

Quick Reference Card

DIFFERENTIATION SYNDROME (DS)

HIGH-RISK PATIENTS – Patients on targeted AML therapy

Common Agents

1. **IDH inhibitors:** Ivosidenib, Enasidenib (14-19%)
 2. **Menin inhibitors:** Revumenib, Ziftomenib* (24-47%)
 3. **FLT3 inhibitors:** Gilteritinib, Quizartinib (less common: 3-5%)
- *Pending FDA approval

Diagnosis: 2 or more symptoms required

➤ 7 KEY DIAGNOSTIC CRITERIA & FREQUENCY OF SYMPTOMS

1. Dyspnea/Hypoxia	Shortness of breath, low O2 saturation (25.8%)
2. Pulmonary Infiltrates/Effusions	Imaging or clinical findings (22.6%)
3. Edema/Weight Gain	Peripheral edema, rapid weight gain (22.6%)
4. Fever	Unexplained temperature elevation (19.4%)
5. Acute Renal Failure	Rising creatinine (6.5%)
6. Unexplained Leukocytosis	WBC >10,000 cell/L (common)
7. Rash/Lymphadenopathy	More common with IDH inhibitors (3.2%)

Severity	Grading
Indeterminate	2 signs/symptoms present
Moderate	3-4 signs/symptoms present
Severe	5 signs/symptoms present

➤ Next steps upon confirmation of suspected DS

1. Notify oncology team immediately- patients need evaluation TODAY!
2. Consider preparing for admission- Many patients require hospitalization.
3. Anticipate dexamethasone order: IV or PO for a minimum of 3 days.
4. Do not stop targeted therapy without oncology consultation. Recommendations for holding vary on agent.

Early Recognition Saves Lives!

- When in doubt, escalate to the oncology team!
- **Dyspnea is a common presenting symptom in AML, often attributable to anemia. A thorough medication review is essential to distinguish anemia-related symptoms from those associated with differentiation syndrome.**
- A single sign or symptom is insufficient for diagnosis; assessment should focus on patterns of presentation.
- Prompt dexamethasone initiation is key to successful DS management.