

Research question

Patient: Patients with severe asthma
Intervention: Omalizumab + standard therapy
Comparison: Standard therapy alone
Outcome: Cost, QALY

If omalizumab is not cost-effective

- What is needed to improve the cost-effectiveness of omalizumab?

QALY: quality-adjusted life year

5

Previous research

Author	Clinical input	Perspective	Model	Results (ICER)
Campbell et al. ¹	INNOVATE study ⁶	US payer	Markov	\$287,200/QALY
Wu et al. ²	Pooled data	US societal	Emphasis on lung function	\$821,000/QALY
Brown et al. ³	ETOPA study (open-label) ⁷	Canadian societal	Markov	€31,200/QALY
Dewilde et al. ⁴	INNOVATE study ⁶	Swedish societal	Markov	€56,090/QALY
Oba et al. ⁵	two RCTs	US payer	Cost per controlled day	\$523/successfully controlled day

¹Campbell JD, et al. Allergy 2010.

²Wu A, et al. J Allergy Clin Immunol 2007.

³Brown R, et al. Allergy 2007.

⁴Dewilde S, et al. Curr Med Res Opin 2006.

⁵Oba Y, et al. J Allergy Clin Immunol 2004.

⁶Humbert M, et al. Allergy 2005.

⁷Ayres J, et al. Allergy 2004.

6

Objectives

To perform economic evaluation of omalizumab in the Japanese setting

To investigate the efficient use of omalizumab

7

2. Methods

8

Study design

Cost-utility analysis from the societal perspective

Estimating ICER per QALY gained

- omalizumab + standard therapy vs standard therapy

$$\text{ICER (incremental cost-effective ratio)} = \frac{\Delta \text{Cost}}{\Delta \text{QALY}}$$

Discount rate

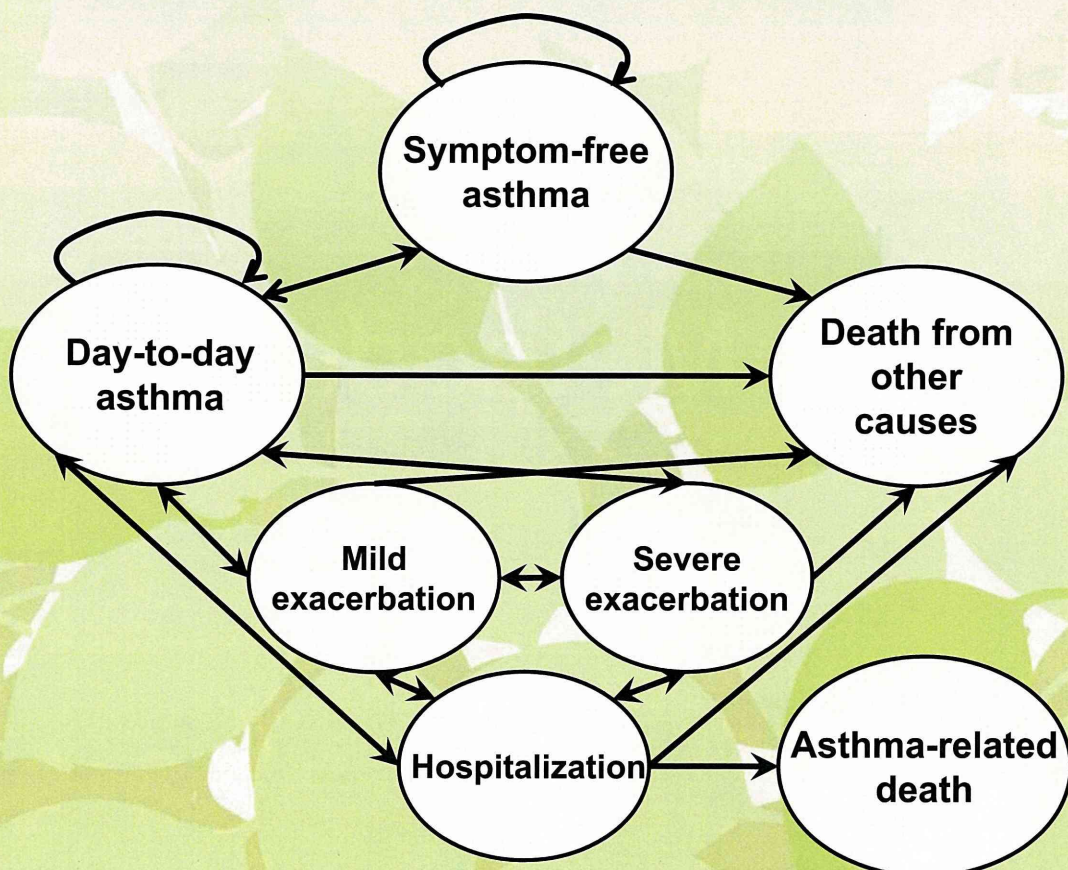
- 3% per annum

Software

- TreeAge Pro 2009, Healthcare

9

Markov model structure 1



Markov model structure 2

Cycle length

- 1 week

Time horizon

- Lifetime horizon
 - 5-year omalizumab therapy
 - Standard therapy alone for the rest of lives

Study cohort

- Starting at the age of 50 years
- 50% men

11

Clinical input

A randomized controlled trial (RCT) in Japan*

- Placebo-controlled & double-blinded
 - [omalizumab + standard therapy] vs [placebo + standard therapy]
- Enrolled 315 patients, aged 20–75 years, with severe asthma

The RCT assessed the number of

- Symptom-free weeks
- Mild exacerbation weeks
- Severe exacerbation weeks
- Hospitalizations

➔ Rates and risk ratios ➔ Transition possibilities

*Ohta K, et al. *Respirology* 2009.

12

Response to omalizumab 1

Omalizumab provides

- Great benefit for some patients (responders)*
- Little benefit for the others (non-responders)*

Predicting the response is possible?

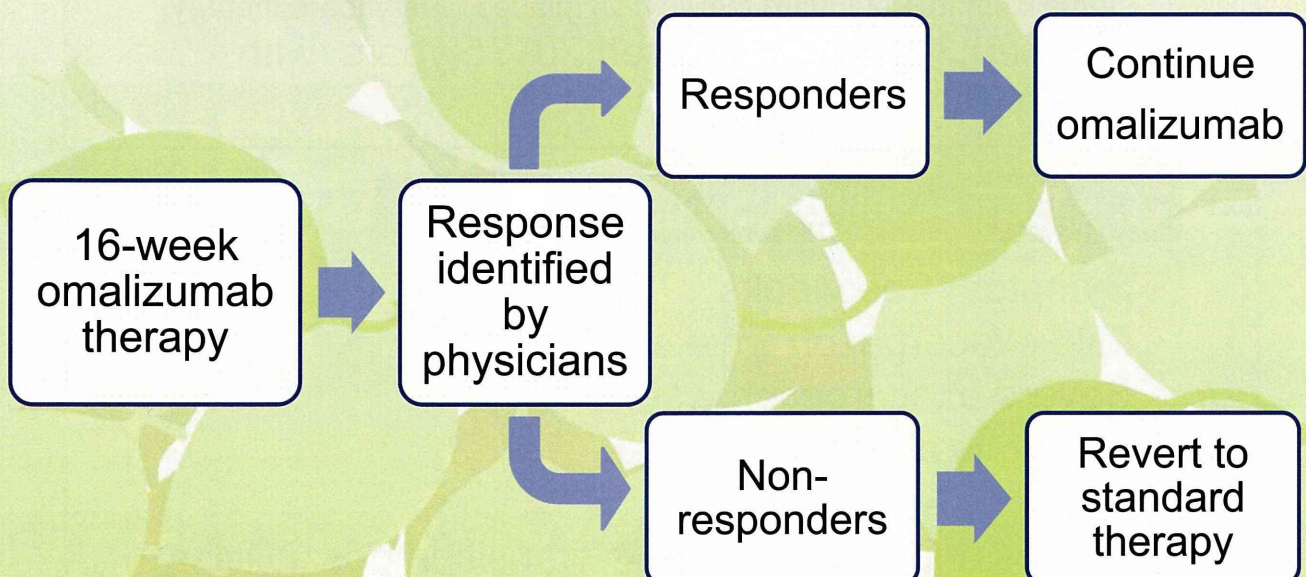
- No prediction methods at present

*Bousquet J, et al. Respir Med 2007.

13

Response to omalizumab 2

Identifying the response*



*Bousquet J, et al. Respir Med 2007.

14

Response to omalizumab 3

Clinical outcomes of responders

- Response percentage = 60.5%*
- Parameters from another large trial conducted outside Japan*

Responders as a subgroup

- The ICER of omalizumab in responders as a subgroup analysis

*Humbert M, et al. Allergy 2005.

15

Mortality estimate

Mortality risk given a hospitalization

- Estimated from Japan's two official databases*†
- Risk = 1.55%

Mortality risk from other causes

- Estimated from Japan's official database

*Patient survey in 2008.

†Vital statistics in 2009.

16

Utility estimate

Utility values came from another study* because of the lack of detailed HRQoL measures in the RCT.

Markov states in our model	Asthma control level described by another study*
Symptom-free	Good control
Day-to-day	Mildly reduced control
Mild exacerbation	Moderately reduced control
Severe exacerbation	Poor control
Hospitalization	

*Szende A, et al. Pharmacoeconomics 2004.

17

Cost input

Cost	Source
Direct medical cost	
Omalizumab	<ul style="list-style-type: none"> • Dose distributions observed in the RCT • Official price
Standard therapy	<ul style="list-style-type: none"> • Model case
Healthcare resource use	<ul style="list-style-type: none"> • Survey of medical care activities in public health insurance in 2009 • QIP*
Indirect cost	
Productivity loss	<ul style="list-style-type: none"> • Labour force survey in 2009: annual report

*QIP: Quality Indicator/Improvement Project, which our department manages to collect clinical and claims data from more than 200 hospitals in Japan.

18

Sensitivity analysis

Probabilistic sensitivity analysis

- 5000 Monte Carlo simulations

One-way sensitivity analyses

- Risk ratios for exacerbation risk
- Utility values
- Asthma-related mortality
- Omalizumab cost
- Standard therapy cost
- Indirect cost
- Unit cost of emergency department visit
- Unit cost of hospital stay

19

Value of information 1

What EVPI means

- Expected value of perfect information (EVPI)
- The price that the society would be willing to pay for further research to gain access to perfect information

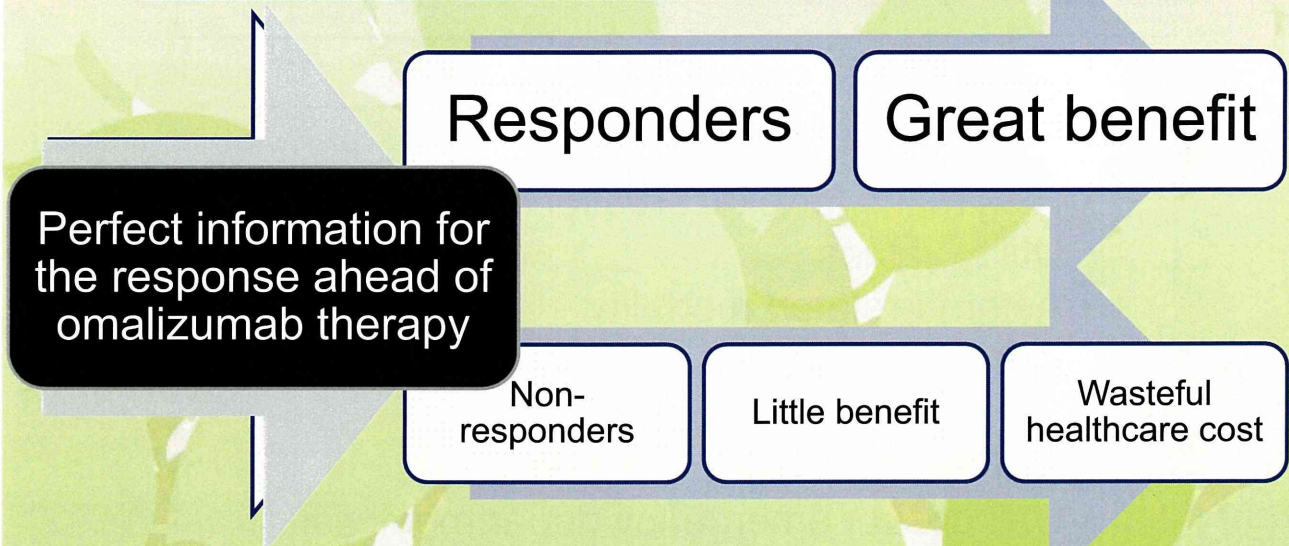
Why is the society willing to pay?

- Eliminating the possibility of making a wrong decision based on existing information

20

Value of information 2

How is perfect information for patients' response to omalizumab useful?



21

Value of information 3

How to calculate EVPI

Individual EVPI

Individual EVPI for the omalizumab response
= NMB (the responder subgroup) – NMB (the omalizumab group)

Population EVPI

Population EVPI per year
= Individual EVPI × the annual incidence of eligible patients in Japan

NMB: net monetary benefits

Omalizumab group: the overall patients treated with omalizumab

22

3. Results

23

Lifetime outcomes and costs

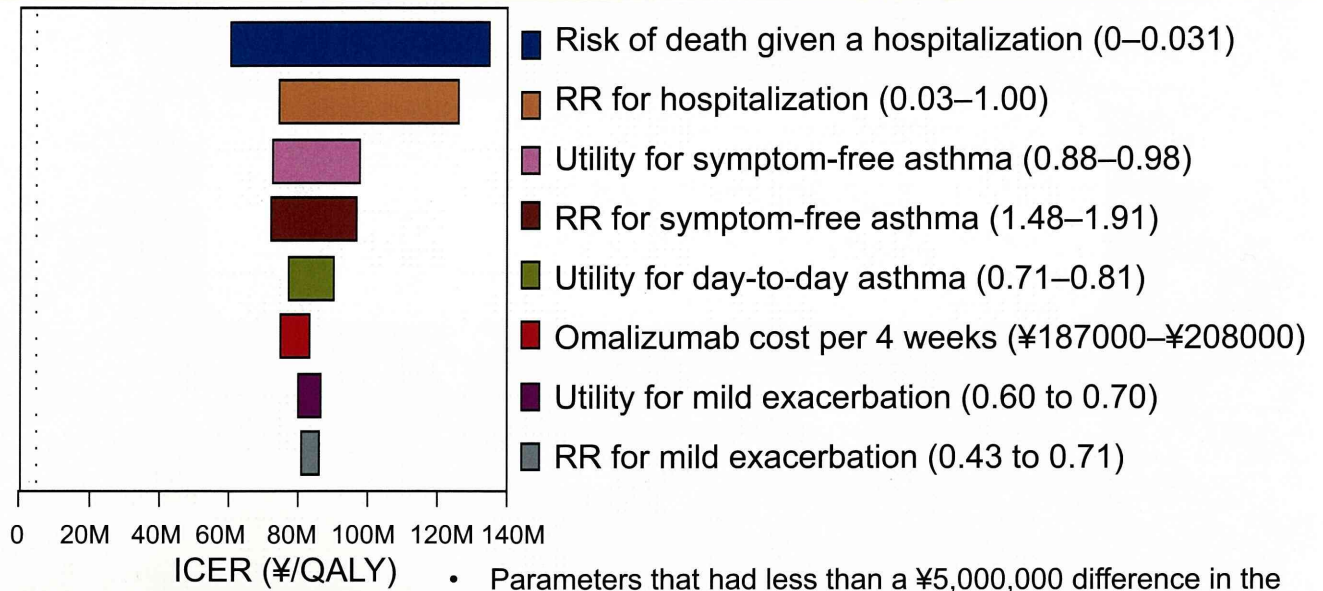
	Standard therapy group	Omalizumab group* (95% CI)	Responder subgroup†
QALYs	16.00	16.10 (16.050–16.118)	16.19
Total costs (¥)	5,230,000	13,080,000 (13,060,000–13,120,000)	17,620,000
ICER (¥/QALY, vs baseline)	Baseline	83,350,000 (67,450,000–145,220,000)	65,160,000

*Omalizumab group indicates the overall patients treated with omalizumab plus standard therapy.

†Responder subgroup indicates a subgroup of patients who obtain great benefit from omalizumab plus standard therapy.

24

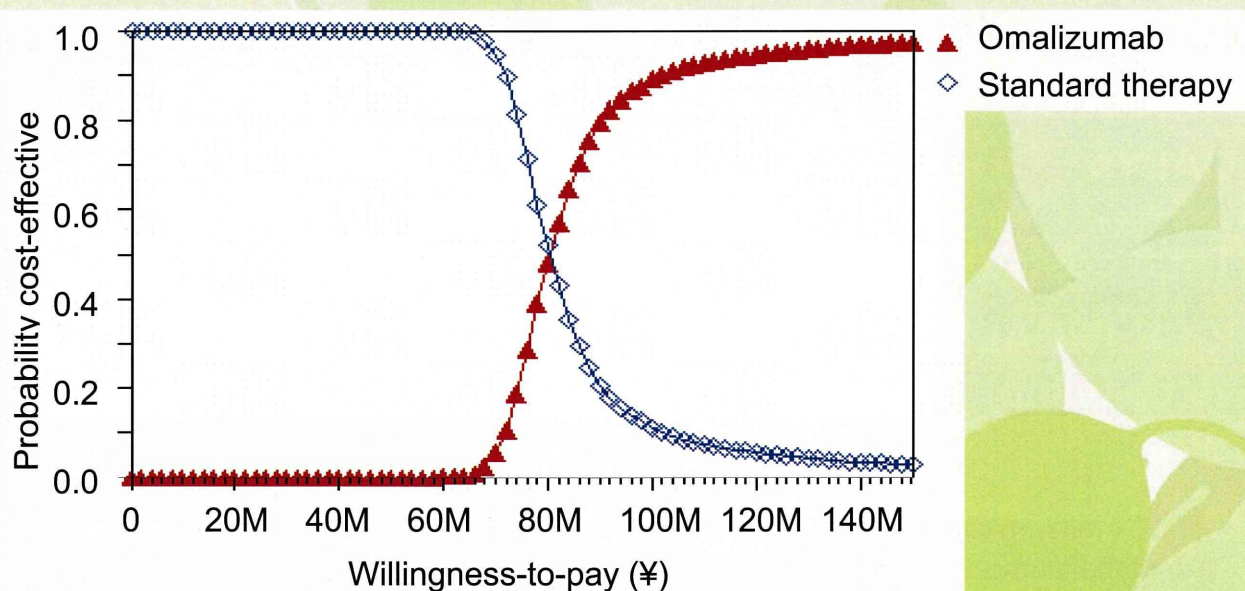
Tornado diagram summarizing one-way sensitivity analyses



- Parameters that had less than a ¥5,000,000 difference in the ICER are not displayed.
- RR: risk ratio of omalizumab plus standard therapy relative to standard therapy.

25

Cost-effectiveness acceptability curve



26

EVPI for omalizumab response

Individual EVPI = ¥435,000

Given a threshold value of ¥5,000,000 per QALY*



Population EVPI = ¥3.1 billion per year

The entire Japanese eligible population = 7200

*Shiroiwa T, et al. Health Econ 2010.

27

4. Discussion

28

Key results 1

The ICER of omalizumab add-on therapy relative to standard therapy alone
= **¥83,350,000** per QALY gained.

Omalizumab was **not cost-effective** given a willingness-to-pay of ¥5,000,000 per QALY in Japan.*

*Shiroiwa T, et al. Health Econ 2010.

29

Key results 2

The ICER was sensitive to omalizumab cost.

The ICER for the responder subgroup was **22% lower** than that for the overall patients treated with omalizumab.

The value of research investigating prediction methods for identifying responders
= **¥3,100,000,000**

30

How to improve the cost-effectiveness

Decreasing the price of omalizumab

- The ICER was sensitive to omalizumab cost.

Selective patients to be treated with omalizumab

- Confining omalizumab therapy to previously-predicted responders identified based on pre-treatment patient characteristics
- This confinement is impossible now.

31

Research implications

What research should be done?

- Research for developing omalizumab response prediction methods

If prediction methods are developed

- Prediction methods will help physicians decide whether to begin omalizumab add-on therapy.

32

Reason for inconsistency in results between our study and others

Including symptom-free state in the model

- For suiting the model to the endpoints that were assessed in the RCT

Asthma-related death state linked with the other states in the model

- Linked with hospitalization in our study and Campbell et al.
- Linked with severe exacerbation in Dewilde et al. and Brown et al.

33

Limitations

Utility values from another study

- The results were sensitive to utilities
- Further research to assess HRQoL in detail among patients treated with omalizumab in Japan

Clinical parameters from different clinical trials

- Parameters of the overall patients treated with omalizumab from the RCT in Japan
- Parameters of responders from another trial outside Japan
- Little is known about the effect of race on the response to omalizumab

34

Summary

Is omalizumab cost-effective?

- Not cost-effective given a WTP per QALY in Japan.

What is needed for the efficient use?

- Discounting the price of omalizumab
- Confining omalizumab therapy to previously-predicted responders

What future research should be aimed at?

- Investigating prediction methods for the identification of responders

35

Thank you very much for your attention

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36

平成23年度厚生労働科学研究費補助金（政策科学総合研究事業（政策科学推進研究事業））
（H22-政策-一般-028）総括研究報告書
医療・介護政策と地域の資源・連携・受療行動が平均在院日数と費用に影響を及ぼす
要因の分析

研究成果の刊行に関する一覧表

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