Appeal against NICE decision for Inotuzumab Ozogamicin (IO)

Ground(s) for appeal

This is an appeal on the grounds of the recommendation being unreasonable in the light of the evidence submitted to NICE.

The appealed is being made against

1. An incorrect assumption made in section 3.13, administration costs; specifically, length of stay assumptions.
2. An incorrect assumption of the number of cycles of IO. Section 5.2.3 of the Evidence Review Group (ERG) report indicates that all of the ERG scenarios are based on costing up to a maximum of six cycles of IO. The FAD does not recognise the most likely scenario of two cycles with maximum three, at all.

The reasons why the aspect(s) of the FAD or appraisal process being appealed against fall within the specified ground(s) of appeal, are discussed below:

1. Length of stay

We are pleased that the NICE committee accepted that "inotuzumab ozogamicin could be an important treatment option for people with relapsed or refractory B-cell acute lymphoblastic leukaemia." Cost seems to be the main ground for making a negative decision. We are all cognisant of and understand the need for realistic pricing and cost containment. However, we are concerned that some major aspects of calculation of cost have been based on incorrect assumptions.

NICE made their conclusion upon an “analysis with the administration cost of inotuzumab ozogamicin based on INO-VATE 1022 and an average length of stay of 9.5 days in both arms.” NICE rejected other estimates of inpatient stay, saying “1 day to 14 days is too overly-favourable a ratio to inotuzumab when considering administration.” Expert advice at the first committee meeting suggested chemotherapy would actually require several weeks of in-patient stay and inotuzumab far less/possibly none. It is not clear why this claim was ignored or at the least, not further explored. If the veracity of evidence of the expert is in question, it would be easy to consult other independent experts or to request real-world data to further demonstrate or refute the veracity of the claim of the expert. There are important reasons why the company did not base the UK-relevant calculation of inpatient days on INO-VATE 1022, which NICE would have preferred. The INOVATE study encompassed sites from a large number of different countries with different health care models which make interpretation of length of stay difficult. As an example, ‘ambulatory care’ is a common therapeutic option in some sectors and is costed differently to either inpatient or outpatient therapy.

It is also particularly difficult to interpret length of stay within a clinical trial where certain trial-related procedures and assessments which do not carry over to routine care are mandated on very specific days. It is also important to note that there were only 6 UK centres participating in this trial. This had the effect that patients travelled from around the UK to participate. This phenomemon also favours a longer length of inpatient stay for the exploratory arm for purely logistic reasons, since patients can rarely afford to take hotel accommodation locally, for a trial duration.

Since the conduct of the trial, there has been a compassionate use program for IO within the UK. In one large London leukemia unit, IO has been given on compassionate grounds to 10 patients since the closure of the trial.
Data on length of stay for FLAG, FLAG-Ida or FLA-Ida are also available during a reasonably comparable time period. It would not be unreasonable (nor costly, nor time consuming) to obtain actual length of stay audit data from the real world taking 4 or 5 large units which have used IO on the compassionate program. On a modest scale, this can easily be organised by relevant clinicians and centres. Length of stay data from such an audit will be presented at appeal.

2. *An incorrect assumption of the number of cycles of IO*

The company basecase model costed up to 6 cycles of IO but suggested that the analysis relevant to the UK should consider a maximum of 3 cycles. Section 5.2.3 of the Evidence Review Group (ERG) report indicates all of the ERG scenarios are based on costing of 6 cycles per patient. The FAD fails to discuss the different cycle number scenarios at all nor take into account different costing models based on cycle number.

Below is an extract from the SPC for IO which clearly **does not** recommend 6 cycles for all patients

For patients proceeding to haematopoietic stem cell transplant (HSCT), the recommended duration of treatment is 2 cycles. A third cycle may be considered for those patients who do not achieve a complete remission (CR) or complete remission with incomplete haematological recovery (CRi) and minimal residual disease (MRD) negativity after 2 cycles (see section 4.4). For patients not proceeding to HSCT, additional cycles of treatment, up to a maximum of 6 cycles, may be administered. Patients who do not achieve a CR/CRi within 3 cycles should discontinue treatment.

The ERG calculated the cost of IO in line with the full INO-VATE trial full dosing schedule. However, only 45 of 164 patients in this trial received more than 3 cycles of drug.

The concluding statement indicating whether the appellant wishes to be heard at an oral or written appeal

The appellants are willing for either a written or oral appeal.

Dr Rachael Hough, Consultant Haematologist and Senior Lecturer

The North Thames teenager and young adults cancer network coordinating group (TYACNCG)

National Clinical Lead Children & Young Adult Cancer Clinical Reference Group (CRG)
Representing RCP

Professor Adele Fielding, Consultant Haematologist and Professor of Haematology
Chair, UK National Research Institute Adult ALL Subgroup
Representing RCPath

Report prepared in consultation with **Professor Ajay Vora** Consultant in Paediatric Haematology, Great Ormond Street so as to represent all affected age groups of patient