MDS & MPN Review Handout

MDS Diagnosis

MDS

dysfunctional maturation of the bone marrow

UNDER-production of one or more cell line

MPN

dysfunctional activation of the bone marrow

OVER-production of one or more cell line

RISK FACTORS
Age (Avg 60s)
Gender (Male)
Chemotherapy exposure Radiation therapy exposure

TYPES

- MDS with single lineage dysplasia
- MDS with multi lineage dysplasia
- MDS with ring sideroblasts
- MDS with excess blasts
- MDS with del(5q)
- Unclassifiable MDS

MDS Risk

Risk Group	R-IPSS Score	OS (years)
Very Low	< 1.5	8.9
Low	1.5 - 3	5.3
Intermediate	3 - 4.5	3.0
High	4.5 - 6	1.6
Very High	> 6	0.8

5q Disease

Lenalidomide

* Low/Intermediate IPSS

Low IPSS (non 5q)

EPO (if EPO < 500) +/- GCSF

Hypomethylating Agent (HMA)

ATG + Cyclosporine

Luspatercept (SF3B1+)

Lenalidomide

Clinical Trial

Intermediate/High IPSS (non 5q)

Transplant Candidate = HMA or ASCT

Not Transplant Candidate = HMA

Revised IPSS (International Prognostic Scoring System)		
BMB Blasts	0	< 2%
	1	2-5%
	2	5-10%
	3	> 10%
Cytogenetics	0	very good (del11q)
	1	good (del5q, del12p, del20q)
	2	intermediate (del7q, trisomy 8, inv17q, +19)
	3	poor (inv3, del3q, -7)
	4	very poor (complex)
Hemoglobin	0	> 10
	1	8-10
	2	< 8
Platelets	0	> 100
	0.5	50-100
	1	< 50
ANC	0	> 800
	1	< 800

MPN Diagnosis

MDS	MPN
dysfunctional maturation of the bone marrow	dysfunctional activation of the bone marrow
UNDER-production of one or more cell line	OVER-production of one or more cell line

Common

- CML
- Polycythemia Vera
- Essential Thrombocytosis
- Primary Myelofibrosis

Rare

- Chronic Neutrophilic Leukemia
- Chronic Eosinophilic Leukemia
- Mast Cell Disease
- Unclassifiable MPN

MPN Types

CML	Over-production WBCs
Polycythemia Vera	Over-production RBCs
Essential Thrombocytosis	Over-production of Plts
Primary Myelofibrosis	Burned out BM

Three major mutations in MPN: JAK2, CALR, MPL

JAK2

- JAK/STAT proliferation pathway
- Most common mutation in MPN
- 90% PV
- 50-60% ET/PMF

CALR

- Ca binding protein
- Rare in PV
- 70% of ET/PMF [w/o ΔJAK2]

MPL

- Encodes thrombopoietin receptor (TPO-R)

CML Diagnosis

CML = Overproduction of WBCs	
LAB HYPERPLASIA	Leukocytosis : often 20-700K Left shift to immature cells * Sometimes thrombocytosis
GENETIC MUTATION	BCR-ABL t(9;22)
BONE MARROW BIOPSY	Hypercellular

CML Phases

CML Phases	
Chronic	
Accelerated	Increasing WBC Basophils > 20% Myeloblasts/promyelocytes > 30% Peripheral/BMB blasts 10-19% Plts > 1 million or < 100K Splenomegaly
Blast	> 20 % BMB blasts

CML Treatment

First Generation TKI

Imatinib	QTC Rash Diarrhea Muscle cramps Fluid Retention

* Usually only used in chronic phase

Second Generation TKI

Dasatinib * Penetrates CNS	QTC Pleural Effusion Pericardial Effusion Pulmonary HTN Thrombocytopenia	Bosutinib	Rash Diarrhea GI/Liver toxicity
Nilotinib	QTC Pancreatitis Hyperglycemia Hyperlipidemia GI/Liver toxicity		

Third Generation TKI

Ponatinib	QTC Thrombosis CHF Liver toxicity Pancreatitis Fluid retention
Asciminib	URIs Rash GI Toxicity

* Used for T315I mutation

MPN Diagnosis

PV = Overproduction of RBCS	
LAB HYPERPLASIA	**Hb > 16** * Sometimes Thrombocytosis
GENETIC MUTATION	**JAK2 (90%)** V617F or exon 12
BONE MARROW BIOPSY	**Hypercellular**
Minor Criteria	**Low EPO**
Symptoms/Complications	Splenomegaly Thrombosis Acquired VWD

ET = Overproduction of Plts	
LAB HYPERPLASIA	**Plts > 450**
GENETIC MUTATION	**JAK2 (60%)** **CALR (20%)** **MPL (3%)**
BONE MARROW BIOPSY	**Megakaryocytes**
Minor Criteria	**Rule out reactive thrombocytosis**
Symptoms/Complications	Vasomotor: HA, palpitations, livedo reticularis, erythromelalgia Splenomegaly Thrombosis Acquired VWD

MF = Bone Marrow Fibrosis	
LAB HYPOPLASIA	**Pancytopenia** Tear drops
GENETIC MUTATION	**JAK2, CALR, MPL**
BONE MARROW BIOPSY	**BM Fibrosis** Megakaryocyte proliferation, atypia
Extramedullary Hematopoiesis (Liver and Spleen)	**HSM** Tear drops

MPN Treatment

MPN RISK FACTORS
- Age > 60
- Thromboembolism

PMF TREATMENT PARADIGM

Low Risk + Asymptomatic → Observe

Low Risk + Symptomatic → Treat

Intermediate/High Risk → HSCT

PV LOW/HIGH RISK TREATMENT

Aspirin 81 mg

Phlebotomy
goal Hct < 45

PV HIGH RISK TREATMENT

Front Line

Hydroxyurea

IFN alpha

Second Line

Ruxolitinib (Jakafi)

ET LOW/HIGH RISK TREATMENT

Aspirin 81 mg

ET HIGH RISK TREATMENT

Front Line

Hydroxyurea

IFN alpha

Second Line

Anagrelide

MF + Anemia

EPO

Danazol

Lenalidomide +/- Steroids

MF + Thrombocytopenia

Pacritinib

MF + Splenomegaly

Splenectomy

Fedratinib

Ruxolitinib (Jakafi)

Hydroxyurea

CMML Diagnosis

CMML is an overlap syndrome between MDS and MPN

MDS Features

Cell-line dysplasia
Anemia
Thrombocytopenia

MPN features

Cell-line hyperplasia
Leukocytosis
Monocytosis
Splenomegaly

Diagnosis:

Monocytosis:	**>1K**
Associated Genes:	**PDGFRA, PDGFRB, FGFR**
Rule Out Related Conditions:	**CML, secondary monocytosis**

CMML Treatment

CMML Types	Peripheral Blasts	BMB Blasts
Type 1	< 5%	< 10%
Type 2	5-20%	10-20%

CMML

Transplant Candidate = AlloSCT

Not Transplant Candidate = HMA