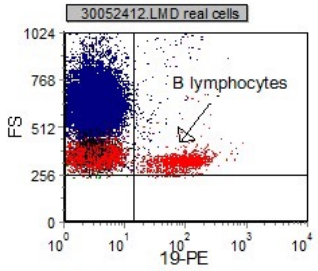
AML & APML Reference Handout

Lab Techniques

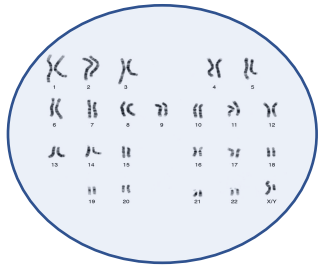
Flow Cytometry



Cell shape/size and CD marker identifies the cell population

Blood or Bone Marrow Flow Cytometry Result:
There is a 20% abnormal CD20+ population

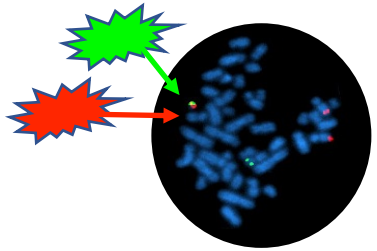
Karyotyping



Visual inspection of metaphase chromosomes reveals large gene changes

Karyotype result:
There is trisomy 21

FISH



Fluorescently tagged DNA probes can detect target DNA sequences

FISH result:
There are X copies of a BCR-ABL translocation

NGS

GGCCTAA → GGTCCAA

Gene Sequencing sequences specific genes and detects ANY gene mutations

NGS result:
There is a FLT3 mutation

AML Diagnosis

Peripheral Labs:

- 2 green top tubes (Peripheral Flow & Cytogenetics)
- In-house NGS (FLT3, CEBPA, NPM1, C-Kit, BCR-ABL, TP53, JAK2)
- CBC w/ diff, CMP BID-TID
- DIC labs (INR, PTT, fibrinogen) BID-TID
- TLS labs (uric acid, LDH, K, Ca, PO4) BID-TID, G6PD
- HIV, hepatitis, CMV
- Type & Cross, Fe studies
- Blood cultures

Other Tests

- EKG
- TTE
- CXR or CT if symptoms
- IVF
- Consider TLS/ID ppx
- Pseudomonal AB coverage if fever

Flow Cytometry

#1) 20% leukemia cells in the marrow or blood

Karyotyping | FISH | NGS

#2) AML defining cytogenetic mutation

t(15,17)	inv(16)
t(8,21)	t(16,16)

AML Presentation

PRIMARY DISORDER	SYMPTOM/LAB FINDING
Leukocytosis/Leukopenia	**Infections/Fever** **Fatigue** **Peripheral blasts**
Anemia Myelophthisic	**Fatigue** **Pallor** **SOB** **Peripheral teardrop RBCs**
Thrombocytopenia Myelophthisic	**Petechiae** **Mucocutaneous bleeding**
Leukemic Cell Organ Infiltration	**Bone infiltration → Pain** **Skin infiltration → Rash/Leukemia cutis** **Liver/Kidney → liver/kidney dysfunction** **CNS → HA, neuropathy**
DIC Activation of the clotting cascade	**INR/PTT, D-dimer elevation** **Thrombocytopenia, Low fibrinogen** **Low Factor levels (including F8)** **Increased bleeding/clotting**
TLS Increased leukemic cell turnover	**Hyperkalemia** **Hyperuricemia** **Hyperphosphatemia** **Hypocalcemia**
Leukostasis Increased viscosity, endothelial damage, cytokine release	**HA, neuropathy, visual changes, tinnitus** **SOB/respiratory failure, MI**

AML Risk Assessment

Good Risk	High Risk
t(15;17); PML-RARA	t(6;9)
t(8;21)	inv3
Inv(16)	t(9;22); BCR-ABL1
t(16;6)	FLT3 positive
Biallelic mutated CEBPA	ASXL1
FLT3 negative	RUNX1
NPM1 mutation With FLT3 negative/low	TP53
IDH2	MLL (11q23)
	Complex or monosomal karyotype

AML Induction Therapy

7 = CYTARABINE

Continuous infusion D1-7
100-200 mg

3 = ANTHRACYCLINE

IV Push D1-3
Idarubicin = 12 mg/m2
Daunorubicin = 60-90 mg/m2

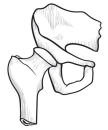
FLT3+ = Midostaurin

CD33+ = Gemtuzumab
*Risk of VOD/SOS

Age > 60 or Poor PS

HMA (AZA/decitabine) +/- Venetoclax

Monitor BMB:
Goal < 5% blasts



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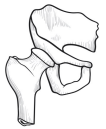


D28
*** Send Cytogenetics, NGS**

Treatment Paradigm

INDUCTION
achieve remission

→ **Chemotherapy**

CONSOLIDATION
maintain remission

→ Low Risk **Chemotherapy**

→ Intermediate/High Risk **BMT**

AML Consolidation Therapy

Low Risk

Intermediate & High Risk

Relapsed/Refractory

HiDac = high dose cytarabine

1 Conditioning Chemotherapy
* myeloablative (MAC) >> Reduced Intensity (RIC)

2 Allogeneic Stem Cell Transplant
* from umbilical cord, peripheral blood, bone marrow

- Targeted agent (ex: IDH inhibitor)
- HMA +/- venetoclax
- FLAG +/- IDA, CLAG +/- IDA
- 7 & 3

AML Prophylaxis

PROPHYLAXIS TARGET	PROPHYLAXIS MEDICATION
Bacterial	**Levofloxacin 750 mg QD** * Can defer inpatient until patient has fever, however if fever consider broad spectrum AB
Viral	**Acyclovir 400 mg BID**
Fungal	**Posaconazole 300 mg QD (load 300 mg BID x1)** * Can cause LFT abnormalities * Covers mucor, aspergillus
TLS	**Allopurinol 300 mg QD** * Renally dose if AKI
Neutropenia	**GSCF** * used in consolidation, not often used for induction (consider in neutropenic fever)

AML Complications

COMPLICATIONS	MANAGEMENT
Neutropenic Fever	**Cefepime +/- vancomycin +/- flagyl** * Pan-culture (peripheral & central line if present) * Consider CT scan of chest or abdomen
Anemia/Thrombocytopenia	**Hb > 7** **Plts >10 (>30 if fever, >50 if bleeding/procedure)** **If not responsive to plts, run slowly over 4H** * Check 1 hour post-transfusion CBC * TBW blood bank re: matched plts * Consider sending platelet AB
TLS	**IVF** **Allopurinol** **Rasburicase 0.1 mg/kg if uric acid > 10** * If G6PD negative * Up to 4.5 mg max
DIC	**FFP or Cryo for goal INR < 1.5, fibrinogen >100** * Confirm no suspicion for APML, consider ATRA
CNS/CSF Disease	**IT Methotrexate**
Leukocytosis/Leukostasis	**Cytoreduction (chemotherapy or hydroxyurea)** **Leukopheresis** * Usually only if WBC >50 -100 * Consider avoiding transfusions, can increase viscosity

APML Diagnosis

APML is a sub-set of AML
Defined by the **t(15,17)** translocation of **PML-RARA** (mostly)

Good Prognosis
Complete remission = 80-90%

Poor Early Survival
30-day mortality = 20%

APML Treatment

RISK	WBC	Platelet
LOW	< 10	> 40
INTERMEDIATE	< 10	< 40
HIGH	> 10	

LOW RISK TREATMENT

ATRA + ARSENIC

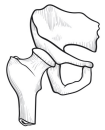
HIGH RISK TREATMENT

ATRA + ARSENIC with Anthracycline or Gemtuzumab

* ATRA causes differentiation of APML → mature myeloid cells

APML Complications

COMPLICATIONS of APML	
DIC	• Activation of clotting cascade • Symptoms = bleeding/clotting • Treatment = FFP/Cryoglobulin
DIFFERENTIATION SYNDROME	• Maturing myeloid cells → cytokine release • Occurs in 25% of patients that get ATRA • Symptoms = fever, hypotension, weight gain, effusions, hypoxia, renal/hepatic dysfunction • Treatment = Steroids (dexamethasone 10 mg BID)
PSEUDOTUMOR CEREBRI	• Caused by ATRA • Discontinue ATRA
QTC Prolongation	• Caused by arsenic • Daily EKG



BMB @ 4-6 weeks
* Delayed because of differentiation