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To Reviewers

The title "Insights into Cardio-oncology: Quinazoline-based α(1)-adrenoceptor antagonists". was changed to "Insights into Cardio-oncology: Polypharmacology of quinazoline-based α_1-adrenoceptor antagonists." as request from reviewer.

A core type has been added.

The reference numbers were put in square brackets in superscript before the end

The text "These old cardiovascular drugs haven't high cost but there was not conduct noninferiority, randomized, controlled trials [33] comparing cited old cardiovascular drugs with new anticancer therapies. Doubts, controversies and pitfalls have emerged regarding some cardioprotective strategies [1,12,25-27] as well as regarding the prices of new anticancer treatments[33] and their very expensive widespread distressing, unnecessary toxicities, suffering, or "collateral damage" [34]" has been changed to These old cardiovascular drugs haven't high cost however, but there was a lack in noninferiority randomized, controlled trials [33], comparing them with new anticancer therapies.

The text "and new molecules have been synthesized [36]. Gefitinib, erlotinib, and afatinib are orally effective protein-kinase targeted quinazoline derivatives that are used in the treatment of ERBB1-mutant lung cancer. Lapatinib is an orally effective quinazoline derivative used in the treatment of ErbB2-overexpressing breast cancer[26,36]." Has been changed to "and new molecules have been synthesized as gefitinib, erlotinib, afatinib, lapatinib[26,36].".

The text "Furthermore it has been reported that a β- plus α_1-blocker pretreatment (propranolol + prazosin) has leaded to better severity reduction of postresuscitation myocardial tissue injury and myocardial dysfunction with better neurologic function and prolonged duration of survival than propranolol treatmen alone [41]. This latter finding will require certainly further evaluation."has been added

The text "also inhibiting prostate cancer cells growth and downregulating expression of androgen receptor [53]. Doxazosin also prevents p27 downregulation [54]" has been changed to "also leading to prostate cancer cells growth inhibition[54] Doxazosin also downregulates expression of androgen receptor [54] and also prevents p27 downregulation [55]

The text "Several signalling are also inhibited from doxazosin VEGF antagonism including PI3K, Akt, 3-phosphoinositide-dependent protein kinase 1 (PDK1), mammalian target of rapamycin (mTOR), and hypoxia-inducible factor 1 (HIF-1α) [49]" was added

The text in red on "Terazosin, another quinazoline-based antihypertensive α_1-adrenoceptor antagonist [57] is also a HERG ligand [58],a cancer cells growth inhibitor[59],and an apoptosis and anoikis inductor [58,60] ." has been added

The text :accumulation of ubiquitinated-proteins and down-regulation of proteasome activity [46]. has been added

The text :Terazosin seems to have weaker or no effects regarding CMDR [55]. has been added

A Table Tab. 1 : Structure and polypharmacology of quinazoline-based α_1-adrenoceptor antagonists doxazosin, prazosin and terazosin in cardio-oncology
has been added

Three references (41, 59 and 60) have been added

A reference (32) has been changed

With Regards