AstraZeneca's comments on gefitinib's Appraisal Consultation Document (ACD)

Section	Comment
2.4 and 4.17	AstraZeneca welcomes the comments made by the Appraisal Committee relating to the likely simple administration of the proposed patient access scheme in the NHS.
4.2	AstraZeneca welcomes the Committee's comments that pemetrexed/cisplatin should be used as the main comparator of interest in this appraisal since it is likely to become standard of care for previously untreated non-squamous NSCLC patients (TA181)
4.3	AstraZeneca welcomes Committee's views on the implementation of EGFR-TK mutation testing not being a limiting factor for the NHS.
4.8	From AstraZeneca's own experience of EGFR mutation testing in the United Kingdom, 342 tests reported with 59 mutations found (17.25%) from 7 testing centres across the United Kingdom. The Manufacturer presents this information in further detail in the response to the Appraisal Committee's questions.
4.9	AstraZeneca supports the view of the appraisal committee that standard combination therapies have very similar (but not equivalent) efficacy. It should be clarified that pemetrexed/cisplatin has significant benefits in OS only as the current text in the ACD implies benefit in OS and PFS against standard combination therapy in a non-squamous population. In addition, AstraZeneca supports the view that the currently immature OS data for gefitinib is similar to pemetrexed/cisplatin and that gefitinib has significantly higher PFS than pemetrexed/cisplatin and standard combination therapies.
4.11	AstraZeneca looks forward to sharing with the Committee the additional requested analyses for the Overall Survival estimates. However AstraZeneca does not routinely share individual patient level data with third party organisations.
4.12	AstraZeneca welcomes the views of the individual clinical specialists that previously untreated NSCLC patients can be treated with up to 6 cycles if the patient responds to treatment. This is in line with ESMO and ASCO clinical guidelines which recommend 4-6 cycles of chemotherapy and also NICE clinical guidelines which do not state a maximum number of cycles.
4.14	Since the publication of the ACD, AstraZeneca has spoken to twelve Oncologists and Pathologists concerning repeat biopsy rates. The consensus was only 2-3% of specimens need to be rebiopsied. This low biopsy rate has largely been attributed to the hisotlogical diagnosis required before pemetrexed/cisplatin can be prescribed. Histological diagnosis requires a bigger sample size than EGFR mutation testing.

4.18

The criteria for End of Life supplementary advice states in 2.3.1: 'The estimates of the extension to life are robust and can be shown or reasonably inferred from either progression free survival or overall survival'

In the Appraisal Consultation Document (ACD), the Committee states that it has concerns that gefitinib has not shown a survival advantage over pemetrexed/cisplatin. Whilst AstraZeneca would agree that there has not been a trial comparing gefitinib to pemetrexed/cisplatin however the AZ submission provides indirect evidence from the Network Meta-Analysis (NMA) and the Weibull regression analysis where paclitaxel/carboplatin was used as a baseline. In this analysis conducted following the Guidance to Manufacturers gefitinib demonstrated a progression-free survival advantage of 3.4 months over pemetrexed/cisplatin.