



IL PARERE DEL CARDIOLOGO

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LA TERAPIA ANTI- IPERTERTENSIVA

Hypertension and carfilzomib

Hypertension is a very common collateral effect of Carfilzomib (14%)

Hypertensive crises are very uncommon (<0.1%) (www.drugs.com)

All patients should be routinely evaluated for hypertension and treated as needed BEFORE beginning of therapy

Medical therapy optimized (statins, etc.)

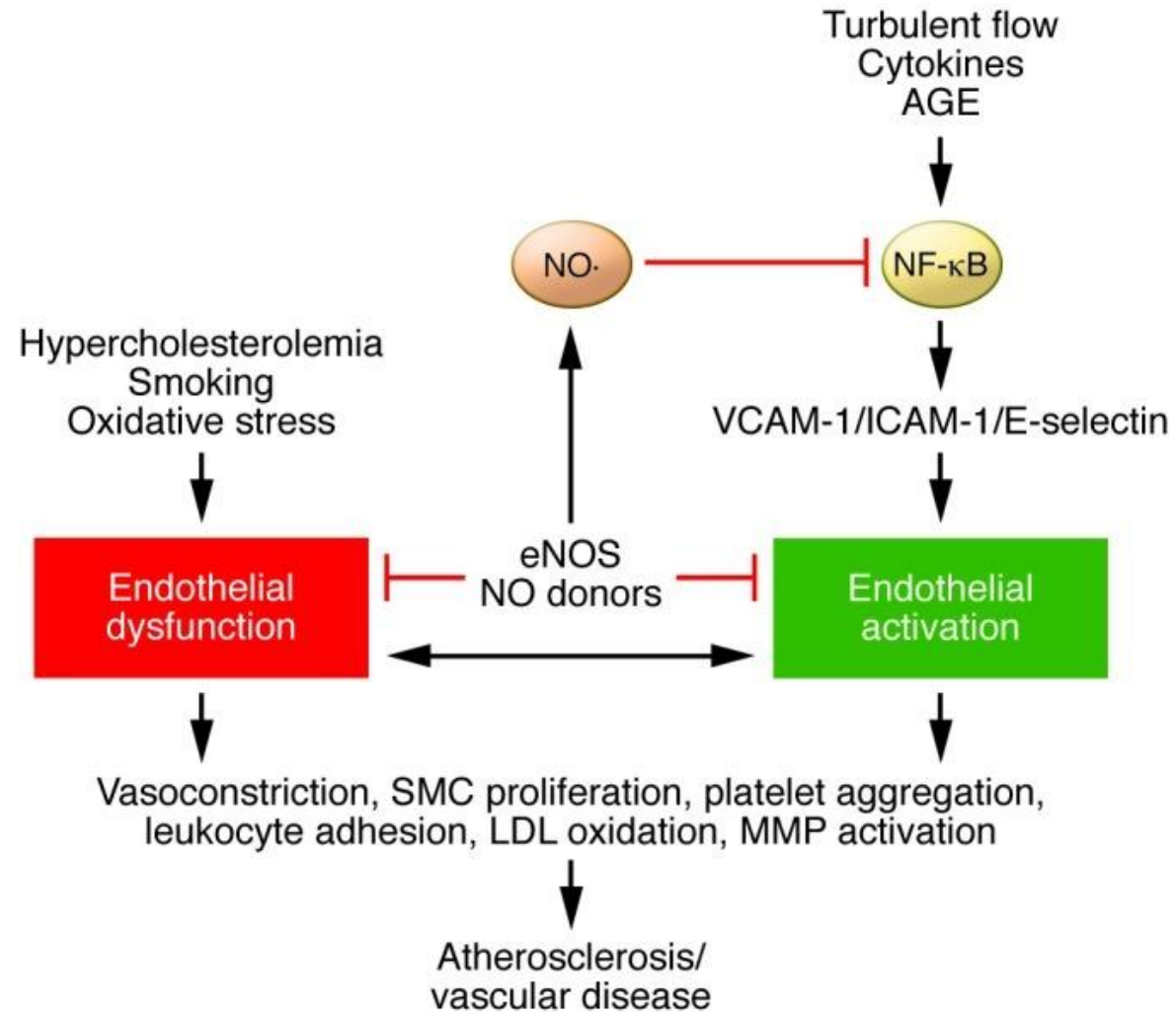
WHAT THERAPY?
FOR WHO?

MECHANISM OF ACTION

Carfilzomib can cause endothelial dysfunction

Cardiac events are more frequent in patients with preexistent heart disease (known coronary artery disease or cardiac amyloidosis). (Rosenthal Blood Cancer J. 2016)

ENDOTHELIAL DAMAGE



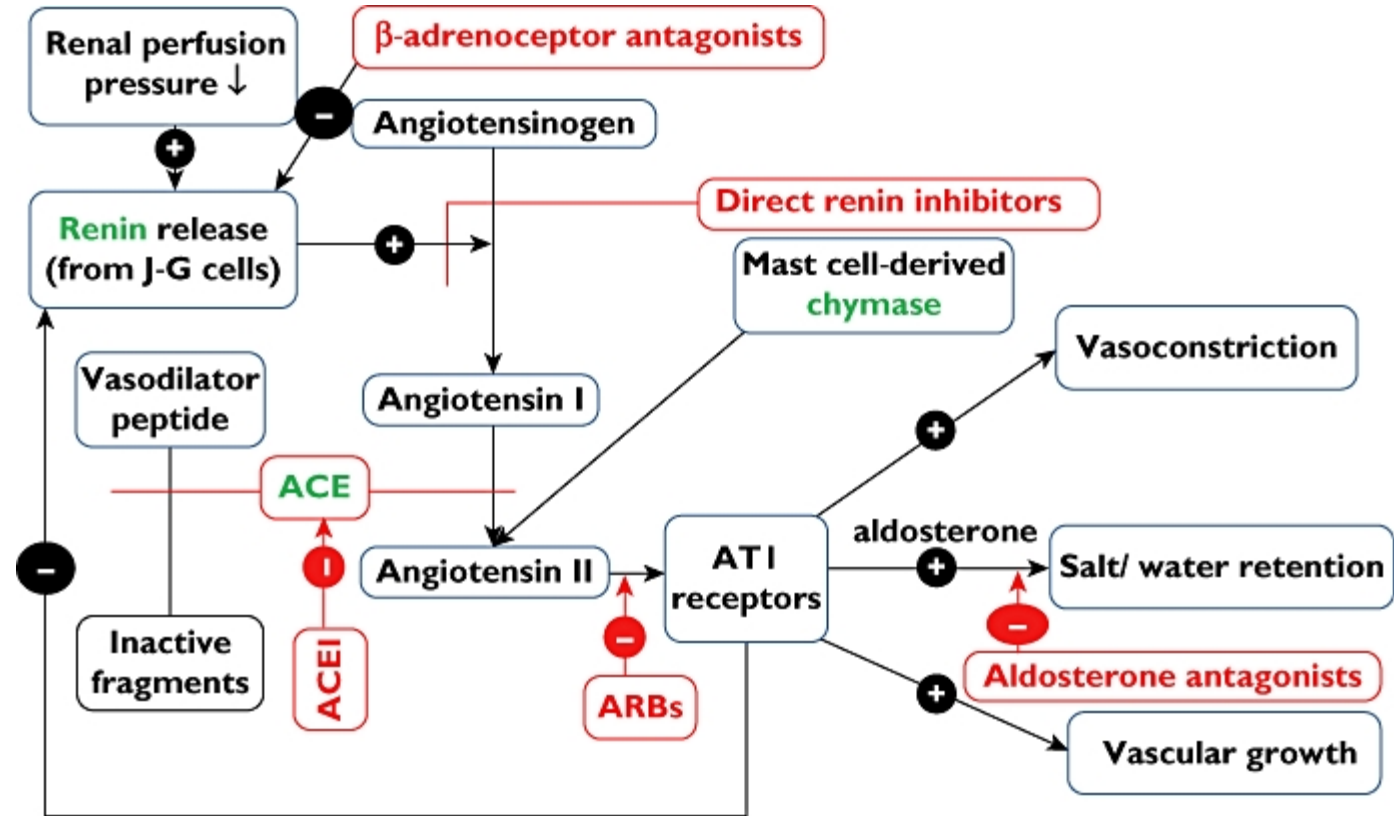
What therapy?

Calcium channel blockers

RAAS inhibitors

Beta-blockers/diuretics

RAAS

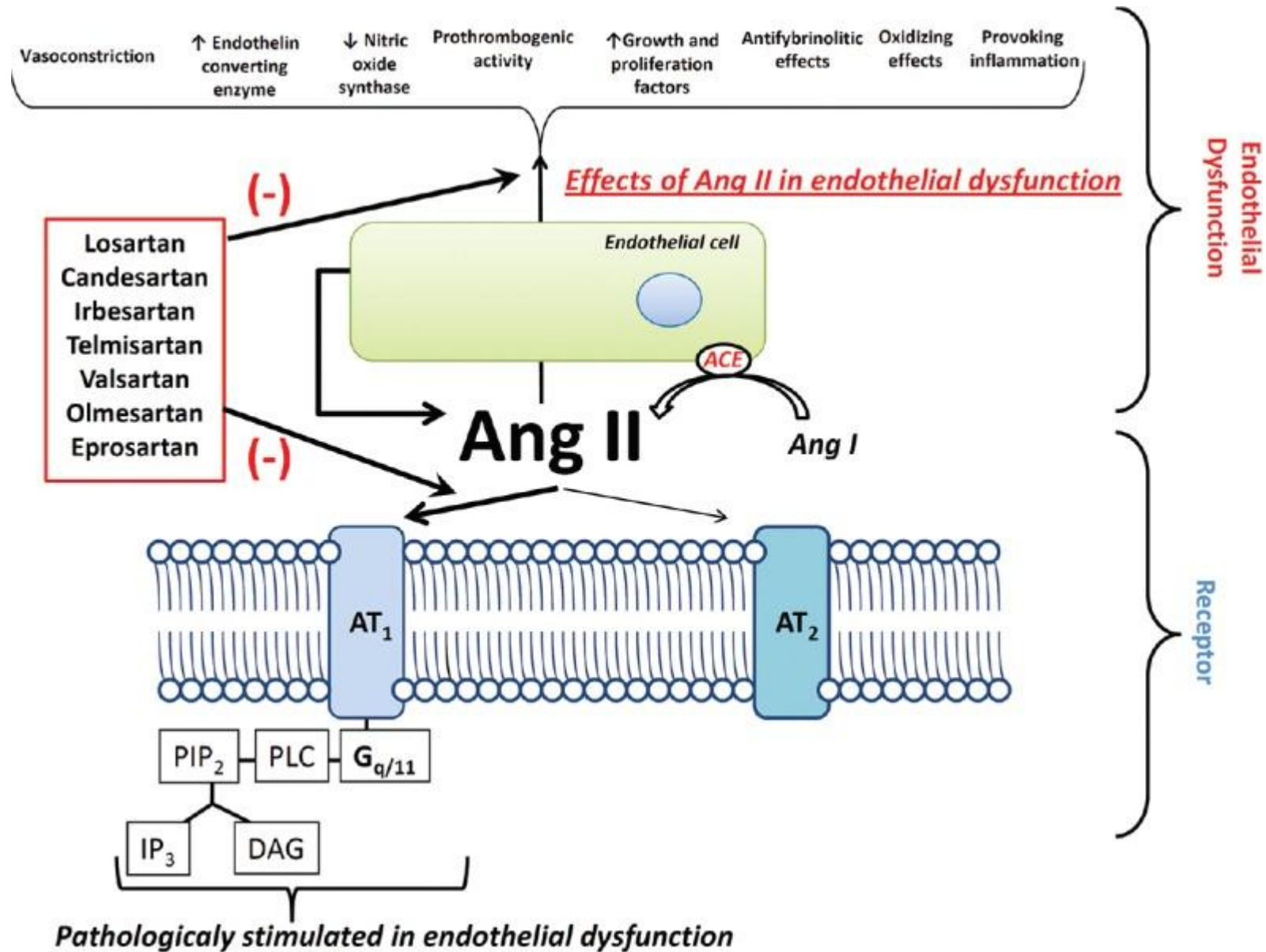


ENDOTHELIAL PROTECTION

- Angiotensin converting enzyme ACE inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) improve endothelial function and prevent vascular remodelling. Calcium channel blockers also improve endothelial function, although to a lesser extent than ACEIs and ARBs. Mineralocorticoid receptor blockers improve endothelial function and reduce arterial stiffness, and have recently become more established as antihypertensive drugs.(Cameron AC et Al., Drugs 2016)

ACE Inhibitors

- Ramipril 5-10 mg
- Collateral effects: cough
- Controind. GFR<30 cc/m
- Periodic check Creat. Na K



ARBs

- Telmisartan 20-80 mg
- Valsartan 80-320 mg
- Candesartan 4-32 mg
- Irbesartan 150-300 mg
- Losartan 12,5-100 mg

ARBs

Candesartan decreases PTX3 and hs-CRP plasma levels more powerful than other classes of antihypertensive drugs (beta blockers, calcium channel blockers, and diuretics), so we may assume that candesartan has a more potent action in reversing endothelial dysfunction and that it offers a higher vascular protection than other classes of antihypertensive drugs.

(Buda v. Ir. J.Med. Sci. 2017)

Calcium channel blockers

- Amlodipine was highly effective for the treatment of HTN and stable angina as evidenced by the fewer hospitalisations for unstable angina and revascularisation in randomised controlled trials.
- Amlodipine has also shown robust reductions on CV end points (especially stroke) but has not altered the prognosis in HF.
- Its abilities to prevent activation of counter-regulatory mechanisms, to slow the progression of atherosclerosis, to confer antioxidant properties and to enhance NO production are all unique actions. (Hassan Fares et Al., Open Heart 2016)
- (5-10 mg) Collateral effects: tachycardia, edema

Beta blockers

- Current evidence suggests that initiating treatment of hypertension with beta-blockers leads to modest CVD reductions and little or no effects on mortality. These beta-blocker effects are inferior to those of other antihypertensive drugs. Further research should be of high quality and should explore whether there are differences between different subtypes of beta-blockers or whether beta-blockers have differential effects on younger and older people (Cochrane Database System. Review, 2017)

Beta blockers

- NO (nitric oxide) is a paracrine factor derived from endothelial cells that has been shown to alleviate ROS-mediated oxidative damage.
- Nebivolol is a third-generation β -blocker with vasodilator activity, both actions contributing to decreased blood pressure in hypertensive patients. Its vasodilatory function is mediated by the endothelial L-arginine NO pathway. Nebivolol increases the bioavailability of NO in the vasculature. Its efficacy and safety profile is comparable to other commonly used antihypertensive agents (Coats A. et Al. J.Hum Hypertens. 2017)
- Clinically nebivolol's ability to modulate endothelial dysfunction may offer additional vascular protection in treating hypertension (Shameki Amiri F. Nephrol. Ther. 2017) Nebivolol 5 mg

Diuretics

The latest hypertension guidelines have underscored the importance of diuretics for all patients, but particularly for those with salt-sensitive and resistant hypertension. For reducing cardiovascular events (CVEs), HCTZ is less effective than enalapril and amlodipine in randomized trials, and, in network analysis of trials, it is less effective than CTDN and HCTZ-amiloride. (Roush GC et Al., Am.J Hypertens.2016)

Useful in fluid retention

Caution in patients with electrolyte disorders, diarrhea or dehydration

Hydrochlorothiazide 12,5-25 mg

CONCLUSIONS

Antihypertensive therapy should be tailored to the known mechanisms of action of the drug.

In this patient, drugs that restore endothelial function must be preferred

There is a growing recognition that angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, calcium antagonists or thiazide diuretics can be used as a first-line therapy for hypertension.

Evidence also supports the use of combination drug therapy as opposed to monotherapy for more synergistic effect on lowering of BP, offsetting side effects and for improved adherence to a drug regimen. (Ahluwalia M et Al., Curr Opin in Cardiol 2017)



GRAZIE PER L'ATTENZIONE

IPERTENSIONE E CARFILZOMIB

Effetto collaterale molto comune (14%)

Effetti comuni (1-10%) scompenso cardiaco (EPA, FE ridotta), fibrillazione atriale, tachicardia, cardiopalmo, flushing

Effetti non comuni(0.1-1%): IMA, arresto cardiaco, pericardite con versamento pericardico

Molto meno frequenti le crisi ipertensive (<0.1%)

www.drugs.com