Sacubitril-valsartan: Hope or hype in the battle against cardiotoxicity due to cancer treatment? Authors' reply

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We read with interest the letter to the editor entitled "Sacubitril-valsartan: Hope or hype in the battle against cardiotoxicity due to cancer treatment?" by Yalta et al. [1]. It emphasizes the importance of the problem we are discussing and contains several important remarks and comments, which we will try to address below.

The authors rightly emphasize the role of biomarkers, such as cardiac troponins and N-terminal pro-B-type natriuretic peptide (NT-proBNP), in diagnosing cardiotoxicity of oncological treatment (especially early cardiotoxicity). In our patient, both biomarkers remained normal throughout the therapeutic process, which could have a calming effect but is not a reason for not using cardioprotection in the case of worsening left ventricular (LV) systolic function [2]. The presence of elevated levels of troponin suggests that myocardial cell death has already occurred, raising questions about its role as an effective early marker of cardiotoxicity. Therefore, also the new European Society of Cardiology recommendations on the definition of cardiotoxicity mainly focus on echocardiographic parameters [3].

Our patient was initially treated with ramipril 5 mg twice daily, bisoprolol 2.5 mg twice daily, and atorvastatin 20 mg daily. Such treatment was used for 3 months before the implementation of mineralocorticoid receptor antagonist (MRA) and angiotensin receptor-neprilysin inhibitor (ARNI).

The question of whether the earlier use of sacubitril-valsartan could have prevented the deterioration of left ventricular ejection fraction (LVEF) remains unanswered for the time being, as it would require a study on this subject. However, it remains a possibility because the drug has a hemodynamic effect — it relieves LV by reducing the afterload, as well as the effect on myocellular level, as evidenced in our patient by the significant reduction in LV end-systolic and end-diastolic dimensions, along with its volumes. Fortunately, the patient tolerated ARNI well, which was accompanied by reduced blood pressure values (about 100/60 mm Hg), but it did not cause any discomfort.

The patient was treated for breast cancer with doxorubicin and cyclophosphamide, then paclitaxel, and finally trastuzumab. Yalta et al. [1] indicate that the decrease in LVEF could be caused mainly by trastuzumab, which is well known to induce a completely reversible form of cardiomyopathy, therefore, the improvement observed in our patient was spontaneous after temporarily withholding trastuzumab, and not after administration of sacubitril-valsartan.

We agree with this and, based on one clinical case, we would not dare to state that it was certainly only an ARNI effect. Even in our conclusions, we emphasize that ARNI may be a valuable component of cardioprotective regimens.

This has been indirectly confirmed by the observations of Canale et al. [4], who used ARNI in a group of patients in whom, due to the cardiotoxicity of various chemotherapy regimens, it was necessary to use the wearable cardioverter defibrillator (WCD) [4]. It resulted in protecting patients against life-threatening ventricular tachyarrhythmias in the period of low LVEF, as well as in significant improvement in LVEF seen in the long term. As a result, the patients did not require implantation of an implantable cardioverter-defibrillator (ICD).

Perhaps we will see the results of randomized trials on this subject conducted in numerically appropriate groups of patients. Until

then, we believe that our clinical vignette provides valuable data on the complex problem of cardiotoxicity.

Answering the title question of Yalta et al. [1], on the basis of the research conducted so far, by paraphrasing the words of Camilli et al. [5] we can say that "In ®Entresto we trust".

We hope that further research will confirm our expectations, which will contribute to better prognosis in cancer patients.

Article information

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