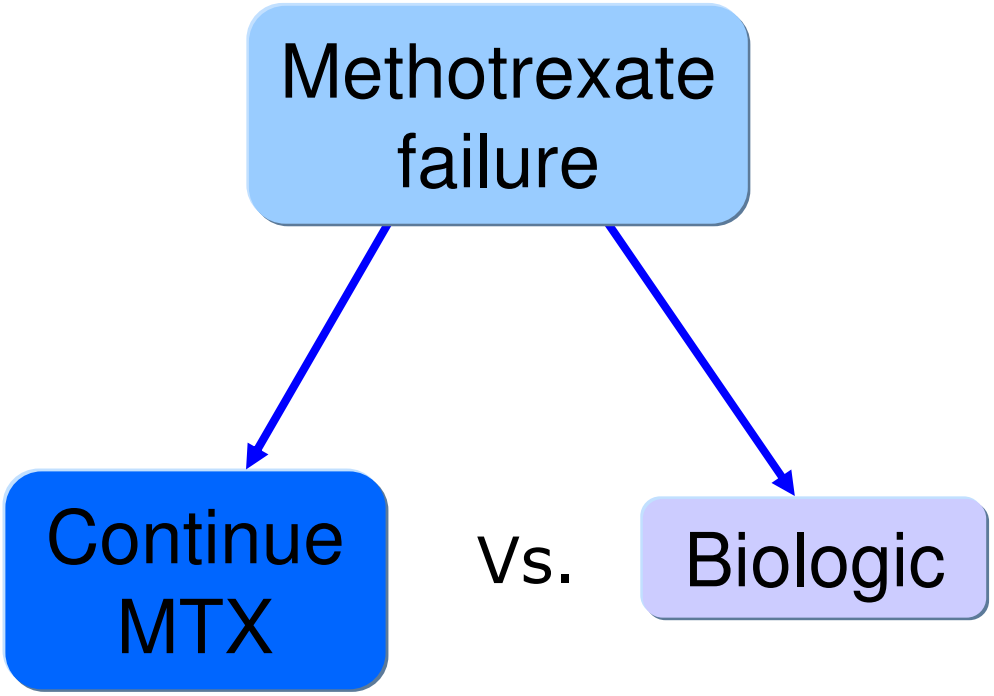


- Anti-TNF
  - Infliximab
  - Etanercept
  - Adalimumab
  - Certoluzimab Pegol
  - Golimumab
- Abatacept
- Rituximab
- Tociluzimab

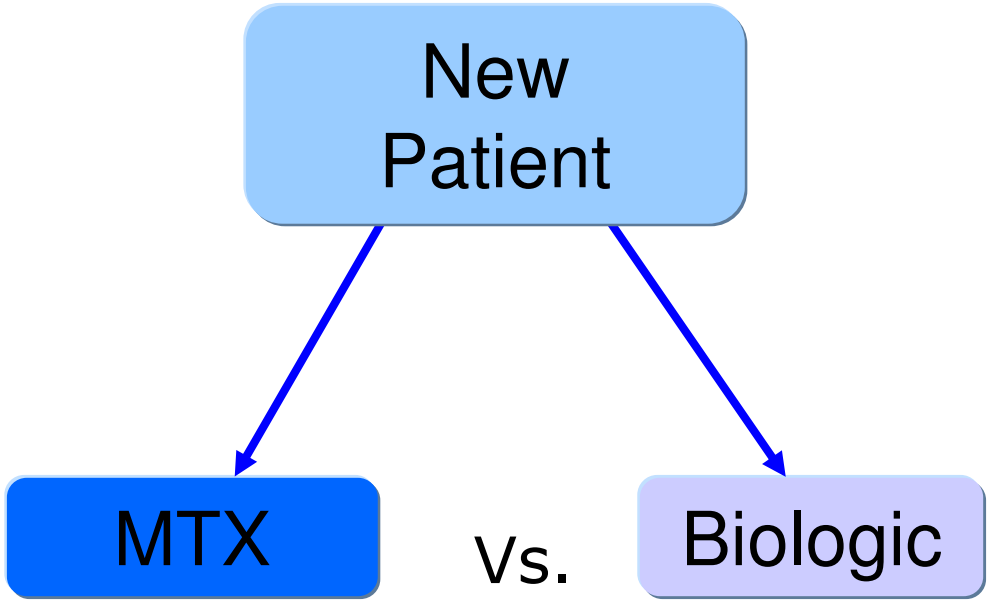


What are the main efficacy questions in trials?

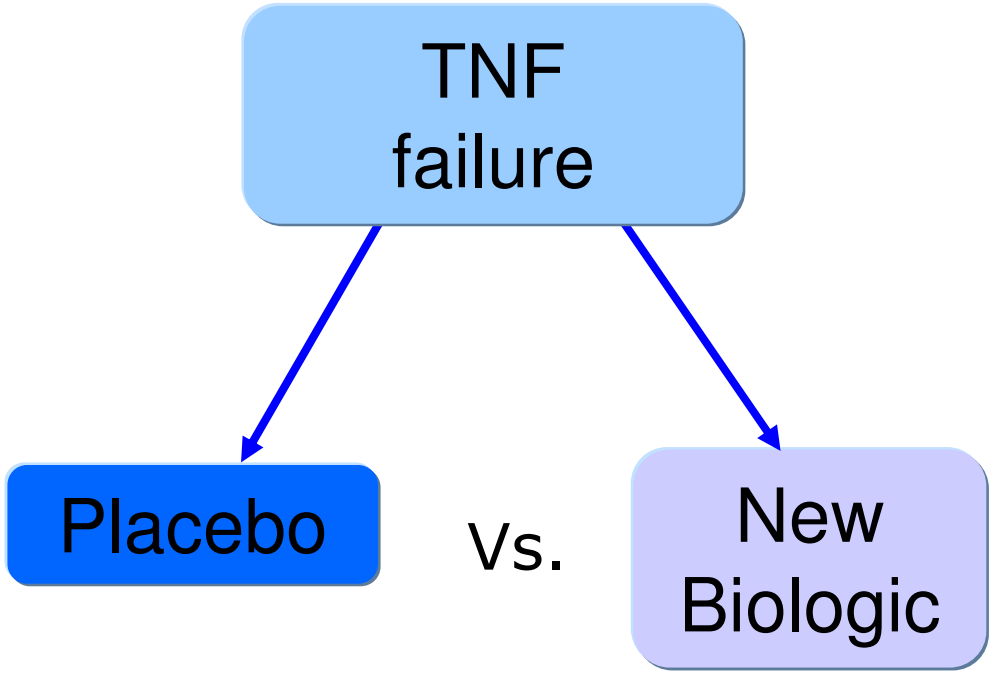
Standard licensing



Early RA



TNF failure



What constitutes failure?

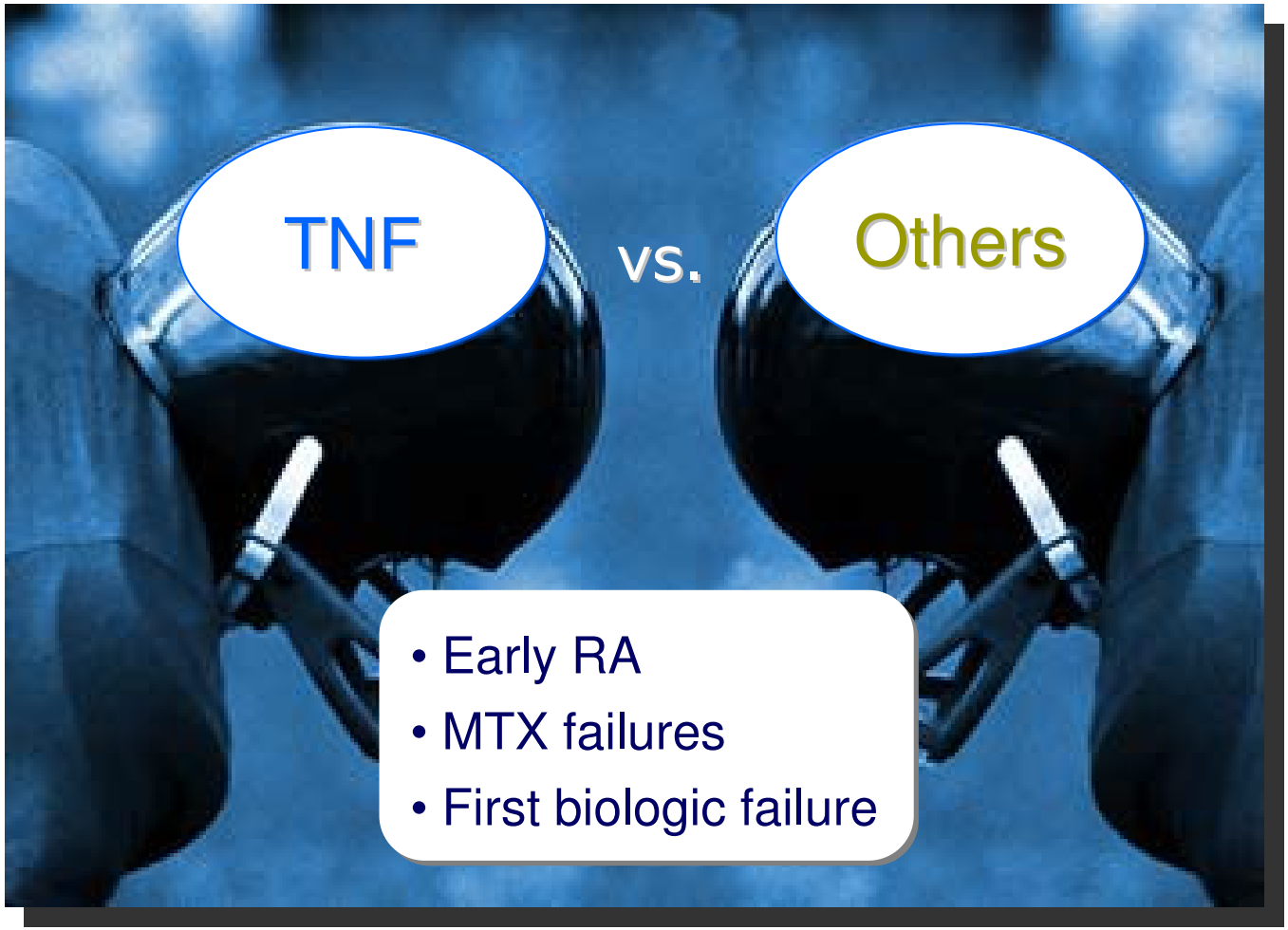
- Lack of efficacy
- Adverse events
- Physician/patient preference
- Availability of alternatives

Other clinical trial designs

- Biologics ‘Head to Head’

- Withdrawal vs. continuing

Head to head



Role of head to head

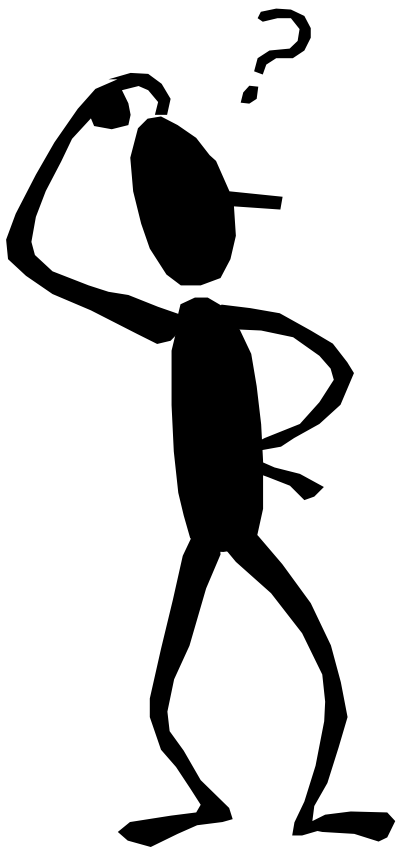
- Efficacy benefit unlikely
- Cost issues
- Main issue is comparative safety

Discontinuation study

Discontinuation of infliximab after attaining low disease activity in patients with rheumatoid arthritis: RRR (remission induction by Remicade in RA) study

Tanaka *et al*, ARD April 2010; epub

Questions from efficacy trials



- Inclusion criteria
- Outcome assessment
- What is failure?

Subject selection questions

1. Do entry criteria to trials reflect the patients we wish to be treated?
2. Do entry criteria as published give accurate picture of who was studied?
3. Is it possible to reconcile trial differences from clinical practice cohorts using available data?

Limitations of Randomised Clinical Trials: External Validity

- Results not extrapolatable outside subjects recruited
- Major multi-centre trials
  - Often handful subjects per centre
- Typical inclusion criteria:
  - No co-morbidity
  - Consenters
  - Certain disease characteristics

Efficacy vs. effectiveness

Economic evaluation

Unanswered effectiveness questions

- First choice of biologic
- Subs
- T vs. other classes
- When to stop

Personalised Medicine

How much does do the drugs cost?

Etanercept	£9,295
Adalimumab	£9,295
Infliximab	£3,775 + £7,553 or £8,812
Rituximab	£3,492
Abatacept	£9,444 - £10,176

Source: NICE 2010

Closing questions

- What would these achieve?
- Can they be done?
- Who would pay?