DeNovo Acute Myeloid Leukemia

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New Orleans Summer Cancer Meeting

MOFFITT CANCER CENTER

Overview

- Discuss tenants of AML care
- Review new classification
- Present treatment options for standard and special considerations

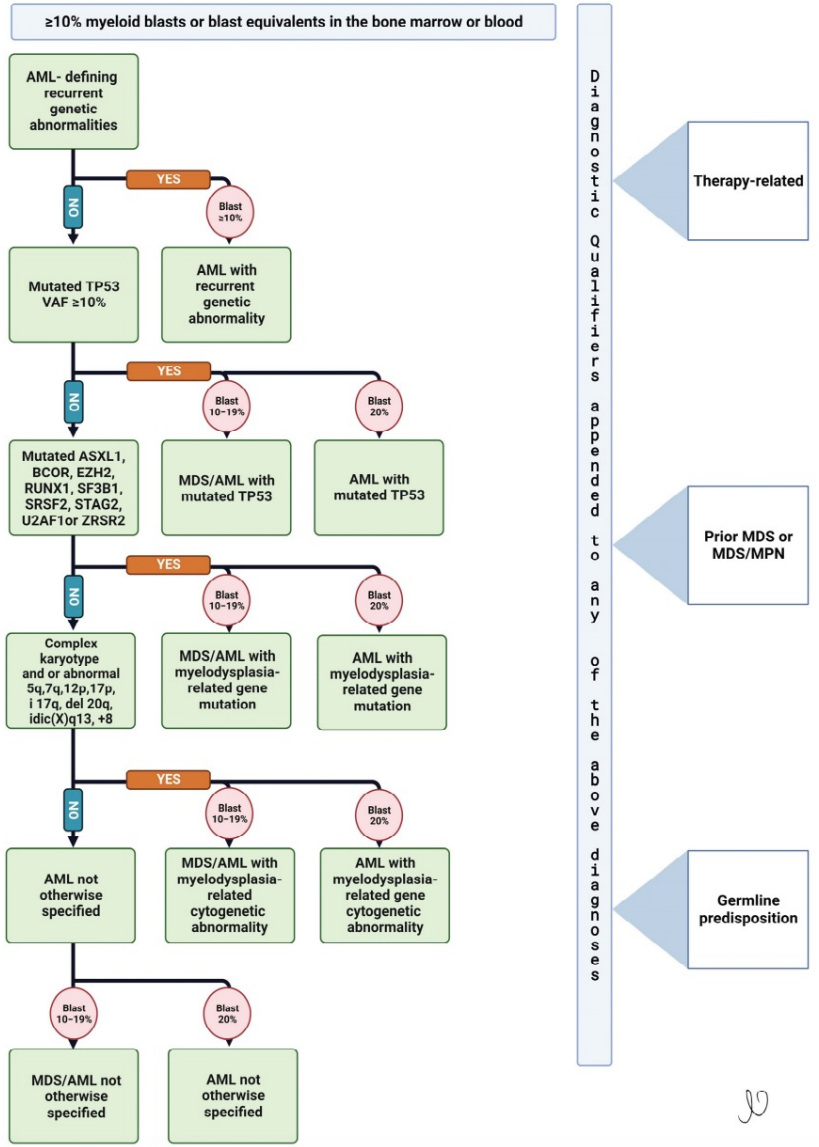
Tenants of AML Care 2024

- Treatment is better than best supportive care in a majority of cases[1]
- Fitness/ comorbidities determine approach[2,3]
- Age is just a number
  - Curative intent can be considered
- Use molecular information to its fullest
- Multiple FDA approved agents/combinations
- Comprehensive AML center partnering

1. Juliusson Leukemia 2006, 2.Sekeres Blood Adv 2020, 3. Ritchie Blood Adv 2022

New Classifications

- ICC
  - 10% blasts is defining for MDS/AML
  - AML if cytogenetic abnormalities present
  - *TP53* is a distinct entity
  - Mutations/muti-lineage dysplasia are important
  - t(9;22) requires >20%
- WHO
  - Cytogenetic/mutational abnormalities are AML irrespective of blast count
  - *KMT2A, MECOM and NUP98* are AML defining



Falini Am J Hem 2023, Premnath Cancers 2023

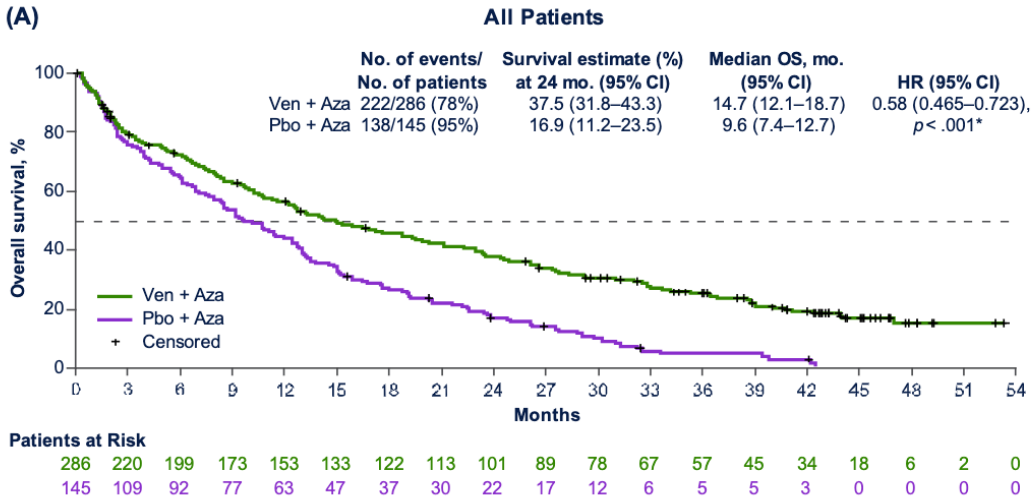
Favorable Risk

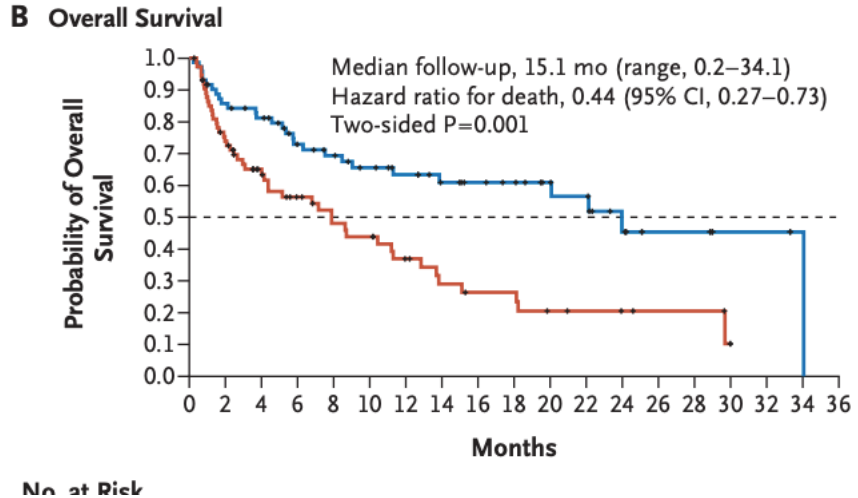
Younger/ Fit

- 7 + 3 + Gemtuzumab Ozogamycin (GO)[1]
- 7 + 3
- Consolidation with HiDAC +/- GO

Older /Unfit

- Azacitidine+ venetoclax[2]
- Aza+ ivosidineb/enasidinib (IDH1/2 positive)[3]





1. Burnett Heamatologica 2016 2. DiNardo NEJM 2020 3. Montesinos NEJM 2022

Intermediate Risk

Younger/ Fit

- 7 + 3 [1,2] followed by consolidation with HiDAC
- Addition of FLT3 inhibitor for FLT3 positive disease
  - Midostaurin[3] or quizartinib[4] (ITD only)

Older /Unfit

- Azacitidine (Aza)+ venetoclax or cytarabine
- Decitabine + venetoclax[5]
- Aza + venetoclax + gilteritinib[6]

1. Fernandez NEJM 2009, 2. Luskin Blood 2016, 3.Stone NEJM 2017,4. Erba Lancet 2023 , 5. DiNardo Lancet Haematol 2020, 6. Short J Clin Onc 2024

Unfavorable and TP53

Multiple cytogenetic and mutational abnormalities

ELN 2022 guidelines- complex karyotype; monosomies in chromosomes 5, 7, and 17; t(11q23); mutations involving *TP53*, *ASXL1*, or *RUNX1*; and MECOM AML

AML-MRC/ secondary AML

> 60 years consider liposomal daunorubicin/cytarabine (CPX-351)[1]

Traditional chemo in TP53- Abysmal results

More intense IC (FLAG-IDA, CLIA) + Venetoclax [2,3]

Clinical Trial

1. Lancet J Clin Onc 2018 2. DiNardo Jclin Onc 2021 3. Kadia Lancet Haematol 2021

Allogeneic HCT

Option for intermediate/ unfavorable risk patient only

Patient informed decision

- Risk/death/benefit reviewed with TC team
- Early HLA typing / donor search
- Expanded donor pool with haploidentical and MMUD

Remission a must

- MRD preferred but not absolute

Review

Offer patients therapy based on:

- Risk
- Targetable mutations
- Fitness

Consolidation

- Risk and response based

Comprehensive and lifelong approach


THANK YOU!