AFATINIB AS FIRSTLINE TREATMENT FOR ADVANCED RETROSPECTIVE ANALYSIS OF CARBOPLATIN DOSING

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kinase domain of EGFR
Somatic mutations in the tyrosine background and importance

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Background and importance Somatic mutations in the tyrosine kinase domain of EGFR, including in-frame deletions in exon 19 (exon-19 del) and the L858R point mutation in exon 21, are common mutations accounting for 80–90% of EGFR mutations in non-small cell lung cancer (NSCLC). NSCLC with these types of mutations is particularly sensitive to afatinib treatment which covalently binds to and irreversibly blocks signalling from all homo- and heterodimers formed by the ErbB family members EGFR (ErbB1), HER2 (ErbB2), ErbB3 and ErbB4.

Aim and objectives We present the case of a male patient, who never smoked, diagnosed with stage IV NSCLC harbouring an exon 19 deletion mutation who achieved a complete response to firstline afatinib treatment.

Material and methods This was an observational retrospective study of the use of afatinib in a 46-year-old man diagnosed with NSCLC. Data were obtained from the electronic medical records.

Results The patient was diagnosed with non-squamous NSCLC stage IV in February 2019. He had a considerable lesion localised in the right lower lobe (RLL), 6.28×5.27 cm in transverse and craniocaudal diameter and metastatic lesions (cerebellum metastasis (2.4×2.1 cm), bilateral lung metastases). The patient had no comorbidities. He started treatment with afatinib 40 mg/day in February 2019. After 10 months, the RLL lesion diminished considerably, from 6.28×5.27 cm to 4.4×3.2 cm, and cerebellum metastasis from 2.4×2.1 cm to 1.6×1.8 cm, achieving a durable partial response. In February 2020, bilateral lung metastases had disappeared and he underwent a right lower lobectomy and lymphadenectomy and in March brain radiosurgery, reaching a complete response which was maintained. This patient continued treatment for 19 months. Side effects were grade 1 diarrhoea which allowed him to continue his treatment without delays.

Conclusion and relevance Afatinib represents an important first-line option for patients with advanced NSCLC harbouring an EGFR sensitising mutation, having been shown to prolong progression free survival compared with chemotherapy and the first generation EGFR TKI. Moreover, subanalyses of the prospective LUX-Lung 3, 6, and 7 and FLAURA trials indicated that afatinib and osimertinib were active in patients with CNS lesions. These agents should be considered as firstline treatments of choice in patients with EGFR mutation positive NSCLC and brain metastases.

REFERENCES AND/OR ACKNOWLEDGEMENTS

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RETROSPECTIVE ANALYSIS OF CARBOPLATIN DOSING PRESCRIBED IN A CHEMOTHERAPY REGIMEN AND ITS RELATIONSHIP WITH TOXICITY

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Background and importance Carboplatin is one of the anti-neoplastic agents in which the dose must be adjusted according to the glomerular filtration rate (GFR) and the area under the curve (AUC). The Cockroft–Gault equation is the most widely used for the calculation of GFR and the Calvert formula is the most commonly used for carboplatin dosing. The Cockroft–Gault equation has two variables (weight and serum creatinine) that depend on the body composition of the patient, and therefore overweight and cachectic people are at risk of undergoing inappropriate carboplatin dosing.

Aim and objectives To analyse carboplatin dosage in cancer patients to determine whether they are over or underdosed in comparison with the theoretical dose during the first cycle, and to determine the relationship between the dosage received in this cycle and dose reduction in subsequent cycles, as a result of side effects.

Material and methods This was a retrospective analysis of prescriptions of chemotherapy with carboplatin conducted in 2019. The variables collected were: anthropometric data (age and sex), number of cycles, chemotherapy scheme, diagnosis, analytical data and dose of carboplatin prescribed based on the AUC of the scheme. They were used as tools to support pharmaceutical validation: creatinine clearance (CrCl) according to the Cockroft–Gault equation and Calvert formula. The mean per cent error (MPE) was used to determine the relationship between the dose received and the theoretical dose calculation during the first cycle. The Shapiro–Wilks test was used to see if the cohort was parametric and the Mann–Whitney U test to assess the possible relationship between the patient’s dosage during the first cycle and dose reduction in subsequent cycles.

Results 50 patients were selected, 84% were men and mean age was 66.72±6.66 years. After assessment, 25 patients (50%) received higher doses than the theoretical dose calculation. The mean MPE value (with standard error) for this group was 15.88 ±2.7%. In total, six patients in this group underwent dose reduction due to toxicity related to overdose. No link was found with dose reduction in subsequent cycles.