CORRESPONDENCE

Clinical Practice Guideline: Colorectal Carcinoma—The Management of Polyps, (Neo)Adjuvant Therapy, and the Treatment of Metastases

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in volume 51–52/2009

Resistance Tests Were Not Mentioned

Clinical practice guidelines for the treatment of a disease assume that disease course does not vary much. However, this is not the case for advanced colorectal cancer (CCRC). The demand for individualized chemotherapy is based on the fact that malignant tumors can escape the growth inhibiting effect of medications by means of numerous complex and individually varying mechanisms and thus become resistant to treatment.

In the clinical practice guidelines for colorectal cancer, which include recommendations for the drug treatment of cancers that have reached advanced stages, no mention is made of possibilities of diagnosing tumor resistance. It is not understandable that resistance tests are not mentioned in the guidelines. The development of resistance tests started in the 1960s, and after initial setbacks, such tests have greatly improved in terms of accuracy. The accuracy of the tests for diagnosing resistance with cell cultures taken from fresh tumor tissue can meanwhile exceed 90% (1, 2). Monitoring cancer drug resistance by means of positron emission tomography (PET scanning) constitutes another great step forward, since it enables doctors to identify not only very small tumor foci but also metabolic changes, and thus resistance (3).

The currently promoted individualized cancer treatments apply to subgroups of patients who are selectively chosen on the basis of biomarker measurement and receive specific treatment. Experience to date has shown, however, that subgroup therapy cannot replace resistance tests.

Guidelines are of great clinical importance, because—as for colorectal cancer—they inform doctors about the latest therapeutic options. However, in the context of drug treatment of CRC, it should not be overlooked that these days measuring tumor resistance provides a means of saving patients from ineffective treatments.

DOI: 10.3238/arztebl.2010.0399a

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Conflict of interest statement

The author declares that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

In Reply:

We thank Lippert for his correspondence, in which he points out the importance of resistance testing for chemotherapeutic drugs by means of cell cultures. He is at a loss as to why these tests were not included in the latest S3 guidelines.

Methodologically, it is important to point out the following: guidelines at developmental stage 3 have to explicitly include scientific findings (evidence) in their recommendations (1). In vitro resistance tests have thus far not been sufficiently evaluated for colorectal cancer in terms of their clinical value. On the one hand, it isn't clear which resistance test has the highest sensitivity and specificity for predicting a non-response to planned chemotherapy. On the other hand, prospective, randomized, studies of possible clinical benefit for patients as a result of additional chemotherapy resistance testing are lacking. To date it has not been prospectively analyzed whether chemoresistance testing can actually help avoid side effects, and whether treatment can thus be individualized. Consequently, there is insufficient evidence on which to base a recommendation for resistance testing.

By contrast, tissue biomarkers—such as the onco-gene k-ras—as negative predictive markers for anti-EGFR therapies have been confirmed in the context of several prospective randomized studies in patients with metastatic colorectal cancer (2). Analysis of the k-ras mutation is already included the approval documentation (FDA, EMEA) for the anti-EGFR antibodies panitumumab and cetuximab. This test can be used to identify patients who would not benefit from this treatment and is thus an idea resistance test for anti-EGFR therapy. On the basis of the existing evidence the test has been included in the updated clinical practice guideline for colorectal cancer.

DOI: 10.3238/arztebl.2010.0399b

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Conflict of interest statement

Professor Schmiegel has received honoraria for speaking from Merck, Roche, Abbott, Amgen, Pfizer, Falk, and Astra-Zeneca. He has also received travel expenses from Roche, Merck, and Astra-Zeneca, and he has received fees for advisory work from Roche, Amgen, and Astra-Zeneca. He has received funding for study projects from Roche and Sanofi-Aventis. Dr. Pox has received speaker honoraria from Falk, Astra-Zeneca, and Hitachi, as well as travel expenses from Roche. Dr. Arnold has received speaker honoraria from Roche, Sanofi-Aventis, Pfizer, Merck, and Amgen, travel expenses from Roche, Sanofi-Aventis, Pfizer, and Merck, as well as study support from Roche, Sanofi-Aventis, Pfizer und Merck. Professor Porschen has received honoraria for speaking from Sanofi-Aventis, Pfizer, und Roche as well as study support from Roche and Sanofi-Aventis. Professor Rödel has received honoraria from speaking from Roche and Sanofi-Aventis and funding for study projects from Merck. Dr. Reinacher-Schick has received honoraria for speaking from Amgen, Roche, Sanofi-Aventis, and Pfizer, as well as project funding from Roche and Sanofi-Aventis.