

Letter to the editor

Revisiting the cost-effectiveness of omalizumab

We read with interest the paper by Brown et al. (1) on the cost-effectiveness of omalizumab in patients with severe persistent allergic asthma. We are concerned by some of the input parameters and assumptions of the model and their potential influence on the results and conclusions.

The authors take Canada as their reference country for the model. A subgroup of patients from the ETOPA European open-label trial, those receiving at least a high-dose ICS plus a LABA, was used to inform key parameters in the model. The rationale for using a subgroup of ETOPA was to mirror the European omalizumab label population. However, the Canadian omalizumab label does not restrict omalizumab eligibility to those with severe persistent disease or to those taking a LABA (2). To be consistent with a Canadian reference case, we think the modeled analysis should include the entire ETOPA population.

The authors report the exacerbation and utility values for standard therapy and omalizumab responders in Table 1. The definition of treatment response is based on improvements in the Mini AQLQ. The Mini AQLQ is also used in the mapping algorithm to generate the utility scores. Thus, it is no surprise to find that omalizumab responders have markedly higher utilities than the standard therapy arm.

We would expect this by definition. However, it is unclear how the response to omalizumab is applied to the model. We would like to see the utility values and results using the entire omalizumab cohort.

The authors make an important assumption that the proportion of severe exacerbations as observed from the INNOVATE trial (3) would be the same as in the subgroup of patients from the ETOPA trial. Average rates of clinically significant exacerbations from INNOVATE were 0.68 for omalizumab and 0.91 for placebo and average severe exacerbation rates were 0.24 for omalizumab and 0.48 for placebo. By our calculations, the proportion of exacerbations that were severe was $0.24/0.68 = 35.3\%$ for omalizumab and $0.48/0.91 = 52.7\%$ for placebo. These proportions however, do not match the proportions reported in Table 1A. We ask the authors to further describe the methods used in establishing the proportion of severe vs nonsevere exacerbations and to show sensitivity analysis around their point estimates. The exacerbation input will likely have a substantial impact on both the incremental cost and effectiveness results.

The authors do not report any costs associated with the side effects of omalizumab, for example anaphylaxis.

The authors indicate that there were no deaths in the ETOPA trial. The model assumes that those who experience a severe exacerbation have a mortality risk of 3.11%. This assumption is based on a small observational study from Sweden (4) that was not designed to estimate the relationship between severe asthma exacerbations and death. The fact that no deaths were observed over the course of 1 year in the standard therapy arm of the ETOPA trial puts into question the model's link between increased mortality and severe exacerbations. If the mortality risk equation from the Swedish study were valid, then one would have expected 4.2 deaths in the standard arm of the ETOPA trial. We commend the authors for investigating the mortality risk parameter in their one-way sensitivity analysis to weigh the influence of their base-case mortality assumption, but think the zero mortality rate parameter should be the base case and the 3.11% mortality risk increase should be the basis for the sensitivity analysis.

*J. D. Campbell, D. E. Spackman,
S. D. Sullivan
Pharmaceutical Outcomes Research and
Policy Program, University of Washington,
Seattle, WA, USA*

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