

Treatment with cetuximab, switch to bi-weekly administration

The Dutch NVMO Committee for Sustainability and Efficiency has formulated recommendations to increase the efficiency of cetuximab administration. Cetuximab can be administered every two weeks at a dose of 500 mg/m², regardless of the indication. This reduces the number of patient visits to day care by half. This makes the treatment more patient-friendly and more cost-effective while reducing use of resources and thus environmental impact.

Introduction

Cetuximab is an antibody that targets the extracellular domain of the epidermal growth factor receptor (EGFR), blocking the activation of the receptor. EGFR inhibitors have demonstrated activity in the treatment of patients with advanced left-sided colorectal carcinoma with a KRAS wild-type, in combination with a MEK inhibitor for advanced colorectal carcinoma with a BRAF-V600E mutation, and in the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck. (1,2,3) The current (European) registration text for cetuximab mentions a weekly dosage of 250 mg/m². However, in 2021, the FDA updated the label, stating that a biweekly dose of 500 mg/m² is equivalent to a weekly dose of 250 mg/m². (2,4)

Rationale

In a study by Kasper et al., published in 2021, it was demonstrated in 1,317 patients with RAS wild-type colorectal carcinoma undergoing first-line cetuximab treatment that biweekly dosing is not inferior to weekly dosing. (5) A study by Taberero et al. indicates that there is sufficient pharmacokinetic and pharmacodynamic evidence to support biweekly dosing. This study shows that the steady-state of a biweekly dose of 500 mg/m² provides the same exposure (AUC) as two weekly doses of 250 mg/m². The minimum plasma concentrations in the biweekly dose of 500 mg/m² were sufficiently high. Moreover, there was no difference in pharmacodynamics between weekly and biweekly dosing in terms of the degree of inhibition of EGFR signal transduction. (6) A recent meta-analysis of 1,164 patients treated across 7 studies shows no significant differences in the efficacy and safety of biweekly versus weekly cetuximab dosing in patients with KRAS wild-type metastatic colorectal carcinoma. (7)

Conclusion

Based on pharmacodynamics, pharmacokinetics, and outcome studies, a cetuximab dosage of 500 mg/m² every two weeks is equivalent to 250 mg/m² weekly. The FDA has already adjusted the label. This dosing schedule provides efficiency gains while maintaining outcomes. In the interest of efficiency, sustainability and patient-friendliness, it is recommended to administer maintenance doses of cetuximab once every 2 weeks (500 mg/m²) instead of 250 mg/m² weekly.

About the Authors:

The committee “sustainability and efficiency” of the Dutch Society of Medical Oncology (NVMO) was initiated in 2022. Their remit is to demonstrate that it is possible to increase both the sustainability as well as the efficiency of medical oncology care. The committee consists of medical oncologists and hospital pharmacists. They regularly publish specific guidelines and suggestions for daily practice based on both published literature and daily experience. All published guidelines are freely accessible at “<https://www.nvmo.org/duurzaam-en-doelmatigheid/>”

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Translated from the original [Dutch version](#).