Dr Nick Slevin comment on the European public assessment report Feb 2006

Thank you for the EPAR and EMAR discussion on Cetuximab; I will obviously restrict my comments to the synchronous RT setting. Cetuximab came to clinical trial from a strong pre-clinical in-vitro and in-vivo background. The document 'accepts' chemoRT as the standard of care in locally advanced head and neck disease whilst acknowledging significant problems with severe acute toxicity/need for considerable supportive care as well as enduring morbidities e.g. chronic dysphagia. The Bonner study is analysed in some detail. Much of the further analyses are subgroup, which the study was not powered to examine. Response rate data is largely irrelevant for RT (as opposed to chemotherapy studies) outcomes. The add on benefit was judged to be smallest in patients with poor performance status; this group we know has high intercurrent death rates,

Making comparisons between relatively small numbers even more misleading. It would be attractive to be able to pigeon hole the particular group of head and neck patients who are likely to derive the greatest benefit from Cetuximab. I concur with the EMAR conclusion that even if Cetuximab+RT was inferior to chemoRT in terms of disease control, the safety profile is relatively favourable such that modified fractionation+ Cetuximab should be considered an alternative to standard RT with synchronous chemo in some patients. Which patients? Head and Neck patients are extremely heterogeneous in terms of patient and disease characteristics. I believe we should avoid stipulating strict and detailed criteria for the use of Cetuximab versus the use of chemoRT (fit patients with heavy node positivity are likely to receive chemo); it is likely that a maximum of 10-20% of head and neck patients would be suitable for Cetuximab. (700-1400 patients nationally):

T1/2N0	40%
Stage 3/4 primary surgery	30%
Very unfit/RT only, or palliative	10%
ChemoRT or Cetuximab RT	20%

My clinical judgement is that Cetuximab would constitute no more the half of the latter group. If the RTOG study shows a benefit for chemoRT+ this would rise to 20 %(Cetuximab and RT for less fit patients).

Nick Slevin