BEYOND ANTHRACYCLINES: NEW DRUGS AND CLINICAL PHENOTYPES OF CARDIOTOXICITY

G. Minotti, Dept. of Medicine University Campus Bio-Medico, Roma

It was not until a few decades ago when cardio-oncology was established to devise new modalities of assistance for patients treated by cancer drugs, primarily anthracyclines. Prevention or treatment of heart failure (HF) from cumulative anthracycline doses was identified as the main target of cardio-oncology. Things have now changed. Dose reductions nearly abated the risk of acute or subacute HF but not the risk of HF that occurs long after chemotherapy, sometime 20-30 years after the last anthracycline course. Asymptomatic diastolic dysfunction with preserved ejection fraction seems to precede HF but proof-of-concept studies that validate this pathophysiologic trajectory and identify optimal treatment are only cursory at this point in time. Things have changed also for the pharmacologic portfolio of onco-hematologists, which now includes monoclonal antibodies against a wide array of receptors or small tyrosine kinase inhibitors. Clinical phenotypes of cardiotoxicity have changed in accordance. HF risk remains for the majority of new drugs but the actual dimension of the problem is uncertain. Arterial thrombosis, venous thromboembolism, QT prolongation, acute myocarditis or rhabdomyolysis are only few examples of clinical events associated with new generation drugs.

Anthracyclines and other old fashioned chemotherapeutics are increasingly replaced by, or combined with the new drugs, which causes mixed clinical phenotypes to occur. Oncologists, hematologists and cardiologists are therefore faced with growing cohorts of long term cancer survivors who were treated by the old drugs and with equally sizeable cohorts of patients who only recently were exposed to new oncologic regimens. This clearly calls for novel modalities of surveillance and management that need to be tailored to patient characteristics and pharmacokinetic/pharmacodynamic correlates of drugs or combinations of drugs.1 Also drug development needs to be reconsidered as the available evidence suggests that for many new drugs, primarily tyrosine kinase inhibitors, risk of cardiovascular events is determined by pitfalls of fast track approval like e.g., registration of unnecessarily high dosages. Cardio-oncology is for cardiologists, oncologists, hematologists, and for pharmacologists too.2

1. Zamorano JL et al. 2016 ESC Position Paper on cancer treatments and cardiovascular toxicity developed under the auspices of the ESC Committee for Practice Guidelines (Achenbach S and Minotti G, CPG coordinators). Eur Heart J (2016) 37:2768-2801

2. Minotti G, Salvatorelli E and Menna P. Pharmacology of Cardio-Oncology. In: Cancer and the Heart (Ewer MS and Yeh ET eds) (2017) in press.