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

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In cardio-oncological practice, the term "cardiotoxicity" is defined as a new-onset myocardial injury/dysfunction mostly in response to a variety of chemotherapeutic regimens including anthracyclins and trastuzumab, etc. [1–3]. In their recently published article, Sławiński et al. [1] have reported the favorable impact of sacubitril-valsartan (an angiotensin receptor-neprilysin inhibitor) on the recovery of left ventricular (LV) systolic dysfunction associated with cancer treatment in a patient with breast cancer. Accordingly, we would like to have further information regarding that interesting case and make a few comments on cardiotoxicity and its management with sacubitril-valsartan in cancer survivors.

In particular, "early (incipient) cardiotoxicity" due to cancer treatment denotes an emerging subclinical myocardial dysfunction characterized by a persistent elevation in a variety of conventional markers, including cardiac troponins, natriuretic peptides along with subtle abnormalities in echocardiographic parameters (presenting with a fall in global longitudinal strain [GLS] and occasionally a slight reduction in the left ventricular ejection fraction [LVEF] value) [2–4]. However, when these initial changes go unnoticed following a cardiotoxic regimen, "early cardiotoxicity" generally progresses to "overt cardiotoxicity" that usually emerges as a form of late cardiomyopathy (universally characterized by a 10% reduction in the LVEF value from baseline to an ultimate value of <53% [or 50]) [2–4]. Apparently, the patient [1] initially seemed to have a pattern of "early cardiotoxicity" (presenting with slight reductions in LVEF and GLS values) that ultimately ended up with overt cardiotoxicity in the later stages. However, the diagnosis of "cardiotoxicity" traditionally needs also to be substantiated with persistent increases (mostly weeks apart) in troponins and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels [2, 3]. Accordingly, we are interested in the levels and elevation patterns of these biomarkers (and other markers, if any) in the patient, particularly during the "early cardiotoxicity" stage.

Importantly, timely initiation of cardioprotective agents (statins, β-blockers, etc.) might have the potential to block or slow down the progression of "early cardiotoxicity" [2–4]. However, despite the initiation of these agents (all were previously documented to have significant favorable effects in this context [4]), the patient was reported to ultimately progress to late cardiomyopathy [1]. Accordingly, we are interested in the dosages and duration of the use of these cardioprotective agents.

More interestingly, sacubitril-valsartan seemed to induce a substantial LV reverse remodeling leading to a significant increase in the LVEF value of the patient with overt cardiomyopathy [1]. This might imply that this agent might be even more efficacious when initiated during the stage of "early cardiotoxicity" and might potentially prevent transition to late cardiomyopathy. Therefore, LVEF [1] might have been already stabilized and preserved if the patient had received sacubitril-valsartan much earlier. Specifically, we also wonder whether the LV reverse remodeling, besides presenting with an increase in LVEF, also constituted a significant reduction in LV volumes and diameters, which potentially suggests that the improvement in LV systolic functions might be more likely due to the permanent effects of sacubitril-valsartan on LV morphology at the myocellular level rather than its favorable impact on preload and af-

terload. Notably, side effects of this agent (including severe hypotension) might be more prevalent in fragile cancer survivors with a reduced physiological reserve and need close monitoring. Did the patient report any side effects regarding sacubitril-valsartan?

Finally, cardiotoxicity in the patient might have been primarily due to trastuzumab therapy [1] which is well known to trigger a completely reversible form of cardiomyopathy in this context [2, 3]. Therefore, there also exists a potential possibility that LV reverse remodeling in the patient might have been a spontaneous and coincidental phenomenon rather than a consequence of sacubitril-valsartan therapy.

In conclusion, the authors [1] should be commended for their didactic case. However, further studies are needed to establish the value of sacubitril-valsartan in the prevention and management of cardiotoxicity due to cancer treatment.

Article information

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