

Infection Care Pathway

Prevention

Prevention

[Systemic Prophylaxis](#)

Assessment

Assessment: Onset of FN

Fever:

- single oral temperature $\geq 38.5^{\circ}\text{C}$ or $\geq 38^{\circ}\text{C}$ for 1 hour or more
- single axillary temperature $\geq 38^{\circ}\text{C}$ or $\geq 37.5^{\circ}\text{C}$ for 1 hour or more

Neutropenia:

- $\text{ANC} < 0.5 \times 10^9/\text{L}$

Obtain blood cultures at onset of FN from all lumens of central venous catheters and from a peripheral vein

Obtain urinalysis and, if feasible, urine culture at onset of FN

Do not obtain chest X-ray in absence of respiratory signs or symptoms

Assessment: Prolonged FN (≥ 96 Hours of Broad-spectrum Antibacterials with Persistent or New Fever)

Obtain CT of sinuses, chest and abdomen

Do not obtain galactomannan, β -D-glucan or blood fungal PCR

Treatment

Treatment: Empiric Antibacterial Therapy

[Initial Empiric Antibacterial Therapy](#)

[Modification and Cessation of Therapy](#)

Treatment: Empiric Antifungal Therapy

Use caspofungin

Infection Care Pathway

PJP Prophylaxis

Give PJP prophylaxis to all patients except those with/receiving:

- APL
- vinblastine monotherapy
- targeted oral agents such as temozolomide or dabrafenib
- radiation only

Able to tolerate
sulfamethoxazole-
trimethoprim

Unable to tolerate
sulfamethoxazole-
trimethoprim

Use sulfamethoxazole-
trimethoprim PO twice daily
on Saturdays and Sundays

LFTs increased, bone
marrow suppression,
unable to take PO
medicine or vomiting

G6PD deficiency, rash,
anaphylaxis or
methemoglobinemia

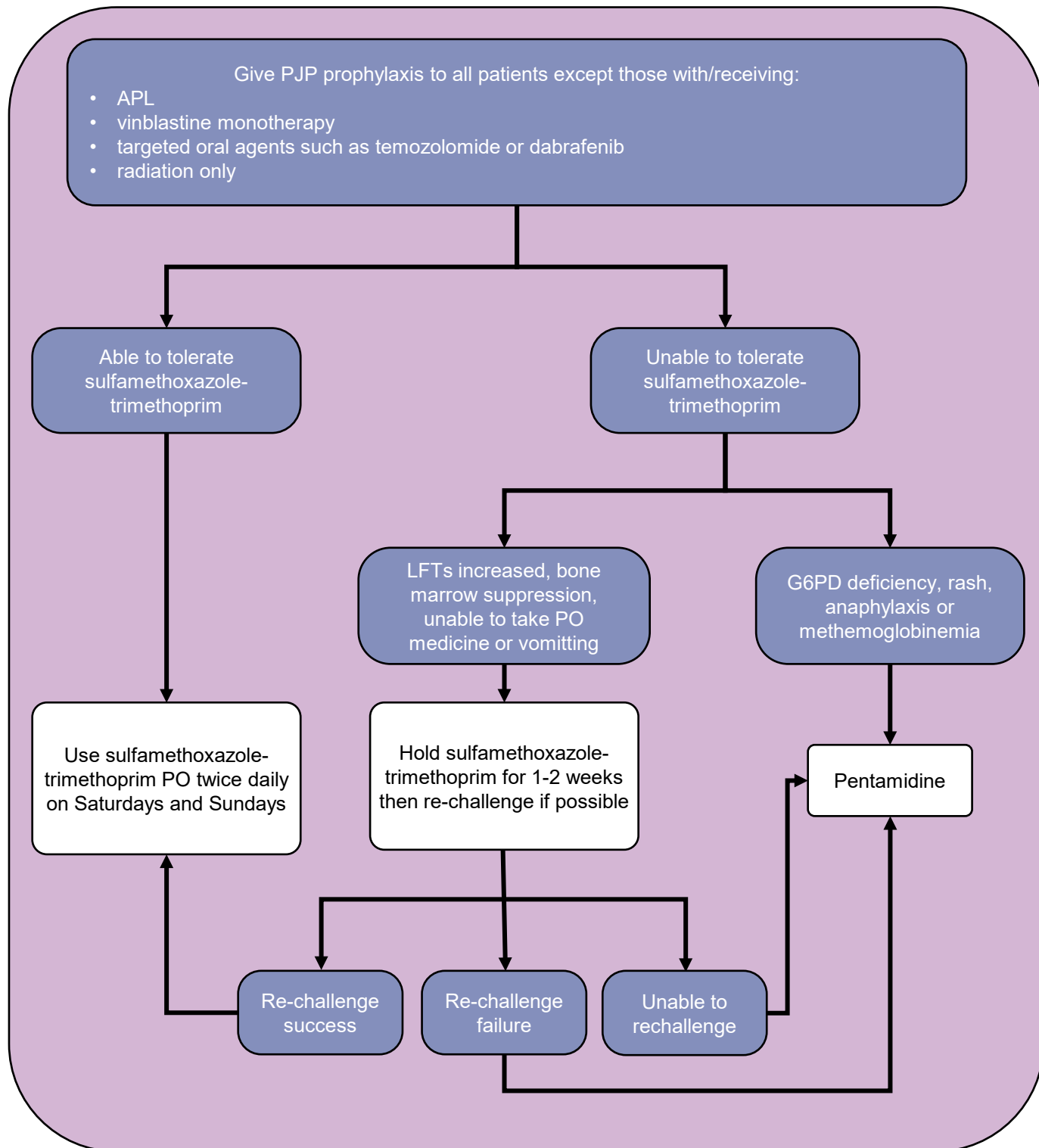
Hold sulfamethoxazole-
trimethoprim for 1-2 weeks
then re-challenge if possible

Pentamidine

Re-challenge
success

Re-challenge
failure

Unable to
rechallenge



Infection Care Pathway

Systemic Antibacterial and Antifungal Prophylaxis

[PJP Prophylaxis](#)

Start levofloxacin (antibacterial prophylaxis) or caspofungin (antifungal prophylaxis) according to the table below:

Diagnosis	Agent(s)	Protocol*	Treatment Block	Discontinuation
AML except APL	Levofloxacin and caspofungin	All protocols except APL	All blocks starting on the day after the completion of chemotherapy	ANC at least $0.2 \times 10^9/L$ post nadir
ALL	Levofloxacin	AALL1732	Delayed Intensification when the ANC is less than $0.5 \times 10^9/L$	ANC at least $0.5 \times 10^9/L$ post nadir
Ph+ ALL	Levofloxacin	AALL1631	Induction A and B, DI 1 and 2 when the ANC is less than $0.5 \times 10^9/L$	ANC at least $0.5 \times 10^9/L$ post nadir
	Levofloxacin and caspofungin	AALL1631	Consolidation 1, 2 and 3 when the ANC is less than $0.5 \times 10^9/L$	ANC at least $0.5 \times 10^9/L$ post nadir
Infant ALL	Levofloxacin and caspofungin	All protocols	All blocks before maintenance when the ANC is less than $0.5 \times 10^9/L$	ANC at least $0.5 \times 10^9/L$ post nadir
Relapsed ALL	Levofloxacin	AALL1821	VXLD reinduction when the ANC is less than $0.5 \times 10^9/L$	ANC at least $0.5 \times 10^9/L$ post nadir
	Levofloxacin	AALL1331	Blocks 1,2 and 3 when the ANC is less than $0.5 \times 10^9/L$	ANC at least $0.5 \times 10^9/L$ post nadir

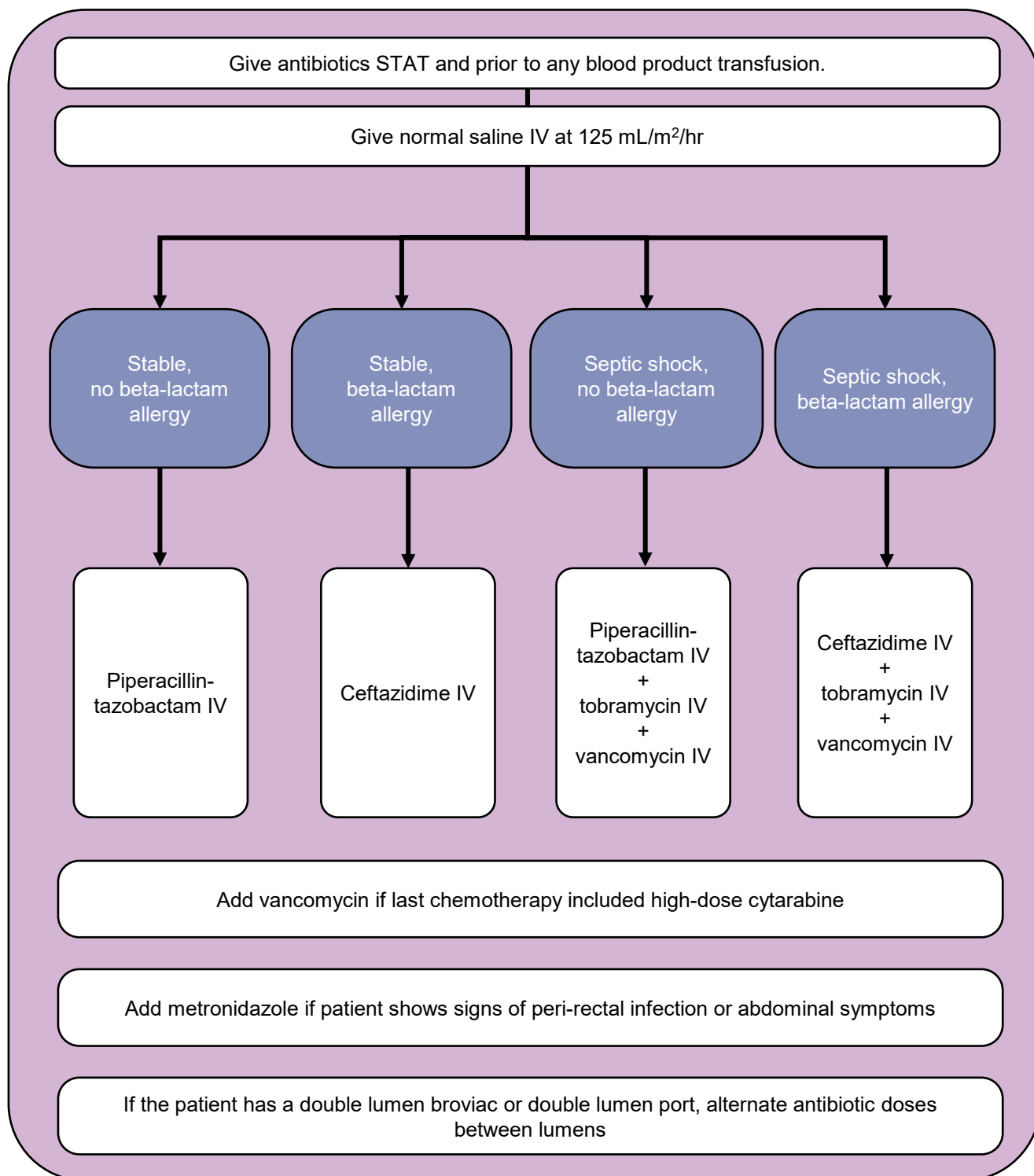
*Unless dictated otherwise by treatment protocol

When empiric antibacterial therapy (e.g. [onset of FN](#)) is initiated, hold levofloxacin and resume if still neutropenic post completion of empiric therapy

When empiric antifungal therapy (e.g. [prolonged FN](#)) is required, continue caspofungin and assess need for alternate antifungals

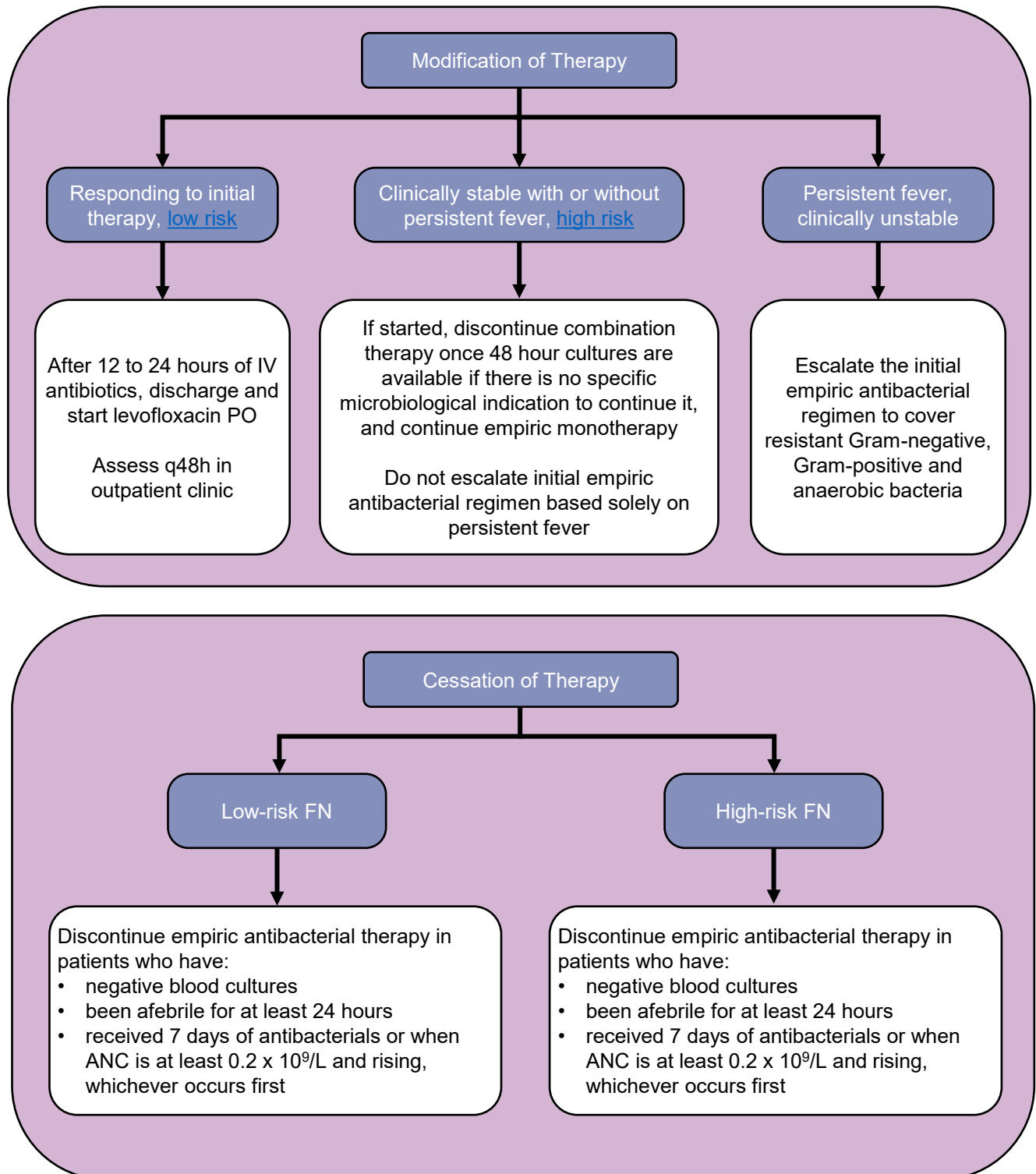
Infection Care Pathway

Initial Empiric Antibacterial Therapy



Infection Care Pathway

Modification and Cessation of Therapy



Infection Care Pathway

Risk Stratification: FN

High-risk FN

- history of overwhelming sepsis within the previous 6 months
- age < 12 months
- Down syndrome
- HSCT patient within 6 months of transplant and/or receiving immunosuppressants
- diagnosis of:
 - AML
 - Burkitt lymphoma or leukemia
 - ALL in induction or delayed intensification
 - advanced stage ALCL
 - stage 4 neuroblastoma
 - relapsed leukemia or
 - progressive/relapsed malignancy with bone marrow involvement
- presents with any one or more of the following:
 - sepsis syndrome
 - hypotension
 - tachypnea, hypoxia or new infiltrates on chest X-ray
 - altered mental status
 - severe mucositis
 - vomiting
 - abdominal pain
 - evidence of significant local infection (e.g. tunnel infection, peri-rectal abscess, cellulitis)

Low-risk FN

No high risk factors

[Initial Empiric Antibacterial Therapy](#)

Infection Care Pathway

Prevention

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[Systemic Antibacterial and Antifungal Prophylaxis](#)

[PJP Prophylaxis](#)

Assessment

Assessment: Onset of FN

Fever:

- single oral temperature $\geq 38.3^{\circ}\text{C}$ or $\geq 38^{\circ}\text{C}$ for 1 hour or more
- single axillary temperature $\geq 37.8^{\circ}\text{C}$ or $\geq 37.5^{\circ}\text{C}$ for 1 hour or more

Neutropenia:

- $\text{ANC} < 0.5 \times 10^9 / \text{L}$

Obtain aerobic blood cultures from all lumens of indwelling venous lines and peripheral blood cultures

Obtain midstream clean catch urine culture

Obtain nasopharyngeal swab for respiratory virus panel if symptomatic

Do not obtain chest X-ray in absence of respiratory signs or symptoms

Assessment: Prolonged FN (≥ 5 days Fever and Broad-spectrum Antibiotics)

Obtain CT of chest

Obtain abdominal ultrasound

Obtain CT of sinuses only if there are local signs or symptoms

Only obtain serum galactomannan in consultation with ID

Do not obtain β -D-glucan or blood fungal PCR

Treatment

Treatment: Empiric Antibacterial Therapy

[Initial Empiric Antibacterial Therapy](#)

[Continuation of Therapy](#)

[Cessation of Therapy](#)

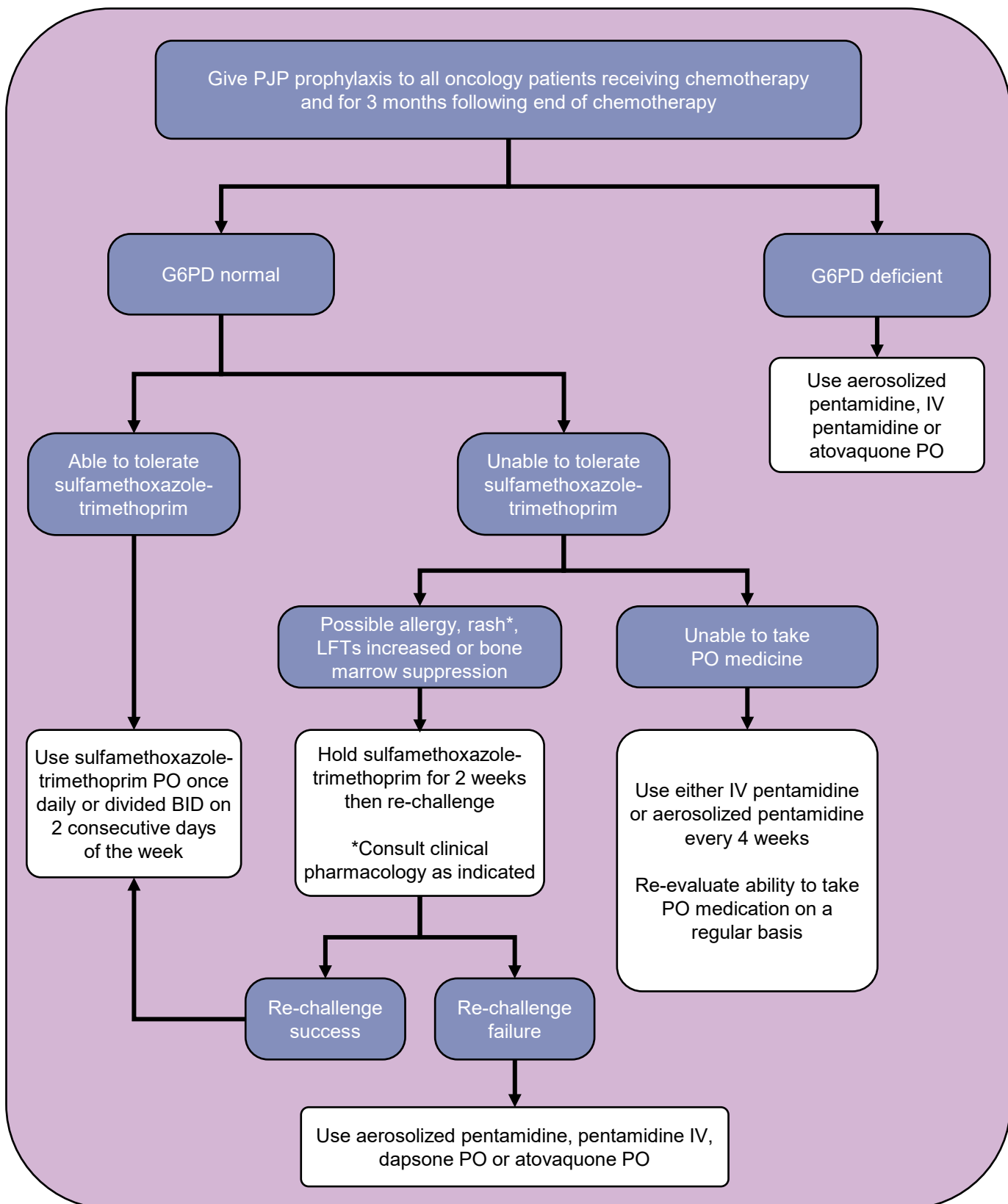
Do not remove the central venous line routinely as part of initial empiric management of FN

Treatment: Empiric Antifungal Therapy

Use caspofungin

Infection Care Pathway

PJP Prophylaxis



Infection Care Pathway

Systemic Antibacterial and Antifungal Prophylaxis

For diagnoses listed in the table below, start levofloxacin (antibacterial prophylaxis) and caspofungin (antifungal prophylaxis):

- For patients with newly diagnosed disease or at relapse – start levofloxacin and caspofungin immediately with the start of chemotherapy
- For patients in other phases who are in remission – start levofloxacin and caspofungin when the ANC < 0.5 x 10⁹/L

Diagnosis	Protocol	Treatment Block
AML (including Down syndrome) <ul style="list-style-type: none"> Upfront AML except APML Relapsed AML 	All protocols	All blocks
Relapsed ALL	AALL 1331	Reinduction Blocks 1-3 (not during blinatumomab blocks if receiving in lieu of Blocks 2 & 3, while admitted only)
Down syndrome ALL or lymphoblastic lymphoma (LLy)	AALL 1731	Induction, consolidation, interim maintenance and delayed intensification
Burkitt lymphoma – Group C	ANHL 1131	Not during R-CYVE2 or maintenance
Burkitt lymphoma – Group B	ANHL 1131	COPADM blocks only
Infant ALL	AALL 15P1	Induction, interim maintenance and delayed intensification
Ph+ ALL	AALL 1631	Consolidation, double delayed intensification

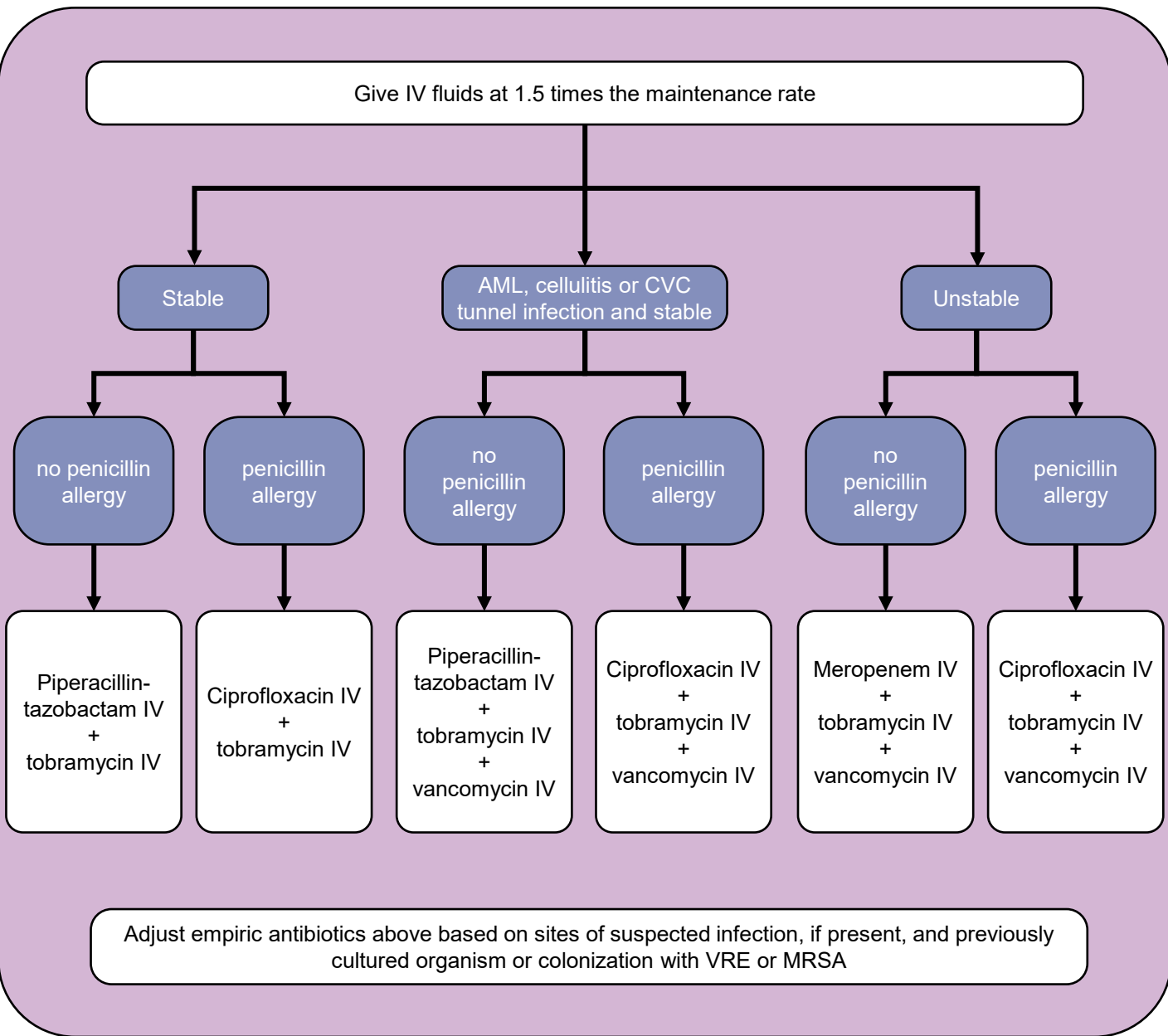
Discontinue levofloxacin and caspofungin when ANC ≥ 0.3 x 10⁹/L post nadir for 2 consecutive days

When empiric antibacterial therapy (e.g. [onset of FN](#)) is initiated, hold levofloxacin and resume if still neutropenic post completion of empiric therapy

When empiric antifungal therapy (e.g. [prolonged FN](#)) is required, continue caspofungin and assess need for alternate antifungals

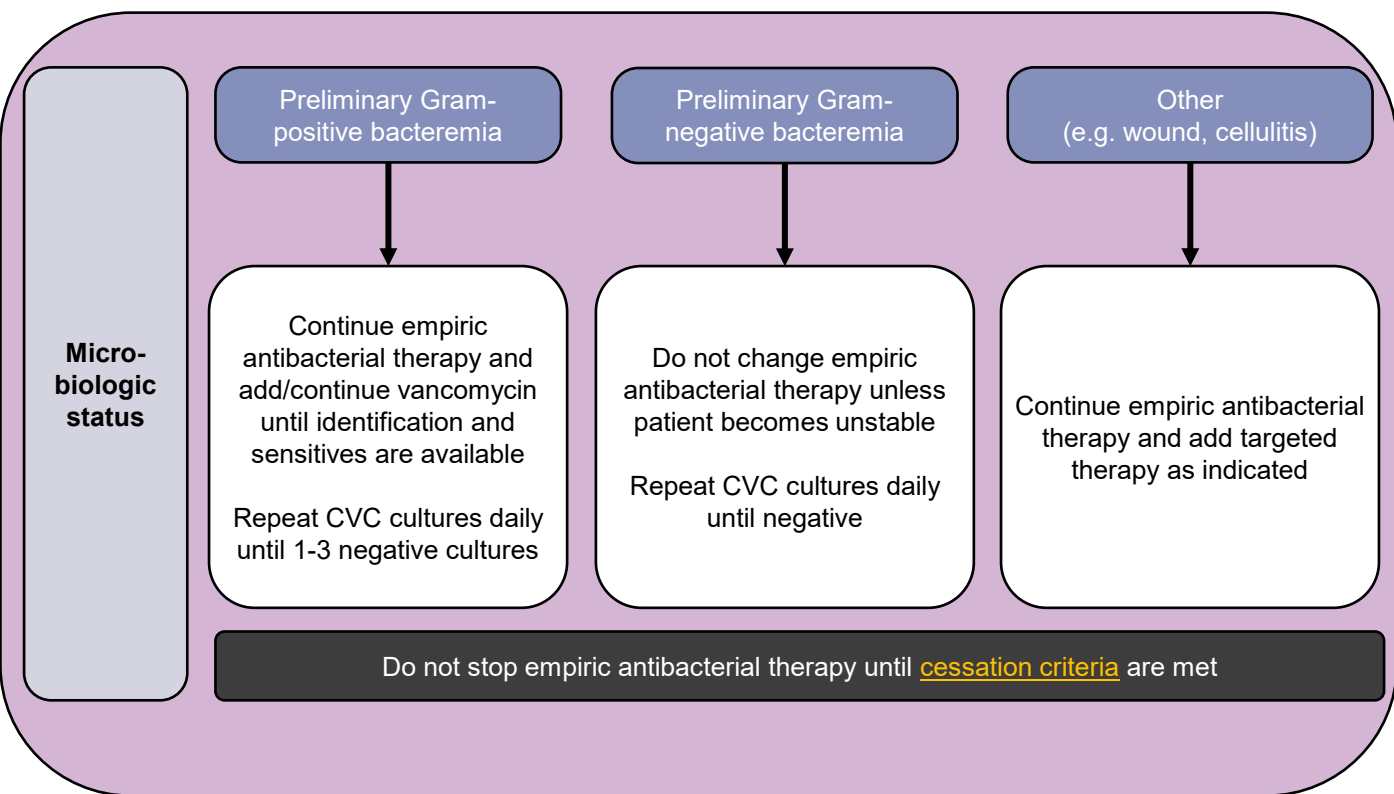
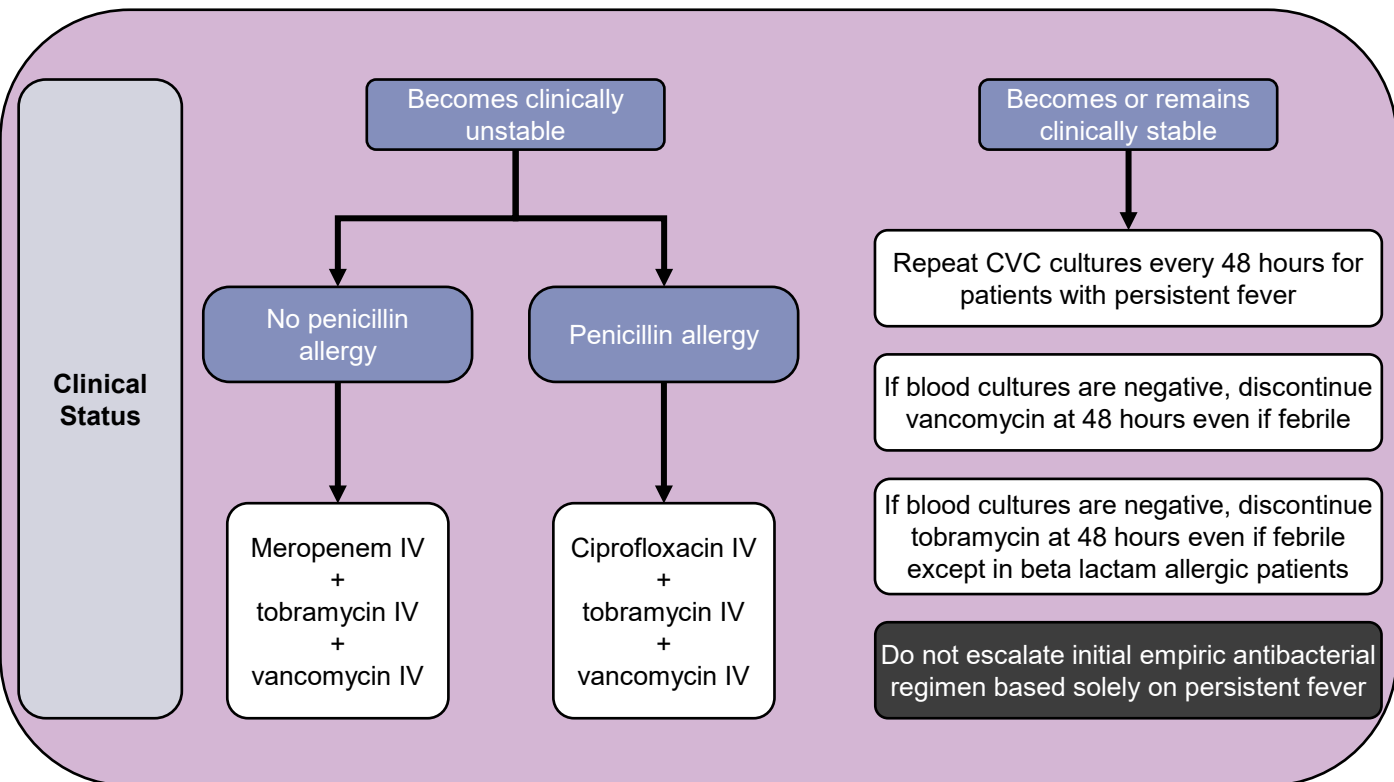
Infection Care Pathway

Initial Empiric Antibacterial Therapy



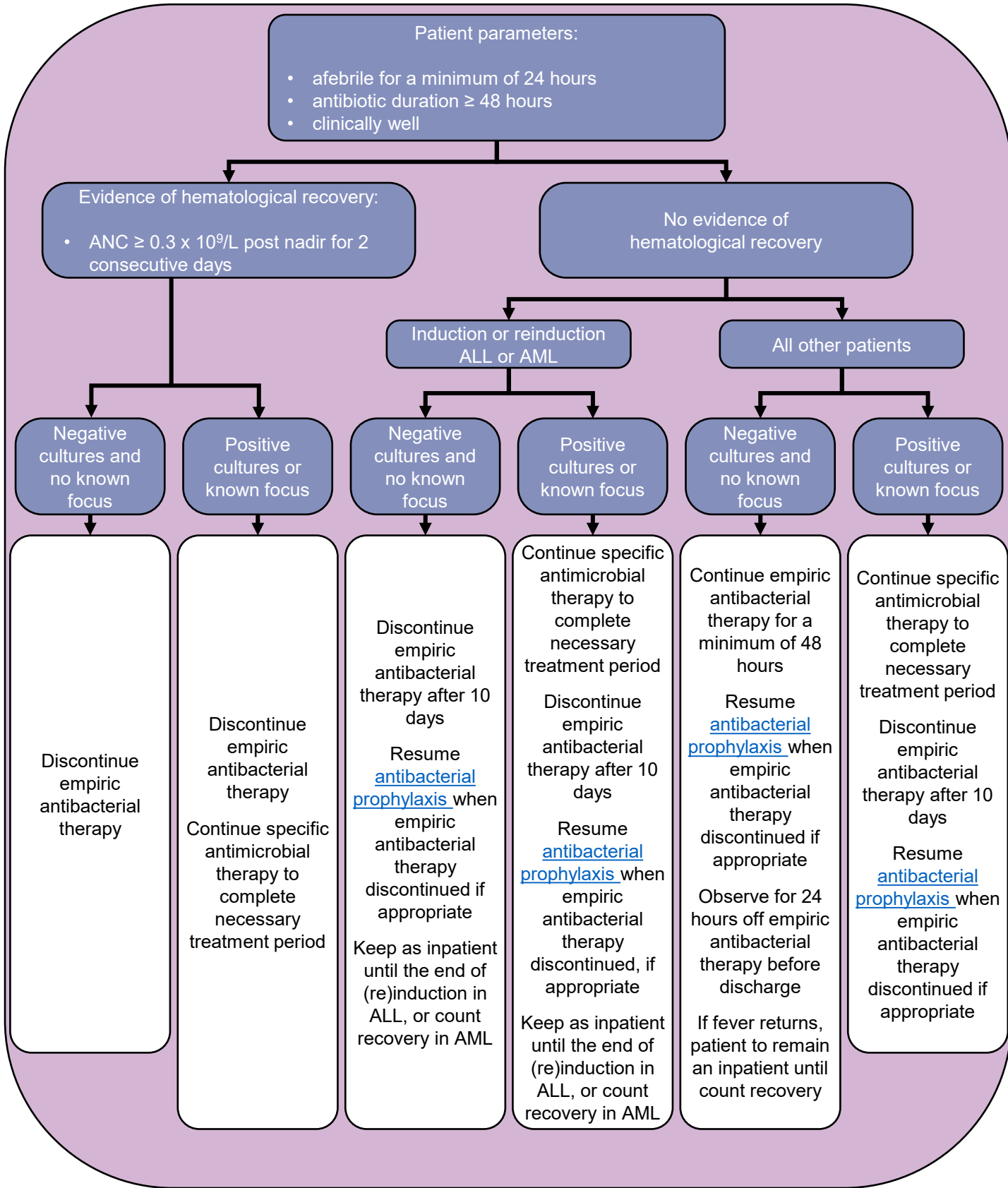
Infection Care Pathway

Continuation of Therapy

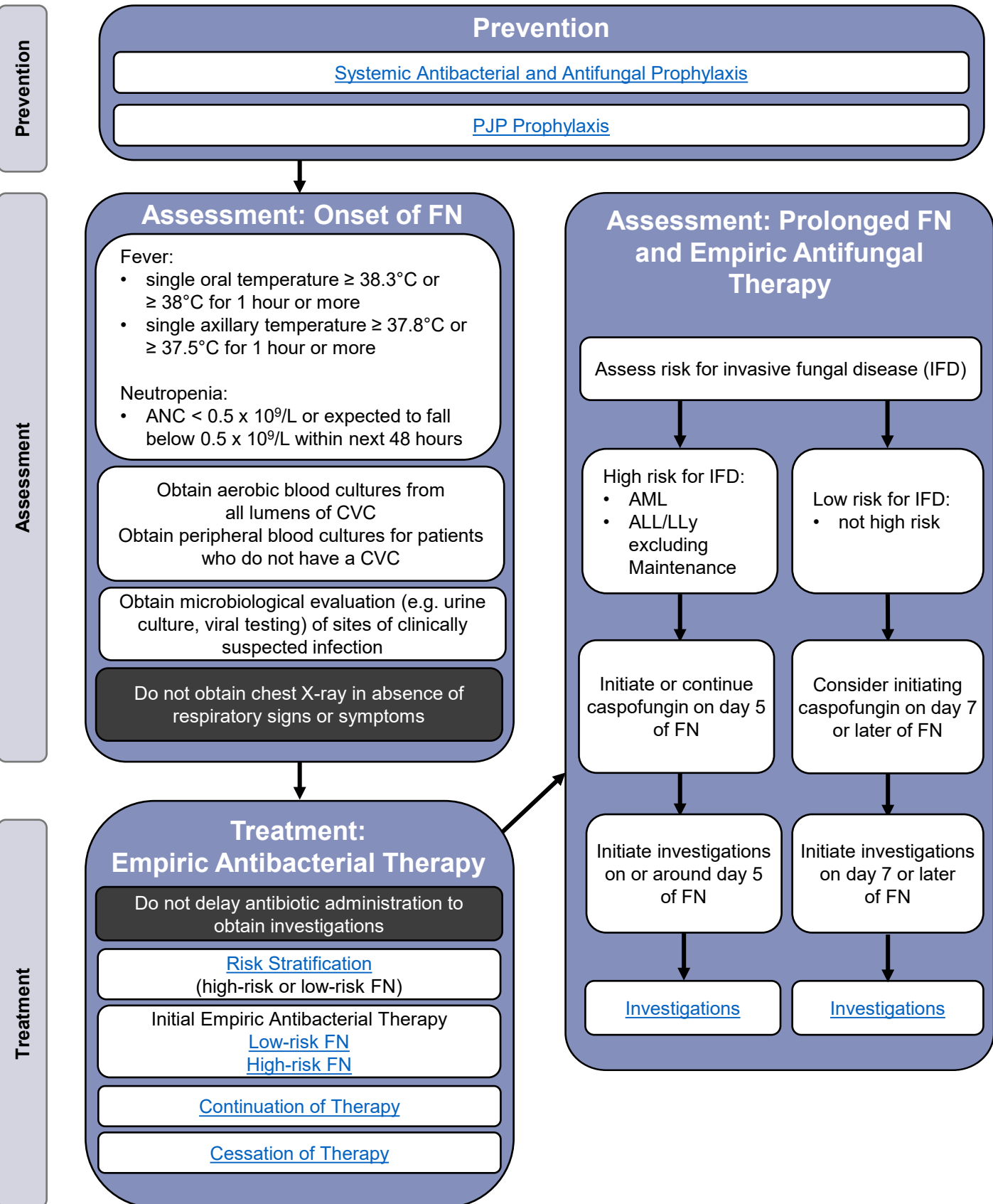


Infection Care Pathway

Cessation of Therapy



Infection Care Pathway: Oncology



Infection Care Pathway: Oncology

PJP Prophylaxis

Give PJP prophylaxis to patients who:

- are undergoing treatment for ALL or AML
- are undergoing treatment for other cancers where steroids are given in moderate to high doses, defined as > 20 mg/day of prednisone or equivalent for periods longer than 4 weeks
- have an underlying primary immunodeficiency

G6PD normal

G6PD deficient

Use aerosolized pentamidine, IV pentamidine or atovaquone

Able to tolerate sulfamethoxazole-trimethoprim

Unable to tolerate sulfamethoxazole-trimethoprim

Possible allergy, rash, LFTs increased or bone marrow suppression

Unable to take PO medicine

Use sulfamethoxazole-trimethoprim PO once daily on 2 consecutive days of the week

Hold sulfamethoxazole-trimethoprim for 2 weeks then re-challenge

For age < 5 years, use IV pentamidine every 2 weeks

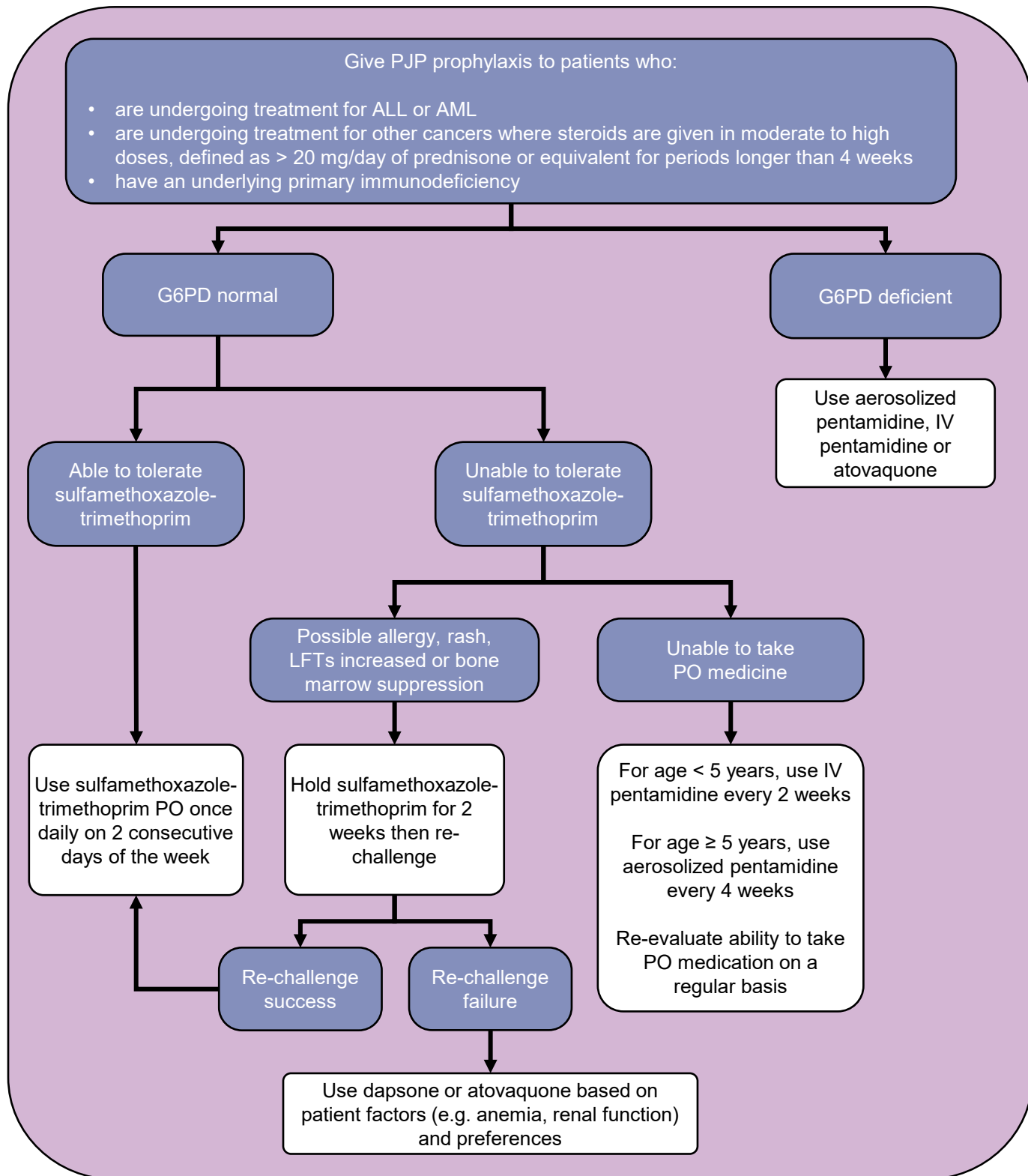
For age ≥ 5 years, use aerosolized pentamidine every 4 weeks

Re-evaluate ability to take PO medication on a regular basis

Re-challenge success

Re-challenge failure

Use dapsone or atovaquone based on patient factors (e.g. anemia, renal function) and preferences



Infection Care Pathway: Oncology

Systemic Antibacterial and Antifungal Prophylaxis

Start levofloxacin (antibacterial prophylaxis) and caspofungin (antifungal prophylaxis) on day 5 of each block of systemic chemotherapy (initiation may be deferred until $ANC < 0.5 \times 10^9/L$) for patients receiving the following therapy:

Diagnosis	Protocol/SOC	Treatment Block
AML (including Down syndrome) • Upfront AML except APL • Relapsed AML	All protocols	All blocks
Down syndrome ALL or lymphoblastic lymphoma (LLy)	SOC SR B-ALL AALL 1731 (SR or LLy)	Induction, Delayed Intensification
	SOC HR B-ALL AALL 1731 (DS-high) SOC T and Advanced B LLy	Induction, Consolidation, Delayed Intensification
Infant ALL	SOC Infant ALL	Induction, Interim Maintenance Part 2
Relapsed ALL	SOC Relapsed ALL	Induction and post-Induction, intensive, non-blinatumomab blocks
Ph+ ALL	SOC Ph+ ALL	Consolidation block 1, 2, 3
	AALL 1631	SR Arm A or HR Consolidation block 1, 2, 3

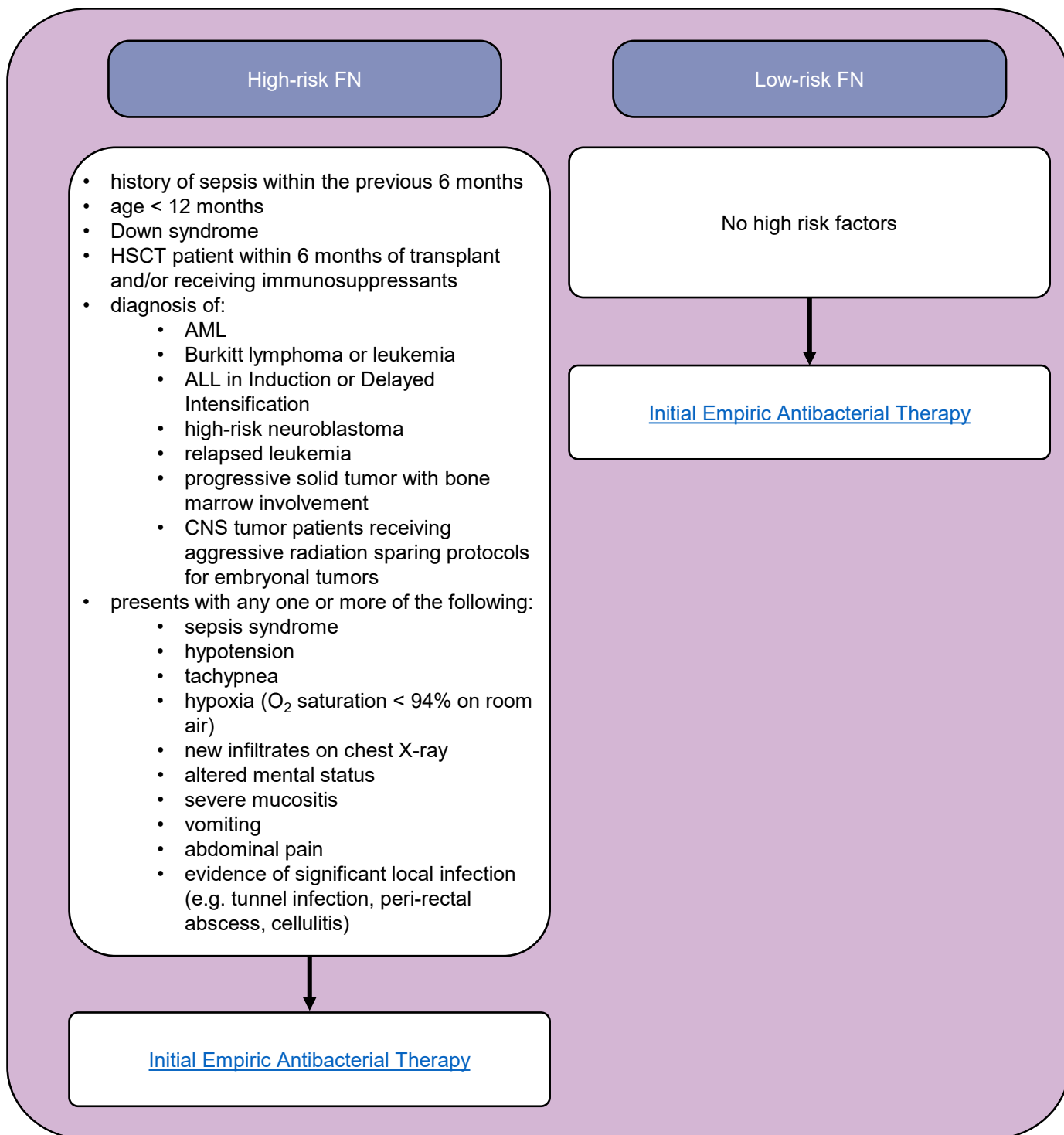
Discontinue levofloxacin and caspofungin when $ANC \geq 0.1 \times 10^9/L$ post nadir

When empiric antibacterial therapy (e.g. [onset of FN](#)) is initiated, hold levofloxacin and resume if still neutropenic post completion of empiric therapy

When empiric antifungal therapy (e.g. [prolonged FN](#)) is required, continue caspofungin and assess need for alternate antifungals

Infection Care Pathway: Oncology

Risk Stratification: Initial Onset of FN



Infection Care Pathway: Oncology

Initial Empiric Antibacterial Therapy

Low-risk FN

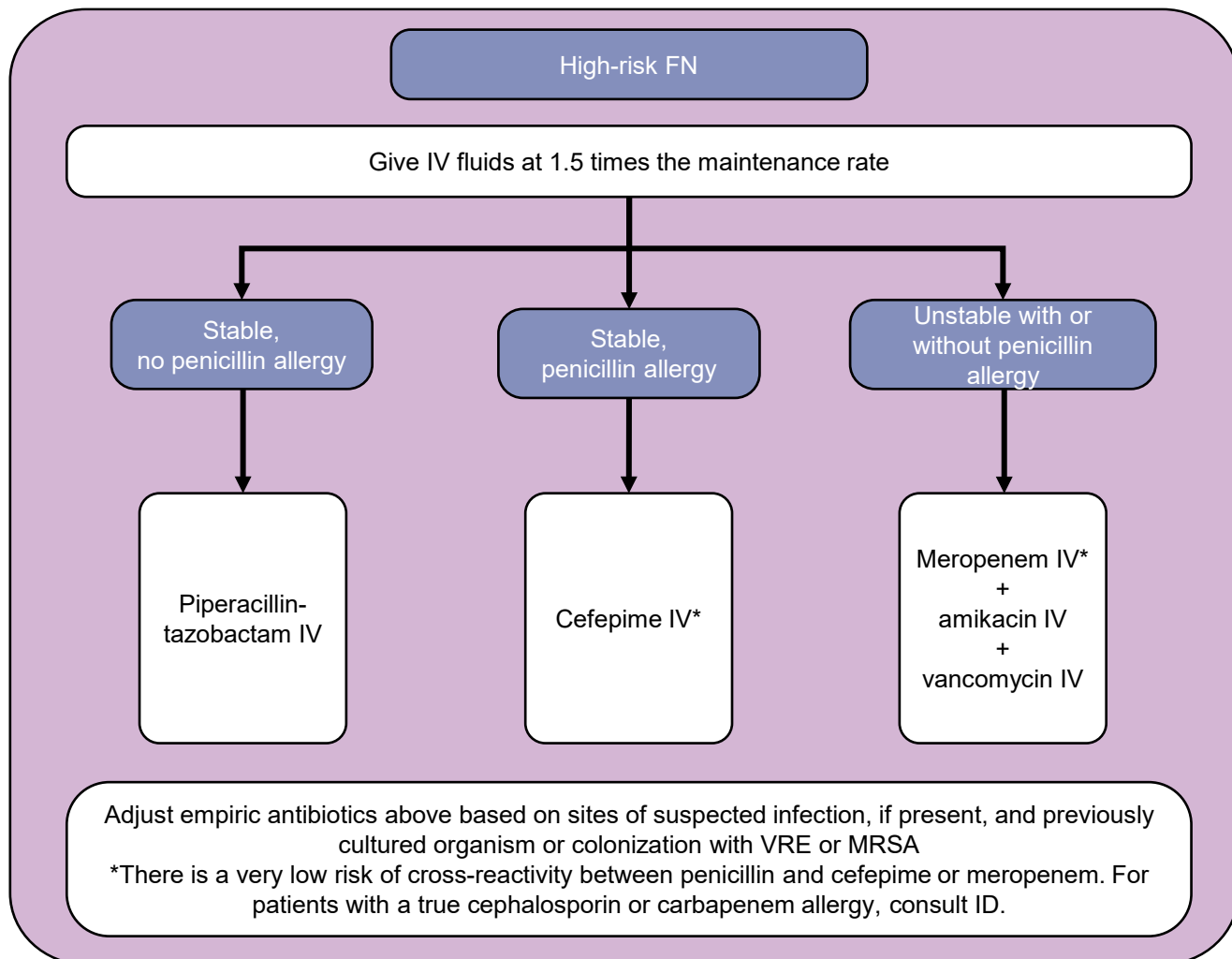
Use initial or step-down outpatient management if appropriate If admitted, give IV fluids at 1.5 times the maintenance rate

Levofloxacin PO or IV



Infection Care Pathway: Oncology

Initial Empiric Antibacterial Therapy



Infection Care Pathway: Oncology

Continuation of Therapy

Clinical Status

Becomes clinically unstable

Meropenem IV*
+
amikacin IV
+
vancomycin IV

Becomes clinically stable

Redraw CVC cultures only once at 24 to 36 hours for patients with persistent fever and negative initial blood culture (two sets of blood cultures within first 48 hours). Repeat blood cultures only if there is a clinical status change (e.g. hypotension).

For patients who were initially unstable, step down to [regimen for stable inpatients](#) at 48 hours

Do not modify initial empiric antibacterial regimen based solely on persistent fever

Evaluate for evolving infection at specific sites

Microbiologic status

Preliminary Gram-positive bacteremia

Continue empiric antibacterial therapy and add vancomycin until identification and sensitivities are available

Repeat CVC cultures daily until negative

Preliminary Gram-negative bacteremia

Continue empiric antibacterial therapy and consider adding amikacin if any clinical concerns until sensitivities are available

Repeat CVC cultures daily until negative

Other
(e.g. wound, cellulitis)

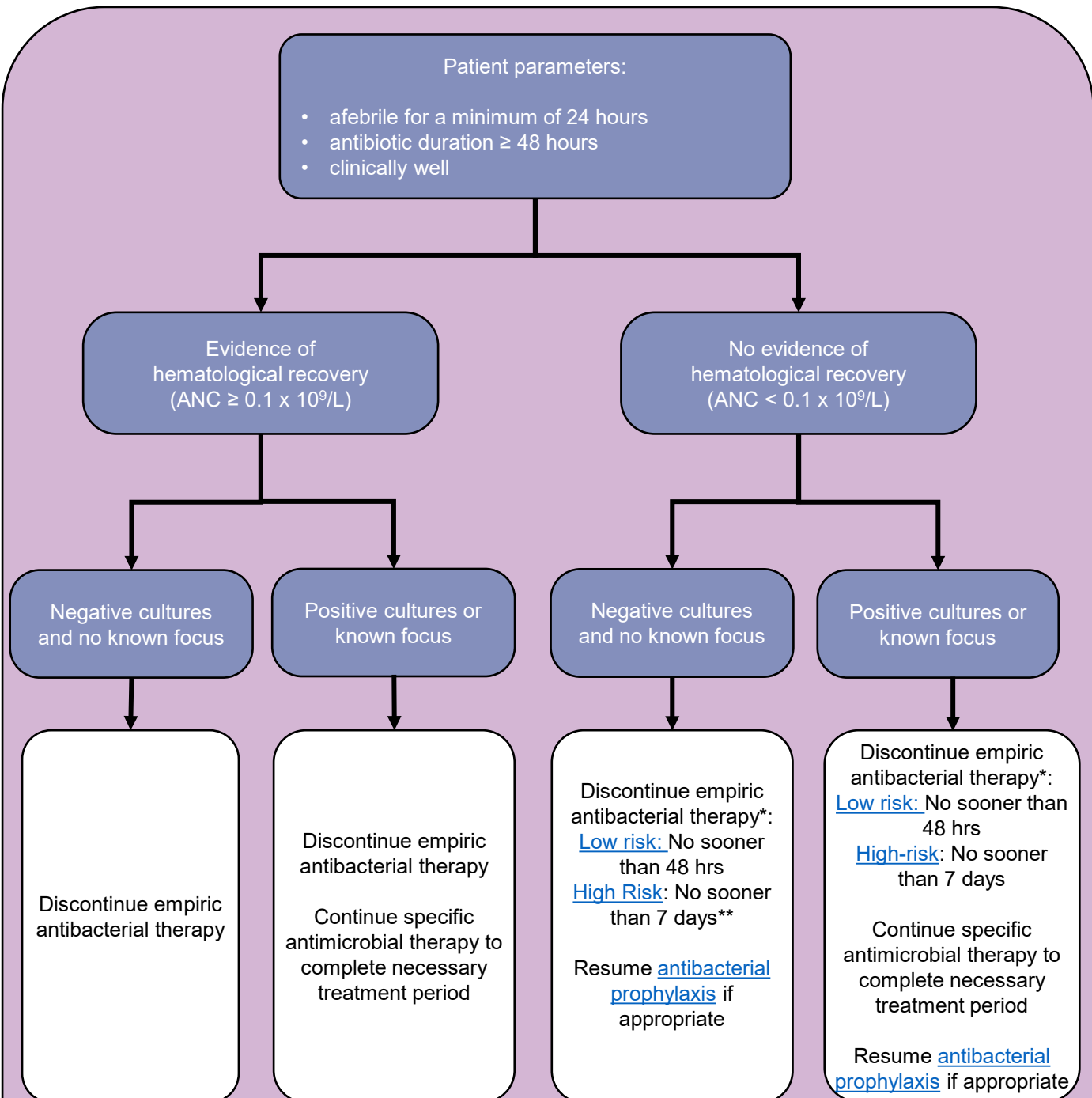
Continue empiric antibacterial therapy and add targeted therapy as indicated

Do not stop empiric antibacterial therapy until [cessation criteria](#) are met

* For patients with penicillin allergy, there is a very low risk of cross-reactivity between penicillin and meropenem. For patients with a true carbapenem allergy, consult ID.

Infection Care Pathway: Oncology

Cessation of Therapy



*Administration of empiric antibacterials for longer than 14 days may entail a risk of drug toxicity and superinfection with fungi or drug-resistant bacteria

**HSCT patients: Consider discontinuing antibiotics after 48 hours if levofloxacin prophylaxis to be resumed

Infection Care Pathway: Oncology

Investigations: Prolonged FN

Obtain chest CT

Obtain abdominal ultrasound

If there is any suspicion of IFI of the sinonasal area, obtain sinus CT in children aged 2 years and older and consider ENT consult

If there is any suspicion of pulmonary IFD:

- obtain serum galactomannan
- consider BAL with galactomannan

For other clinically suspected sites of IFD, obtain imaging and consider sampling where feasible

Do not obtain β -D-glucan or blood fungal PCR