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

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In cardio-oncology 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 their 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 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 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 to be substantiated with persistent increases (mostly weeks apart) in troponins and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels as well [2, 3]. Accordingly, we wonder about 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, beta 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 (that 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 wonder about the dosages and duration of therapy regarding 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 an 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, the LVEF of the patient [1] might have been already stabilized and preserved, if she had received sacubitril-valsartan much earlier. Specifically, we also wonder whether the LV reverse remodelling, besides presenting with an increase in LVEF, also constituted a significant reduction in LV volumes and diameters of the patient (which potentially suggests that the improvement in LV systolic functions might more likely be due to the permanent effects of sacubitril-valsartan on LV morphology at the myocellular level rather than its favorable impact on preload and afterload). 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 having emerged as a consequence of sacubitril-valsartan therapy.

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

REFERENCES


