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Rush Algorithms for Cardiovascular Management of Patients on Cancer Therapies

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Introduction

Background

Advances in cancer therapeutics have paved the way for the development of several novel anti-cancer treatments. Many of these agents carry a risk of potentially life-threatening cardiotoxicities.

Due to the exclusion of patients with cancer from cardiology studies; it is often difficult to generalize cardiology guidelines to patients with cancer. Therefore, it is important to provide guidelines on the cardiovascular management of patients on cancer therapies.

Objective

The goal of this document is to provide guidance to clinicians practicing at Rush across various disciplines, both in the outpatient and inpatient setting, on the cardiovascular management of patients on cancer therapies. We conducted a literature search and created 23 algorithms focusing on the monitoring, evaluation, and management of cardiac toxicities of cancer treatments.

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[1] By alphabetical order

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List of Possible Cardiotoxicities of Cancer Therapies[2]

Cancer Therapies associated with Left Ventricular Dysfunction

1. **Anthracyclines (Dose-dependent)**
   - Doxorubicin (1-20%)
   - Epirubicin (0.9-3.3%)
   - Idarubicin
   - Daunorubicin
   - Mitoxantrone
   - Other anthracycline formulations:
     - Liposomal doxorubicin
     - Liposomal daunorubicin and cytarabine (Vyxeos)

2. **Tyrosine Kinase Inhibitors (TKIs)**

Small molecule

- Dabrafenib (when combined with trametinib)
- Dasatinib
- Lapatinib
- Pazopanib
- Ponatinib
- Sorafenib
- Sunitinib (11-16%)
- Trametanib
- Imatinib
- Osimertinib (3%)

MAb-based

- Ado-Trastuzumab emtansine
- Pertuzumab
- Trastuzumab
- Neratinib
- Alemtuzumab

Angiogenesis inhibitors

- Bevacizumab (1% ; 4% with anthracycline use)
- Ramucirumab

3. **Proteasome Inhibitors**
   - Bortezomib (≤1%)
   - Carfilzomib

4. **Cyclophosphamide** (Mainly with higher doses >1.55g/m2 (and as low as 100 mg/kg)

5. **OTHERS**

Alkylating Agents

- Ifosfamide (Ifex)
- Cisplatin

[2] Frequencies listed in parenthesis after each agent where available in Lexicomp®.

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Antimetabolites
- Decitabine (Hypomethylating agent) (5%)
- Cytarabine (more common when combined with cyclophosphamide)

Antimicrotubule agents
- Docetaxel
- Paclitaxel

Miscellaneous
- ATRA (6%)
- Mitomycin
- Interferon-α
- Pentostatin (<3%)

Cancer therapies associated with Hypertension

1. TKIs

Small molecule TKIs
- Acalabrutinib (3%)
- Axitinib (40%)
- Cabozantinib (30-61%)
- Ibrutinib (14-19%; cumulative over time)Nilotinib (10-11%)
- Pazopanib (40-42%)
- Ponatinib (31-53%; severe hypertension: 3% - 13%)
- Ramucirumab (16-25%)
- Regorafenib (30-59%; hypertensive crisis: <1%)
- Sorafenib (9-41%)
- Sunitinib (15-39%)
- Trametinib (15%)
- Vandetanib (≤33%)
- Zanubrutinib (12%)
- Ziv-aflibercept (41%)
- Brigatinib (21-32%)
- Lenvatinib (45-73%)

MAb-based
- Ado-Trastuzumab emtansine (5-6%)

Angiogenesis Inhibitors
- Bevacizumab (24-42%)
- Ramucirumab (16-25%)

2. OTHERS

Antimetabolites
- Decitabine (Hypomethylating agent) (6%)

Alkylating agents
- Cisplatin

Monoclonal antibodies
- Alemtuzumab
- Ibritumomab-Tiuxetan(7%)
- Ofatumumab (5%)
- Rituximab (6-12%)

mTOR Inhibitors
- Everolimus (17-30%)
- Temsirolimus (7%)

Proteasome Inhibitors
- Bortezomib
- Carfilzomib (15-42%)

Antiandrogen Therapy
- Abiraterone (9-37%)

Cancer therapies associated with Venous Thromboembolism (VTE)

1. **Immunomodulatory imide drugs**
   - Lenalidomide (2-4%)
   - Thalidomide (13%)
   - Pomalidomide

2. **Alkylating agents**
   - Cisplatin

3. **Histone deacetylase inhibitor**
   - Vorinostat (5%; Pulmonary embolism)
   - Belinostat
   - Panobinostat

4. **Monoclonal Antibody-based TKI**

   Angiogenesis inhibitors
   - Bevacizumab (5-11%; grade 3-4)
   - Ramucirumab

5. **Antimicrotubule Agents**
   - Paclitaxel (≤1%)

6. **mTOR inhibitors**
   - Everolimus

7. **Small molecule TKIs**
   - Axitinib (1%)
   - Cabozantinib (6-7%)
   - Dabrafenib (Mostly when combined with trametinib)
   - Erlotinib (4% - in combination with gemcitabine: 11%)
   - Nilotinib
   - Pazopanib (1-5%)
   - Ponatinib (2%)
   - Sorafenib (<1%)
   - Sunitinib (4%)
   - Trametinib
   - Ziv-aflibercept (9%)

8. **Endocrine Therapy**
   - Tamoxifen (≤2%)

- Raloxifene (1-2%)
- Anastrozole (2%)
- Letrozole (≤3%)
- Exemestane (<1%)

Cancer therapies associated with Bradycardia

1. **Angiogenesis Inhibitors**
   - Thalidomide (≥3%)

2. **Antimicrotubule agents**
   - Paclitaxel (AV block) (3%)

3. **Antimetabolites**
   - Cytarabine

4. **Small molecule TKIs**
   - Ceritinib (1-4%)
   - Crizotinib (5-14%)
   - Pazopanib (2-19%)
   - Trametanib
   - Alectinib (8-18%)
   - Brigatinib (8-12%)

Cancer therapies associated with Arrhythmias

1. **BTK Inhibitors**
   - Ibrutinib (Atrial fibrillation ≤8% – VT/VFib ≤1%)
   - Zanubrutinib (Atrial fibrillation 2%)
   - Acalabrutinib (Atrial fibrillation ≤5%)

2. **Antimetabolites**
   - Capecitabine (Atrial fibrillation <5%; Premature ventricular complexes <5%)
   - 5FU

3. **Interleukins**
   - IL-2 (10%)

4. **OTHERS**

Anthracyclines
   - Epirubicin
   - Idarubicin
   - Daunorubicin
   - Mitoxantrone (3-18%)
   - Doxorubicin

Antimicrotubule agents
   - Paclitaxel (PVCs – VT) (≤1%)

Proteasome inhibitors
   - Carfilzomib

Alkylating Agents
- Ifosfamide (Ifex)

Monoclonal Antibodies
- Rituximab

Small molecule TKIs
- Osimertinib (SVT)

Cancer therapies associated with Myocarditis

1. **Immune checkpoint inhibitors (with/without Pericarditis)**[3]

PD-1 inhibitors
- Pembrolizumab (≤1%)
- Nivolumab
- Cemiplimab
- Dostarlimab

PD-L1 inhibitors
- Atezolizumab
- Avelumab
- Durvalumab

CTLA-4 inhibitors
- Ipilimumab

2. **Cyclophosphamide**

3. **OTHERS**

Anthracyclines (with/without Pericarditis)
- Epirubicin
- Idarubicin
- Daunorubicin
- Mitoxantrone
- Doxorubicin

Alkylating Agents (with/without Pericarditis)
- Cyclophosphamide [Mainly with higher doses >1.55g/m2 (and as low as 100 mg/kg)]

Cancer therapies associated with QT Prolongation

1. **Arsenic Trioxide (ATO) (40%; >500 msec)**

2. **TKIs**

ALK Inhibitors
- Ceritinib (4-12%)

BRAF Inhibitors
- Dabrafenib
- Vemurafenib (≤55%)

MEK Inhibitors
- Trametanib

[3] Up to 1.3% with combination IO/IO; particularly combination ipilimumab/nivolumab

EGFR Inhibitors
- Osimertinib (≤10%)

ROS1 Inhibitors
- Crizotinib (5-6%)

CDK4/6 Inhibitors
- Ribociclib (1-6%)

IDH Inhibitors
- Ivosidenib (10-26%)
- Enasidenib

FLT3 Inhibitors
- Midostaurin (11%)
- Gilteritinib (1-10%)

Multikinase Inhibitors
- Vandetanib (14%)
- Pazopanib (2%)
- Dasatinib (≤1%)
- Lapatinib
- Nilotinib (>60 msec from baseline: 4%; >500 msec: <1%)
- Sunitinib

3. OTHERS

Histone deacetylase inhibitors
- Belinostat (11%; grades 3/4: 4%)
- Vorinostat
- Romidepsin

Monoclonal Antibodies
- Gemtuzumab-ozogamicin

Cancer therapies associated with MI/Ischemia

1. Angiogenesis inhibitors
- Lenalidomide
- Pomalidomide

2. Antimetabolites
- Capecitabine
- Fluorouracil

3. TKI

Small molecule
- Nilotinib (5-9%)
- Ponatinib (2%)
- Erlotinib (2%)
- Sorafenib (2-3%)

Monoclonal antibody – based TKI

Angiogenesis Inhibitors
- Bevacizumab
- Ramucirumab

4. OTHERS

Alkylating agents

- Cisplatin
- Carboplatin
- Oxaliplatin

Antimicrotubule agents

- Paclitaxel

Proteasome inhibitors

- Carfilzomib

Vinca alkaloids

Interferon-α

Cancer therapies associated with Hypotension

- Etoposide (1-10%; due to rapid infusion)
- Paclitaxel (4-12%)
- Alemtuzumab
- Cetuximab
- Rituximab (10%)
- IL-2 (71%, grade 4: 3%)
- Denileukin
- Interferon-α
- All-trans retinoic acid (14%)
- Omacetaxine mepesuccinate

Cancer therapies associated with Pericardial Disease

Immune checkpoint inhibitors → pericarditis
Cytarabine/Ara-C → pericarditis (rare, hemorrhagic pericarditis)
ATRA → pericardial effusion (3%)
Imatinib → pericardial effusion

Miscellaneous

Busulfan → Endomyocardial fibrosis + Tamponade
Fluorouracil → Cardiogenic shock

Abbreviation List:

- 2D: Two-Dimensional
- 5FU : 5-Fluorouracil
- ABI: Ankle-Brachial Index
- AC: Anticoagulation
- ACEi: Angiotensin Converting Enzyme Inhibitor
- ACLS: Advanced Cardiovascular Life Support
- Ara-C: Arabinosylcytosine
- ARB: Angiotensin-II Receptor Blocker
- ASCVD: Atherosclerotic Cardiovascular Disease
- ATO: Arsenic Trioxide
- ATRA: All-Transretinoic Acid
- AV: Atrio-ventricular
- BB: Beta Blocker
- BCR/ABL: Breakpoint Cluster Region/Abelson protooncogene
- BNP: B-Natriuretic Peptide
- CABG: Coronary Artery Bypass Graft
- CAD: Coronary Artery Disease
- CCB: Calcium Channel Blocker
- CV: Cardiovascular
- DDI: Drug-Drug Interaction
- DM: Diabetes Mellitus
- DP-CCB : Dihydropyridine Calcium Channel Blocker
- ECG: Electrocardiogram
- EPO: Epogen (or erythrocyte stimulating agents in general)
- FP : Fluoropyrimidine
- GDMT: Goal-Directed Medical Therapy
- GFR: Glomerular Filtration Rate
- GLS: Global Longitudinal Strain
- Gy: Grays
- HBPM: Home Blood Pressure Monitoring
- HDACi: Histone Deacytelase inhibitor
- HER2: Human Epidermal Growth Factor Receptor-2
- HF: Heart Failure
- HR: Heart Rate
- HTN: hypertension
- ICIs: Immune Checkpoint Inhibitors
- IL-2: Interleukin-2
- IMiDs: Immunomodulatory Imide Drugs
- irAEs : Immune-related Adverse Events
- LHC: Left Heart Catheterization
- LV: Left Ventricle
- LVEF: Left Ventricular Ejection Fraction
- MAb: Monoclonal Antibody
- MI: Myocardial Infarction
- NDP-CCB: Non-dihydropyridine Calcium Channel Blocker
- PAD: Peripheral Artery Disease
- PCI: Percutaneous Coronary Intervention
- PI: Proteasome Inhibitor
- PNA: Pneumonia
- PVC: Premature Ventricular Complex
- SVT : Supraventricular Tachycardia
- TKI: Tyrosine Kinase Inhibitor
- TLS: Tumor Lysis Syndrome
- TOR: Target of Rapamycin
- TSH: Thyroid Stimulating Hormone
- TTE: Transthoracic Echocardiogram
- VEGF: Vascular Endothelial Growth Factor
- VFib: Ventricular Fibrillation
- VT: Ventricular Tachycardia
- VTE: Venous Thromboembolism

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Patients at Baseline Increased Risk for Cardiovascular Toxicity, particularly LV dysfunction

1. High-dose anthracycline (e.g., doxorubicin ≥250 mg/m2, epirubicin ≥600 mg/m2).
2. High-dose radiotherapy (≥30 Gy) where the heart is in the treatment field.
3. Lower-dose anthracycline (e.g., doxorubicin <250 mg/m2, epirubicin <600 mg/m2, daunorubicin <900 mg/m2, idarubicin <225 mg/m2, mitoxantrone <200 mg/m2[4]) or *HER2* inhibitors, *VEGF* inhibitors, Proteasome inhibitors, *BCR/ABL* inhibitor **PLUS** of any of the following factors:
    a. Age ≥65 years
    b. Lower-dose radiotherapy (<30 Gy) where the heart is in the treatment field
    c. ≥2 Risk factors, including hypertension, diabetes mellitus, smoking, dyslipidemia, chronic kidney disease, and obesity.
4. History of cardiovascular disease
5. Elevated cardiac biomarkers (NT-proBNP/BNP and/or Troponin), before the initiation of anti-cancer treatment

***Specific risk factors are included in the following algorithms*

Pre-treatment Work-up for Patients at Baseline Increased Risk

1. History and physical examination (including blood pressure measurement)
2. 12-Lead ECG
3. Blood glucose – calculated GFR – TSH; consider troponin, BNP (or NT-proBNP) based on risk profile
4. Transthoracic echocardiography (TTE)
5. To include left ventricular ejection fraction (LVEF) measurement and Global Longitudinal Strain (GLS) measurement.
    - Low threshold to utilize LV contrast agents for the 2D echocardiography
        i. [Can include the text in "5" under the "comments" section on the TTE order]
    - 3-dimensional preferred over 2-dimensional LVEF, if 2D; at least 2D Simpson biplane method
6. Optimize electrolytes; e.g, potassium >4 mmol/L, magnesium >2 mg/dL, calcium >8 mg/dL, phosphorus > 2 mg/dL (refer to institutional outpatient/inpatient replacement guidelines).
7. Counsel the patient on the importance of exercising on a regular basis and healthy dietary habits.

Other Pre-treatment considerations; by oncology, cardio-oncology/cardiology

1. Troponin, BNP (or NT-proBNP), Lipid panel, HbA1c, TSH
2. Calculation of the 10-year ASCVD risk score
3. For TTE: In the absence of GLS quantification of LV longitudinal function, assess diastolic function
4. Cardiac magnetic resonance imaging is recommended if the quality of the TTE is suboptimal
    - It is recommended to use the same imaging modality for monitoring of cardiac function after the initiation of treatment
5. Manage modifiable cardiovascular risk factors and diseases (obesity, smoking, hypertension, dyslipidemia, coronary artery disease (CAD), peripheral arterial disease (PAD), arrhythmias).

[4] See Appendix-1 for anthracycline toxicity equivalence ratios

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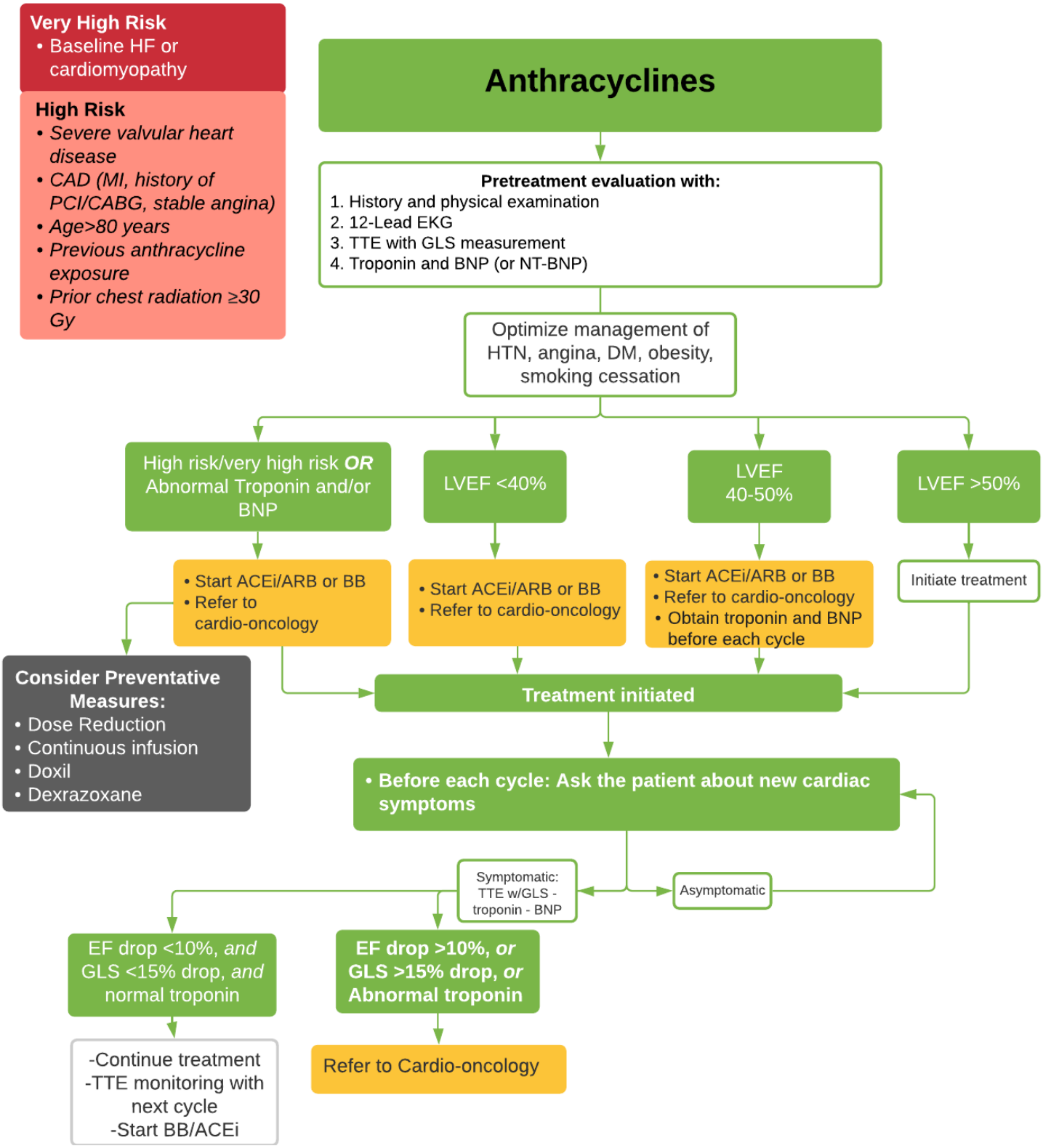
Cardiomyopathy



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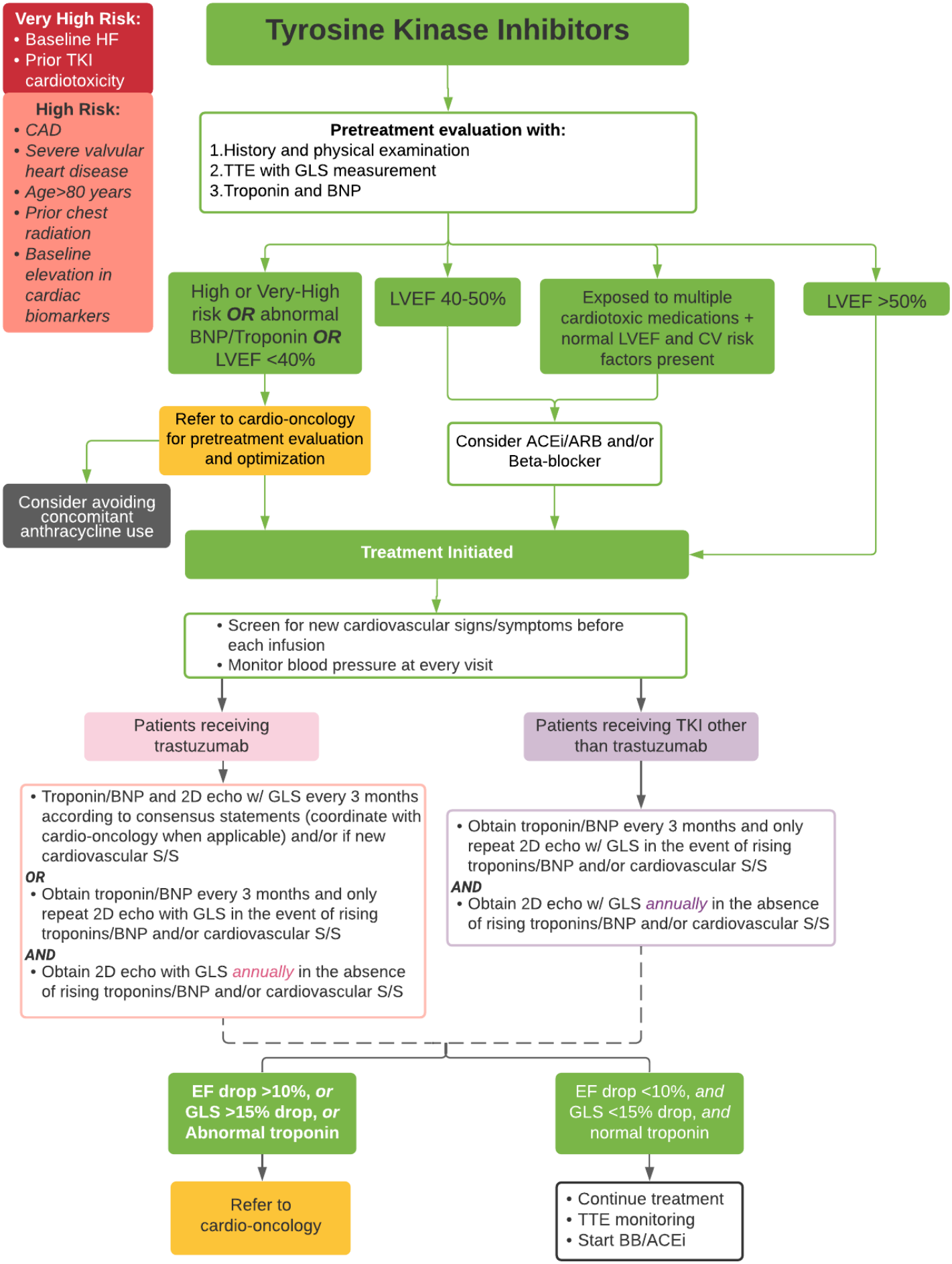
Very High Risk:
• Baseline HF
• Prior TKI cardiotoxicity
High Risk:
• CAD
• Severe valvular heart disease
• Age>80 years
• Prior chest radiation
• Baseline elevation in cardiac biomarkers
Tyrosine Kinase Inhibitors
Pretreatment evaluation with:
1.History and physical examination
2.TTE with GLS measurement
3.Troponin and BNP
High or Very-High risk OR abnormal BNP/Troponin OR LVEF <40%
LVEF 40-50%
Exposed to multiple cardiotoxic medications + normal LVEF and CV risk factors present
LVEF >50%
Refer to cardio-oncology for pretreatment evaluation and optimization
Consider ACEi/ARB and/or Beta-blocker
Consider avoiding concomitant anthracycline use
Treatment Initiated
• Screen for new cardiovascular signs/symptoms before each infusion
• Monitor blood pressure at every visit
Patients receiving trastuzumab
Patients receiving TKI other than trastuzumab
• Troponin/BNP and 2D echo w/ GLS every 3 months according to consensus statements (coordinate with cardio-oncology when applicable) and/or if new cardiovascular S/S
OR
• Obtain troponin/BNP every 3 months and only repeat 2D echo with GLS in the event of rising troponins/BNP and/or cardiovascular S/S
AND
• Obtain 2D echo with GLS annually in the absence of rising troponins/BNP and/or cardiovascular S/S
• Obtain troponin/BNP every 3 months and only repeat 2D echo w/ GLS in the event of rising troponins/BNP and/or cardiovascular S/S
AND
• Obtain 2D echo w/ GLS annually in the absence of rising troponins/BNP and/or cardiovascular S/S
EF drop >10%, or GLS >15% drop, or Abnormal troponin
EF drop <10%, and GLS <15% drop, and normal troponin
Refer to cardio-oncology
• Continue treatment
• TTE monitoring
• Start BB/ACEi

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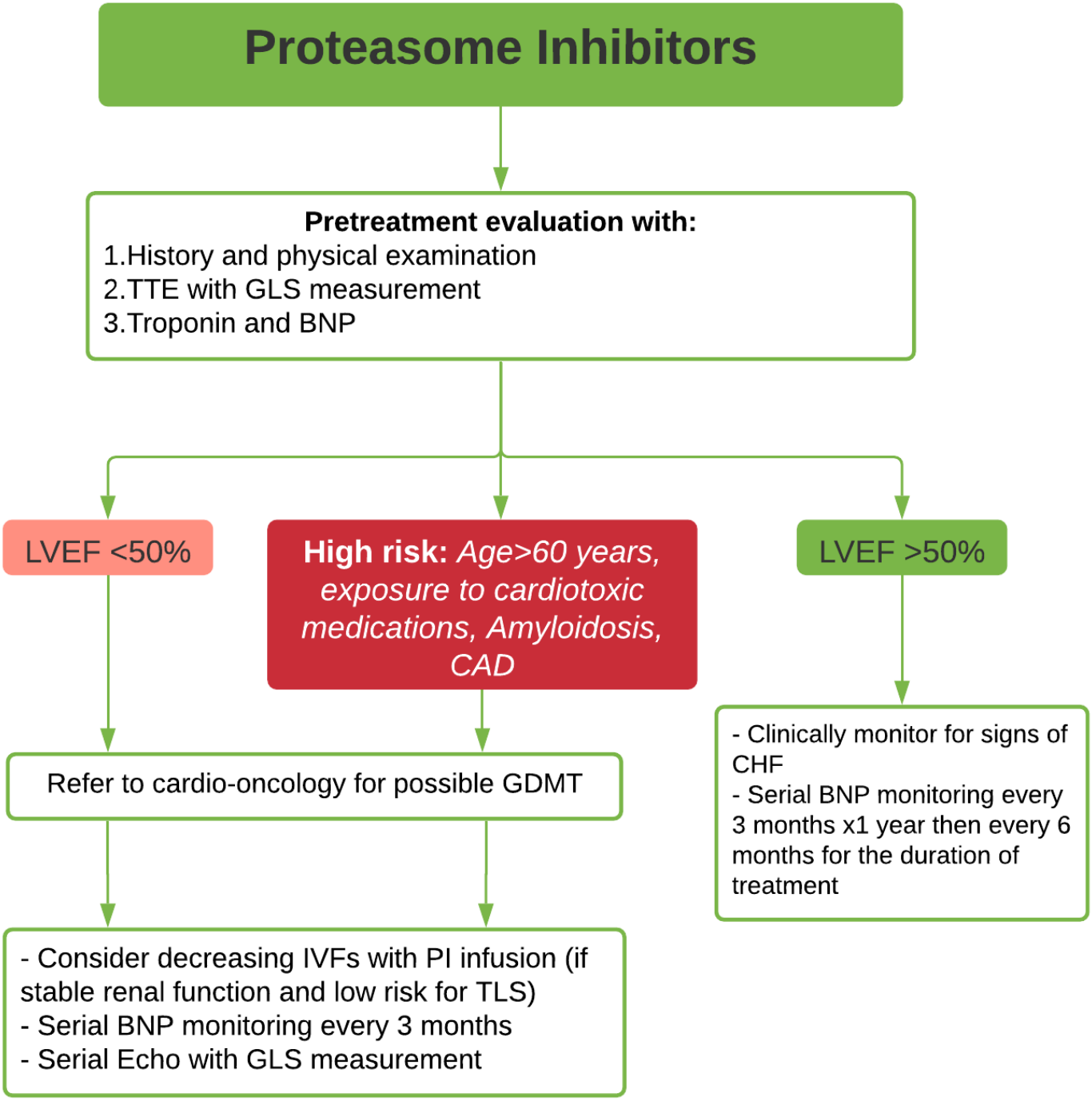

See next algorithm for management of proteasome-inhibitor related cardiotoxicity

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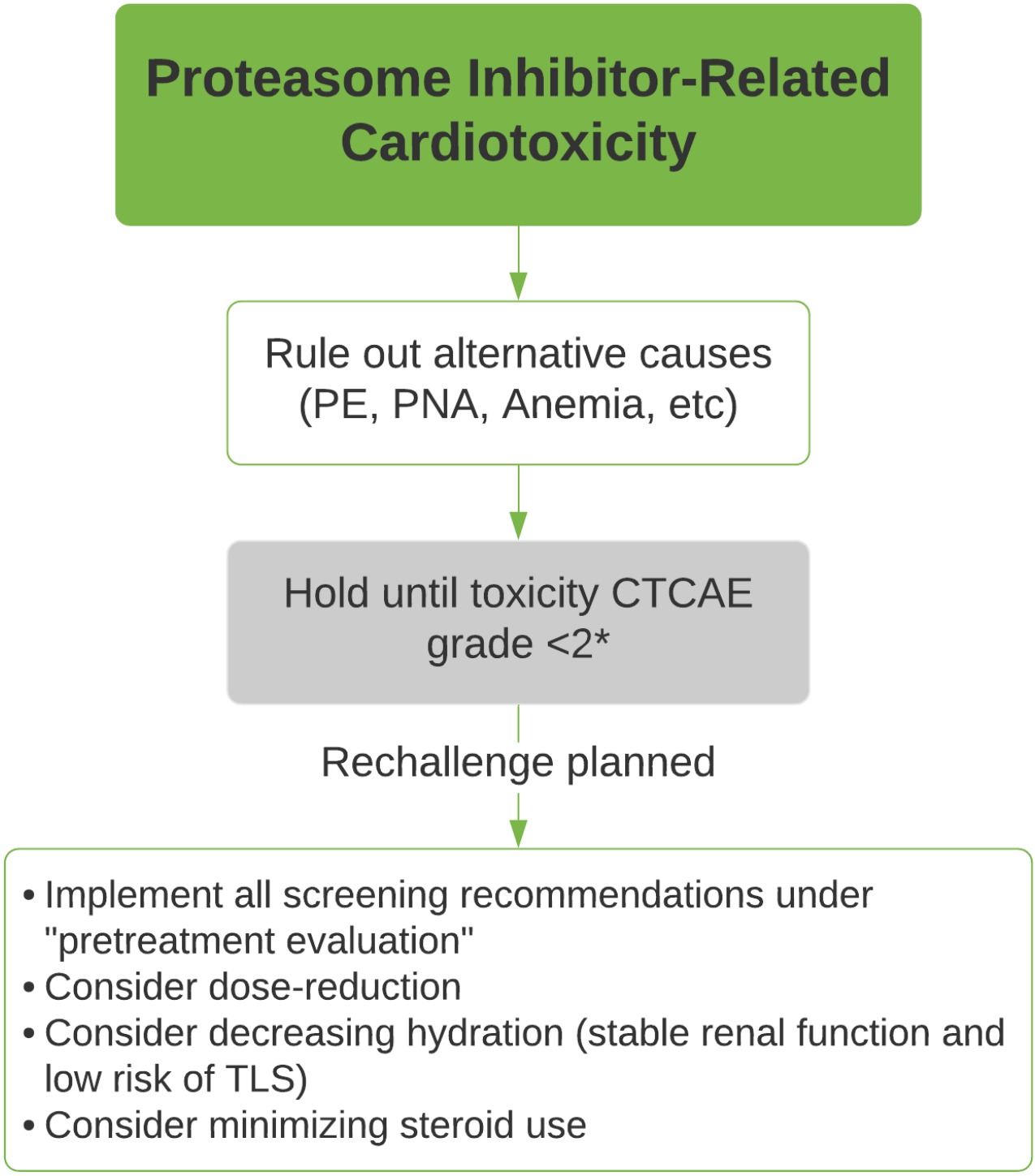
Proteasome Inhibitor-Related Cardiotoxicity



***Grade 2:** symptoms with mild exertion

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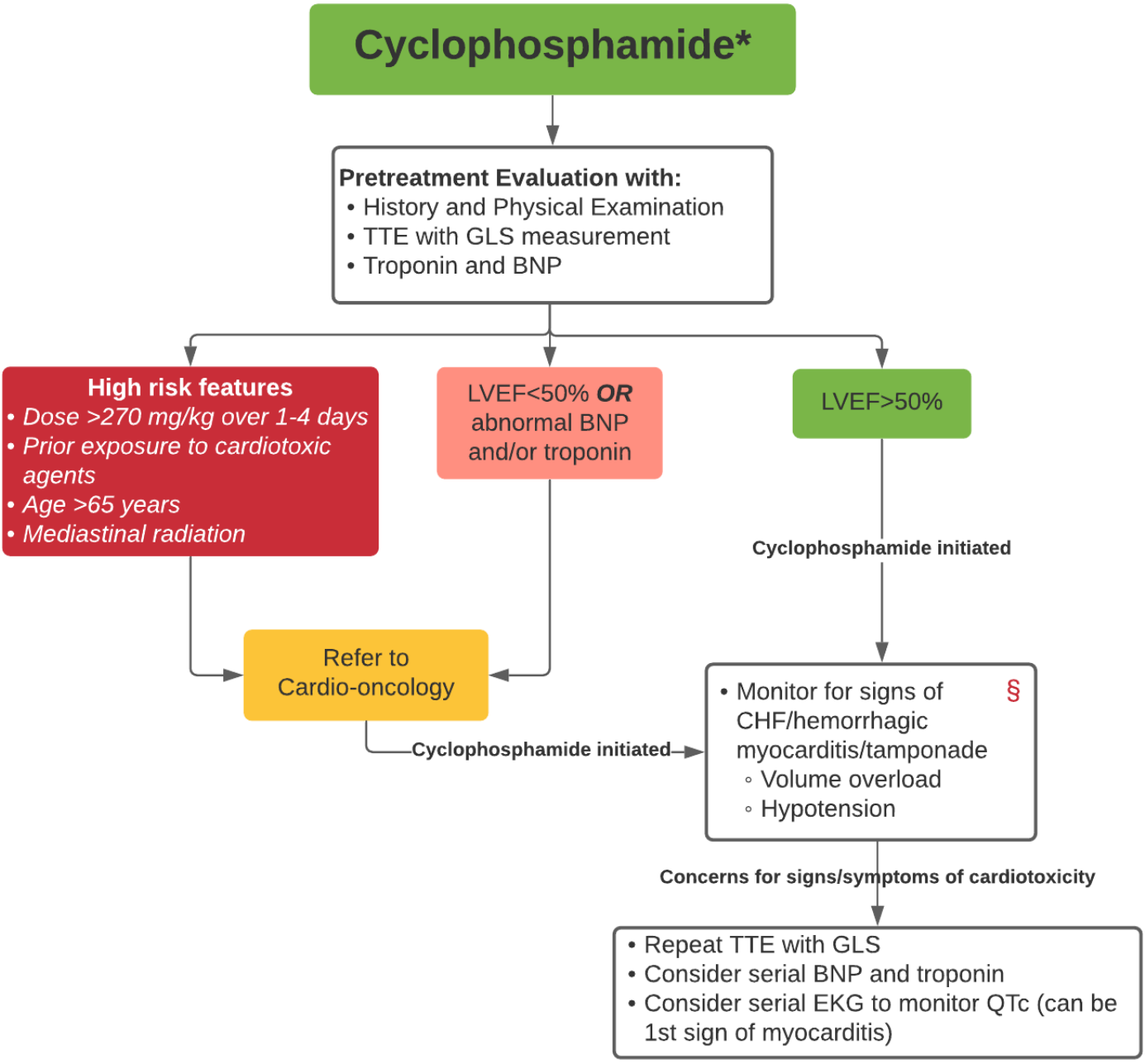

*Risk for cardiotoxicity mainly with higher doses > 1.55g/m2 (and as low as 100 mg/kg) per dose
§ Maintain a low threshold to repeat TTE if any new symptoms or changes in markers

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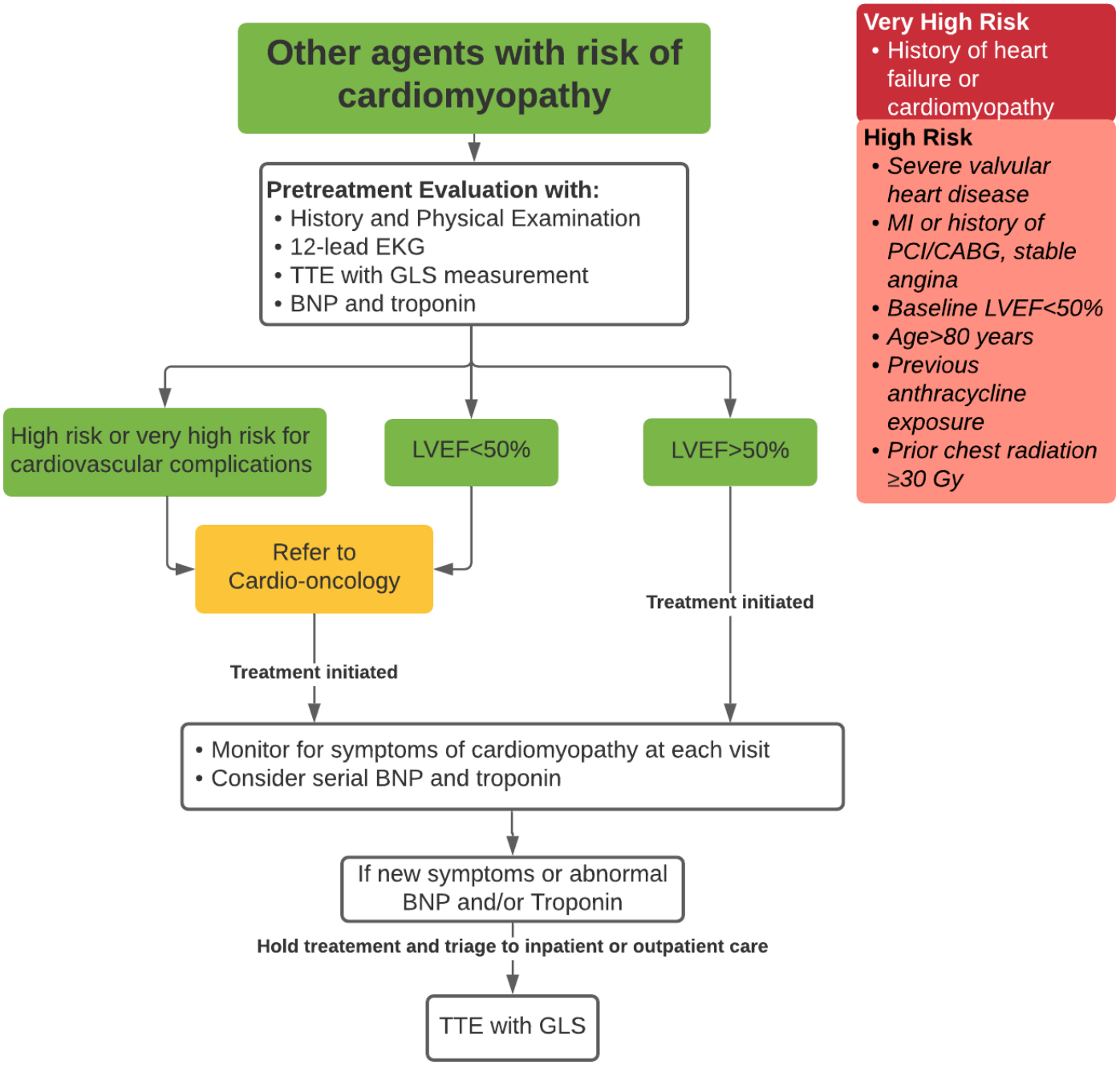

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Hypertension

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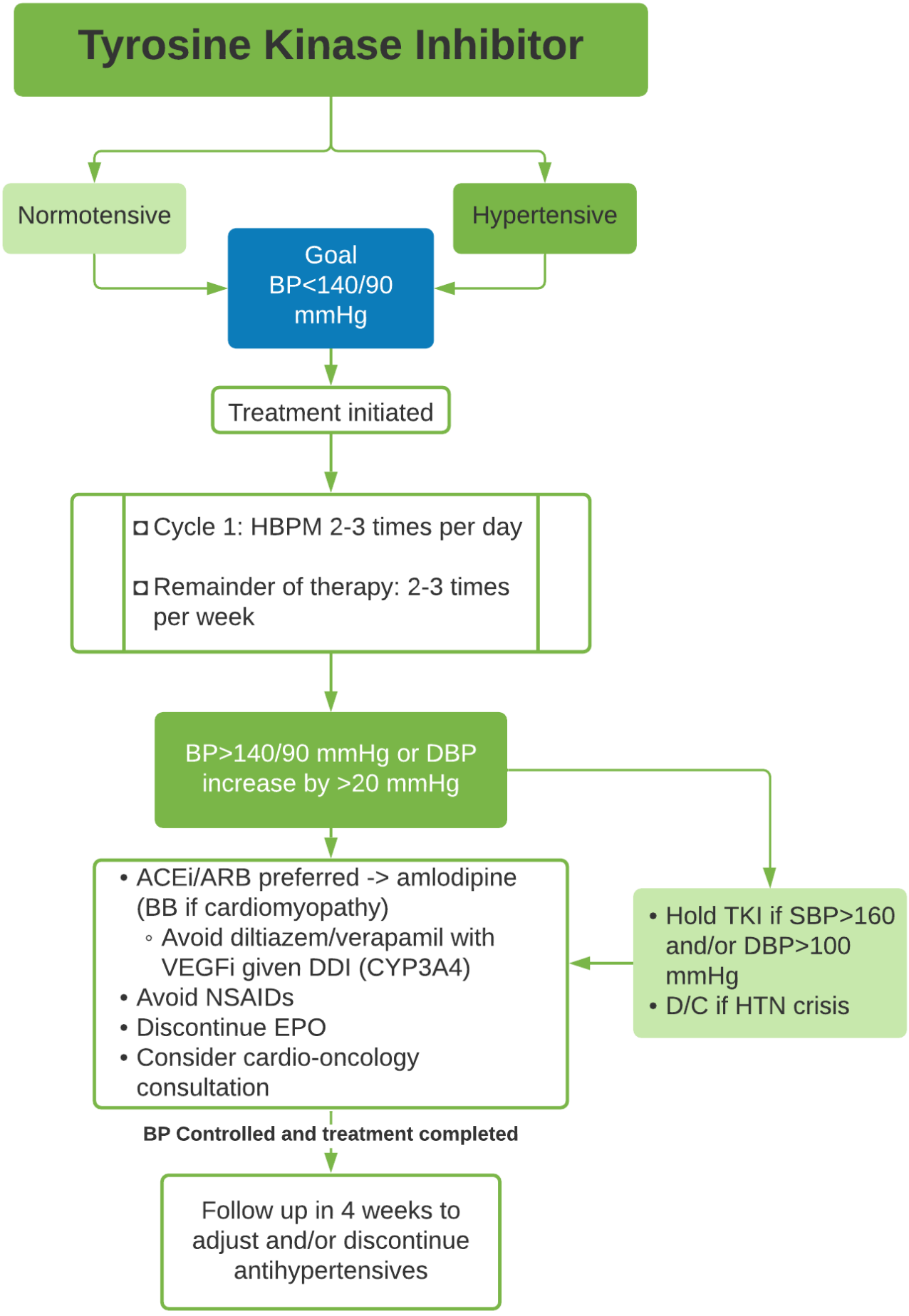

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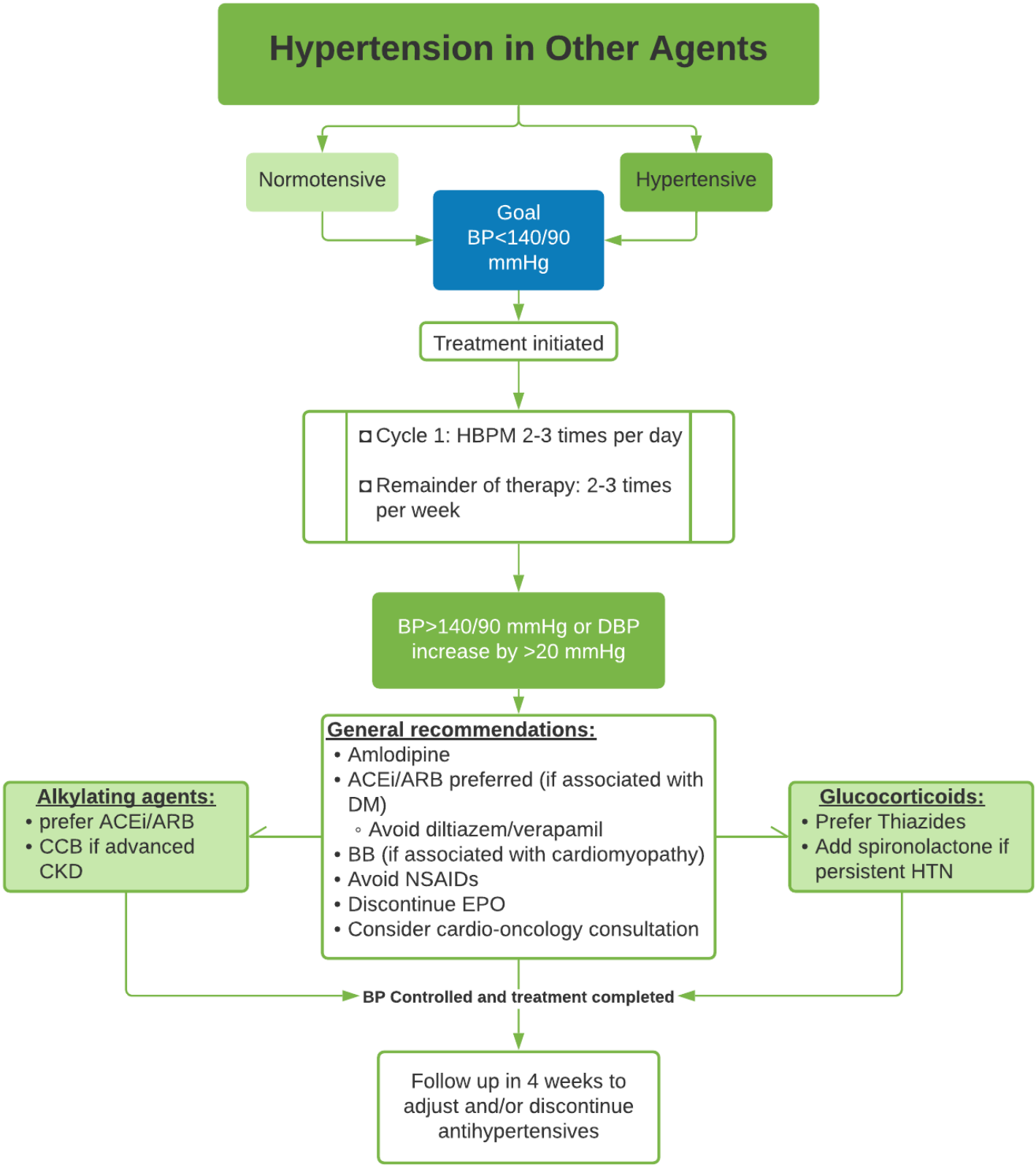
Hypertension in Other Agents



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Venous Thromboembolism

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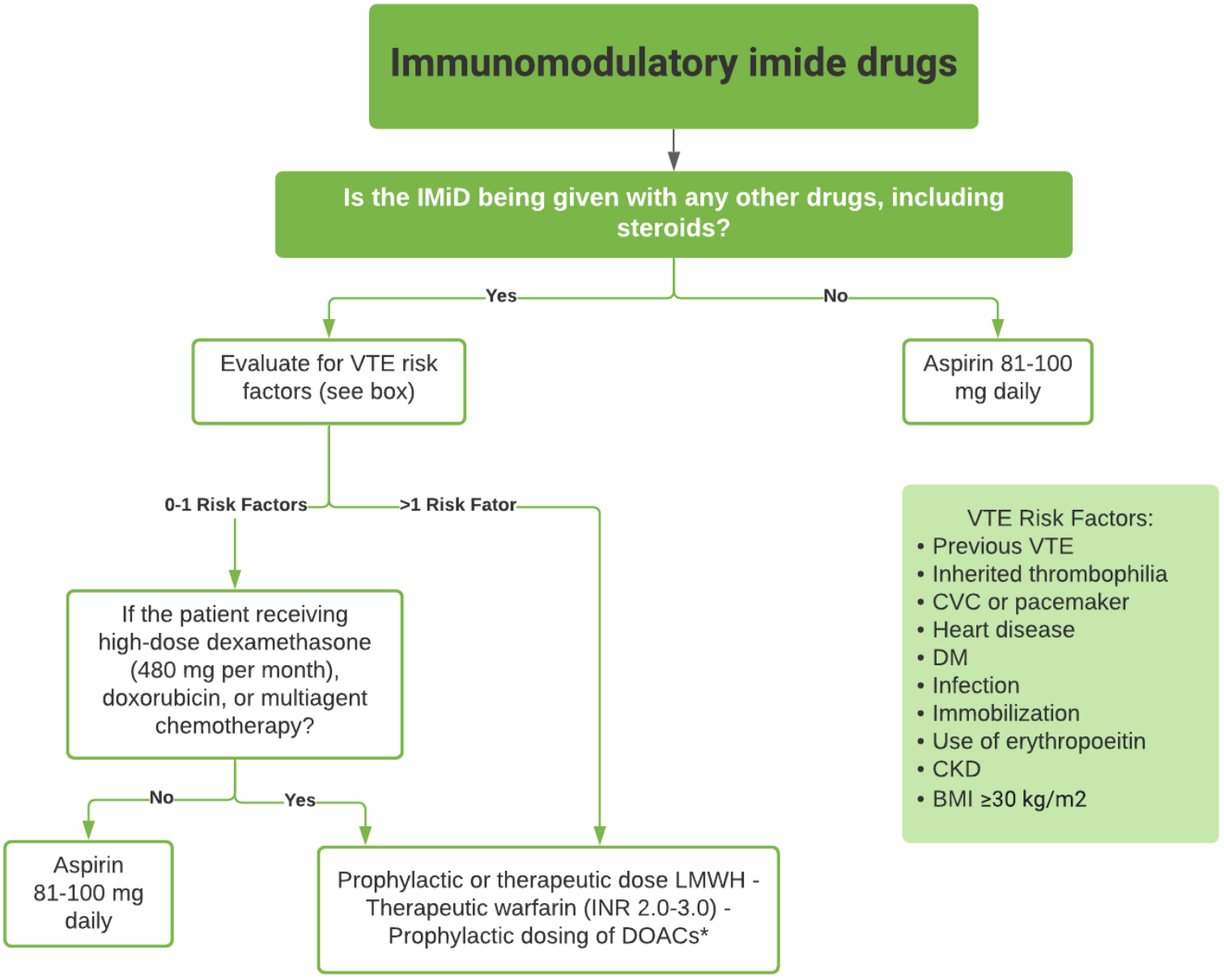

*Limited data for DOAC use

Algorithm adapted from UpToDate®

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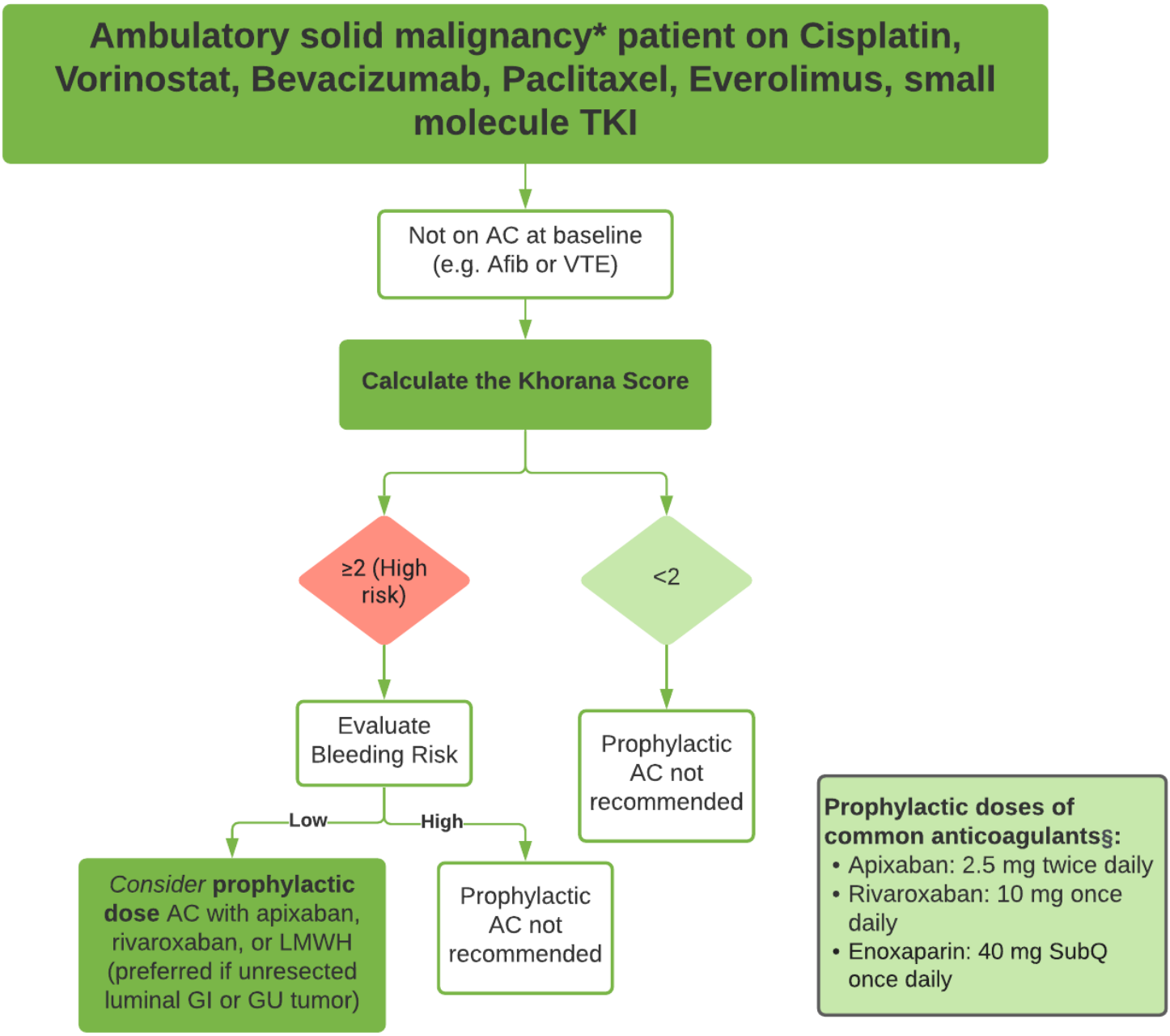

*Generally solid cancer and lymphoma, does not apply to patients with CNS cancer, acute leukemia or multiple myeloma

§ Dose adjustment may be necessary in patients with renal or hepatic dysfunction

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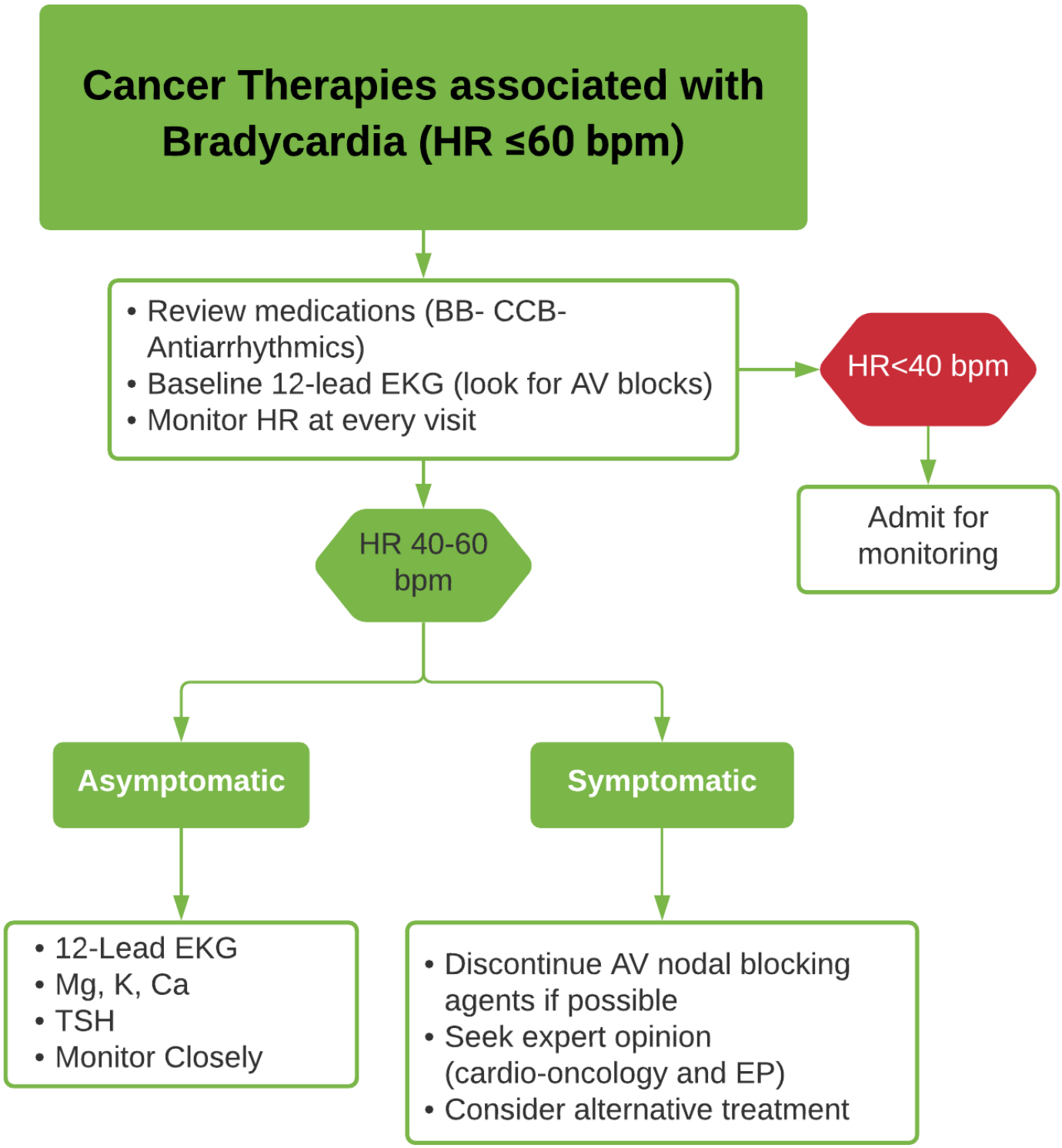
Cancer Therapies associated with Bradycardia (HR ≤60 bpm)
• Review medications (BB- CCB- Antiarrhythmics)
• Baseline 12-lead EKG (look for AV blocks)
• Monitor HR at every visit
HR<40 bpm
Admit for monitoring
HR 40-60 bpm
Asymptomatic
Symptomatic
• 12-Lead EKG
• Mg, K, Ca
• TSH
• Monitor Closely
• Discontinue AV nodal blocking agents if possible
• Seek expert opinion (cardio-oncology and EP)
• Consider alternative treatment

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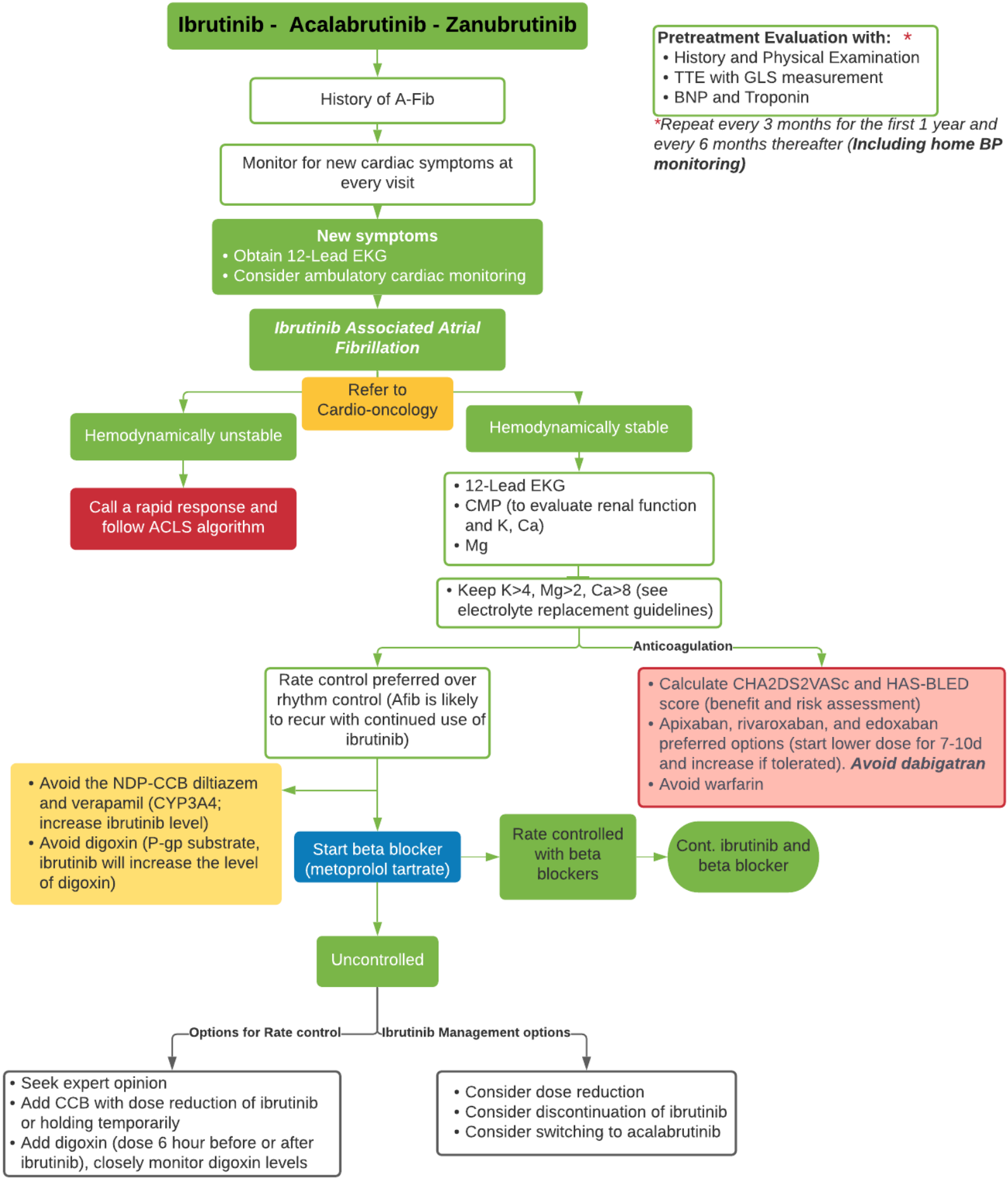
Ibrutinib - Acalabrutinib - Zanubrutinib
Pretreatment Evaluation with: *
• History and Physical Examination
• TTE with GLS measurement
• BNP and Troponin
*Repeat every 3 months for the first 1 year and every 6 months thereafter (Including home BP monitoring)
History of A-Fib
Monitor for new cardiac symptoms at every visit
New symptoms
• Obtain 12-Lead EKG
• Consider ambulatory cardiac monitoring
Ibrutinib Associated Atrial Fibrillation
Refer to Cardio-oncology
Hemodynamically unstable
Call a rapid response and follow ACLS algorithm
Hemodynamically stable
• 12-Lead EKG
• CMP (to evaluate renal function and K, Ca)
• Mg
• Keep K>4, Mg>2, Ca>8 (see electrolyte replacement guidelines)
Anticoagulation
Rate control preferred over rhythm control (Afib is likely to recur with continued use of ibrutinib)
• Calculate CHA2DS2VASc and HAS-BLED score (benefit and risk assessment)
• Apixaban, rivaroxaban, and edoxaban preferred options (start lower dose for 7-10d and increase if tolerated). Avoid dabigatran
• Avoid warfarin
• Avoid the NDP-CCB diltiazem and verapamil (CYP3A4; increase ibrutinib level)
• Avoid digoxin (P-gp substrate, ibrutinib will increase the level of digoxin)
Start beta blocker (metoprolol tartrate)
Rate controlled with beta blockers
Cont. ibrutinib and beta blocker
Uncontrolled
Options for Rate control
Ibrutinib Management options
• Seek expert opinion
• Add CCB with dose reduction of ibrutinib or holding temporarily
• Add digoxin (dose 6 hour before or after ibrutinib), closely monitor digoxin levels
• Consider dose reduction
• Consider discontinuation of ibrutinib
• Consider switching to acalabrutinib

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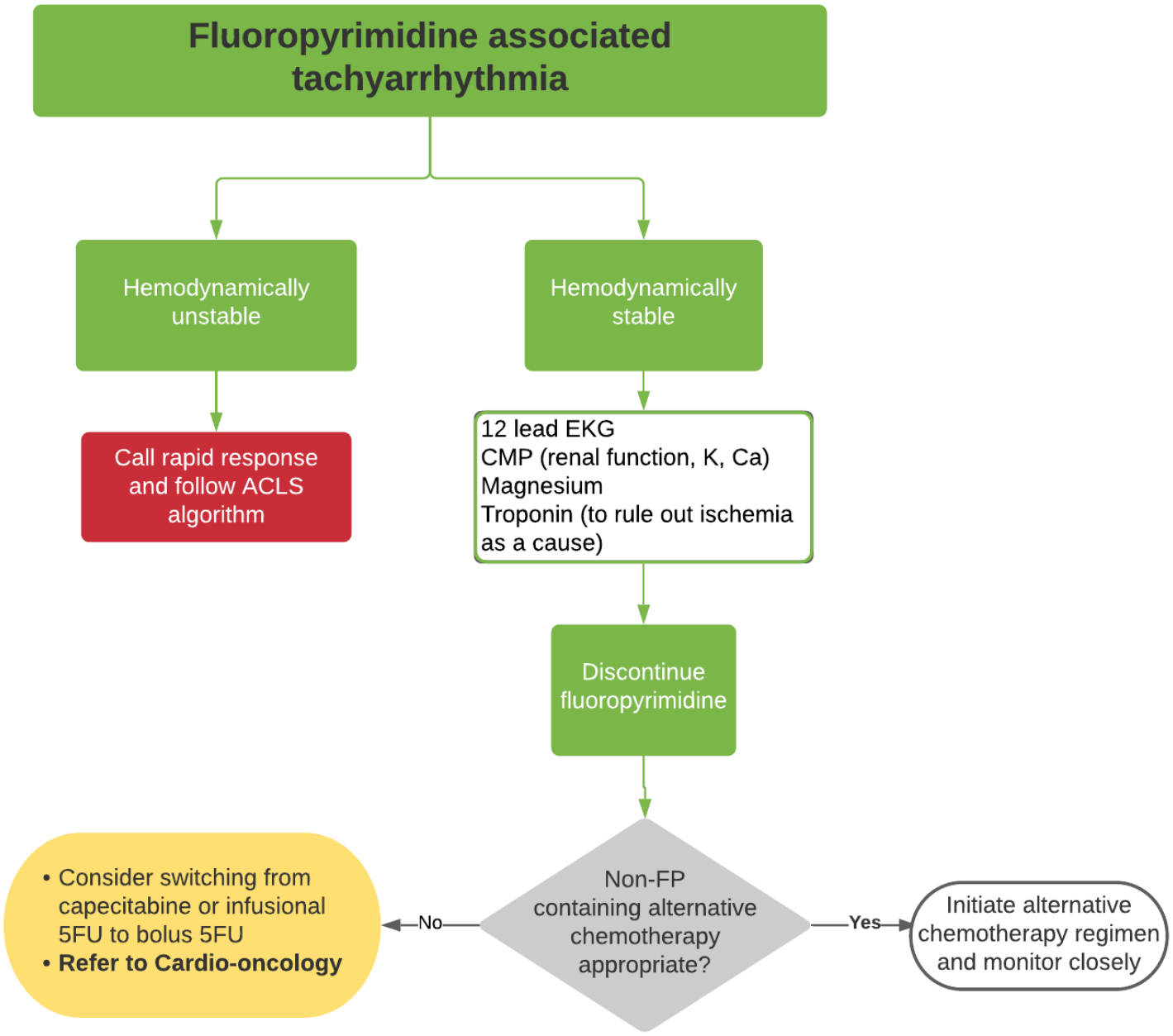

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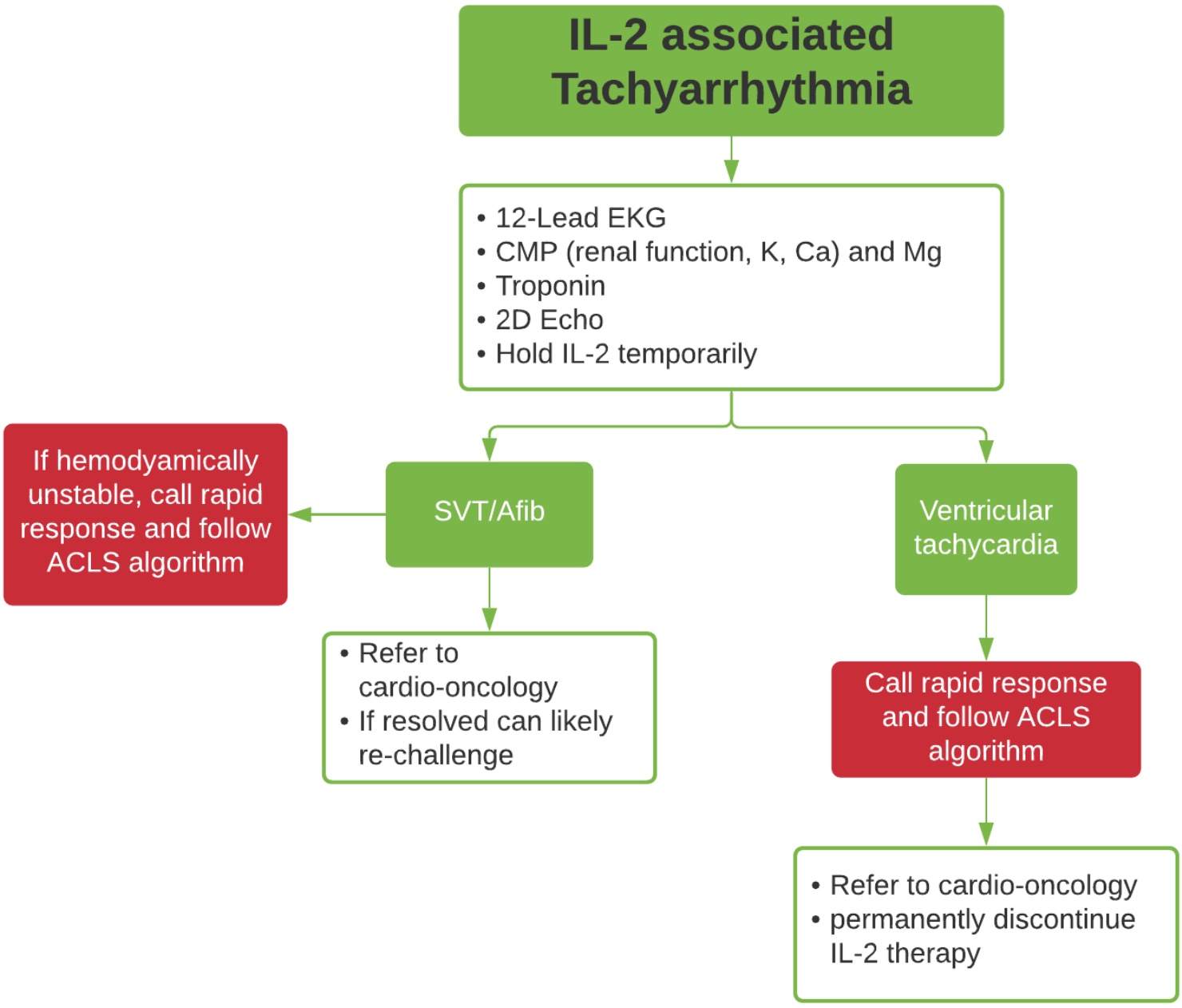

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Other chemotherapy associated Tachyarrhythmias

- Hold chemotherapy
- 12-Lead EKG
- CMP (renal function, K, Ca), and magensium
- Troponin
- TTE with GLS

- Refer to cardio-oncology
- Consider alternative anti-cancer treatments
- If treatment continued, monitor electrolytes closely and keep K>4, Mg>2, Ca>8
- If treatment continued, telemonitoring must be instituted during infusion

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Myocarditis

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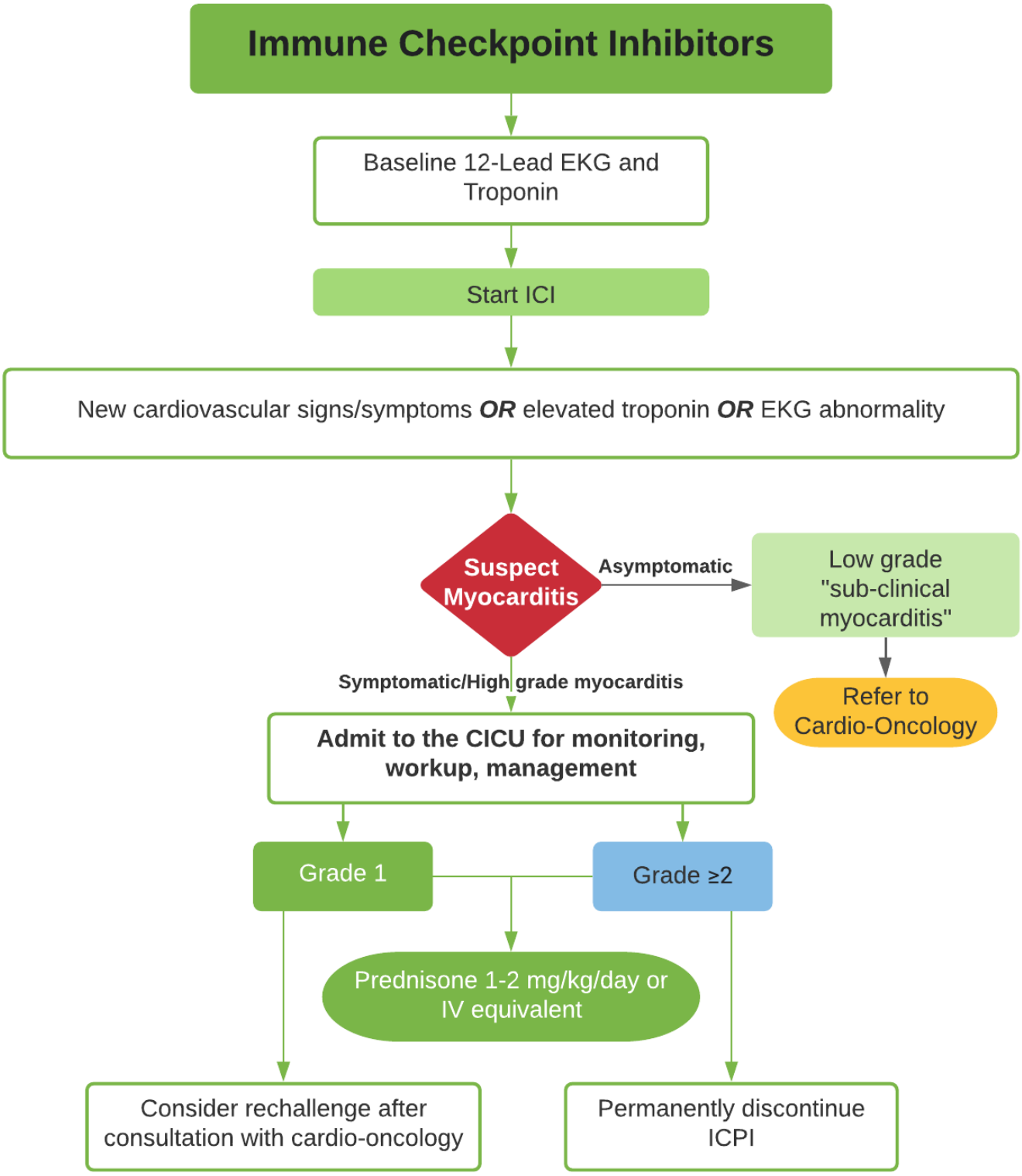

An alternative approach may include checking EKG and troponin before initiation of therapy followed by repeating EKG and troponin within 48 hours before each subsequent cycle **AND/OR in the event of any other irAEs*

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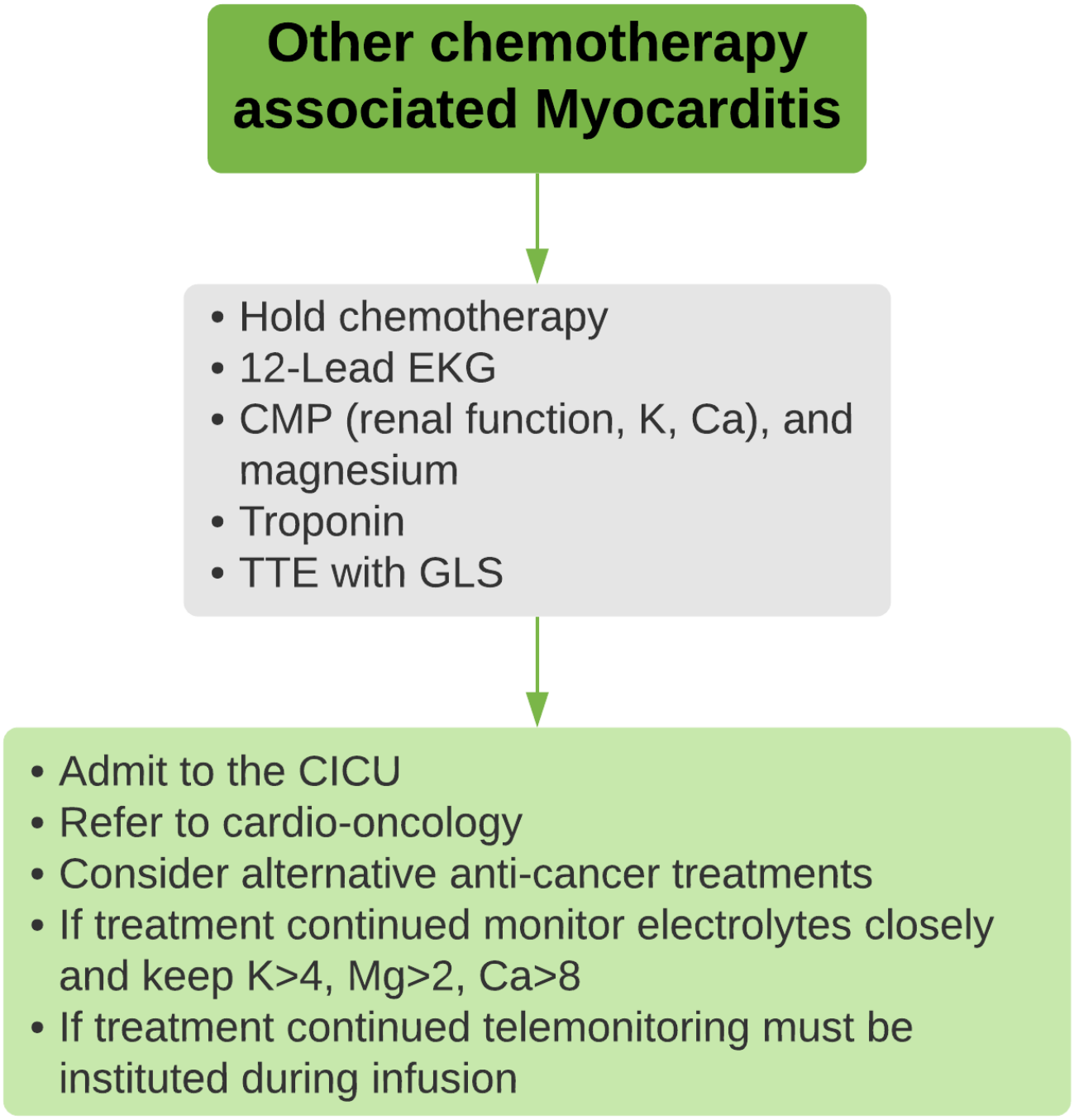

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QT Prolongation

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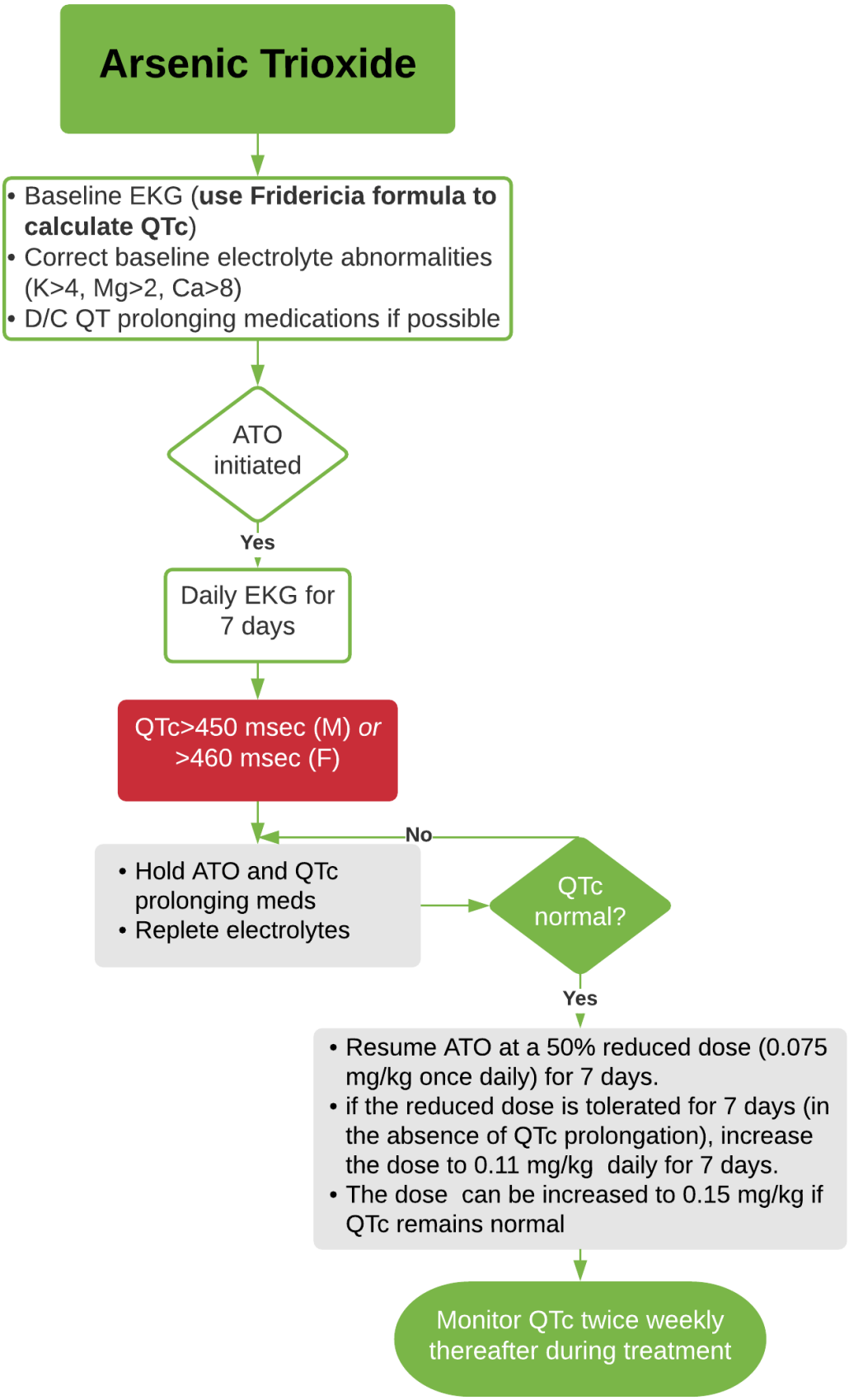

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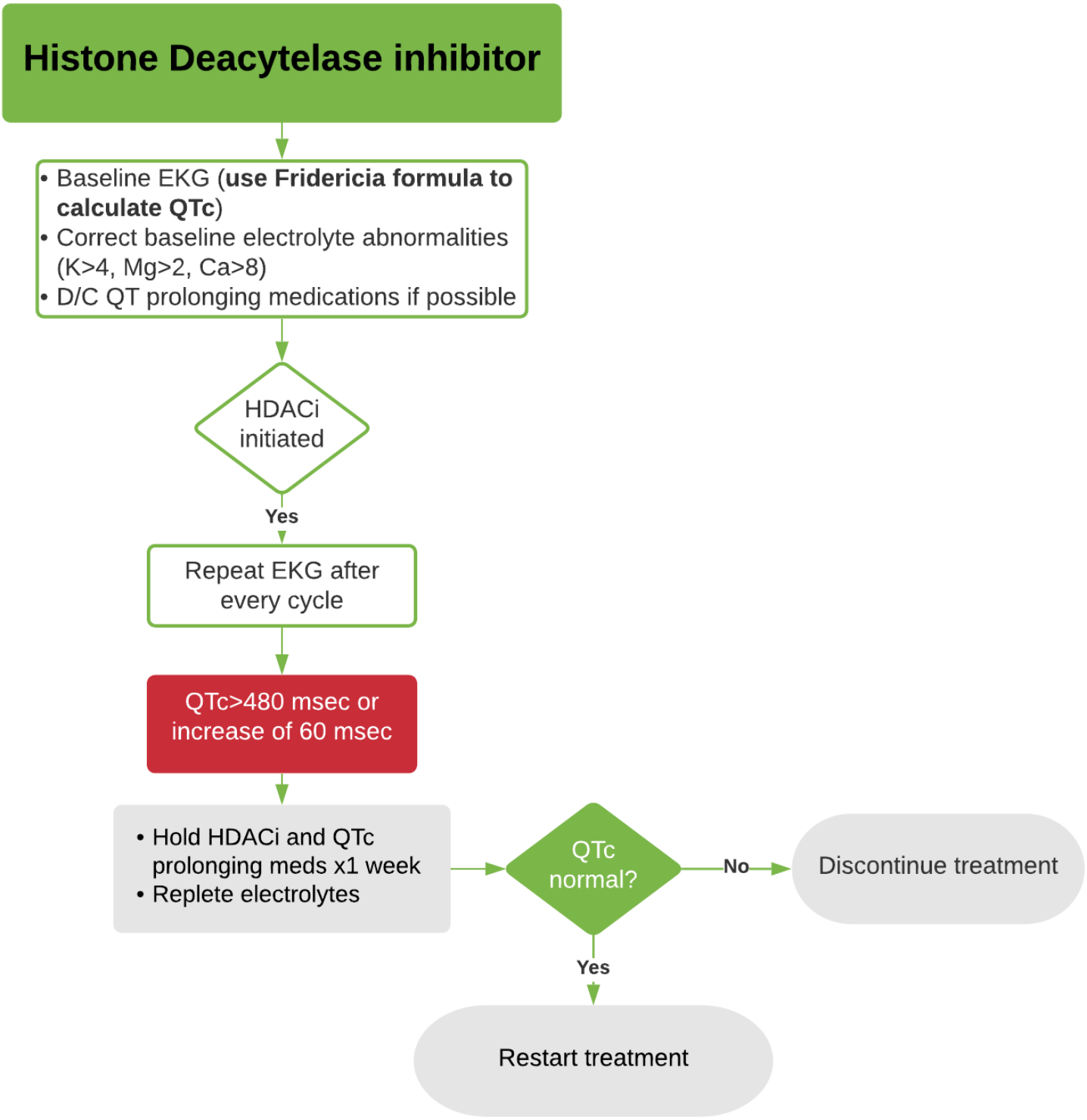
Histone Deacytelase inhibitor
• Baseline EKG (use Fridericia formula to calculate QTc)
• Correct baseline electrolyte abnormalities (K>4, Mg>2, Ca>8)
• D/C QT prolonging medications if possible
HDACi initiated
Yes
Repeat EKG after every cycle
QTc>480 msec or increase of 60 msec
• Hold HDACi and QTc prolonging meds x1 week
• Replete electrolytes
QTc normal?
No
Discontinue treatment
Yes
Restart treatment

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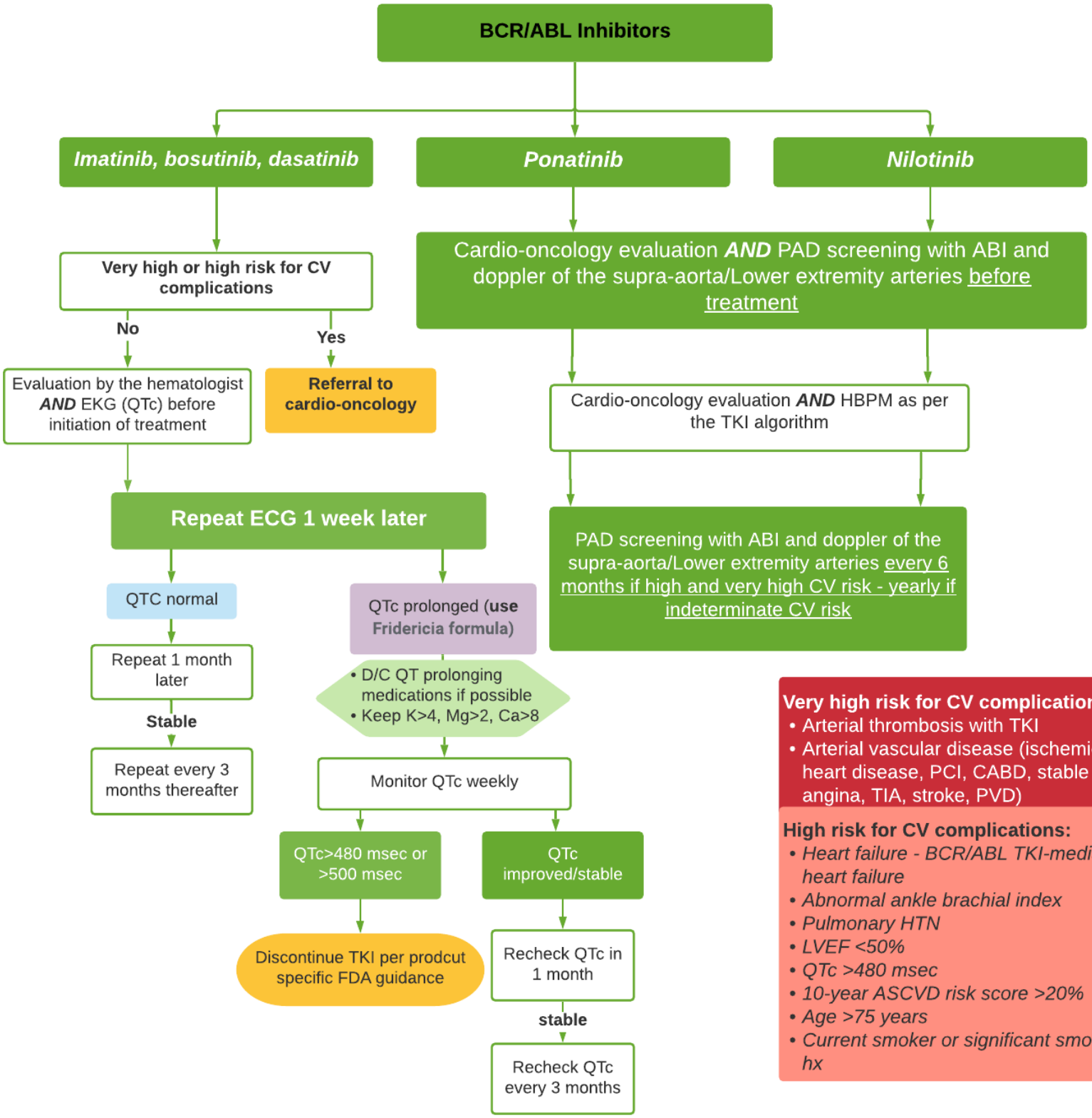

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Myocardial Ischemia

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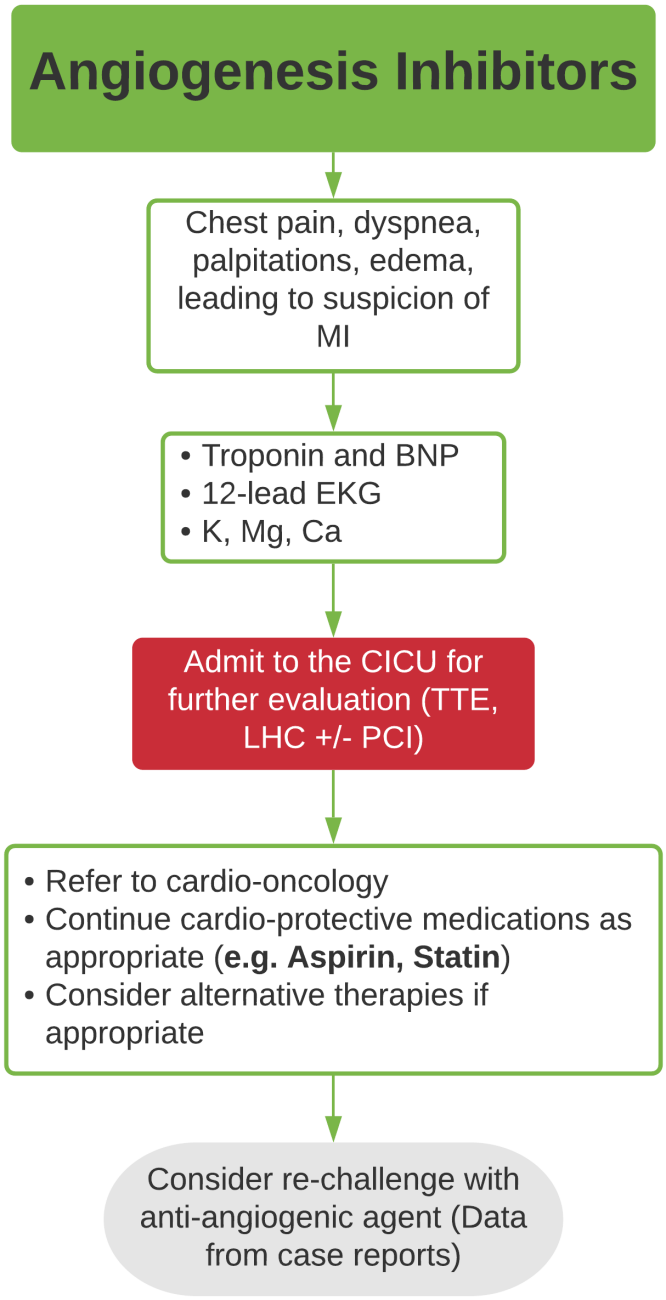

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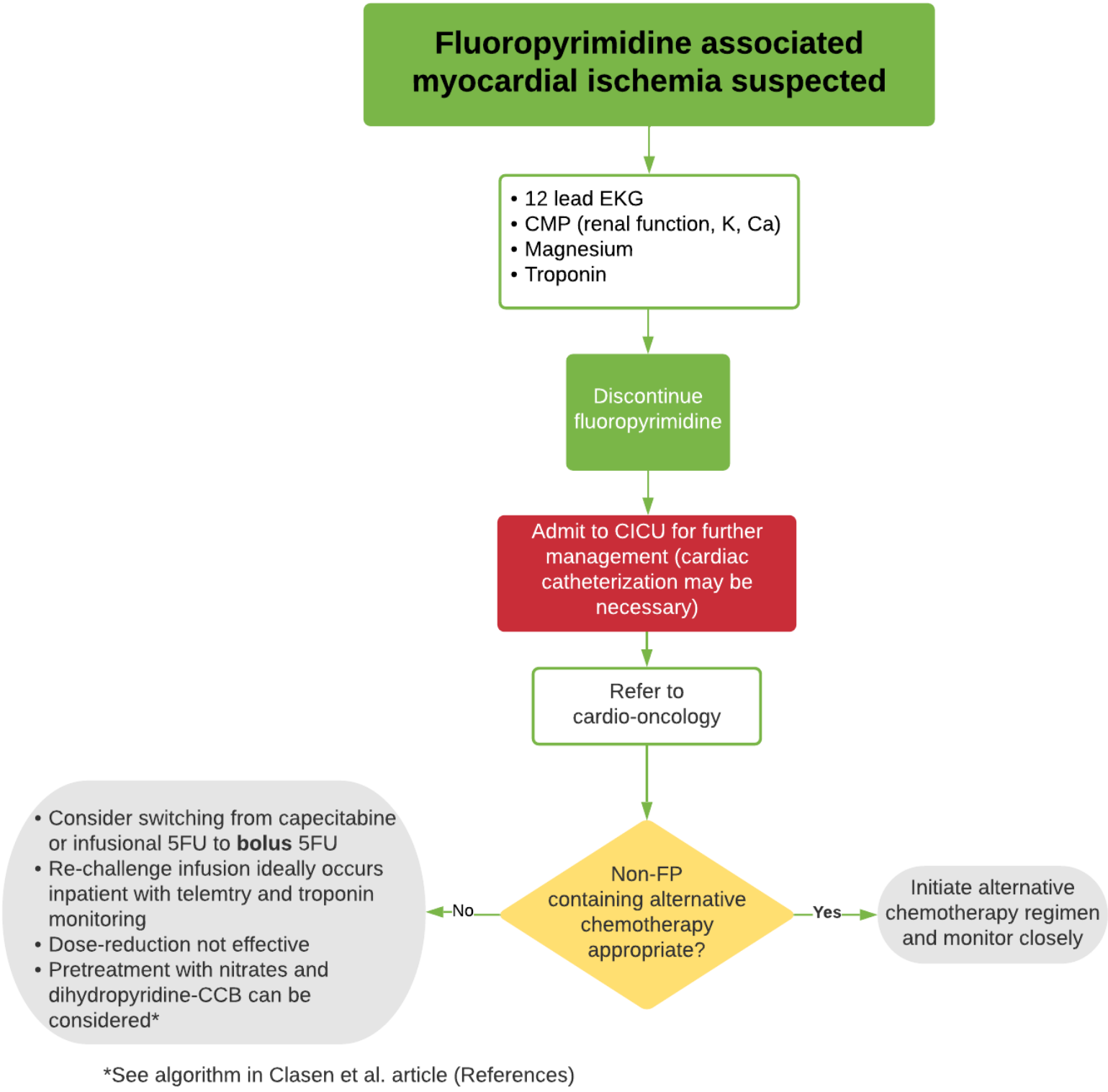

*See algorithm in Clasen et al. article (References)

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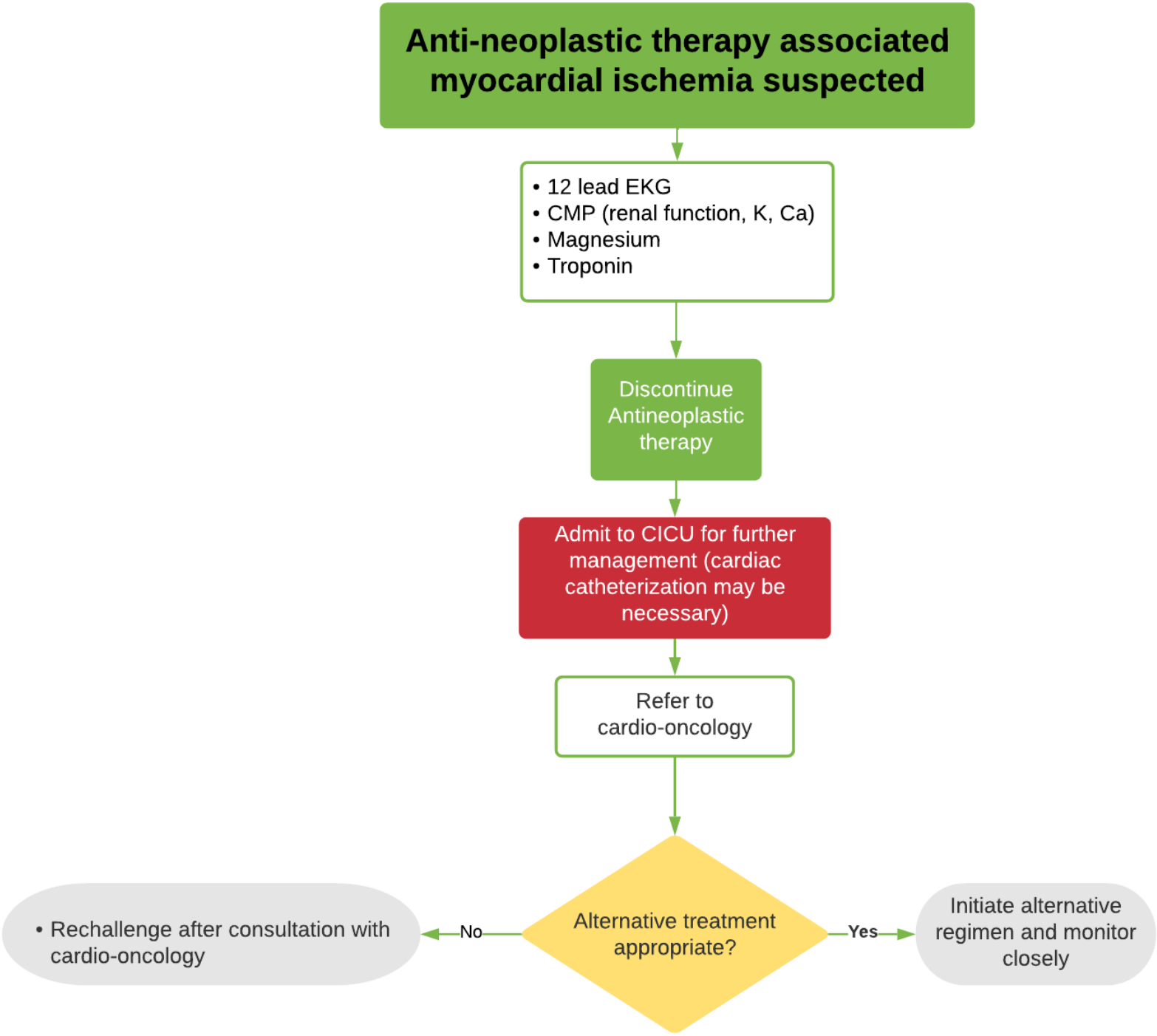

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Appendix-1

Children's Oncology Group Anthracycline Toxicity Equivalence Ratios

Anthracycline	Conversion Factor
Doxorubicin	1
Daunorubicin	1
Idarubicin	5
Epirubicin	0.67
Mitoxantrone	4

[5]

1. Le Deley MC, Leblanc T, Shamsaldin A, et al. Risk of secondary leukemia after a solid tumor in childhood according to the dose of epipodophyllotoxins and anthracyclines: A case-control study by the Société Française d'Oncologie Pédiatrique. *J Clin Oncol.* 2003;21:1074–1081.
2. Andolina JR, Dilley K. Anthracycline-induced cardiac toxicity more likely in underweight childhood cancer survivors. *J Pediatr Hematol Oncol.* 2010;32:411–415.
3. Abosoudah I, Greenberg ML, Ness KK, et al. Echocardiographic surveillance for asymptomatic late-onset anthracycline cardiomyopathy in childhood cancer survivors. *Pediatr Blood Cancer.* 2011;57:467–472.
4. Feijen EA, Leisenring WM, Stratton KL, et al. Equivalence Ratio for Daunorubicin to Doxorubicin in Relation to Late Heart Failure in Survivors of Childhood Cancer. *J Clin Oncol*. 2015;33(32):3774-3780. doi:10.1200/JCO.2015.61.5187

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References

- Chang HM, Moudgil R, Scarabelli T, Okwuosa TM, Yeh ETH. Cardiovascular Complications of Cancer Therapy: Best Practices in Diagnosis, Prevention, and Management: Part 1 [published correction appears in J Am Coll Cardiol. 2018 Feb 6;71(5):587]. J Am Coll Cardiol. 2017;70(20):2536-2551. doi:10.1016/j.jacc.2017.09.1096

- Chang, H.-M., Okwuosa, T. M., Scarabelli, T., Moudgil, R., & Yeh, E. T. (2017). Cardiovascular Complications of Cancer Therapy: Best Practices in Diagnosis, Prevention, and Management—Part 2. Journal of the American College of Cardiology, 70(20), 2552–25

- Yeh, E. T. (2016). MD Anderson Practices in Onco-Cardiology. Department of Cardiology, The University of Texas MD Anderson Cancer Center.

- Alexandre Joachim, Cautela Jennifer, Ederhy Stéphane, Damaj Ghandi Laurent, Salem Joe-Elie, Barlesi Fabrice, Farnault Laure, Charbonnier Aude, Mirabel Mariana, Champiat Stéphane, Cohen-Solal Alain, Cohen Ariel, Dolladille Charles, & Thuny Franck. (2020).

- Chari, A., & Hajje, D. (2014). Case series discussion of cardiac and vascular events following carfilzomib treatment: Possible mechanism, screening, and monitoring. BMC Cancer, 14(1), 1–9. https://doi.org/10.1186/1471-2407-14-915

- Wu, P., Oren, O., Gertz, M. A., & Yang, E. H. (2020). Proteasome Inhibitor-Related Cardiotoxicity: Mechanisms, Diagnosis, and Management. Current Oncology Reports, 22(7), 66. https://doi.org/10.1007/s11912-020-00931-w

- Dhesi, S., Chu, M. P., Blevins, G., Paterson, I., Larratt, L., Oudit, G. Y., & Kim, D. H. (2013). Cyclophosphamide-Induced Cardiomyopathy. Journal of Investigative Medicine High Impact Case Reports, 1(1). https://doi.org/10.1177/2324709613480346

- Mohammed, T., Singh, M., Tiu, J. G., & Kim, A. S. (2021). Etiology and management of hypertension in patients with cancer. Cardio-Oncology, 7(1), 14. https://doi.org/10.1186/s40959-021-00101-2

- Lyman, G. H., Carrier, M., Ay, C., Di Nisio, M., Hicks, L. K., Khorana, A. A., Leavitt, A. D., Lee, A. Y. Y., Macbeth, F., Morgan, R. L., Noble, S., Sexton, E. A., Stenehjem, D., Wiercioch, W., Kahale, L. A., & Alonso-Coello, P. (2021). American Society

- Palumbo, A. et al. Prevention of thalidomide- and lenalidomide-associated thrombosis in myeloma. Leukemia 22, 414–423 (2008).

- American Society of Hematology 2021 guidelines for management of venous thromboembolism: Prevention and treatment in patients with cancer. Blood Advances, 5(4), 927–974. https://doi.org/10.1182/bloodadvances.2020003442

- Key NS, Khorana AA, Kuderer NM, Bohlke K, Lee AYY, Arcelus JI, Wong SL, Balaban EP, Flowers CR, Francis CW, Gates LE, Kakkar AK, Levine MN, Liebman HA, Tempero MA, Lyman GH, Falanga A. Venous Thromboembolism Prophylaxis and Treatment in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol. 2020 Feb 10;38(5):496-520. doi: 10.1200/JCO.19.01461. Epub 2019 Aug 5. PMID: 31381464.

- Mirza, A.-S. et al. Validation of the Khorana score in acute myeloid leukemia patients: a single-institution experience. Thrombosis Journal 17, 13 (2019).
- Ibrutinib-Associated Cardiotoxicity. (n.d.). American College of Cardiology. Retrieved May 11, 2021, from http%3a%2f%2fwww.acc.org%2flatest-in-cardiology%2farticles%2f2020%2f01%2f21%2f08%2f46%2fibrutinib-associated-cardiotoxicity
- Fluoropyrimidine Cardiotoxicity. (n.d.). American College of Cardiology. Retrieved May 11, 2021, from http%3a%2f%2fwww.acc.org%2flatest-in-cardiology%2farticles%2f2019%2f04%2f05%2f07%2f34%2ffluoropyrimidine-cardiotoxicity
- Managing Toxicities of High-Dose Interleukin-2. (n.d.). Cancer Network. Retrieved May 11, 2021, from https://www.cancernetwork.com/view/managing-toxicities-high-dose-interleukin-2
- Diagnosis and Treatment of Immune Checkpoint Inhibitor-Associated Myocarditis and ACS. (n.d.). American College of Cardiology. Retrieved May 11, 2021, from http%3a%2f%2fwww.acc.org%2flatest-in-cardiology%2farticles%2f2020%2f10%2f30%2f15%2f06%2fdiagnosis-
- Arsenic Trioxide (TRISENOX)[package insert]. North Wales, PA:Teva Pharmaceuticals USA, Inc.
- Coppola, C., Rienzo, A., Piscopo, G., Barbieri, A., Arra, C., & Maurea, N. (2018). Management of QT prolongation induced by anti-cancer drugs: Target therapy and old agents. Different algorithms for different drugs. Cancer Treatment Reviews, 63, 135–143.
- Zhao, B., Wood, L. S., James, K., & Rini, B. I. (2015). Is It Safe to Restart Antivascular Endothelial Growth Factor Therapy in Patients with Renal Cell Carcinoma after Cardiac Ischemia? Case Reports in Oncological Medicine, 2015, e817578. https://doi.or
- Clasen SC, Ky B, O'Quinn R, Giantonio B, Teitelbaum U, Carver JR. Fluoropyrimidine-induced cardiac toxicity: challenging the current paradigm. J Gastrointest Oncol. 2017;8(6):970-979. doi:10.21037/jgo.2017.09.07
- Fluoropyrimidine Cardiotoxicity. (n.d.). American College of Cardiology. Retrieved May 11, 2021, from http%3a%2f%2fwww.acc.org%2flatest-in-cardiology%2farticles%2f2019%2f04%2f05%2f07%2f34%2ffluoropyrimidine-cardiotoxicity
- Swain, S. M., Whaley, F. S. & Ewer, M. S. Congestive heart failure in patients treated with doxorubicin. Cancer 97, 2869–2879 (2003). 1.
- Armstrong, G. T. et al. Modifiable risk factors and major cardiac events among adult survivors of childhood cancer. J Clin Oncol 31, 3673–3680 (2013).
- Cancer Therapy-Related Cardiac Dysfunction: An Overview for the Clinician. Clin Med Insights Cardiol 13, (2019).
- Joseph Bubalo, P. Ibrutinib-Related Atrial Fibrillation: An Anticoagulant Challenge. (2019).
- Waliany S, Zhu H, Wakelee H, Padda SK, Das M, Ramchandran K, Myall NJ, Chen T, Witteles RM, Neal JW. Pharmacovigilance Analysis of Cardiac Toxicities Associated With Targeted Therapies for Metastatic NSCLC. J Thorac Oncol. 2021 Aug 18:S1556-0864(21)02377-7. doi: 10.1016/j.jtho.2021.07.030. Epub ahead of print. PMID: 34418561

- Lyon AR, Dent S, Stanway S et al (2020) Baseline cardiovascular risk assessment in cancer patients scheduled to receive cardiotoxic cancer therapies: a position statement and new risk assessment tools from the Cardio-Oncology Study Group of the Heart Failure Association of the European Society of Cardiology in collaboration with the International Cardio-Oncology Society. Eur J Heart Fail 22(11):1945–1960