Webcast Wednesday Metabolic March Madness Part 1: Updates in Hypertension

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Disclosures

- The activity planners and speakers do not have any financial relationships with commercial entities to disclose.
- The speakers will not discuss any off-label use or investigational product during the program.

Objectives

- Discuss updates in the management of hypertension in persons with HIV
- Apply evidence-based recommendations to non-pharmacologic and pharmacologic treatment
- Identify counseling pearls for pharmacologic and non-pharmacologic therapies

Abbreviations

- Hypertension (HTN)
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Chronic Kidney Disease (CKD)
- Cardiovascular Disease (CVD)
- Black box warning (BBW)
- Contraindication (CI)
- Beta Blocker (βB)
- Angiotensin Converting Enzyme Inhibitor (ACEi)
- Angiotensin Receptor Blocker (ARB)
- Calcium Channel Blocker (CCB)
- Aldosterone Antagonist/African American (AA)

Statistics

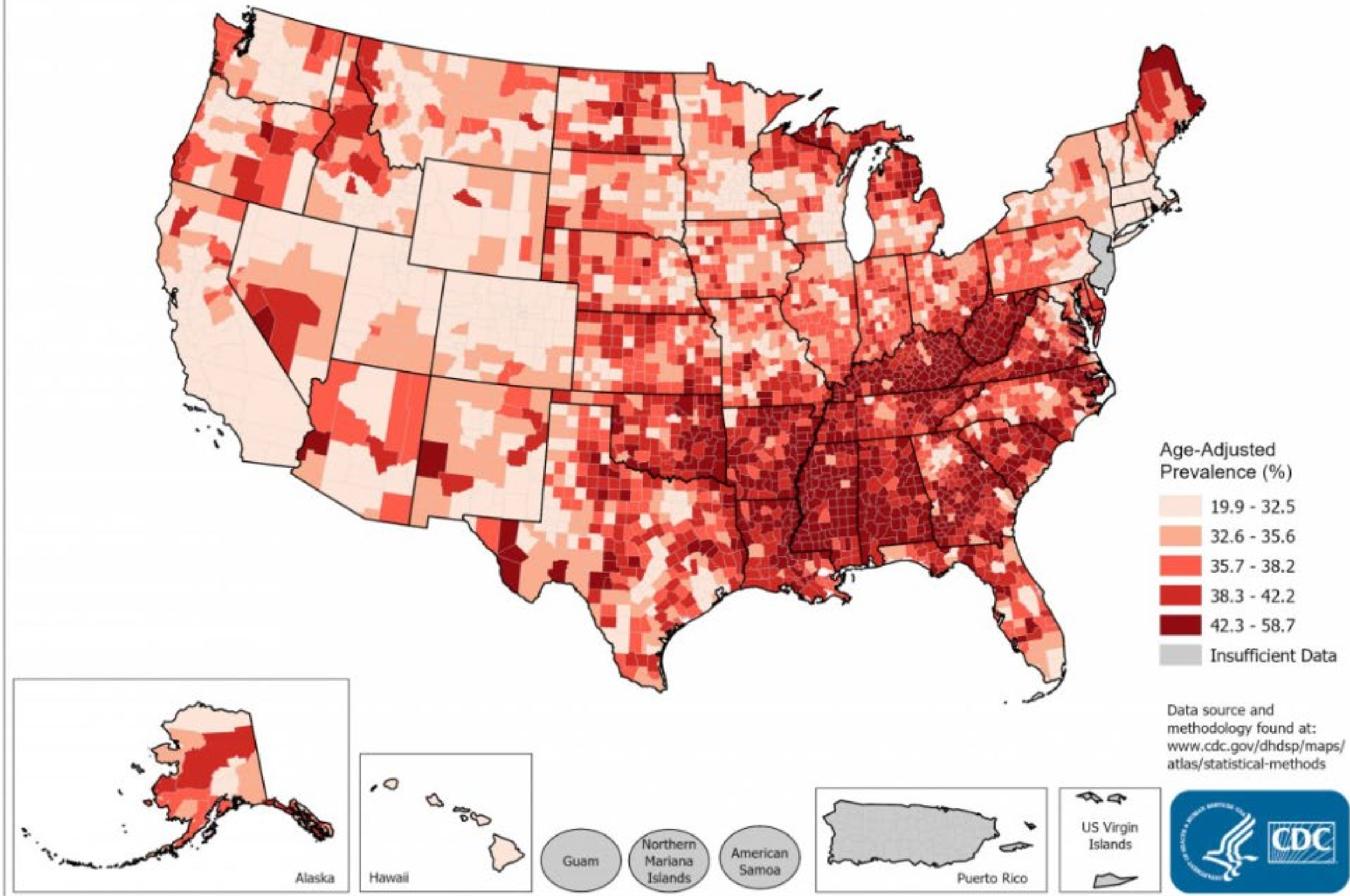
- HTN was the primary cause of 670,000 deaths in the US
- 47% of adults in the US have HTN
- 24% of adults with HTN are controlled
- HTN costs the US approximately $131 billion annually between 2003-2014
- 56% of non-Hispanic black adults have HTN
  - Non-Hispanic white adults (48%)
  - Non-Hispanic Asian adults (46%)
  - Hispanic adults (39%)

Centers for Disease Control and Prevention, National Center for Health Statistics. About Multiple Cause of Death, 1999–2020. CDC WONDER Online Database website. Atlanta, GA: Centers for Disease Control and Prevention; 2022

Cardiovascular Disease in PWH

- Increased risk of developing CVD in PWH compared to those uninfected
- Increased risk of MI, ischemic stroke, HF, pulmonary HTN, and venous thrombosis
  - Likely due to chronic immune activation and inflammation
  - Lower CD4 count associated with higher MI risk
  - Lower CD4/CD8 ratio associated with grater risk of coronary atherosclerosis
- Combination of low CD4 count and higher HIV viremia or coinfection with hepatitis C are associated with increased risk of stroke

Circulation. 2019 Jul 9;140(2):e98-e124



The map shows that concentrations of counties with the highest hypertension prevalence – meaning the top quintile – are located primarily in Mississippi, Louisiana, Arkansas, Oklahoma, Texas, Kentucky, Tennessee, Alabama, Georgia, South Carolina, North Carolina, Virginia, Maine, and Michigan. Pockets of high-rate counties also were found in Florida, New Mexico, Arizona, Nevada, and Missouri.

Centers for Disease Control and Prevention, National Center for Health Statistics. About Multiple Cause of Death, 1999–2020. CDC WONDER Online Database website. Atlanta, GA: Centers for Disease Control and Prevention; 2022

Drug Induced Secondary HTN

- Estrogens
- Herbal/Dietary Supplements
  - Licorice, ephedra, ma huang, bitter orange
- Decongestants (e.g. pseudoephedrine)
- Caffeine
- Corticosteroids
- NSAIDs, COX 2 Inhibitors
- Calcineurin inhibitors (e.g. cyclosporine and tacrolimus)
- Erythropoietin stimulating agents (e.g. erythropoetin, darbepoetin)
- Antidepressants (e.g. venlafaxine, desvenlafaxine, bupropion)
- Illicit drugs: cocaine (cocaine withdrawal), amphetamines
- Nicotine and nicotine withdrawal
- Certain ARTs

2017 Adult BP Classification

Stage	SBP (mmHg)		DBP (mmHg)
Optimal	<120	**and**	<80
Elevated	120-129	**and**	<80
Stage I HTN	130-139	**or**	80-89
Stage II HTN	≥140	**or**	≥90

AETC AIDS Education & Training Center Program
Southeast

J Am Coll Cardiol. 2018 May 15;71(19):e127-e248

J Am Coll Cardiol. 2018 May 15;71(19):e127-e248

Let's Meet Tyler (Ty) Lenol…TL is a 58 y/o AAM who presents to your HTN clinic with a BP of 136/76 and 138/72 taken two weeks apart. TL has no other PMH and denies any other medications. What is TL's BP Classification?

- Elevated BP
- Stage 0.5 HTN
- Stage I HTN
- Stage II HTN

Start the presentation to see live content. For screen share software, share the entire screen. Get help at **pollev.com/app**

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http://tools.acc.org/ASCVD-Risk-Estimator-Pl

Other Information

- TC: 210 mg/dl
- LDL: 130 mg/dl
- HDL: 30 mg/dl
- TG:250 mg/dl
- Social hx: (-) alcohol, + TOB, or (-) illicit drugs
- No aspirin
- No statin

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ASCVD Risk Estimator Plus

Estimate Risk

16.9% Current 10-Year ASCVD Risk

Lifetime ASCVD Risk | Optimal ASCVD Risk: 5.3%

Current Age * 58
Age must be between 40-79

Sex * ✔ Male | Female

Race * White | ✔ African

Systolic Blood Pressure (mm Hg) * 138
Value must be between 90-200

Diastolic Blood Pressure (mm Hg) 76
Value must be between 60-130

Total Cholesterol (mg/dL) * 210
Value must be between 130 - 320

HDL Cholesterol (mg/dL) * 30
Value must be between 20 - 100

LDL Cholesterol (m 130
Value must be between 30-

History of Diabetes? * Yes | ✔ No

Smoker: * ✔ Yes | Former

On Hypertension Treatment? * Yes | ✔ No

On a Statin? Yes | ✔ No

On Aspirin Therap Yes

http://tools.acc.org/ASCVD-Risk-Estimator-Plus/

WHEN DO WE TREAT?

BP Thresholds for Drug Initiation and Treatment

- Normal BP → Promote Optimal Lifestyle Habits
- Elevated BP → Nonpharmacological Therapy
- Stage 1 → Clinical ASCVD or 10 year CVD risk of ≥10%
  - Yes → Initiate Nonpharmacological Therapy AND Antihypertensive
  - No → Nonpharmacological Therapy
- Stage 2 → Initiate Nonpharmacological Therapy AND Antihypertensive(s)

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Once pharmacologic treatment is started, what is the BP goal?

<130/80

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Therapy

Non-Pharmacologic
- Limit sodium
- Limit alcohol
- Increase physical activity
- Limit caffeine
- Smoking cessation
- DASH Diet

First Line
- Thiazide
- ACEi
- ARB
- CCB

African American
- CCB
- Thiazide

CKD
- ACEi or ARB

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Thiazide Diuretics

Medication	Usual Dose Range	Frequency
Hydrochlorothiazide (HydroDIURIL)	12.5-*50 mg*	1
Chlorthalidone	12.5*-25 mg	1
Indapamide	1.25-2.5 mg	1
Metolazone (Zaroxolyn)	2.5-5 mg	1

Thiazide Considerations

- Advise on appropriate time of day dosing
- Photosensitivity
- Gout
- May have benefit in osteoporosis
- OTC medications/diet
- Monitoring: Blood pressure; BUN, serum creatinine; serum electrolytes (potassium, magnesium, calcium, sodium); uric acid
  - Consider blood glucose and cholesterol
  - Renal function consideration
    - Lack of efficacy in CrCl <10 ml/min
    - May consider metolazone

Angiotensin Converting Enzyme Inhibitors (ACEI)

Medication	Usual Dose Range	Frequency
Benaze**pril** (Lotensin)	10-40 mg	Divided in 1-2 doses
Capto**pril** (Capoten)	12.5-150 mg	Divided in 2-3 doses
Enala**pril** (Vasotec)	5-40 mg	Divided in 1-2 doses
Fosino**pril** (Monopril)	10-40 mg	Divided in 1-2 doses
Lisino**pril** (Zestril, Prinivil)	10-40 mg	1
Moexi**pril** (Univasc)	7.5-30 mg	Divided in 1-2 doses
Perindo**pril** (Aceon)	4-16 mg	1
Quina**pril** (Accupril)	10-80 mg	Divided in 1-2 doses
Rami**pril** (Altace)	2.5-20 mg	Divided in 1-2 doses
Trandola**pril** (Mavik)	1-4 mg	1

Angiotensin Receptor Blockers (ARBs)

Medication	Usual Dose Range	Frequency
Azil**sartan** (Edarbi)	40-80 mg	1
Cande**sartan** (Atacand)	8-32 mg	1
Epro**sartan** (Teveten)	600-800 mg	Divided in 1-2 doses
Irbe**sartan** (Avapro)	150-300 mg	1
Lo**sartan** (Cozaar)	25-100 mg	Divided in 1-2 doses
Olme**sartan** (Benicar)	20-40 mg	1
Telmi**sartan** (Micardis)	20-80 mg	1
Val**sartan** (Diovan)	80-320 mg	Divided in 1-2 doses

ACEi and ARB Considerations

- Contraindications
  - Pregnancy
  - Bilateral renal artery stenosis
- Dry Cough?
- Angioedema?

Hot Off the Press

- Antihypertensive Class and Cardiovascular Outcomes in Patients With HIV and Hypertension
  - BBs may increase CVD in PWH if used as initial therapy
  - ACEi/ARBs may have additional benefits in PWH
    - May lower the risk of developing heart failure

Hypertension. 2021;77:00–0

Dihydropyridine (DHP) CCBs

Medication	Usual Dose Range	Frequency
Amlo**dipine** (Norvasc)	2.5-10 mg	1
Felo**dipine** (Plendil)	2.5-10 mg	1
Isra**dipine** (DynaCirc)	5-10 mg	Divided in 2 doses
Nicar**dipine** sustained release (Cardene SR)	60-120 mg	Divided in 2 doses
Nife**dipine** long acting (Adalat CC, Procardia XL)	30-90 mg	1
Nisol**dipine** (Sular)	17-34 mg	1

Considerations in PWH: Potential Drug Interactions: CCBs

- PIs, cobicistat/elvitegravir/emtricitabine/tenofovir DF, or cobicistat/elvitegravir/emtricitabine/tenofovir AF may increase levels of amlodipine, nifedipine, and felodipine
  - Consider starting at lower doses
- Diltiazem's dose should be dose reduced by 50% in coadministration with atazanavir

Corbett AH, Sheffield CI. Key Pharmacologic Principles and Drug-Drug Interactions in HIV Patient Care. June 2019.

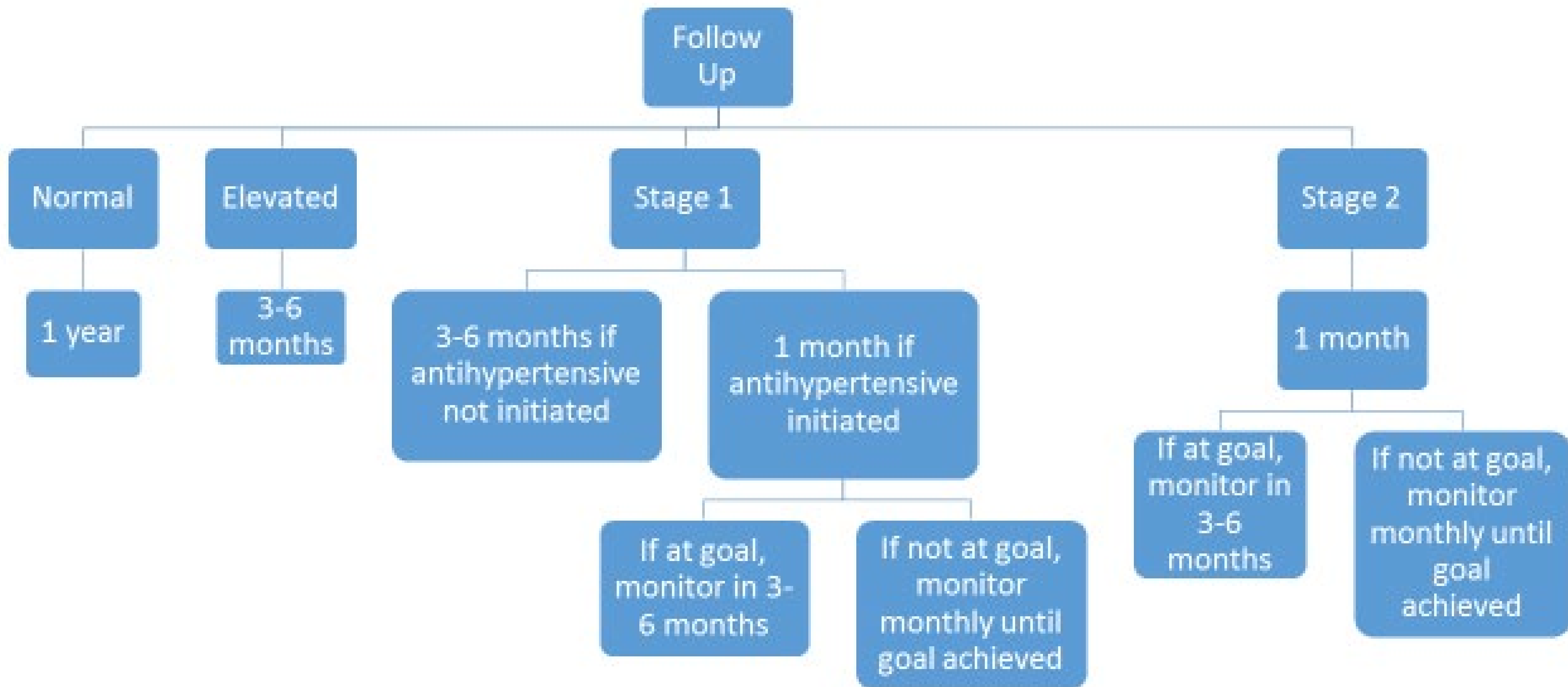
Considerations in PWH: Potential Drug Interactions: BB

- PIs may increase the concentration of metoprolol, carvedilol, and propranolol
- Tipranavir/ritonavir may increase concentrations of metoprolol and carvedilol
- Cobicistat/elvitegravir/emtricitabine/tenofovir DF and cobicistat/elvitegravir/emtricitabine/tenofovir AF may increase concentrations of metoprolol and timolol
- Consider starting above BB at low doses
- Atazanavir/cobicistat or darunavir/cobicistat in combination with a BB should be monitored

Corbett AH, Sheffield CI. Key Pharmacologic Principles and Drug-Drug Interactions in HIV Patient Care. June 2019.

Alternative Agents

- Should be used as add-on therapy to 1st line agents
  - βBs
  - α-βBs
  - Loop diuretics
  - Potassium sparing diuretics
  - Aldosterone Antagonists
  - *α1 Blockers*
  - Direct Renin Inhibitor
  - Central Acting α2 Agonists
  - Direct Acting Vasodilators
  - *Reserpine*



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Dosing Strategies

- Stage 1:
  - Start **one** drug and titrate to maximum effective dose (if needed)
  - If not at goal, **add** a second drug
- Stage 2:
  - SBP: 140-150 mmHg
    - Start **one** medication and titrate/add additional drug if necessary
  - SBP: >150 mmHg (SBP >20mmHg above goal)
    - Start **two** drugs at the same time either as two separate tablets or a single formulation and titrate/add additional agent if necessary

Follow up

- Efficacy
  - Patient should be evaluated 4 weeks (1 month) after initiation of therapy or changes to therapy
  - Once at goal, monitor every 3-6 months thereafter
- Toxicity
  - Monitor labs at baseline and 3-4 weeks after initiation of therapy or dose increases
  - Monitor every 6-12 months thereafter once stable

Getting to Goal

- If BP goal is not achieved within 1 month of initiation
  - Consider dose titration or the addition of a second medication
- If BP goal is not achieved with 2 medications
  - Add 3rd medication
  - Do not use ACEI and ARB together
  - Consider ACEi or ARB + thiazide or CCB for dual therapy
  - Try avoiding βB and Non DHP CCB combination
- If requiring more than 3 medications, may need to choose from a second line option

Summary

- Choose guideline directed therapy
- Ensure patient counseling
- Pair pharmacologic therapy with non pharmacologic recommendations

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