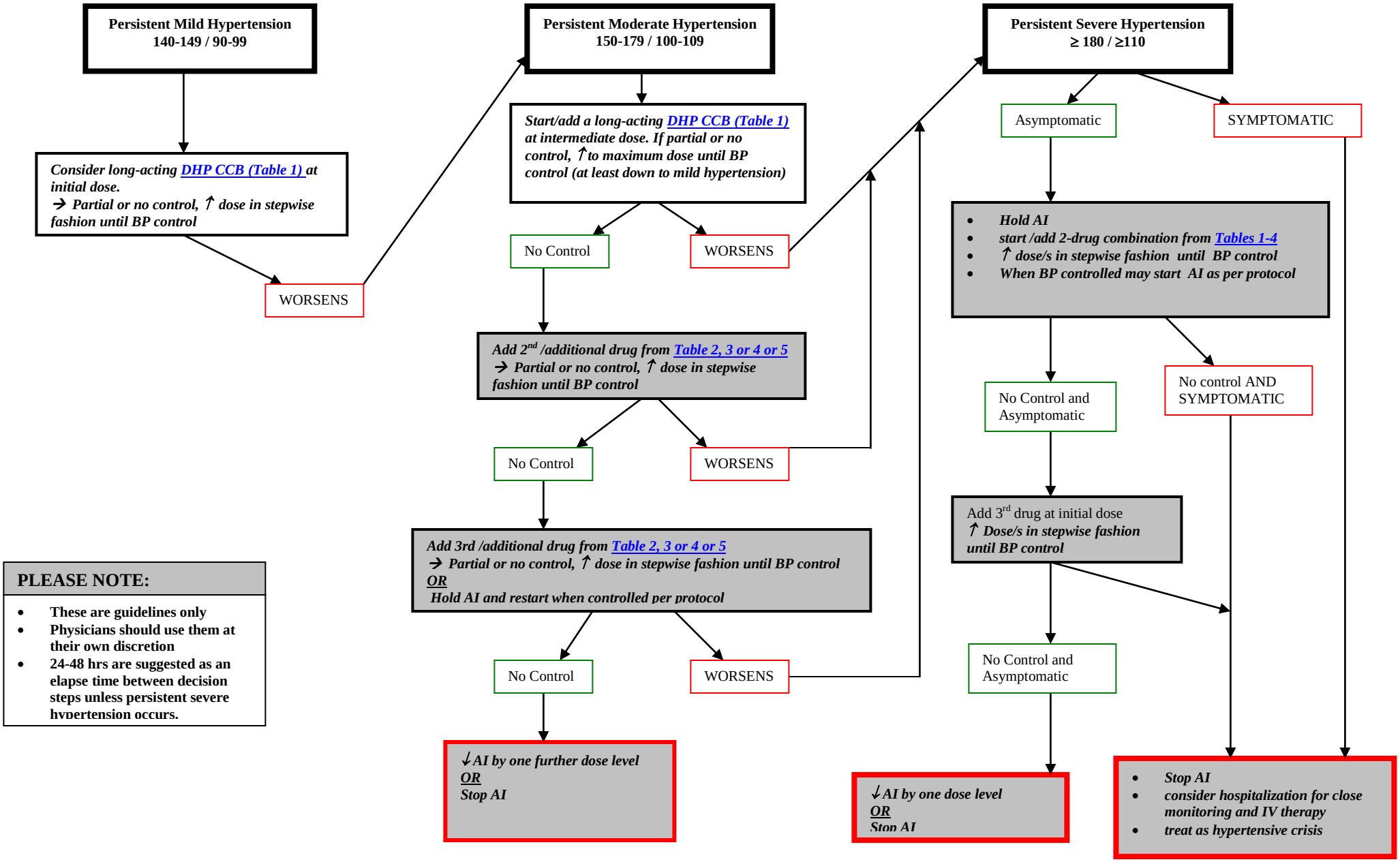
Appendix 8: Management of Angiogenesis Inhibitor (AI)-induced Hypertension



Reference : Gauthier I, Laurie SA, Arnold A, Goss G, Ellis P, Shepherd FA, Chen E, Matthews S, Walsh W, Robertson J, Seymour L. Hypertension (HTN): Experience in IND.171, a phase I dose-seeking trial combining AZD2171 with standard chemotherapy in patients with advanced incurable non-small cell lung cancer (NSCLC). Angiogenesis 2006, La Jolla, January 2006.

Table 1. Dihydropyridine calcium-channel blockers

Agent	Initial dose	Intermediate dose	Maximum dose	Hepatic metabolism?
Nifedipine XL	**30 mg po qd**	**60 mg po qd**	**90 mg po qd**	**CYP 3A4 substrate**
Amlodipine	**2.5 mg po qd**	**5 mg po qd**	**10 mg po qd**	**CYP 3A4 substrate**
Felodipine	2.5 mg po qd		10 mg po qd	CYP 3A4 substrate + inhibitor

▲ Top

Table 2: Selective β blockers

Agent	Initial dose	Intermediate dose	Maximum dose	Hepatic metabolism?
Metoprolol	25 mg po bid	50 mg po bid	100 mg po bid	CYP 2D6 substrate
Atenolol	**25 mg po qd**	**50 mg po qd**	**100 mg po qd**	**No**
Acebutolol	100 mg po bid	200mg-300 mg po bid	400 mg po bid	Yes (CYP 450???)
Bisoprolol	2.5 mg po qd	5-10 mg po bid	20 mg po qd	Yes (CYP 450???)

▲ Top

Table 3. Angiotensin Converting Enzyme Inhibitors (ACEIs)

Agent	Initial dose	Intermediate dose	Maximum dose	Hepatic metabolism?
Captopril	12.5 po tid	25 mg po tid	50 mg po tid	CYP 2D6 substrate
Enalapril	5 mg po qd	10-20 mg po qd	40 mg po qd	CYP 3A4 substrate
Ramipril	2.5 mg po qd	5 mg po qd	10 mg po qd	Yes (CYP 450???)
Lisinopril	**5 mg po qd**	**10-20 mg po qd**	**40 mg po qd**	**No**
Fosinopril	10 mg po qd	20 mg po qd	40 mg po qd	Yes (CYP 450???)
Rarely used:				
Perindopril	**4mg po qd**	**none**	**8mg po qd**	**Yes but not per CYP 450**
Quinapril	**10mg po qd**	**20 mg po qd**	**40 mg po /qd**	**No**

▲ Top

Table 4. Angiotensin II Receptors Blockers (ARBs)

Agent	Initial dose	Intermediate dose	Maximum dose	Hepatic metabolism?
Losartan	25mg po qd	50 mg po qd	100 mg po qd	CYP 3A4 substrate
Candesartan	4mg po qd	8-16 mg po qd	32mg po qd	CYP 2C9 substrate
Irbesartan	75mg po qd	150 mg po qd	300 mg po qd	CYP 2C9 substrate
Telmisartan	**40 mg po qd**	**none**	**80 mg po qd**	**Yes but not per CYP 450**
Valsartan	**80 mg po qd**	**none**	**160mg po qd**	**Yes but not per CYP 450**

▲ Top

Table 5. α and β blocker

Agent	Initial dose	Intermediate dose	Maximum dose	Hepatic metabolism?
Labetolol	100 mg po bid	200 mg po bid	400 mg po bid	CYP 2D6 substrate and inhibitor

▲ Top

NB. Agents in bold characters are suggested as optimal choices to avoid or minimize potential drug-interactions with angiogenesis inhibitors metabolised through CYP-450 (e.g. sunitinib and sorafenib)

Reference : Gauthier I, Laurie SA, Arnold A, Goss G, Ellis P, Shepherd FA, Chen E, Matthews S, Walsh W, Robertson J, Seymour L. Hypertension (HTN): Experience in IND.171, a phase I dose-seeking trial combining AZD2171 with standard chemotherapy in patients with advanced incurable non-small cell lung cancer (NSCLC). Angiogenesis 2006, La Jolla, January 2006.

Date: May, 2007