From: [redacted]
Sent: 12 September 2008 16:04
To: Jeremy Powell
Subject: Re: NICE Appraisal: Head and neck cancer (squamous cell carcinoma) - cetuximab

Single Technology Appraisal (STA)
Appraisal of Cetuximab for the treatment of metastic and/or recurrent squamous cell carcinoma of the head and neck.

Submission from [redacted]/[redacted] of Let's Face It a Support Network for the facially disfigured.

Dear Jeremy,

On reading the comments made by a variety of people involved with this appraisal, I, as a patient find some of the technical wording complicated and confusing. Therefore, my submission is from a personal experience of radiotherapy and chemotherapy treatment for a squamous cell carcinoma, and the shared experience of hundreds of other patients who are no longer living.

In my first submission to NICE sent in February 2007 I was aware of the lack of evidence from Merck, however, the data from the Bonner study does show that Cetuximab can augment the response to radiotherapy, and the benefit of cetuximab plus radiotherapy is achieving a 10% improvement in survival over 3 years. Despite these facts, the Evaluation report presupposed that cetuximab would be reserved for the cases that were not considered for chemoradiation.

The pain and discomfort to the patient undergoing chemoradiation is unbelievable agony. The inability to swallow, to speak, the agony of living with a dry, ulcerated mouth leaves both patient and families in turmoil. If Cetuximab were available to these patients as an alternative to Cisplatin and your loved one was being treated for this disabling cancer - what would you choose?

Cetuximab offers less toxicity to the patient, it shows that a 10% improvement to patients on Cetuximab. Considering there are over 8,000 new patients each year suffering from oral cancer in the UK there is evidence that this treatment is kinder, less aggressive than Cisplatin/radiotherapy. Quality of life is an issue that seems to have been overlooked by NICE , and I urge you to take this into account when assessing the information before you.

Patient/carer organisation statement template

Thank you for agreeing to give us your views on the technology and the way it should be used in the NHS.

Patients and patient advocates can provide a unique perspective on the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Please do not exceed the 8-page limit.

About you

Your name:

Name of your organisation: Mouth Cancer Foundation

Are you (tick all that apply):

- ~~a patient with the condition for which NICE is considering this technology?~~
- ~~a carer of a patient with the condition for which NICE is considering this technology?~~
- an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, member, etc)
- other? (please specify)

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

1. **Advantages**
(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make.

Head and neck cancer is very difficult to treat and these patients have a very poor outcome. Up to 30% of patients with one primary head and neck tumour will have a second primary malignancy. About 20% of people with recurrent head and neck cancer have metastatic disease. Depending on the stage of cancer spread, different treatment options are recommended for oral cancer. Surgery is suggested when the cancer has become invasive. If there is repeated recurrence, radiation therapy is an option. Where a patient is not a candidate for surgery or radiation, chemotherapy has been the option.

This is time in 25 years that the a systemic therapy has shown a survival benefit over platinum-based chemotherapy in head and neck cancer.

(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology. These might include the effect of the technology on:

- the course and/or outcome of the condition
- physical symptoms
- pain
- level of disability
- mental health
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example family, friends, employers)
- other issues not listed above.

This treatment is not curative but improves lifespan. For a patient, any chance of prolonging life with quality is worth having as long as the side-effects of treatment are tolerable and do not impair the quality of life further. Having a treatment that can prolong life gives hope and improves mental health and gives additional time to be with family and friends.

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition? (continued)

2. **Disadvantages**
Please list any problems with or concerns you have about the technology.
Disadvantages might include:

- aspects of the condition that the technology cannot help with or might make worse.
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient and/or their family (for example cost of travel needed to access the technology, or the cost of paying a carer).

The results of the EXTREME study show that the treatment of chemotherapy –plus-cetuximab significantly increased the adverse effects of sepsis. The incidence of hypomagnesemia also increased. There was also slightly more vomitting and diarrhea. The cetuximab treated patients also had acne-like skin reactions (9%) and infusion related reactions (3%) that are consistent with the adverse-effect profile of cetuximab. Accordingly, treatment providers need to be aware of these issues and manage informed patients appropriately.

According to patient reports (monitored on the Mouth Cancer message board) of patients reporting experiences of treatment with cetuximab and radiotherapy, the side-effects of the rash and itchiness are transient and stop after treatment. Some patients have reported being given infusions of benadryl to help with the side effects and using betametasone valearte cream for the rash to successfully ameliorate the terrible itching thet cetuximab causes. However we have had a report of an 18 year old in Surrey who was treated with cetuximab and radiotherapy for a tonsil cancer still having side affects of a painful itchy red scalp hair loss and skin problems 18 months latter.

3. Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.

The overall survival of patients being treated with cetuximab was a median of 2.7 months. Patients who are able to have it are grateful for any weapon in the treatment arsenal that will help them survive longer. But we must ask if the fight against cancer is really being won if improvements are so incremental.

4. Are there any groups of patients who might benefit **more** from the technology than others? Are there any groups of patients who might benefit **less** from the technology than others?

The EXTREME study seemed to show that survival was better in patients whose primary tumour site had been in the oral cavity/hypopharynx.

Comparing the technology with alternative available treatments or technologies

NICE is interested in your views on how the technology compares with with existing treatments for this condition in the UK.

(i) Please list any current standard practice (alternatives if any) used in the UK.

Depending on the stage of cancer spread, different treatment options are recommended for oral cancer. Surgery is suggested when the cancer has become invasive. If there is repeated recurrence, radiation therapy is an option. Where a patient is not a candidate for surgery or radiation, platinum based chemotherapy has been the option.

(ii) If you think that the new technology has any **advantages** for patients over other current standard practice, please describe them. Advantages might include:

- improvement in the condition overall
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in hospital)
- side effects (please describe nature and number of problems, frequency, duration, severity etc.)

Overall survival is improved. It appears from the results of the EXTREME study that for patients with recurrent and/or metastatic head and neck cancer who are not candidates for radiation or surgery, we have a new standard treatment of platinum-based chemotherapy plus cetuximab, if their condition allows them to tolerate this.

(iii) If you think that the new technology has any **disadvantages** for patients compared with current standard practice, please describe them. Disadvantages might include:

- worsening of the condition overall
- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

None that are not tolerable or manageable.

Research evidence on patient or carer views of the technology

If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their routine NHS care reflects that observed under clinical trial conditions.

Based on patient comments on the Mouth Cancer Foundation message board, it appears that the rash and itching is the main discomfort noted when cetuximab is used. The other side-effects are also seen with platinum based chemotherapy. So yes, the side-effects described in the Extreme study mirror side-effects described by patients who have had cetuximab with radiotherapy but we have no reports from patients who have had platinum-based chemotherapy pus cetuximab for recurrent disease or metastasis as such treatment would have been palliative if used.

Are there any adverse effects that were not apparent in the clinical trials but have come to light since, during routine NHS care?

Not aware

Are you aware of any research carried out on patient or carer views of the condition or existing treatments that is relevant to an appraisal of this technology? If yes, please provide references to the relevant studies.

Not aware.

Availability of this technology to patients in the NHS

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

It appears from the results of the EXTREME study that for patients with recurrent and/or metastatic head and neck cancer who are not candidates for radiation or surgery, we have a new standard treatment of platinum-based chemotherapy plus cetuximab, if their condition allows them to tolerate this.

What implications would it have for patients and/or carers if the technology was **not** made available to patients on the NHS?

Distress.

Are there groups of patients that have difficulties using the technology?

Those unable to tolerate cetuximab owing to allergy or severe side-effects.

Other Issues

Please include here any other issues you would like the Appraisal Committee to consider when appraising this technology.

None.

Professional organisation statement template

Thank you for agreeing to give us a statement on your organisation's view of the technology and the way it should be used in the NHS.

Healthcare professionals can provide a unique perspective on the technology within the context of current clinical practice which is not typically available from the published literature.

To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: [redacted]

Name of your organisation, Royal College of Nursing

Are you (tick all that apply):

- a specialist in the treatment of people with the condition for which NICE is considering this technology?
  [redacted]
- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?
- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)? **Member**
- other? (please specify)

What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant clinical guidelines and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

Currently for this group of patients there is very limited treatment available. Some may be offered salvage surgery, which in itself has huge impact and morbidity depending on the location of recurrence as it will cause body image issues, may affect a patient's swallowing and make them dependent on Enteral Feeding. It may cause speech problems too. Others depending on where the metastases may be offered best supportive care which may be appropriate for some patients with widespread metastases, however Cetuximab ought to be available to those patients with a good Karnofsky Score.

This group of patients are often from poorer socio economic backgrounds, have alcohol and drug issues too and therefore are not the most vocal group of patients. This may be evident in trusts which serve a large geographical area, which contains some very deprived areas as well as the more affluent areas.

In the trust which our reviewer works in, Cetuximab has shown in the Extreme Trial, to have been tolerated well by the patients. The patients were seen weekly, receiving an infusion which required them to be in Oncology Day care for less time than when they were receiving Platinum based chemotherapy. Increasingly some patients with other cancers are receiving chemotherapy agents at home; perhaps this could be looked at for these patients too?

Attending for treatment weekly may be seen as a disadvantage for patients who are trying to maintain some normality, i.e. going to work.

As a designated Head and Cancer Unit, these patients are well served by having a team, who work closely and well together in the interests of these patients. The trust was also involved in the 'Extreme' trial when it was open and found although recruited a small number of patients, patients tolerated Cetuximab well.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

Cetuximab is administered over a shorter period than Platinum based chemotherapy and patients would be spending less time in Oncology Day Care. They are also less likely to require admission to the ward as an in patient as they would be seen weekly in Oncology Day Care and their symptoms monitored. This would reduce admissions to the ward. These patients would therefore have a better quality of life as they would not have lengthy stays on the ward.

Patient's main side effect related to Cetuximab is the Acne type rash they experience. However this can be treated with various creams.

A disadvantage could be in the frequency of visits to the Oncology Day Care and for some patients who are trying to maintain some normality in their day to day routines, attending weekly may be difficult.

Patients with metastatic and or /recurrent disease are incurable from their cancer, therefore the outcome measures would be progression free survival, symptomatic relief and improving their current quality of life. We are not aware of any adverse effects which were not reported in the trial and have now come to light. Head and Neck cancers over recent years have not experienced new drug treatments being developed as other cancers, however Cetuximab has shown promising results for this group of patients and should be licensed for metastatic and or/recurrent SCC of head and neck.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

Not Applicable

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

Additional education or training would not be required as it is currently administered for other cancers in Oncology Day Care on an outpatient basis.

The nurses administering it are already familiar with Cetuximab and its side effects.

There would not be additional equipment required in the administering of Cetuximab as it is administered via a standard intravenous infusion pump.

Professional organisation statement template

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To help you in making your statement, we have provided a template. The questions are there as prompts to guide you. It is not essential that you answer all of them.

Please do not exceed the 8-page limit.

About you

Your name: [redacted]

Name of your organisation The Royal College of Pathologists

Are you (tick all that apply):

√ - a specialist in the treatment of people with the condition for which NICE is considering this technology?

- a specialist in the clinical evidence base that is to support the technology (e.g. involved in clinical trials for the technology)?

- an employee of a healthcare professional organisation that represents clinicians treating the condition for which NICE is considering the technology? If so, what is your position in the organisation where appropriate (e.g. policy officer, trustee, member etc.)?

- other? (please specify)

What is the expected place of the technology in current practice?

How is the condition currently treated in the NHS? Is there significant geographical variation in current practice? Are there differences of opinion between professionals as to what current practice should be? What are the current alternatives (if any) to the technology, and what are their respective advantages and disadvantages?

Are there any subgroups of patients with the condition who have a different prognosis from the typical patient? Are there differences in the capacity of different subgroups to benefit from or to be put at risk by the technology?

In what setting should/could the technology be used – for example, primary or secondary care, specialist clinics? Would there be any requirements for additional professional input (for example, community care, specialist nursing, other healthcare professionals)?

If the technology is already available, is there variation in how it is being used in the NHS? Is it always used within its licensed indications? If not, under what circumstances does this occur?

Please tell us about any relevant **clinical guidelines** and comment on the appropriateness of the methodology used in developing the guideline and the specific evidence that underpinned the various recommendations.

The treatment of head and neck cancers is adequate summarised in the final scoping document and in the comments from the British Association of Head and Neck Oncologists.
As the majority of squamous carcinomas of the head and neck appear to over-express EGFR, the use of inhibitors of this molecule has attraction as an adjunct to conventional treatment methods.
The Royal College of Pathologists publishes national, evidence-based guidance on the laboratory investigation of head and neck cancers. Biomarker evaluation is not currently included in this guidance. Should molecular therapies directed against specific targets on cancer cells become a standard treatment option, then it may be necessary to include in our guidance information specific laboratory tests that may be used to determine those patients who are most likely to benefit from the treatment.

The advantages and disadvantages of the technology

NICE is particularly interested in your views on how the technology, when it becomes available, will compare with current alternatives used in the UK. Will the technology be easier or more difficult to use, and are there any practical implications (for example, concomitant treatments, other additional clinical requirements, patient acceptability/ease of use or the need for additional tests) surrounding its future use?

If appropriate, please give your view on the nature of any rules, informal or formal, for starting and stopping the use of the technology; this might include any requirements for additional testing to identify appropriate subgroups for treatment or to assess response and the potential for discontinuation.

If you are familiar with the evidence base for the technology, please comment on whether the use of the technology under clinical trial conditions reflects that observed in clinical practice. Do the circumstances in which the trials were conducted reflect current UK practice, and if not, how could the results be extrapolated to a UK setting? What, in your view, are the most important outcomes, and were they measured in the trials? If surrogate measures of outcome were used, do they adequately predict long-term outcomes?

What is the relative significance of any side effects or adverse reactions? In what ways do these affect the management of the condition and the patient's quality of life? Are there any adverse effects that were not apparent in clinical trials but have come to light subsequently during routine clinical practice?

The RCPath is primarily interested in the potential role of laboratory tests on cancer tissue that might help to predict response to molecular therapies. My informal impression of the experience from other cancers suggests that neither EGFR protein nor gene expression is a good predictor of response. It is important to validate laboratory tests in the setting of head and neck cancers, as predictors may or may not be the same as for other cancers.

Any additional sources of evidence

Can you provide information about any relevant evidence that might not be found by a technology-focused systematic review of the available trial evidence? This could be information on recent and informal unpublished evidence, or information from registries and other nationally coordinated clinical audits. Any such information must include sufficient detail to allow a judgement to be made as to the quality of the evidence and to allow potential sources of bias to be determined.

I have no additional information on predictors of EGFR response than that which is available in the published literature.

Implementation issues

The NHS is required by the Department of Health and the Welsh Assembly Government to provide funding and resources for medicines and treatments that have been recommended by NICE technology appraisal guidance. This provision has to be made within 3 months from the date of publication of the guidance.

If the technology is unlikely to be available in sufficient quantity, or the staff and facilities to fulfil the general nature of the guidance cannot be put in place within 3 months, NICE may advise the Department of Health and the Welsh Assembly Government to vary this direction.

Please note that NICE cannot suggest such a variation on the basis of budgetary constraints alone.

How would possible NICE guidance on this technology affect the delivery of care for patients with this condition? Would NHS staff need extra education and training? Would any additional resources be required (for example, facilities or equipment)?

Should laboratory tests be desirable/necessary as a determinant of treatment, then the cost of this testing should be included in the cost-benefit analysis of the treatment. Precise costs would be determined by the nature of the technology involved.