

From: Catherine Coyle

Sent: 26 February 2007 18:22

To: Michelle Adhemar

Subject: Fwd: single technology assessment - response on behalf of Bahno

>>> Catherine Coyle 2/26/07 6:19 PM >>>

Hello Christopher

I have been asked by the British Association of Head and Neck Oncologists to reply to the initial assessment for Cetuximab in advanced head and neck cancer. I wanted to reply after the ESTRO Head and neck meeting last week because I wanted to ensure a representative reply rather than a personal one.

As you know Cetuximab is the first drug in head and neck cancer that has been licenced by the FDA for over forty years. There is a lot of scientific evidence as to why it may be effective and a lot of interest generally. Prognosis for advanced head and neck cancer has not really improved significantly over the years, and local control as well as survival is a major issue with quality of survival in this group. The current standard of care is chemoradiotherapy with several well designed trials plus updated meta analysis to support its use. However the latest update presented at ASCO in 2006, noted the relative lack of improvement in outcomes in the over 71 year age group. The toxicity of chemoradiotherapy has always been noted and some of the American trials have suggested mortality rates of up to 6%, which with a survival benefit of 10 - 12 % is significant. The patient group also have considerable co morbidities.

The advantages of Cetuximab is said to be the lack of increase in radiation induced toxicity such as dysphagia or mucositis although other side effects particularly the rash are well know and rash presence indicates benefit.

The request for licensing by Merck however relates to only one study.

While this Bonner et al study has been very very well conducted, its age means it did not compare chemoradiotherapy plus or minus cetuximab.

Therefore Merck have extrapolated the patient population to apply for a licence in those unfit for chemoradiotherapy. While there is general scientific support for such a drug there is very very limited experience in the UK with some centres having treated about 10 patients. The major sticking point is that Merck are trying to have the NICE badge for a group of patients which have not been specifically targeted in the

Bonner study. Most patients unfit for chemoradiotherapy are unfit on the basis

of performance status, extreme age, poor cardiac or renal function. The study required patients to have good performance stage and normal renal function and the median age was 58 years. Therefore we are reliant on limited UK practice plus lack of evidence for chemoradiotherapy in 71 years or more. The practice does however seem to favour the tolerability of the drug but of course is not being audited etc.

Minor points about the study also include the preponderance for oropharyngeal cancers, whereas in the elderly the laryngeal and hypopharyngeal are more common. Over 56% had hyperfractionated treatments with radiotherapy which are quite tough and therefore go with the expected good performance status. Those schedules are rarely used in the UK.

Although the study was well received, even at ESTO head and neck conference where Cetuximab was being billed as an option for patients, Kian Ang who was one of the authors of the trial, would not be drawn into when to specifically use the drug, pointing out the experience in less than five hundred patients.

I could not comment on whether the economics of improving survival by 10% in a heavily co morbid and older group is cost effective. Local control would be a huge benefit clinically. I note the significant difference in Qualys assessment by NICE and Merck.

While I struggle with this group of patients clinically and can see potential benefits for patients, I would be concerned that a positive NICE outcome would not be linked to a prospective audit. I would advocate that a group such as the NCRN or even BAHNO via the DAHNO audit already set up should be heavily involved.

A number of us have proposed that a trial in intermediate cancers, ie the group with no benefit from the addition of chemotherapy would benefit from the Bonner style approach. We are of course awaiting the RTOG trial in advanced disease.

Overall with so few options available in head and neck cancer and such a scientifically sound drug I would like to see Cetuximab move into clinical practice. The data extrapolation from the Bonner study into the group of patients Merck are proposing is however very contentious and only anecdotally safe. I would like to see more trials in the particular patient group, plus robust audit. The international community also seem to see this drug as a step forward, but it's exact role remains undetermined by the current literature.

I hope that is a balanced and helpful assessment.

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