JADPRO Clinical Case Series

Case Studies in Myeloid Disorders: The Advanced Practitioner's Role in Patient Management

PRESENTER

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Objectives

- Understand changes in the treatment landscape of patients with myeloid disorders
- Discuss role of advanced practitioners (APs) in the management of these patients
- Review case studies to understand treatment decision-making in myeloid diseases for a multidisciplinary team approach

Case 1:
Myelodysplastic Syndrome

Case 1: Introduction to Mr. Richards

Diagnosed with macrocytic anemia

- Normal B_{12}, folic acid
- Referral to hematologist
- Bone marrow biopsy reveals low-risk MDS, diploid karyotype
- Low symptom burden

Laboratory Values in 2016 for Mr. Richards

Laboratory Parameters	Values in 2016
Serum EPO	5 mIU/mL
WBC	Normal
Platelets	Normal
Hemoglobin	9.2 g/dL

EPO, erythropoietin; MDS, myelodysplastic syndrome; WBC, white blood cells

Case 1: Becomes Symptomatic

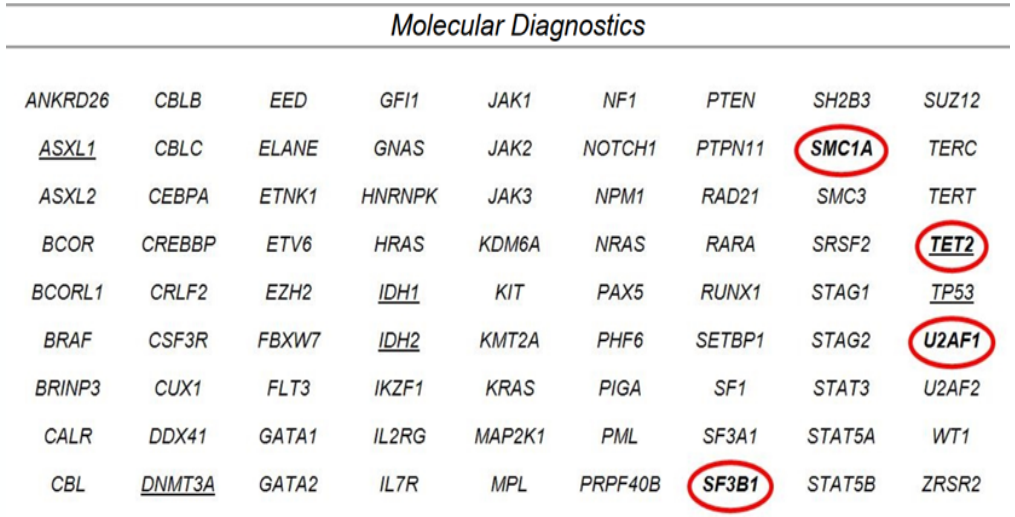
- Low serum EPO level
- Develops symptomatic anemia
- Initiate darbepoetin alfa 300 µg every 2 weeks
  - Dose later increased to 500 µg every 2 weeks
  - Delays in therapy due to insurance complications

Case 1: Increasing Symptoms

Mr. Richards moves and establishes care at new facility

- Increasing SOB, fatigue
  - 1 unit of RBC administered
- Repeat bone marrow biopsy
  - Persistent MDS with multilineage dysplasia and no increase in blasts
  - Cytogenetics revealed trisomy 8 in 19 out of 20 metaphases

Next-Generation Sequencing Panel



Updated Laboratory Values

Lab Parameters	Values in 2016
Serum EPO	91.1 mIU/mL
Hemoglobin	8.5 g/dL

Case 1: Treatment Considerations

- Trend in hemoglobin
- Normal EPO level
- Loss of response to erythropoietin-stimulating agents (ESAs)
- Increased symptom burden and transfusion dependency

Case 1: MDS Polling Question

Given the trend in Mr. Richards' counts, loss of response to ESA, and symptom burden, which of the following is your recommendation?

A. Switch to a different ESA **9%**
B. Initiate regular blood transfusions **9%**
C. Switch to luspatercept **69%**
D. Begin a hypomethylating agent (HMA) **14%**

Case 1: MDS - Luspatercept

Initiated luspatercept

- 1 mg/kg for total 75 mg every 21 days

No improvement after 2 injections

- No change in hemoglobin
- Symptoms of fatigue and SOB with exertion

Increased luspatercept dose to 1.33 mg/kg

Response to luspatercept

- Median hemoglobin, 11.1 g/dL
- Improvement in clinical symptoms
- Site irritation noted

Luspatercept

Hemoglobin
- >11.5 g/dL → HOLD
- ≥ 2 g/dL → CHANGE

Blood pressure
- Systolic ≥160 mm Hg → HOLD
- Diastolic ≥100 mm Hg → HOLD

Case 1: Luspatercept Considerations

- Mechanism of action: erythroid maturation agent
- Dose adjustments
- Adverse side effects
  - Hypertension
  - Arthralgias
  - GI symptoms
  - Irritation at injection site

GI, gastrointestinal

Case 2: Myelofibrosis

Case 2: Introduction to Mr. Brown

72-year-old man with history of myelofibrosis (MF) diagnosed in 2012

- WBC 15,000
- Asymptomatic splenomegaly
- No anemia/thrombocytopenia
- No symptom burden

Bone Marrow Biopsy Results in 2012

Features	Values in 2016
Cellularity	60%
Megakaryocytes	Atypical
BCR-ABL fusion	Negative
JAK2 mutation	Positive
MF grade	1

Case 2: Increasing Grade With Minimal Symptoms

- Mild thrombocytopenia noted in 2013
  - Platelets 113,000 /mcL
  - Referred to leukemia department
- Minimal symptom burden
- Treatment indications?

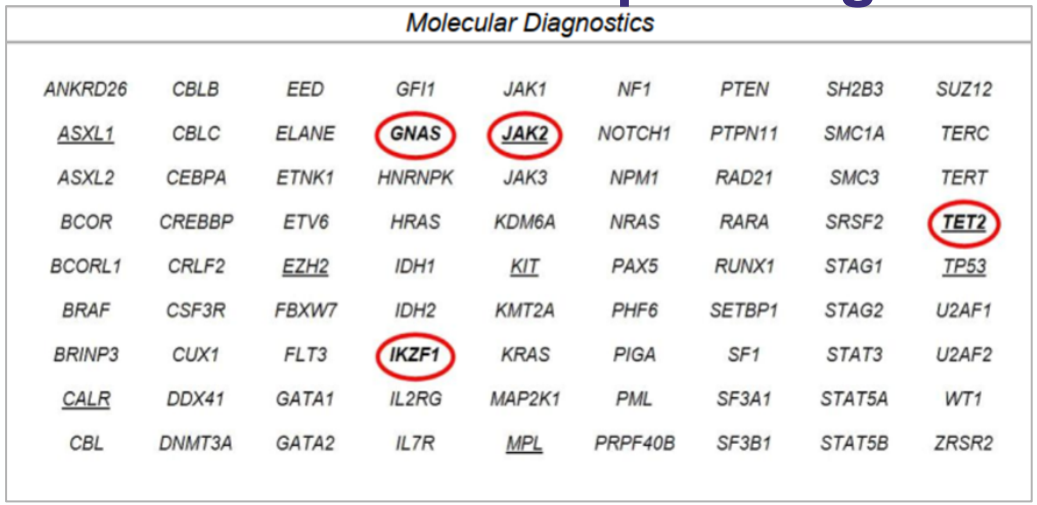
Repeat bone marrow biopsy in 2013

- Persistent myeloproliferative neoplasm with MF grade 3, not associated with any dysplastic changes

Case 2: Increasing Symptoms

- Observation until 2020
  - Progressive splenomegaly
  - Decrease appetite with residual weight loss
  - Progressive thrombocytopenia
  - Worsening fatigue
- Treatment indications?

Next-Generation Sequencing Panel



Laboratory Values in 2020

Lab Parameters	Values
WBC	17,000 /mcL
Hemoglobin	16.3 g/dL
Platelets	60,000 /mcL

Case 2: Treatment Selection

Ruxolitinib vs fedratinib

- Frontline therapy for intermediate-risk MF with progressive symptom burden and splenomegaly
- Platelet count

Initiated fedratinib 400 mg PO daily with meals with weekly monitoring by APs

Case 2: Improving Symptoms

Initiated fedratinib

- Complained of nausea, reflux with residual weight loss
- Consideration of GI prophylaxis?

Evaluation at 4 weeks

- Stable spleen size
- Mild increase in appetite

Evaluation at 6 weeks

- Elevated ALT/AST consistent with grade 1 toxicity
- Rule out other hepatoxic regimens
- Continue and monitor with repeat labs

ALT, alanine aminotransferase; AST, aspartate aminotransferase

Case 2: MF Polling Question

If a patient experiences a mild to moderate (grade 1) ALT and/or AST elevation while taking fedratinib, what are your typical recommendations?

A. Continue fedratinib and monitor liver function tests **67%**
B. Hold fedratinib until the ALT/AST elevation resolves **4%**
C. Switch to another agent **15%**
D. I'm unsure **15%**

Case 2: Myelofibrosis

Mr. Brown was re-evaluated at 6 months

- Reduction in spleen size ~7 cm
- Liver enzymes stable
- GI symptoms manageable
- Symptom burden improved
- CBC stable
- Continuation of treatment
  - Compliance

CBC, complete blood count

Case 3: Acute Myeloid Leukemia

Case 3: Introduction to Mr. Green

- 35-year-old male otherwise healthy with no past medical history presents to ED for new acute leukemia
  - Reports fatigue and “small red dots all over body”
  - Noted to have pancytopenia with peripheral blasts
  - CMP WNL
  - Vitals unremarkable
  - Physical exam only showed petechiae
  - PS = 1

Initial Laboratory Values for Mr. Green

Lab Parameters	Values
WBC	4.3 x 10^9/L
Hemoglobin	9.6 g/dL
Platelets	36 x 10^9/L
ANC	0.82
Peripheral blasts	28%

ANC, absolute neutrophil count; ED, emergency department; PS, performance status

Case 3: Work-up

Acute myeloid leukemia (AML) with multilineage dysplasia (AML-MRC)

- NGS panel positive for mutations in *NRAS*, *ASXL1*, and *IDH2* (allelic burden <2%)
- Baseline chest x-ray, CT chest, echo were all within normal limits

Initial Bone Marrow Biopsy Results

Features	Values in 2016
Blasts	37%
MPO expression	Positive
IHC blast staining	
BCL-2	Positive
MYC	Subset positive
p53	Negative
NPM1	Negative
Cytogenetics	45,X,Y[10]/46,XY,del(9)(q13q34)[2]/46,XY[8]

IHC, immunohistochemistry; MPO, myeloperoxidase

Case 3: Treatment Selection

Induction protocol: CLIA + venetoclax

- Day 28 marrow: 2% blast, diploid karyotype, flow negative for MRD
- Complications: rectal abscess, prolonged myelosuppression

Consolidation cycles 2 & 3 dose reduced 25%

- Complications: rectal abscess, prolonged myelosuppression
- Cycle 4 further dose reduced

SCT vs maintenance therapy?

- 10/10 MUD
- Socioeconomic concerns

Case 3: Maintenance Therapy

Mr. Green decides to proceed with maintenance

- Oral azacitidine 300 mg PO daily on days 1-14 of 28-day cycle
- Oral ondansetron ODT 4 mg sublingual 30 minutes prior to each dose as prophylaxis
- Cycle 1 Day 1 Mr. Green had complete count recovery with ANC >1.00 and platelets >100 /L

Case 3: AML Polling Question

What are some common side effects associated with oral azacitidine that you counsel your patients about? Select all that apply.

A. Nausea **32%**
B. Diarrhea **25%**
C. Myelosuppression **24%**
D. Infections **19%**

Case 3: Monitoring Oral Azacitidine

Monitoring on oral azacitidine

- GI toxicity, myelosuppression
- Labs monitored twice weekly

Required 1 unit of RBC and 2 platelet transfusions during Cycle 1

Transfusion dependency increased in Cycle 2

- Day 28 follow up ANC <1.00
- Platelets 50 x 10^9/L
- Delay cycle 3?
- Mr. Green also complaining of increased nausea and reflux

Case 3: Oral Azacitidine Considerations

Monitoring on oral azacitidine

- Pharmacokinetics/pharmacodynamics versus IV/SC azacitidine
- How often to monitor patients?
- Prophylaxis for nausea? GI toxicities?

Conclusions

- The treatment paradigm in low-risk MDS has evolved, with additional options for those who no longer respond to ESAs
- Managing potential side effects of therapy allows patients to derive maximal benefit from their treatment regimen
- Monitoring patients for potential adverse effects is important to maintain quality of life

The Role of the AP

- ✓ Monitor and dose-adjust patients on anti-cancer therapy
- ✓ Collaborate with other members of the healthcare team to choose the most appropriate treatment option based on the patient's individual risk factors
- ✓ Educate patients regarding toxicity profiles and efficacy of anti-cancer therapies
- ✓ Manage side effects of anti-cancer therapy

Q & A

Please type your questions for Allyson Price
into the **question box** in the control panel.

Thank You