Cost effectiveness analysis of Omalizumab for the treatment of chronic spontaneous urticaria in China

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Introduction

- Chronic spontaneous urticaria (CSU) is a skin disease, with itchy hives and/or angioedema which last for at least 6 weeks without obvious causes.
- Epidemiological survey shows that the worldwide prevalence of chronic urticaria (CU) range from 0.1% to 3.4% , while the prevalence of CU in Chinese population was 1.4%[1],among which CSU is the most common type(about 68.1%) [2].
- From the guideline for diagnosis and treatment of urticaria in China(2018), due to the lack of licensed alternatives, the second generation H1-antihistamines are still the main therapeutic drugs for CSU patients prior to the approval of Omalizumab by NMPA.
- Omalizumab is a humanized anti-IgE recombinant monoclonal antibody that has shown good efficacy and safety in treatment of Chinese CSU patients inadequately controlled by H1-antihistamines from Phase III clinical study (*CIGE025E2305*) and various real world studies.
- CSU is associated with a considerable negative impact on patient quality of life and also reduces patient productivity through absenteeism and presenteeism[3-4].

Objective

- To estimate the cost effectiveness of Omalizumab (150mg/4weeks, 12 week-course) combined with H1-antihistamines treatment compared to placebo combined with H1-antihistamines in patients with moderate or severe CSU from the perspective of Chinese medical service system.

Methods

Model structure

- The structure of the model was defined by five disease activity health states (free, well controlled, mild, moderate, severe) based on Urticaria Activity Scores over 7days (UAS7) and three additional states (relapse, spontaneous remission and death), presented in ***Figure 1***.
- The model cycle length was 4 weeks, and the time horizon was 10 years in base case analysis.
- After the treatment, the CSU patients in the free, well controlled and mild states were at risk of relapse (UAS7≥16), for the patients experiencing relapse will be re-treated with a 12-week course of original regimen assuming an equivalent response to that of initial treatment.
- All patients were also associated with a probability of entering a spontaneous remission state (UAS7=0), in which they received no treatment.
- The model assumed no CSU-related mortality, all-cause mortality was used based on annual mortality rates for each age group, obtained from China population and employment statistical yearbook(2020).

Model input

- Chinese phase III clinical trial study has provided the basis for several clinical inputs to the model:
  - Distribution of patients between UAS7-based health states at each 4-week time point across the treatment period.
  - Data from the follow-up period between 12 and 20 weeks provided relapse rates for patients in each health state, and extrapolations were made for rates beyond 20 weeks.
  - Incidence of adverse events for each group.
- Probabilities of spontaneous remission were based on a linear model constructed from natural history data of Korean CSU population[5].
- Due to the lack of research on the health utility in Chinese CSU population, the values were derived from a study conducted by Korean CSU population[6], presented in ***Table1*** .
- The direct medical costs(including drug cost, registration cost, inspection cost, other related treatment cost) were considered in base case analysis, and the direct non-medical cost and indirect cost were considered as well in scenario analysis, presented in ***Table2&3***.

Sensitivity analysis

- One-way sensitivity analysis (OWSA), scenario analysis and probabilistic sensitivity analysis (PSA) were conducted to explore the impact of key model inputs and assumptions on results.

Results

Base case analysis results

- In the base case analysis, the incremental outcomes for Omalizumab combined with H1-antihistamines treatment were 0.239 QALYs and incremental direct costs were ¥5487 compared with placebo and H1-antihistamines , corresponding to an ICER of ¥22950/QALY which was less than the preset willingness-to-pay threshold (1 time GDP per capita in China was ¥81,000).

Sensitivity analysis results

- One-way sensitivity analysis showed that the health utility made greater influence on the result than price of Omalizumab and other parameters.
- Probabilistic sensitivity analysis(PSA) confirmed the robustness of the model results, the probability of Omalizumab being cost-effective was 84% at the willingness-to-pay threshold, presented in ***Figure 2&3***.

Scenario analysis results

- Different scenario analyses were conducted which including alternative research patients(with/without angioedema), alternative time horizon(20 years/lifetime), alternative research perspective(whole society).
- The scenario analyses exploring key assumptions around model parameters are presented in ***Table 4.***

Table 1. Utility inputs applied in the model

Health state	Value	Source
Severe	0.746	*Kim et al., 2018*[5].
Moderate	0.86	
Mild	0.878	
Well controlled	0.913	
Free	0.953	
Relapse	0.803	

Table 2. Direct medical cost for different health states

Health state	Direct medical cost(without drug cost)			Source
	Registration fee(¥)	Inspection fee(¥)	Other treatment cost(¥)	
Severe	113.21	320.53	0	*Chinese CSU disease burden research (unpublished)*
Moderate	104.5	289.93	51.85	
Mild	98.55	236.14	0	
Well controlled	94.52	97.09	0	
Free	0	0	0	
Relapse	108.86	305.23	25.93	

Table 3. Direct non-medical cost and indirect cost for different health states

Health state	Direct non-medical cost(¥)	Indirect cost(¥)	Source
Severe	260.59	300	*Chinese CSU disease burden research (unpublished)*
Moderate	489.56	340	
Mild	150.42	378.13	
Well controlled	75.21	189.07	
Free	0	0	
Relapse	375.08	320	

Figure 2. Scatterplot for probabilistic sensitivity analysis (PSA)

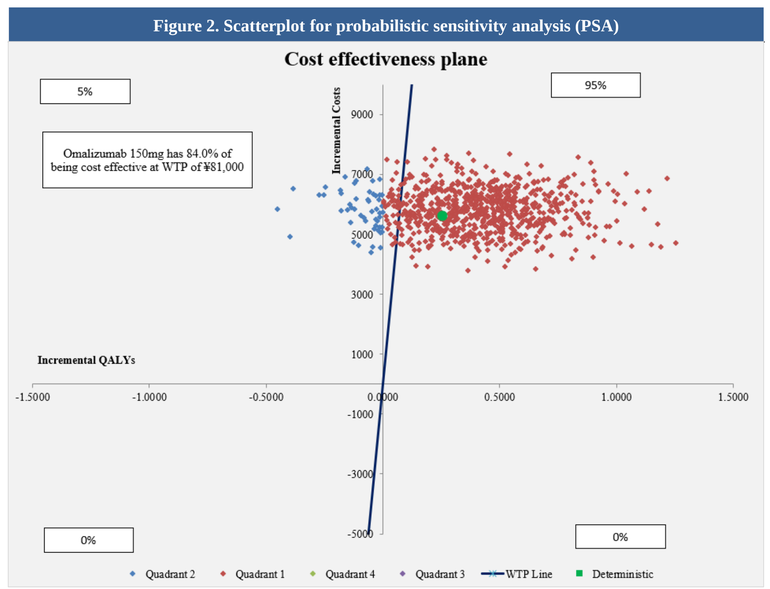


Figure 3. Cost-effectiveness acceptability curve (CEAC) for each group

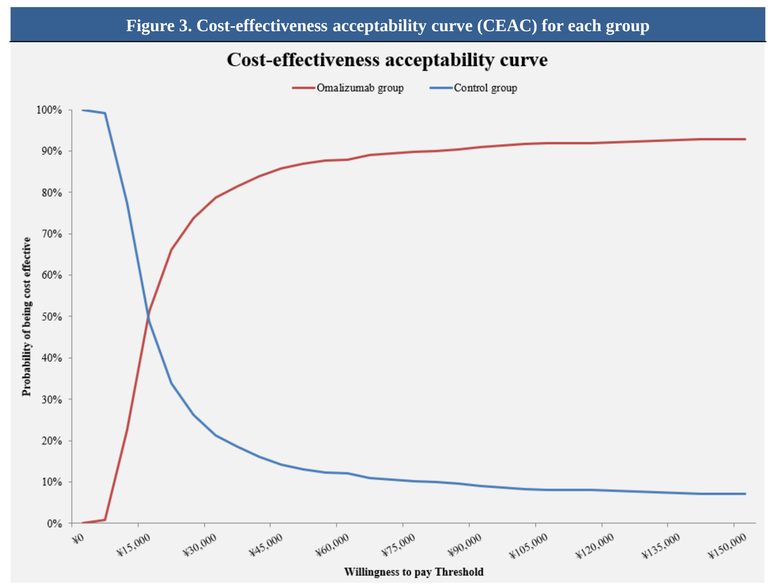
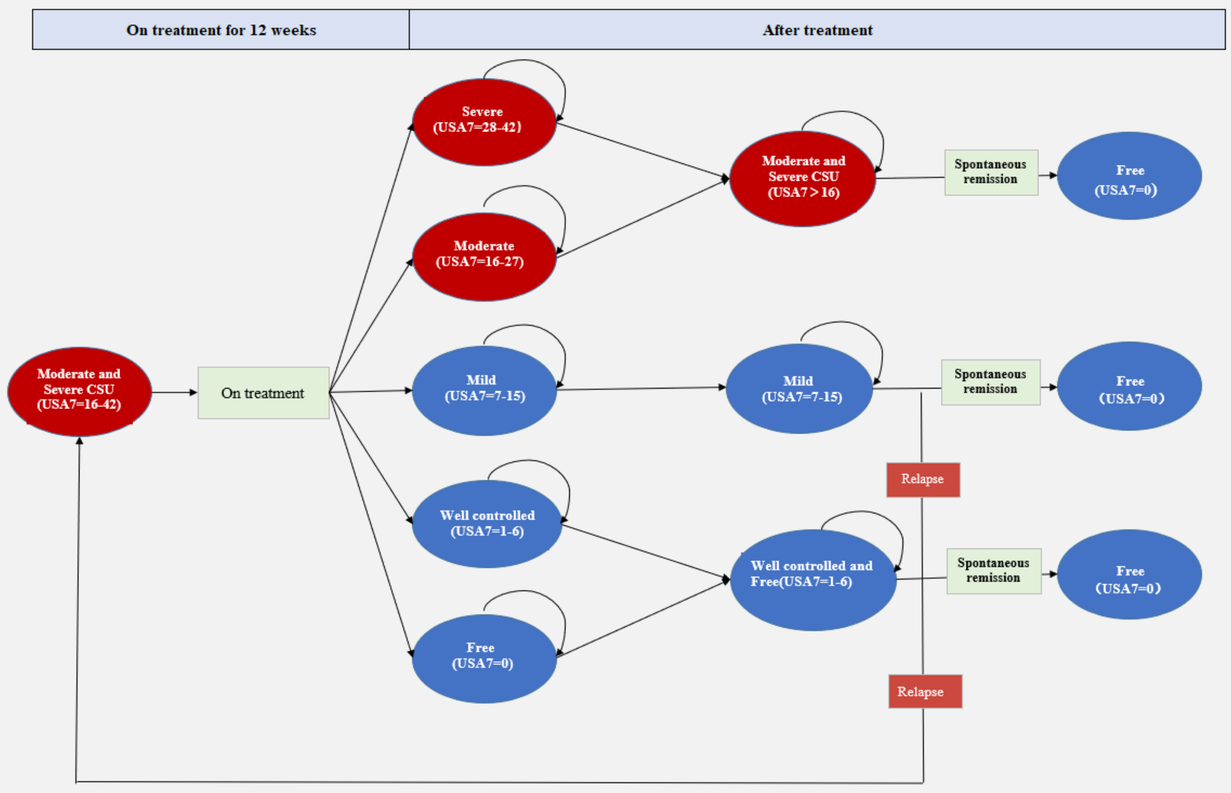


Table4. Result of scenario analyses

Scenarios	Omalizumab group		Control group		ICER(¥/QALY)
	Cost(¥)	QALYs	Cost(¥)	QALYs	
Base case analysis	13495.33	7.21	8008.33	6.9709	22950.00
Alternative research patients					
Patients with angioedema	13214.28	7.17	8182.87	6.94	21852.51
Patients without angioedema	13569.32	7.23	8169.74	6.97	20537.66
Alternative time horizon					
20 years	16276.43	11.66	11213.92	11.31	14353.31
Life time	18264.79	16.11	13372.87	15.69	11581.52
Alternative research perspective					
Whole society	15657.68	7.22	11049.94	6.96	18099.81

Figure 1. Markov model used in cost effectiveness analysis



Discussion

- In the base case analysis, Omalizumab has a high probability of being a cost-effective treatment option in CSU patient at the preset willingness-to-pay threshold. But the heath utility made greater influence on the result than other parameters, so further research on health utility in Chinese CSU population is necessary.
- The pharmacoeconomic evaluation results of omalizumab was consistently cost-effective in a range of different scenarios, which confirmed the robustness of the model results.

Conclusion

- Omalizumab represents a cost-effective treatment for patients with moderate to severe CSU inadequately controlled by H1-antihistamines from the perspective of Chinese medical service system.

Reference

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