CORRESPONDENCE

Cardiotoxicity and Oncological Treatments

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Confusion of Therapeutic Approaches

Schlitt et al. in their review article focused on cardiotoxic oncological treatments (1). Adequate management of adverse effects of cardiotoxic treatments ensures optimal results of oncological treatment. In the article by Schlitt et al., an algorithm was proposed for monitoring, prevention, and treatment in the context of cardiotoxicity, including the VEGFR inhibitors sunitinib and sorafenib.

Schmidinger et al. postulated direct cardiotoxicity for sunitinib and sorafenib on the basis of a retrospective analysis (2). However, prospective clinical studies did not confirm this suspicion (Haas et al, ASCO Annual Meeting Proceedings, *J Clin Oncol* 2012; 30[suppl 18; abstr 4500]; Michel MS et al., ASCO Genitourinary Cancers Symposium, *J Clin Oncol* 2014; 32[suppl 4; abstr 393]). Rather, the discussion concerns cardiac events as a consequence of uncontrolled, treatment-associated, arterial hypertension, a class-specific adverse drug effect of the VEGFR inhibitors (3). Accordingly, monitoring and regulation of blood pressure in patients taking VEGFR inhibitors are essential in order to prevent secondary cardiac events (4). For cytotoxic drugs, such as doxorubicin, the monitoring measures for identifying cumulative myocardial injury described by Schlitt et al may be adequate, but this approach is not sufficient for VEGFR inhibitors.

In sum, my main criticism of the proposed algorithm is the confusion of curative and palliative treatments, as well as the lack of discrimination between acute, sporadically occurring, and cumulative cardiotoxicity, which as a rule have different underlying pathomechanisms. A blanket recommendation to monitor cardiac function often does not do justice to the individual therapeutic scenario and requires an understanding of the class of substance administered. At least for the use of VEGFR inhibitors there is hardly any rationale for the proposed algorithm; instead, the priority should be to proactively regulate and monitor blood pressure during treatment.

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In Reply:

In their contribution, Ivanyi et al. discuss the potential cardiotoxic side effects of the tyrosine kinase inhibitors sunitinib and sorafenib. They describe the side effect of this treatment—namely, restricted left-ventricular ejection fraction (1)—which was reported in what is thus far the only published one full-text study, as a sequela of uncontrolled arterial hypertension, rather than of the treatment itself. The authors cite two studies that have been publish in abstract form.

We thank our correspondents for their comments; in this context we regard the proactive regulation of blood pressure as specious. We refer readers to the study cited in our article (1), product information from Germany regarding both substances, which describes heart failure as a "common" side effect for sorafenib (product information, sorafenib) and "occasional" for sunitinib (product information, sunitinib). Furthermore, we wish to point out that patients who receive treatment with tyrosine kinase inhibitors are described as "stage a heart failure" patients by many authors (2, 3).

In sum, this is consistent with the proposed algorithm of repeated controls (medical history, physical examination, which obviously includes blood pressure measurement, ECG, and echocardiography), which is set out in Figure 3 (4).

Ivanyi et al. subsequently criticize the "confusion of curative and palliative treatments" and the "lack of discrimination between acute, sporadically occurring, and cumulative cardiotoxicities" in our article.

We think that regular monitoring of cardiotoxic side effects is necessary, independent of the therapeutic intention (curative or palliative) or the time of onset, since therapy-related heart failure changes the therapeutic approach, independent of curative or palliative intent. Last, but not least, heart failure adversely affects a patient's quality of life. DOI: 10.3238/arztebl.2014.0405b

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