ESTIMATING UTILITY DATA FOR PATIENT SYMPTOM SEVERITY IN CHRONIC SPONTANEOUS URTICARIA

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BACKGROUND

- According to international guidelines, chronic spontaneous/idiopathic urticaria (CSU/CIU) is defined as the occurrence of itchy hives (wheals), angioedema or both for 6 weeks or longer due to known or unknown causes (Zuberbier T 2014)
- The EuroQol (EQ-5D) is a generic, standardised instrument used as a measure of health outcomes across all diseases
  - It is a descriptive system of health-related quality of life (HRQoL) states consisting of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (Gusi N 2010)
  - Each dimension has 3 levels: no problems, some problems, extreme problems
  - A single index value for health states (called utility) can be calculated from the combination of responses to the 5 questions. The maximum utility value is 1 (perfect health), 0 (corresponds to death)
- EQ-5D allows comparison of HRQoL across diseases and facilitates the calculation of quality-adjusted life years (QALYs)
- The Urticaria Activity Score (UAS) is a validated daily diary, encompassing hives and itch, to assess urticaria severity and monitor treatment outcomes. UAS7 is a weekly composite score, derived by summing daily UAS scores over 7 days. The instrument is used to determine disease activity and response to treatment (Zuberbier T 2014). UAS7 scores range from 0 to 42, with higher scores reflecting worse urticaria

OBJECTIVE

- Currently there is no published information on the relationship between health states and utility values in patients with CSU. The objective of this study was to investigate the relationship between health states defined by UAS7 and EQ-5D utility values in CSU, and provide suitable estimates for use in economic models

METHODS

Data

- Patient-level data from three randomised, double-blind, placebo-controlled phase III clinical trials (ASTERIA I [N=318], ASTERIA II [N=322], and GLACIAL [N=335]) were analysed
- Treatment was administered once every 4 weeks for 24 weeks in ASTERIA I and GLACIAL trials and for 12 weeks in ASTERIA II trial with a follow-up period of 16 weeks in all three trials
- For ASTERIA I and GLACIAL trials, EQ-5D data were collected at baseline, Week 12 and 40; and for ASTERIA II trial at baseline, Week 12 and 28
- For ASTERIA I and GLACIAL trials, UAS7 scores were reported at baseline and every week until Week 40 and for ASTERIA II trial, until Week 28

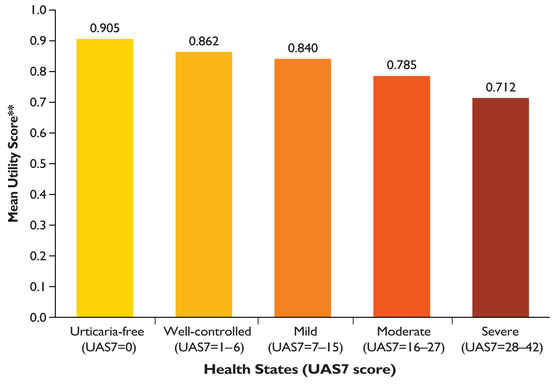
Analytic methods

- Mean utilities were calculated for the following five health states, defined with UAS7 scores (based on expert opinion); Urticaria-free (UAS7=0), Well-controlled urticaria (UAS7=1–6), Mild urticaria (UAS7=7–15), Moderate urticaria (UAS7=16–27), Severe urticaria (UAS7=28–42)
- Individual trial analyses, by treatment arm and time point, showed inconsistent utilities across the UAS7 health states, due to small sample sizes
- To increase the overall sample size, a pooled dataset considering all time points, all treatment arms of the ASTERIA I, ASTERIA II and GLACIAL trials was analysed independent of baseline severity
- To predict EQ-5D utility according to UAS7 health states in the pooled dataset, a mixed effects model (linear mixed model) was used, with EQ-5D as the dependent variable and UAS7 health states as the predictor. Fixed/random effects for trial and patient were included as well as the following covariates: UAS7 health states at baseline (Moderate or Severe), presence of angioedema at baseline and during follow-up (a binary variable indicating presence of one or more angioedema days during weeks 4 to 12), duration of CSU, number of previous CSU medications, and gender of the patient; interaction terms were also considered
- A parsimonious model was selected using the approach of backwards elimination, where covariates that were not significant were sequentially removed from the model according to their p-value, UAS7 health states was forced into the model
- The validity of pooling trials was considered through visual comparisons and interaction terms to evaluate differences in the relationship between health states and utilities among the different trials
- Sensitivity analyses were conducted to confirm the robustness of the results
- Analysis was conducted using Stata (StataCorp; College Station, Texas), mixed models were conducted using the xtmixed command, and utilities were estimated using the margins command

RESULTS

- Mean utility scores were estimated for each of the five health states from pooled patient-level trial data from all studies, all treatment arms and all time points, and independent of baseline severity. Following backwards elimination, the only covariate which remained in the model was the presence of angioedema. There was a consistent improvement in EQ-5D utilities as patient severity of urticaria decreased. Mean utilities at Week 12 ranged from 0.712 in patients with severe urticaria to 0.905 in patients who were urticaria-free (**Figure 1**)

Figure 1. Mean EQ-5D utility scores at Week 12 of each health state in pooled trial data*



*Age, gender, presence of angioedema at baseline, occurrence of angioedema during weeks 4–12, duration of disease, treatment, time point, interaction term between treatment and response, interaction term between time point and response were considered as covariates in the model. The only covariates which remained significant in the model following backwards elimination were the presence of angioedema during follow-up and UAS7 health states; visit, study and patient were included as random effects in the model.

**0=death, 1=perfect health

- Sensitivity analyses of utility estimates were conducted without baseline data, without the presence of angioedema at baseline, and without the presence of angioedema during follow-up. The results were consistent with the pooled patient-level trial data from all studies, all treatment arms and all time points, and independent of baseline severity (**Table 1**)

Table 1. Sensitivity analyses of utility score by UAS7 health states*

Health States (UAS7 score)	Sensitivity analyses of utility score by UAS7 health states*		
	Without baseline data	Without the presence of angioedema at baseline	Without the presence of angioedema during follow-up
	Mean EQ-5D score (SD)	Mean EQ-5D score (SD)	Mean EQ-5D score (SD)
Urticaria-free (0)	0.918 (0.20)	0.904 (0.23)	0.916 (0.23)
Well-controlled (1–6)	0.886 (0.20)	0.869 (0.22)	0.867 (0.22)
Mild (7–15)	0.848 (0.20)	0.838 (0.22)	0.839 (0.21)
Moderate (16–27)	0.796 (0.20)	0.795 (0.22)	0.802 (0.21)
Severe (28–42)	0.721 (0.21)	0.735 (0.25)	0.745 (0.25)

*Age, gender, presence of angioedema at baseline, occurrence of angioedema during weeks 4–12, duration of disease, treatment, time point, interaction term between treatment and response, interaction term between time point and response were considered as covariates in the model. The only covariates which remained significant in all the models following backwards elimination were the presence of angioedema during follow-up and UAS7 health states; study and patient were included as random effects in the model, visit remained significant in models containing baseline information.

CONCLUSIONS

- The results suggest that EQ-5D utility score increased with decreasing severity of urticaria
- The study further demonstrated that with increasing severity of urticaria, patients placed varying preferences for specific health states in CSU
- The robustness of the results was confirmed by the sensitivity analyses and further analyses will be conducted to explore the impact of angioedema on utility values
- The results of this analysis documents the utility associated with severity of CSU health states
- EQ-5D utility scores allow the comparison of HRQoL and patient preferences across diseases by calculating QALYs which are used in economic models
- These are essential components of health technology assessments which contribute to support decision-making for healthcare resource allocation

REFERENCES

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