Dear Mr Feinmann,


In 2000, there were 38,410 new cases of lung cancer diagnosed in the UK. Of these, 80% of patients had NSCLC, of whom 1 in 10 were non-smokers. Overall, lung cancer accounts for 6% of all deaths and 22% of all cancer deaths in the UK. Cure is extremely unlikely for those who have NSCLC. New therapies are urgently required. All therapies need to achieve a meaningful prolongation of life without a deleterious effect on the patient’s quality of life.

Erlotinib is licensed for use in locally advanced or metastatic NSCLC after failure of previously administered chemotherapy. It is an oral preparation and, hence, is cheaper and easier for the NHS to deliver than intra-venous preparations, like docetaxel. Also, and importantly, patients would find this style of therapy considerably more acceptable and preferable than they would docetaxel. Erlotinib has a relatively non-toxic side-effect profile. Again, this feature results in it being easier and cheaper for the NHS and better for patients than docetaxel, which potentially causes severe side-effects, such as febrile neutropenia.

NICE has stated in its Appraisal Consultation Document that it does not recommend erlotinib for second-line treatment of patients with NSCLC who would normally receive docetaxel. Cancer Research UK considers this recommendation, if finalised, would deny patients and their oncologists the opportunity to utilise what today is the only medically advantageous therapeutic option of significant value.

The charity holds the same view, as an extension of logical thinking, about NICE not being “minded” to recommend erlotinib after failure of at least one prior chemotherapy regimen in patients for whom docetaxel is unsuitable.

The indirect comparisons of erlotinib’s median overall survival with that of docetaxel shows a small difference in either direction depending upon whether the manufacturer’s or NICE’s analysis is favoured. Thus, there is little difference in terms of efficacy. There is, however, in terms of side-effects. In the TAX 317 trial docetaxel 75mg/m(2) caused febrile
neutropenia in 1 of 55 treated patients. In the larger trial reported by Hanna et al, 2004, the same dose docetaxel-related incidences of grade 3/4 were: neutropenia 40.2%, febrile neutropenia 12.7%, neutropenia with infections 3.3%, hospitalisations for neutropenic fever 13.4%, hospitalisations due to other drug adverse events 10.5%, use of GCSF support 19.2% and alopecia 37.7%.

Erlotinib, in contrast, did not produce any haematological toxicity or alopecia in the BR.21 trial. It did cause grade 3-5 fatigue 19%, rash 9%, anorexia 9% infection 2% (vs 5% with placebo), and discontinuation of treatment 5% (vs 2% with placebo).

Previous trials of effective anti-cancer therapies have shown improved or equal quality of life (QoL) benefits deriving from the therapies in comparisons with best supportive care. The same has recently been reported for erlotinib from the BR.21 trial (Bezjak et al. J Clin Onc 2006;24:3831). Symptoms of cough, dyspnoea and pain, three common lung cancer symptoms, improved in 44%, 34% and 42% of patients respectively. In addition there were statistically significant improvements in physical function (31% vs 19% with placebo) and global QoL (35% vs 26% with placebo).

The Scottish Medicines Consortium in May 2006 stated, “Indirect comparison of the key studies would suggest erlotinib offers an oral preparation with comparable overall survival outcomes and a more favourable adverse effect profile than docetaxel.” The SMC’s advice is that erlotinib is accepted for use in locally advanced or metastatic NSCLC after failure of at least one prior chemotherapy regimen.

In contrast, the NICE Appraisal Committee considered there is “uncertainty surrounding survival benefits” and it was “unable to conclude that erlotinib is a cost-effective option”. The Committee also noted that a number of trials are ongoing which directly compare erlotinib with docetaxel. It is considered by Cancer Research UK that this is a case of a lack of evidence of effect being interpreted as evidence of a lack of effect. And on this basis for NICE to propose reviewing this therapy as far away as 3 years from now would be to deny very many patients a considerably helpful therapy.

It is strongly proposed, therefore, that NICE should make no recommendation about erlotinib until such time as definitive evidence of the sort wanted by NICE becomes available, and that in the meantime lung cancer specialists, in discussion with their patients, can consider the prescribing of erlotinib for locally advanced and metastatic NSCLC.

Yours sincerely,

Professor John Toy  
Medical Director, Cancer Research UK