UCLA Health

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Abstract Form

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Project Title:	Osimertinib-Associated Cardiac Events and Echocardiographic Changes in Patients with Non-Small Cell Lung Cancer

Research Category (please check one):

☒	**Original Research**	☐	**Clinical Vignette**	☐	**Quality Improvement**	☐	**Medical Education Innovation**

Abstract

Background:
Osimertinib is an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) used as a first line systemic therapy in patients with non-small cell lung cancer (NSCLC). Although Osimertinib has shown improved survival outcomes compared to previous generation TKIs, an increased risk of cardiotoxicity has been observed, including QTc prolongation, heart failure (HF), and a decline in left ventricular ejection fraction (LVEF). Apart from LVEF, a comprehensive analysis of dynamic Osimertinib-associated echocardiographic changes has been lacking. Further, it remains unclear if a decrease in LVEF is the main driver associated with Osimertinib induced HF, if any diastolic dysfunction or valvular disease is contributing, or whether other underlying contributing changes can be elucidated by echocardiogram analysis. These unanswered questions are critical, given the elevated baseline cardiovascular risk of patients with lung cancer and high concomitant use of cardiotoxic treatments. Thus, there is an urgent need for analysis of dynamic echocardiographic changes in patients treated with Osimertinib.

Goals/Aims:
The primary objective of this study is to assess cardiovascular adverse events following treatment with Osimertinib in patients with NSCLC. Secondary goals include analysis of baseline and post-Osimertinib echocardiographic variables to determine if there are any significance changes.

Methods:
A retrospective, single-center study was conducted on patients with NSCLC who received osimertinib between 2007 to 2022 at Cedar-Sinai Medical Center. Patients were excluded if they did not have any echocardiogram after osimertinib administration. Cardiovascular adverse events were defined according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Comparisons for statistical significance were made using paired sample t-test.

Results:
A total of 85 patients, 57 females and 28 males, were evaluated in the study cohort. The mean age was 69 years. Significant CTCAEs (grade 2 or higher) occurred in 17 (20%) patients after osimertinib administration. These CTCAEs included decline in LVEF (n = 5), QTc prolongation (n = 10), arrhythmias (n = 3), valvular disease (n = 5), and pericardial effusion (n = 1). When comparing baseline and post-Osimertinib echocardiographic variables, there was a decline in LVEF (61 ± 8% to 58 ± 11%; $p < 0.001$), an increase in the number of patients with diastolic dysfunction (12 vs. 34; $p < 0.001$), an increase in number with mitral regurgitation (9 vs. 42; $p < 0.001$), and an increase in number of tricuspid regurgitation (9 vs. 38; $p = 0.004$). All other echocardiographic parameters did not show any statistically significant difference before vs. after Osimertinib.

Conclusions:
In our comprehensive retrospective analysis, the incidence of grade 2 or higher CTCAEs was 20% in patients treated with Osimertinib. The classes of CTCAEs were similar to those described in previous studies. In addition to a decline in LVEF that was observed on echocardiograms, patients taking Osimertinib had a higher rate of developing diastolic dysfunction, mitral regurgitation, and tricuspid regurgitation. Continued analysis in this cohort will be performed to determine whether there are any patient or treatment characteristics that increase the risk of Osimertinib-associated cardiotoxicity and/or survival outcomes.