Single technology appraisal (STA)

Gefitinib for the first-line treatment of locally advanced or metastatic non small cell lung cancer

Comments on ACD in relation to the above from Royal College of Pathologists

These comments relate only to points raised that are relevant to the role of the pathologist in testing for the EGFR mutation(s) that would inform treatment options:

EGFR mutation testing

The last year has seen this test being increasingly requested, with data from varying UK groups suggesting that mutations are identified in 10-15% of cases diagnosed as adenocarcinoma. The instigation of a process for sending material from diagnostic pathology laboratories to molecular units has proved relatively straightforward, with a low failure rate in relation to the test (although techniques vary between centres) itself. If anything, the main issue relates to the volume of tumour cells required with a 'failure rate' in terms of tumour volume of around 10% in our experience. However, recent publications state that mutations are identifiable even in fine-needle aspirations (e.g. Garcia-Olivie et al. *Eur Resp J* 2010;35:391) and our College is addressing these issues in relation to its "Tissue Pathways for Lung Disease" document, which is currently being updated to account not just for implementing mechanisms that allow tissue to be saved for potential mutation testing but also for the refinement of the diagnosis of non-small cell lung carcinoma (NSCLC) to either squamous cell carcinoma or adenocarcinoma, whenever possible. As clinicians and pathologists become more aware of the potential need for testing, the 'tumour volume' issue may lessen as the type of sample required may be planned accordingly as part of multidisciplinary review.

The cost for a mutation test is around £150 at present but will come down with increasing volume. There is also research ongoing into immunohistochemical assessment of mutations which may bring the cost down further, although this may be a while into the future.

Population for testing

The amount of testing could be further refined by limiting it those cases that are adenocarcinoma, either morphologically or via immunohistochemistry, which is already part of the diagnostic process in many UK laboratories in relation to NSCLC. However, there is an argument for the group for testing to be those that are 'non-squamous' as the NSCLC population will contain some adenocarcinomas, albeit more poorly differentiated and with a likely lower mutation rate (although this is unproven on biopsies).

At present, there are insufficient data to argue convincingly for testing just "adenocarcinomas" or a larger "non-squamous NSCLC" group. However, the RCPath "Tissue Pathways" updated document intends to make it part of the process to refine NSCLC whenever possible, which may reduce the problem by identifying more cases with an adenocarcinoma immunohistochemistry profile. This subgroup is not a group

that have been validated in relation to mutation status etc., but it would be reasonable to test such cases in patients who were being considered for targeted treatment.

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