bsaci
improving allergy care
through education, training and research

Report on NICE HTA 10/128/01 omalizumab (OZ)

The report expresses the frustrations of inadequate data in the sense that:

(1) On the one hand there is:
   (a) Robust evidence (more limited in children, but there) that OZ shows good short/medium term efficacy and safety in patients treated with OZ within licensed indications and also to a degree outside these indications. The data show a very clear and significant short/medium term reduction in total (26%) and particularly severe (50%) asthma exacerbations in both adults and children (33%), and this difference is even more impressive in sub-analyses of responders in adult studies. This in turn has been shown to reduce hospital admissions and unplanned health care usage (at least 50%) which is the most immediate and significant determinant of quality of life.
   (b) Good evidence for an oral corticosteroid (OCS) sparing effect of OZ compared with placebo in adults, although not in children because the relevant studies simply have not been done.

(2) On the other hand there are:
   (a) Insufficient data relating these changes to changes in quality of life (QoL), which are difficult to estimate especially in short term studies where the principal impact of OZ treatment is on exacerbations and unscheduled health care usage and not on changes in day to day symptoms and lung function.
   (b) Insufficient data to estimate the overall size and longevity of reduction of OCS dosages especially in children where there are virtually no data at all.

The NICE MTA is based on cost per QALY. The principal drivers for “acceptable” cost per QALY when assessing the benefits of OZ are reductions in mortality, the amount of improvement in QoL afforded by OZ therapy *per se* and any additional amount of improvement in QoL that may accrue from reduction in dosages of OCS. Unfortunately, as the widely disparate estimates of ICER and cost per QALY in adults and children performed by the manufacturers and the independent analysers in this MTA well illustrate, there would appear to be no scope in our current state of knowledge for making any sensible and credible estimate of the size of the effect of OZ therapy on:
   (a) Mortality.
   (b) QoL improvement.
   (c) The effect on QoL of the OCS sparing effect.

In addition little attention has been paid so far to:
   (a) The persistence or otherwise of the effects of OZ in reducing exacerbations and OCS usage (excusable since it has not been with us very long).
   (b) Delineation of “responder” or “high risk” groups.
   (c) The possibility that the licensed indications do not delineate optimal target groups (the implication from the existing guidelines that a single positive skin prick test to an arbitrary perennial aeroallergen defines “severe, allergic asthma” is ludicrous. Assessment and diagnosis of severe allergic asthma also requires experience and clinical judgment particularly important if an expensive and potentially life-long therapy is being considered .
   (d) Studies comparing the effects and adverse effects of OZ and OCS side by side.

In short, we have a good drug. We know this from outcome data of the randomised trials but perhaps more pressingly from numerous patient stories which have affirmed many times over that the treatment can change lives. Data from studies in adults affirm that OZ is cost-effective and it appears that NICE have been inadvertently backed into a corner and discriminated against the >12y age group. The problem is we are not in a position to measure how good it is. This is a shameful state of affairs for both the manufacturers and the health service. Given these circumstances the BSACI strongly feels that this ignorance should not be used as an excuse to abandon the therapy which has benefited many patients, but as an opportunity to answer some of the many pressing questions which arise. We suggest:

(a) Further scrutiny of the possible impact of reducing asthma exacerbations on the risk of death (for example by embracing data from the ongoing RCP audit of asthma deaths).
(b) Urgent, controlled trials to assess the OCS sparing effects of OZ treatment in severe adult and child asthmatics in the medium to long term.
(c) "All comers" trials of OZ therapy for unselected adult and child asthmatics at step 4/5 with robust estimates of the effects of therapy on QoL and prospective analysis of the influence of factors such as atopy, baseline lung function and baseline OCS therapy.
(d) Trials of OCS vs OZ therapy in severe asthmatic patients needing to proceed beyond step 4.
(e) A realistic appraisal of the costs and health losses of OCS therapy stratified by the duration and amount of therapy.

Suggestions:

Revise conclusion on Page 3 to regain the *status quo*: 1.1 Omalizumab is not recommended within its marketing authorisation for treating severe persistent allergic asthma but is recommended for adult and adolescent patients in the following groups (see section 4.2.27):

- Population 1: people with very severe persistent allergic asthma who are on maintenance oral corticosteroids and who were hospitalised in the year before treatment.
- Population 2: people with very severe persistent allergic asthma who are on maintenance oral corticosteroids but who have not necessarily been hospitalised in the year before treatment.
- Population 3: people with very severe persistent allergic asthma who are on maintenance or frequent courses of oral corticosteroids (for example, 4 or more courses per year) but who have not necessarily been hospitalised in the year before treatment.

We also note that the Committee concluded that some adverse effects of oral corticosteroid use, such as obesity, hypertension, mood changes, depression, psychosis, thinning skin, delayed wound healing, reduced growth in children, and increased risk of infection were additional important factors that had not been captured when calculating the QALY. The Committee agreed that there could be additional health-related benefits conferred to carers as a result of omalizumab use but that these were currently not quantifiable (page 55). We would suggest that this does not mean that they do not potentially exist and should be discarded out of hand.

On behalf of the BSACI

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29 November 2012