SUPPLEMENTARY MATERIALS

Supplementary Material 1: A: List of collected variables in the literature search and Cardio-

oncology database cases. B: Search strategy for Vigibase®

Supplementary material 1A: List of collected variables in the literature search and Cardio-oncology database cases.

The following parameters were collected: demographic parameters (age, sex); the presence of a previous history of cardiac disease; the presence of cardiovascular risk factors; the ICIs; the number of combination therapy cases; the cancer type; the number of cycles of ICIs before the occurrence of the CAE; the cardiologic clinical features of the initial presentation; the description of the initial ECG; the type of cardiotoxicity; the presence of an associated immune-related adverse event (irAE); the presence of an increased (BNP), pro-BNP or N-terminal pro-BNP level; the presence of an increased troponin level; the presence of a normal left ventricular ejection fraction (LVEF) at baseline; the presence of a LVSD (LVEF drop > 10% and LVEF < 50%); other echocardiogram findings including elevated systolic pulmonary artery pressures; the global longitudinal strain; the coronary angiogram; non-invasive myocardial perfusion test results; MRI findings (late gadolinium enhancement and myocardial edema); treatments involved in the management of the CAE; and outcomes, including the reversibility of LVSD and mortality (heart related and all-cause). In the analysis, we aggregated atrial fibrillation and atrial flutter as supraventricular arrhythmias.

Supplementary material 1B: Search strategy for Vigibase®

VigiBase® uses the Medical Dictionary for Regulatory Activities (MedDRA) terminology to record and report adverse drug reactions. It is hierarchically divided on the basis of System Organ Class to classify diseases. Standardized MedDRA queries (SMQs) have been developed to improve the identification of some diseases of particular interest, and they rely on the transversal non-hierarchical aggregation of disease codes that are named preferred terms. CAEs were classified into 12 categories that could partially overlap: cardiac conductive disorder, cardiac death or shock, cardiac supraventricular arrhythmias, cardiac valve disorders, cardiac ventricular arrhythmias, endocardial disorders, heart failure, hypertension

and related end-organ damages, myocardial infarction, myocarditis, pericardial diseases and torsades de pointes / QT prolongation. The following parameters were extracted from Individual case safety reports: completeness score (which indicates the amount of data available per case, ranging theoretically from 0 (no data) to 1 (complete report)), the adverse event seriousness (dichotomous, serious or not), demographic characteristics (age, sex), the cancer type, the ICI(s) used, whether a combination therapy was used, the onset delay as defined previously, the number of cycles of ICI prior to the CAE, the type of cardiotoxicity, the presence of an associated irAE (dichotomous, presence or absence) and the mortality rate. The seriousness of an adverse event included death, life-threatening situations, hospitalization or prolongation of a current hospital stay, persistent incapacity or disability or any situation judged to be clinically relevant by the physician reporting the case.

Vigibase® search was designed as follows:

- Medications: Atezolizumab OR avelumab OR durvalumab OR ipilimumab OR nivolumab OR pembrolizumab OR tremelimumab

- Reactions (MedDRA version 21.1) : Hypertension (SMQ narrow) OR Myocardial infarction (SMQ narrow), Cardiac valve disorders (HLGT) OR Endocardial disorders (HLGT) OR Supraventricular tachyarrhythmias (SMQ narrow) OR Ventricular tachyarrhythmias (SMQ narrow) OR Torsades de pointes/ QT prolongation (SMQ narrow) OR Cardiac conduction disorders (HLT) OR Cardiac Failure (SMQ narrow), OR Shock associated circulatory or cardiac conditions (excl torsade de pointes)(SMQ narrow) OR Non-infectious pericarditis (HLT) OR Pericardial disorders (HLT)