The Cost-Effectiveness and Value of Information Associated with Biologic Drugs for the Treatment of Psoriatic Arthritis

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BACKGROUND

Recent clinical trials indicate that new ***biologic drugs*** combine efficacy with low toxicity for the treatment of ***PsA*** patients.

Anti-TNFα drugs = etanercept (Enbrel®), infliximab (Remicade®)

Inflammatory arthropathy associated with psoriasis and distinct from R.A.

However, their acquisition costs are substantially higher than standard therapy with DMARDs and evidence on the maintenance of benefits in the long term is very limited. A synthesis of all available evidence was required.

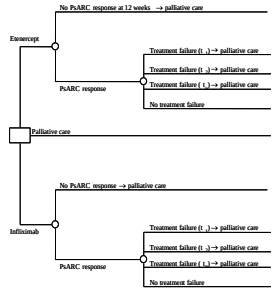
AIM

To estimate the cost-effectiveness of new biologics for the treatment of active PsA in patients with inadequate response to DMARDs, characterize decision uncertainty and identify research priorities which can inform decisions regarding their future use.

METHODS

A probabilistic decision analytic model was constructed to compare the 3 main alternatives (etanercept, infliximab, palliation) in the context of their licensed indications. The model is a cohort model which takes the form of a recursive decision tree (Fig.1).

Fig.1: Simplified model structure



Evidence synthesis

We combine both initial 3 months response to treatment (***PsARC*** criteria) and disease activity (***HAQ***) as efficacy outcomes.

- ***Progressive disability*** – modelled as underlying HAQ natural progression (*N*).
- Quality of life and costs as a function of disability (HAQ scores).

The limited trial evidence was combined using ***Bayesian methods*** of multiple parameter synthesis[1], which enable the indirect comparison of all 3 treatment options and the combination of the main outcome measures, whilst maintaining their correlation structure.

Table 1: Treatment comparisons forming the chain of evidence

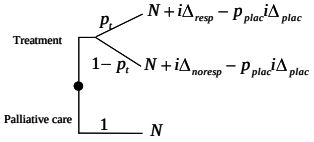
Trials	Treatment option		
	Etanercept	Placebo	Infliximab
Mease et al. 2000	X	X	
Mease et al. 2004	X	X	
Impact 2003		X	X

The evidence synthesis consists of two random baseline, fixed treatment effects meta-analyses that estimated:

- Treatment response rates
- Mean HAQ change from baseline conditional on PsARC response.

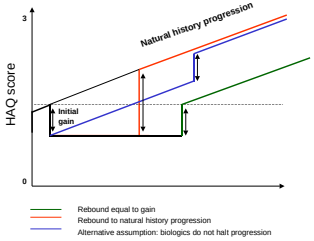
Mean HAQ change is adjusted by placebo effect (Fig.2). We also add the HAQ increment for treatment non-responders.

Fig.2: Placebo effect adjustment



Annual withdrawal rates were modelled based on observational evidence. Given the lack of evidence on the rebound effect after treatment failure we present 3 alternative scenarios (Fig.3)

Fig.3: Alternative rebound scenarios



RESULTS

Decision uncertainty is graphically represented as a cost-effectiveness acceptability curve (Fig.4). Probabilities that each treatment is more cost-effective than the others conditional on different WTP for additional QALY are also shown in Table 2. Etanercept has the highest probability of being cost-effective for a threshold of £30K to £40K per QALY for a 10-year horizon and equal to gain rebound (Base case scenario).

Fig.4: CEAC - Base case

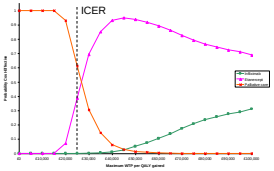


Table 2: Cost effectiveness results

Treatment	Mean costs	Mean QALYs	ICER	Probability cost-effective at: £20,000	£30,000	£40,000
(S1) Rebound equal to gain						
Infliximab	£64,274	4.636	£165,363 [a]	0	0.001	0.009
Etanercept	£44,111	4.514	£26,361 [b]	0.070	0.693	0.931
Palliative Care	£10,718	3.248	NA	0.930	0.306	0.060
(S2) Rebound equal to natural progression						
Infliximab	£64,418	4.455	£205,345 [a]	0	0	0.005
Etanercept	£44,169	4.356	£30,628 [b]	0.005	0.446	0.878
Palliative Care	£10,679	3.263	NA	0.995	0.554	0.117
(S3) Progression whilst responding						
Infliximab	£64,633	4.070	£440,982 [a]	0	0	0
Etanercept	£44,404	4.024	£44,115 [b]	0	0.002	0.210
Palliative Care	£10,632	3.259	NA	1	0.998	0.790

a= ICER calculated as inflimixab vs etanercept; b= etanercept vs palliative

The ICER for Etanercept is £26K per QALY gained for the base-case scenario (S1), which increases to £30K if rebound after treatment failure is equal to natural progression (S2). Infliximab shows a very high ICER that ranges between £165K to £440K. Alternative rebound assumptions have an impact on expected cost-effectiveness.

Expected Value of Perfect Information (EVPI)

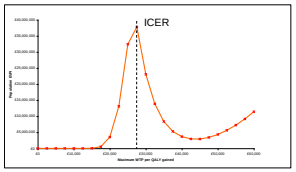
$$EVPI = \underbrace{E_\theta \max_j NB(j,\theta)}_{\text{Expected NB with perfect information}} - \underbrace{\max_j E_\theta NB(j,\theta)}_{\text{Expected NB with current information}}$$

Population EVPI places an upper bound on the value of further research for the population of current and future UK PsA patients.

$$Population \quad EVPI = EVPI \cdot \sum_{t=1}^{T} \frac{I_t}{(1+r)^t}$$

The value of information reaches a maximum when the threshold is equal to the expected ICER of the technology (Fig. 5)

Fig.5: Population EVPI - Base case



References:

[1] Spiegelhalter D, Abrams K, Mules J. (2004) *Bayesian Approaches to Clinical Trials and Health Care Evaluation*. John Wiley & Sons, Ltd.

[2] Ades A, Lu G, Claxton K. (2004) Expected value of sample information calculations in medical decision modeling. *Medical Decision Making* 24: 207-27

Alternative structural assumptions, such as rebound effect and HAQ progression whilst responding to treatment, have an important impact on the value of information (Table 3).

Table 3: Population EVPI for all scenarios

Scenarios	Value of information for threshold of: £20,000	£30,000	£40,000
S1	£3,541,163	£23,046,814	£3,666,444
S2	£154,213	£34,404,661	£5,442,830
S3	£0	£12,584	£9,804,098

Partial EVPI (EVPPI)

$$EVPPI_\varphi = \underbrace{E_\varphi \max_j E_{\psi|\varphi} NB(j,\varphi,\psi)}_{\text{Perfect information for parameter } \varphi} - \underbrace{\max_j E_\theta NB(j,\theta)}_{\text{Expected value with current info for all parameters } (\theta)}$$

The cost of further research should not exceed the population EVPI to make it potentially worthwhile. Population EVPI for parameters can help prioritise research focusing on those parameters where the value of information and so the return of research to society is higher.

Fig.6: Population EVPPI - Base case

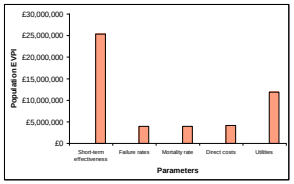


Table 4: Population EVPPI - Base case

Parameters	£ (mill.)
Short-term effectiveness	25,386,153
Failure rate	3,970,126
Mortality rate	3,933,558
Costs = f(HAQ)	4,202,464
Utilities = f(HAQ)	11,923,298

Note: Threshold equal to ICER etanercept (26K); 500/10,000 draws

CONCLUSIONS

Bayesian methods of evidence synthesis can enable the comparison of technologies that have not been directly compared in clinical trial evidence. Policy decisions should benefit from an analytic framework which can structure the decision problem so that all evidence can be combined, all uncertainty surrounding the decision incorporated and evidence of parameters can be updated as evidence accumulates. This project is an example of how Bayesian evidence synthesis and value of information analysis can conform such analytic framework, producing results that are a powerful aid for decision-making, consistent with both the objectives and budget constraints of health care provision.

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