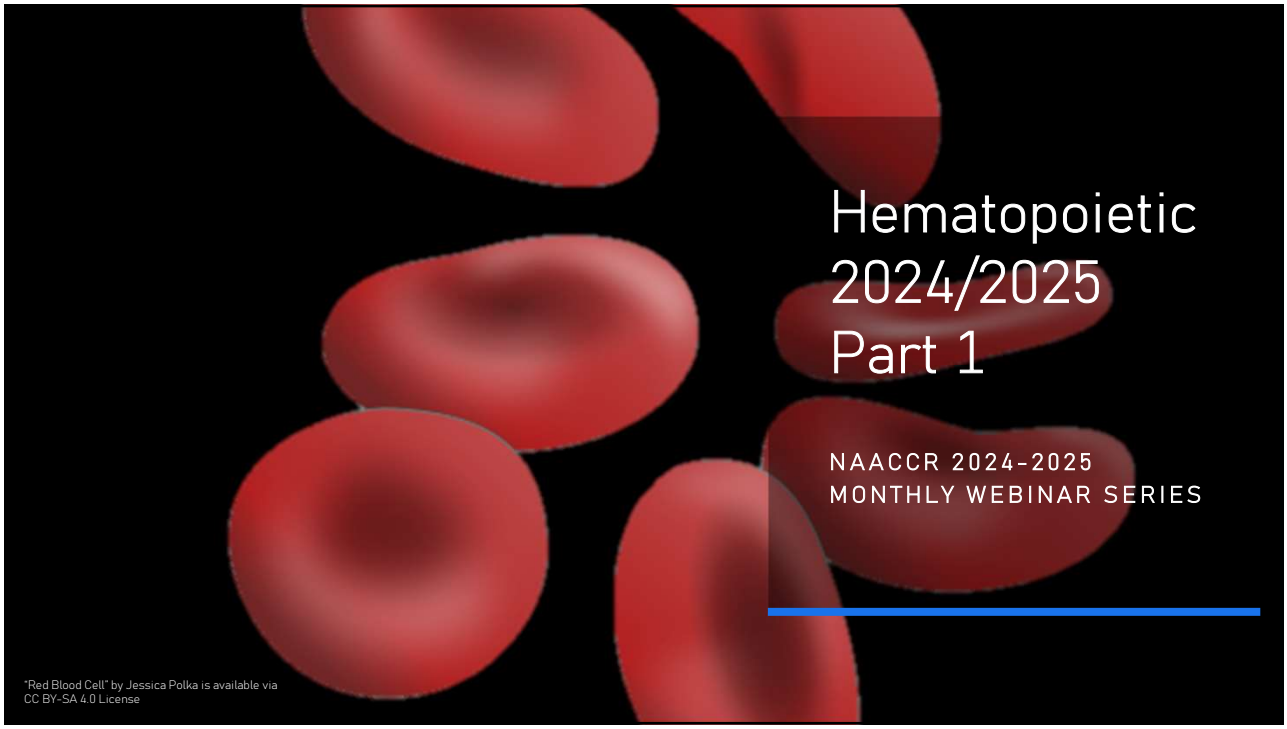


1

Q&A

Please submit all questions concerning the webinar content through the Q&A panel.

If you have participants watching this webinar at your site, please collect their names and emails.

We will be distributing a Q&A document in about one week. This document will fully answer questions asked during the webinar and will contain any corrections that we may discover after the webinar.

2

2

3

NAACCR

GUEST PRESENTER

Juliet Gilliam, MA, ODS

Jennifer Ruhl, MS, CCS, RHIT, ODS

4

OBJECTIVES

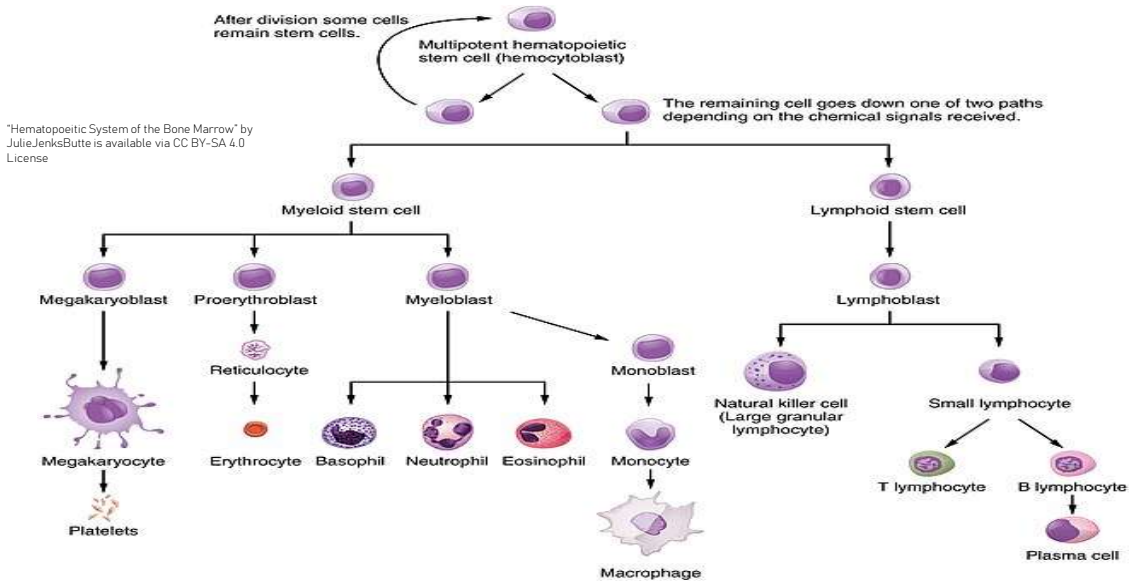
1) Establish some basic HP terminology
2) Explain cell type/lineage
3) Explore HP reportability
4) Discuss the idea of transformation
5) Summarize diagnostic confirmation
6) Review of Multiple Primary Rules
7) Look at myeloproliferative v. myelodysplastic syndromes
8) Review AML histologies

5

INTRODUCTION TO HEMATOPOEITIC CANCERS

6

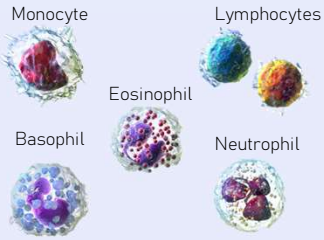
HEMATOPOIETIC CELL DIVISIONS



"Hematopoeitic System of the Bone Marrow" by JulieJenksButte is available via CC BY-SA 4.0 License

7

HEMATOPOIETIC CELL TYPES

Cell Type	Formation	Function	
Red Blood Cells (Erythrocyte/RBC)	-Made in Bone Marrow -Found in Peripheral Blood	-Contain hemoglobin (protein) -Transport oxygen from the lungs throughout the body	
White Blood Cells (Leukocyte/WBC)	-Made in Bone Marrow -Found in Blood & Lymph Tissue	-Part of the immune system -Help fight infection -Types: -Granulocytes -Neutrophils -Eosinophils -Basophils -Monocytes -Lymphocytes -B-Cells -T-Cells	
Plasma Cells (Plasmacyte)	-Develop from activated B-cells -Type of white blood cell	-Make large amounts of a specific antibody	
Platelets (Thrombocyte)	-Formed by the breaking off of a large cell in the bone marrow -Found in the peripheral blood and spleen	-Form blood clots -Slow/stop bleeding -Help wounds heal	

"Red Blood Cell" is available in the Public Domain

"WhiteBloodCells" by BruceBlaus is available by CC BY 3.0 license

"Plasma Cell" by A. Rad et al is available by CC BY-SA 4.0 license

"Platelet" is available by CC BY 3.0 license

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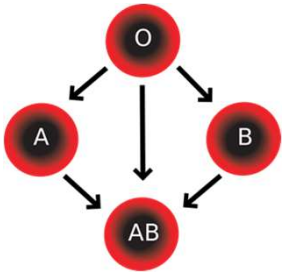
HEMATOPOIETIC TERMINOLOGY

- Eosin/o: Red
- Hemat/o: Blood
- Leuk/o: White
- Mon/o: Single
- Myel/o: Bone marrow, spinal cord
- Poikil/o: Varied, irregular
- Poiesis: Formation
- Thromb/o: Clot
- Splen/o: Spleen
- Ven/o: Vein
- Fibrin/o: Fibrous
- -ac: Pertaining to
- -apheresis: Removal, carrying away
- -blast: Immature cell
- -cytosis: Abnormal condition of cells
- -globin: Protein
- -ia: Condition of, diseased state
- -megaly: Enlarged
- -penia: Abnormal reduction in number
- -phage: Eat, swallow
- -rrhage/-rrhagia: Excessive flow
- -stasis: Stop, stopping, controlling



"Blood Compatibility" by InvictaHOG is public domain

9

10

Use the manual for the first question.
Use the DB for all other questions.

Hematopoietic Database (HPDB) Quiz

1. On what page of the hematopoietic manual do the Multiple Primary Rules start? 29
2. What histology code is assigned to:
   - *Acute myeloid leukemia with t(6;9)(p23;q34);DEK-NUP214* 9865/3
3. What multiple primary rule would we use if the patient was also diagnosed at the same time as a *myeloid sarcoma*? M3

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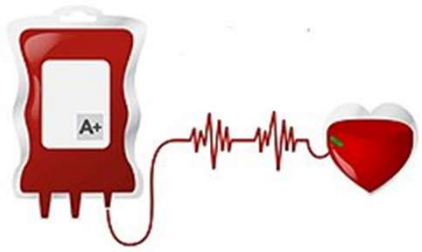
HPDB

4. What is the Diagnostic Confirmation for *Acute myeloid leukemia with t(6;9)(p23;q34);DEK-NUP214?* 3
5. *Acute myeloid leukemia with t(6;9)(p23;q34);DEK-NUP214* can ***transform to*** which of the following? D
   a. 9875/3 Chronic myeloid leukemia, BCR-ABL1-positive
   b. 9920/3 Therapy-related myeloid neoplasms
   c. 9945/3 Chronic myelomonocytic leukemia
   d. None
6. Which of the following is the same primary as *Acute myeloid leukemia with t(6;9)(p23;q34);DEK-NUP214?* C
   a. 9875/3 Chronic myeloid leukemia, BCR-ABL1-positive
   b. 9920/3 Therapy-related myeloid neoplasms
   c. 9860/3 Myeloid leukemia, NOS
   d. 9945/3 Chronic myelomonocytic leukemia

12

REPORTABILITY

Check the Hematopoietic Database (HPDB) and Manual to determine reportability and number of primaries.



Reportability Guidelines
Search the HPDB and Manual to determine reportability.
Report all cases with morphology codes 9590-9993 and a /3 behavior code.
Report hematopoietic and lymphoid neoplasms with morphology codes 9590-9993 and /1 behavior codes when a provider describes them as "malignant". Change the behavior code to /3.
Report hematopoietic neoplasms preceded by ambiguous terms described in the HP manual.
Report the case when the patient is treated for a reportable neoplasm.
Report the case when there is a clinical diagnosis (physician's statement of reportable neoplasms.
Report the case when a reportable diagnosis appears in the text of a report described as a definitive diagnostic method.

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TRANSFORMATIONS

- Certain hematopoietic neoplasms can "transform" to a more serious/acute histology.
- For instance, CLL/SLL (9823/3) can become Diffuse Large B-Cell Lymphoma.
- Do not be fooled by "Chronic" or "Acute" in certain histology names. This use of the terms can refer to the indolence v. aggressiveness of the cancer.
- The HPDB will indicate histologies that can transform under "Transforms From" or "Transforms To"
- Be aware that not all the "chronic" cells will transform at once and use the appropriate timing rules to determine number of primaries. Also, some acute neoplasms can become chronic over time.

Transformations to

9680/3 Diffuse large B-cell lymphoma, NOS

Transformations from

None

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ASSIGNING PRIMARY SITE

- When assigning primary sites:
  - It's important to know what are the common primary sites for the histology you are looking at
    - Primary site information available in the database
    - Note: This doesn't mean you can't have an uncommon primary site
- Instruction #4, Note 1 (pg. 35)
  - Do not simply code the site of a lymph node biopsy, use the information available from scans to determine the correct primary site
  - As a reminder, many times with lymphomas, they will biopsy the most convenient location to get a diagnosis
  - This does not mean this is the primary site
  - Always check your imaging

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ASSIGNING PRIMARY SITE

DID THEY…

Draw blood with a small needle stick in the arm?

"BloodCell State 268" by Sarbasst Brainan is available in the public domain

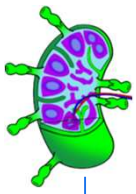
Code to C42.1

Suck out bone marrow with a giant needle stick in the hip?

"Deus Marrow Donor" by Bruce the Deus is available under CC BY-SA 4.0 license

Code to C42.1

Cut out or biopsy a hard, palpable, or shotty lymph node?



"Lymph Node" by Sheldahl is available under CC BY-SA 4.0 license

Code to C77.0-C77.9

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Assigning Hematopoietic Histologies

- Your histology code is based SOLELY on the pathologist's diagnosis
- Do not go through the path report looking at genetics or immunophenotyping to determine the histology
- The main purpose of the immunophenotyping or genetics information in the Heme DB is to help with determining Diagnostic Confirmation
  - Do not use it to determine your histology code
  - Remember, the pathologist or the managing physician must make the diagnosis

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Assigning Hematopoietic Histologies

- Do not try to make a diagnosis based on minor or major criteria that is included in the Heme DB
  - This information, from the WHO Blue Book for Hematopoietic, is used by pathologists to determine the histology
  - It was included in the Heme DB as additional information
  - Some registrars have been using it to determine the diagnosis (which is wrong, registrars do not determine the diagnosis).
  - This type of information will be removed from the Heme DB for the next major update

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UNDERSTANDING THE HP DATABASE

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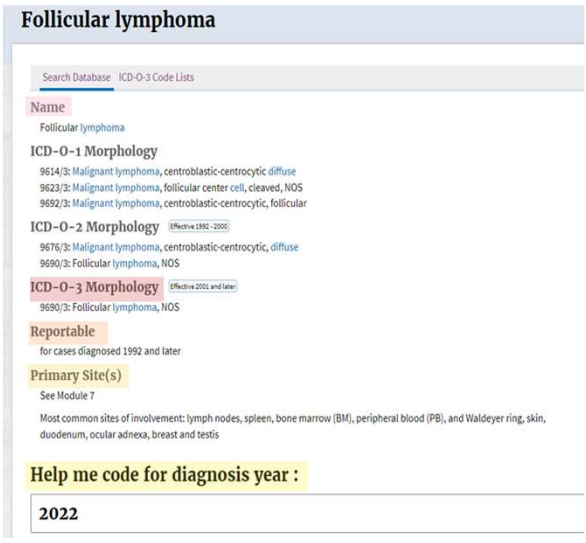
UNDERSTANDING THE HP DATABASE



Name: Gives the preferred term for the HP malignancy.

ICD-O-3 Morphology: Provides the histology code. Be aware that many HP histologies have more specific varients that rely on genetic analysis. ICD-O-1 and ICD-O-2 codes are also provided for historical reference.

Reportable: Explains whether or not the histology is reportable, and if so, for what years. Be sure to verify with STORE and central registry reportability rules.

Primary Site: Assists with determining which module to use to assign primary site and often lists common sites for each histology.

Help Me Code for Diagnosis Year: Gives specific notes on abstracting based on the year of diagnosis. Should match the date of diagnosis in the abstract.

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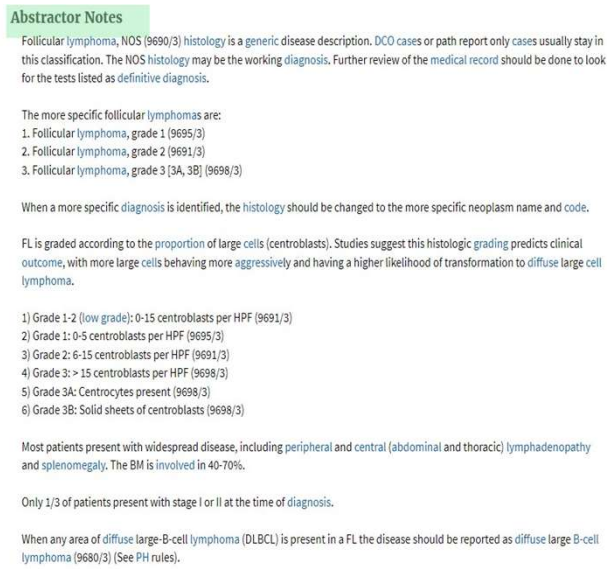
Understanding the HP Database



Abstractor Notes

Follicular lymphoma, NOS (9690/3) histology is a generic disease description. DCO cases or path report only cases usually stay in this classification. The NOS histology may be the working diagnosis. Further review of the medical record should be done to look for the tests listed as definitive diagnosis.

The more specific follicular lymphomas are:
1. Follicular lymphoma, grade 1 (9695/3)
2. Follicular lymphoma, grade 2 (9691/3)
3. Follicular lymphoma, grade 3 [3A, 3B] (9698/3)

When a more specific diagnosis is identified, the histology should be changed to the more specific neoplasm name and code.

FL is graded according to the proportion of large cells (centroblasts). Studies suggest this histologic grading predicts clinical outcome, with more large cells behaving more aggressively and having a higher likelihood of transformation to diffuse large cell lymphoma.

1) Grade 1-2 (low grade): 0-15 centroblasts per HPF (9691/3)
2) Grade 1: 0-5 centroblasts per HPF (9695/3)
3) Grade 2: 6-15 centroblasts per HPF (9691/3)
4) Grade 3: > 15 centroblasts per HPF (9698/3)
5) Grade 3A: Centrocytes present (9698/3)
6) Grade 3B: Solid sheets of centroblasts (9698/3)

Most patients present with widespread disease, including peripheral and central (abdominal and thoracic) lymphadenopathy and splenomegaly. The BM is involved in 40-70%.

Only 1/3 of patients present with stage I or II at the time of diagnosis.

When any area of diffuse large-B-cell lymphoma (DLBCL) is present in a FL the disease should be reported as diffuse large B-cell lymphoma (9680/3) (See PH rules).

Abstractor Notes: Indicates helpful hints for coding, including but not limited to more specific histologies to consider, how grade is determined, presenting symptoms, applicable staging details, statistics, and PH rules to use when coding histology.

These notes should be carefully reviewed for helpful hints on coding, including but not limited to grade, primary site, histology, etc.

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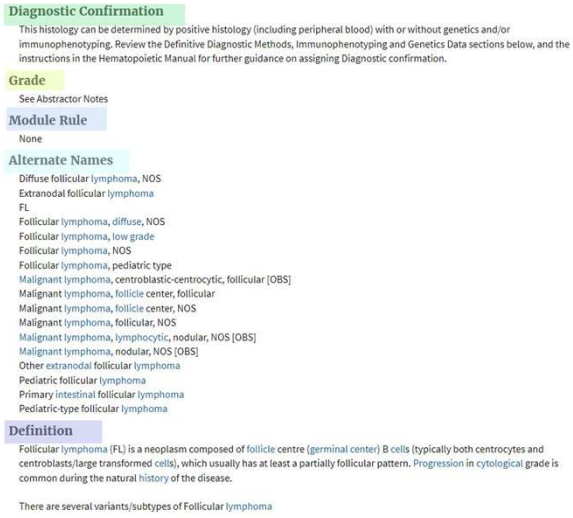
Understanding the HP Database



Diagnostic Confirmation

This histology can be determined by positive histology (including peripheral blood) with or without genetics and/or immunophenotyping. Review the Definitive Diagnostic Methods, Immunophenotyping and Genetics Data sections below, and the instructions in the Hematopoietic Manual for further guidance on assigning Diagnostic confirmation.

Grade

See Abstractor Notes

Module Rule

None

Alternate Names

Diffuse follicular lymphoma, NOS
Extranodal follicular lymphoma
FL
Follicular lymphoma, diffuse, NOS
Follicular lymphoma, low grade
Follicular lymphoma, NOS
Follicular lymphoma, pediatric type
Malignant lymphoma, centroblastic-centrocytic, follicular [OBS]
Malignant lymphoma, follicle center, follicular
Malignant lymphoma, follicle center, NOS
Malignant lymphoma, follicular, NOS
Malignant lymphoma, lymphocytic, nodular, NOS [OBS]
Malignant lymphoma, nodular, NOS [OBS]
Other extranodal follicular lymphoma
Pediatric follicular lymphoma
Primary intestinal follicular lymphoma
Pediatric-type follicular lymphoma

Definition

Follicular lymphoma (FL) is a neoplasm composed of follicle centre (germinal center) B cells (typically both centrocytes and centroblasts/large transformed cells), which usually has at least a partially follicular pattern. Progression in cytological grade is common during the natural history of the disease.

There are several variants/subtypes of Follicular lymphoma

Diagnostic Confirmation: Indicates the types of tests used to determine the particular histology.

Grade: Notes information pertinent to coding the grade fields. Often this will be not applicable or explained in the abstractor notes.

Module Rule: Connects to the appropriate module used to code primary site and/or histology in the HP manual.

Alternate Names: Terms listed here should be considered the same histology for the purposes of coding (see Equivalent Terms and Definitions in the Multiple Primary Rules).

Definition: Explains what this particular type of hematopoietic/lymphoid neoplasm is.

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Understanding the HP Database

Definitive Diagnostic Methods
- FISH
- Genetic testing
- Histologic confirmation
- Immunophenotyping

Genetics Data
- BCL2 mutation
- BCL6 mutation
- CREBBP mutation
- EP300 deletion, mutation
- EPHA7 mutation
- EZH2 mutation
- FAS mutation
- KMT2D (MLL2) mutation
- MEF2B mutation
- MYC gain
- TNFAIP3 (also called A20) deletion, mutation
- TNFRSF14 deletion, mutation
- TP53 deletion, mutation

Immunophenotyping
- BCL2 expression and positive
- BCL6 positive
- CD5 negative
- CD10 expression and positive
- CD19 expression
- CD20 positive
- CD22 expression
- CD23 expression

"Red Blood Cells" by Aseedtolife is available CC BY SA-4.0 license

Definitive Diagnostic Methods: Helps with coding NAACCR data item #490. For example, if genetics/immunophenotyping is not listed, this field should not be coded to 3 for that histology.

Genetics Data: Lists genetic tests used by providers to assign the specific histology. Helps registrars know what to look for in the pathology report.

Immunophenotyping: Lists immunophenotyping used by providers to assign the specific histology. Helps registrars know what to look for in the pathology report.

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Understanding the HP Database

Treatments
- Chemotherapy
- Hematologic Transplant and/or Endocrine Procedures
- Immunotherapy
- Radiation therapy

Transformations to
- 9680/3 Diffuse large B-cell lymphoma, NOS

Transformations from
- None

Same Primaries
- 9590/3 Malignant lymphoma, NOS
- 9591/3 Non-Hodgkin lymphoma, NOS
- 9675/3 Malignant lymphoma, mixed small and large cell, diffuse
- 9691/3 Follicular lymphoma, grade 2
- 9695/3 Follicular lymphoma, grade 1
- 9698/3 Follicular lymphoma, grade 3

Corresponding ICD-9 Codes
- 202.0 Nodular lymphoma

Corresponding ICD-10 Codes
- C82.9 Follicular non-Hodgkin lymphoma, unspecified

Corresponding ICD-10-CM Codes (U.S. only)
- C82.9 Follicular lymphoma, unspecified (effective October 01, 2015)
- C82.8 Other types of follicular lymphoma (effective October 01, 2015)

Signs and Symptoms
- Drenching night sweats
- Fatigue
- Fever (for no known reason)
- Lymphadenopathy (abdominal and thoracic)
- Pain in chest, abdomen or bones (for no known reason)

"Blood Drop Donor" by Karol Krenski is available in the Public Domain

Treatments: Describes treatment modalities in keeping with recognized standards of care (see the NCCN guidelines as well).

Transformations To: Discusses more acute histologies/transformations. If histologies are listed here, the neoplasm should be considered chronic. Some histologies have both chronic and acute transformations.

Transformations From: Discusses more chronic histologies/transformations. If histologies are listed here, the neoplasm should be considered acute. Some histologies have both chronic and acute transformations.

Same Primaries: Suggests alternate names/equivalent histologies.

Signs and Symptoms: Details signs and symptoms common for this particular histology.

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Questions?

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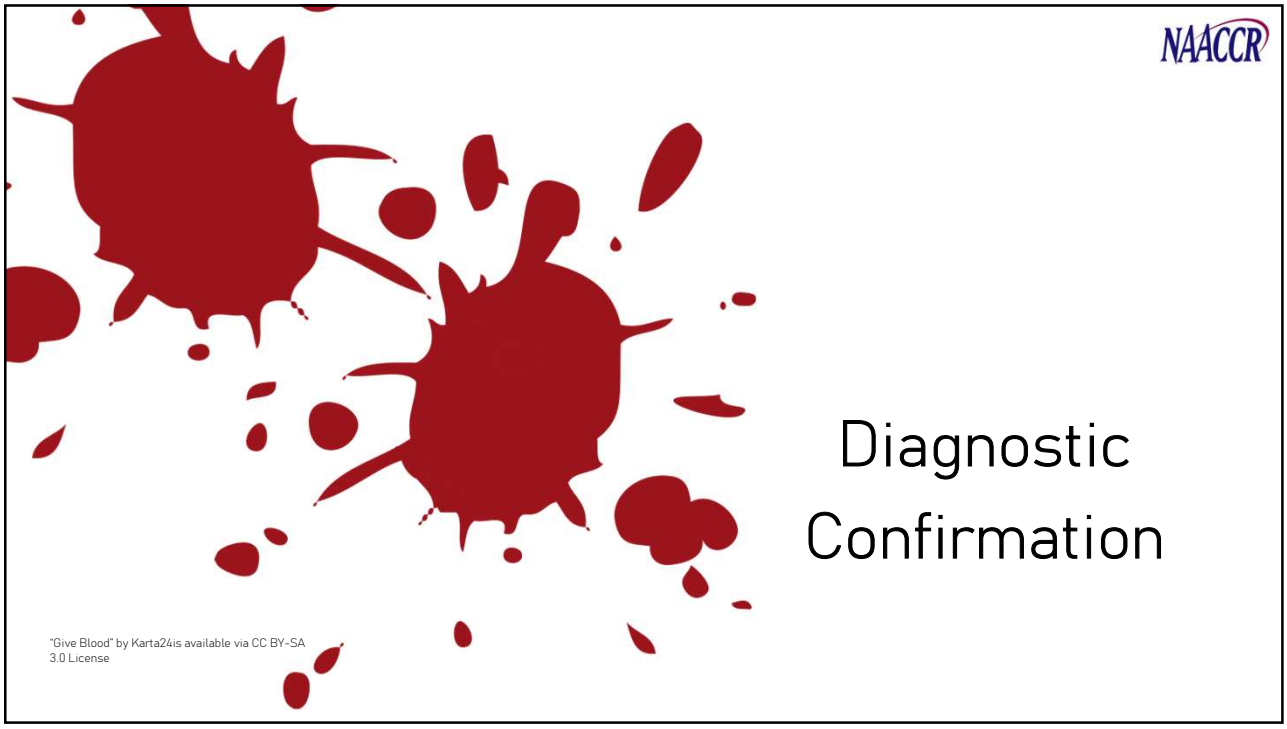
NAACCR
Diagnostic Confirmation
"Give Blood" by Karta24is available via CC BY-SA 3.0 License

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Diagnostic confirmation

- Peripheral blood smears
  - Flow cytometry is frequently done on peripheral blood smears
  - The flow cytometry is looking at immunophenotyping and genetics
    - These are required for diagnostic confirmation code 3
  - If results from the flow cytometry confirm the diagnosis, or identify a more specific diagnosis, then Diagnostic Confirmation is 3.

Microscopically Confirmed

Code	Description
1	Positive histology • Includes: peripheral blood smear only
2	Positive cytology
3	Positive histology PLUS: • Positive immunophenotyping AND/OR • Positive genetic studies • Includes: peripheral blood smear followed by flow cytometry ***(Effective for cases diagnosed 1/1/2010 and later)***

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Example

At this point Dx Conf is 1:
Positive histology

- Patient presents for peripheral blood smear. Physician states the patient results are consistent with *acute myelogenous leukemia*.
- The sample is sent for flow cytometry and based on those results the patient has *acute myeloid leukemia with inv(16)(p13.1q22) or t(16;16) (p13.1;q22), CBFB/MYH11*

The flow cytometry has further defined the diagnosis.
Diagnostic confirmation is now 3

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Diagnostic confirmation

- Some histologies are ALWAYS going to be diagnostic confirmation code 3 because the genetics are part of the term
- Examples:
  - Acute myeloid leukemia, t(8;21)(q22;q22.1); RUNX1-RUNX1T1
  - Acute myeloid leukemia with t(9;11)(p21.3;q23.3); KMT2A-MLLT3
- Under Diagnostic confirmation in the database:
  - This AML is part of the "AML with recurrent genetic abnormalities" group. Since this AML is diagnosed based on genetics, diagnostic confirmation will always be 3.
  - Edits enforced

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"Consistent With" and Heme neoplasms

- "Consistent with" is historically and currently considered ambiguous terminology
- Becoming the standard of reporting Heme diagnoses
- For HEME NEOPLASMS ONLY:
  - "Consistent with" is a definitive diagnosis
  - So, for coding Heme neoplasms, "consistent with" is not ambiguous terminology
  - Discussion under way for Solid Tumors Rules

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Diagnostic confirmation: Example

Case from Ask SEER Registrar

- 9831/3: T-cell large granular lymphocytic leukemia

What would be the correct date and diagnostic confirmation for the case described below? The flow cytometry and DNA Analysis T-Cell Clonality was performed on peripheral blood.

Flow Cytometry Oct 30/23 – an increased proportion of T-cell large granular lymphocytes (T-LGL) with loss of CD5, may be reactive however clonality testing is required to diagnose T-LGL leukemia – positive for CD2, CD3, CD16, negative for CD5, CD56

DNA Analysis T-Cell Clonality Dec 11/23 – positive for a clonal proliferation of T lymphocytes

Heme Onc Consult Jan 8/24 - flow cytometry was consistent with a T-LGL and T clonality was confirmed, believe this patient is having T-LGL, basically asymptomatic of her T-LGL, would recommend CBC q6 months

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Diagnostic confirmation: Example

- Diagnostic confirmation would be a 3 since the flow cytometry confirmed the diagnosis of T-LGL. "consistent with" is not ambiguous terminology for Hematopoietic neoplasms. It has become the standard way of documenting a diagnosis.

Per the SEER Manual, Date of Diagnosis Coding Instructions, #6:

Code the earlier date as the date of diagnosis when

- a. A recognized medical practitioner says that, in retrospect, the patient had cancer at an earlier date or
- b. The original slides are reviewed and the pathologist documents that cancer was present. Code the date of the original procedure as the diagnosis date.

Date of diagnosis 10/30/23.

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Multiple Primary Rules

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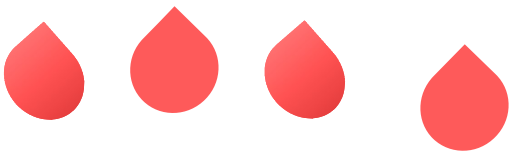
Multiple Primaries for HP & Lymphoid Neoplasms

- Assign a provisional histology
  - While in the database review
    - Transformations
    - Abstractor notes
    - Same primary
    - Hodgkin vs Non-Hodgkin
- Start with M1
- Move through the rules in order.
- STOP at the first rule that applies.



- Notes:
  - During workup, providers *may* begin with a provisional or differential diagnosis and update as testing is completed.
    - These diagnoses do *not* represent multiple primaries.
    - They represent steps in the diagnostic workup.
  - Use the Heme DB Multiple Primaries Calculator *only* when the rules instruct.
  - Always read the general section of the manual first.

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Multiple Primary Rules

- Rule M1
  - Abstract a single primary* when minimal information is available (such as a death certificate only [DCO] case or a pathology-report-only case).
- Rule M2
  - Abstract a single primary * when there is a single histology

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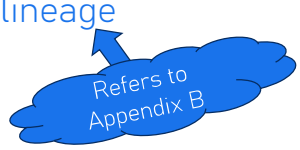
Multiple Primary Rules

- Rule M3
  - Abstract a single primary * when a sarcoma is diagnosed simultaneously *(during the initial clinical work-up)* or after a leukemia of the same lineage



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Example

- Patient with history of *Acute myeloid leukemia with t(6;9)(p23;q34.1); DEK-NUP214* diagnosed in 2023 presents in 2024 with *myeloid sarcoma* of the orbit

- Step 1
  - Use the hematopoietic database to assign a provisional histology
    - Review information in HPDB (abstractor notes for both histologies.
- Step 2
  - Go to the Hematopoietic Manual Multiple Primary Rules.
  - Find the first rule that applies and stop.
  - Per rule M3, this is a single primary
  - Confirm both histologies are of the same lineage using Appendix B Table

37

Example

- Step 1
  - Use the hematopoietic database to assign a provisional histology
    - 9865/3 acute myeloid leukemia with t(6;9)(p23;q34.1); DEK-NUP214
      - Abstractor Notes: If the leukemia occurs before or simultaneously with Myeloid Sarcoma (9930/3), see M3 and Module 5:PH10.
    - 9930/3 myeloid sarcoma
- Step 2
  - Go to the Hematopoietic Manual Multiple Primary Rules.
  - Find the first rule that applies and stop.
  - Per rule M3, this is a single primary (confirmed by lineage
    - Complete a single abstract.
    - Include information concerning the myeloid sarcoma in the text

Table B6: Acute Myeloid Leukemia (AML) and Related Precursor Neoplasms

WHO Preferred Term	ICD-O
Acute myeloid leukemias with recurrent genetic abnormalities	
Acute myeloid leukemia (megakaryoblastic) with t(1;22)(p13.3;q13.1); *RBM15-MKL1*	9911/3
Acute myeloid leukemia with *BCR-ABL1* (2021)+	9912/3*
Acute myeloid leukemia with biallelic mutation of *CEBPA* (2021+)	9878/3*
Acute myeloid leukemia with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2, MECOM*	9869/3
Acute myeloid leukemia with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*	9871/3
Acute myeloid leukemia with mutated *NPM1* (2021+)	9877/3*
Acute myeloid leukemia with mutated *RUNX1* (2021+)	9879/3*
WHO Preferred Term	**ICD-O**
Acute myeloid leukemia with t(6;9)(p23;q34.1) *DEK-NUP214*	9865/3
Acute myeloid leukemia with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*	9896/3
Acute myeloid leukemia with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3*	9897/3
Acute promyelocytic leukemia with *PML-RARA*	9866/3
Acute myeloid leukemia with myelodysplasia-related changes	9895/3
Therapy-related myeloid neoplasms	9920/3
Acute myeloid leukemia, NOS	9861/3
Acute basophilic leukemia	9870/3
Acute megakaryoblastic leukemia	9910/3
Acute monoblastic and monocytic leukemia	9891/3
Acute myeloid leukemia with maturation	9874/3
Acute myeloid leukemia with minimal differentiation	9872/3
Acute myeloid leukemia without maturation	9873/3
Acute myelomonocytic leukemia	9867/3
Acute panmyelosis with myelofibrosis	9931/3
Pure erythroid leukemia	9840/3
Myeloid sarcoma	9930/3
Myeloid proliferations related to Down syndrome	
Myeloid leukemia associated with Down syndrome	9898/3
Transient abnormal myelopoiesis associated with Down syndrome	9898/1
Blastic plasmacytoid dendritic cell neoplasm	9727/3

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Multiple Primary Rules

- **Rules M4-M6** are related to Hodgkin and Non-Hodgkin. Topics we'll discuss next month.
- **Rule M7**
  - Abstract as a single primary* when a more specific histology is diagnosed after an NOS ONLY when the Heme DB Multiple Primaries Calculator confirms that the NOS and the more specific histology are the same primary

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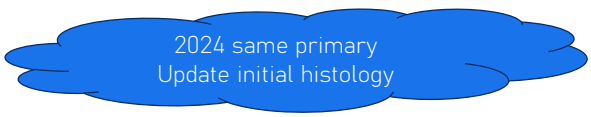
M7 Example

- 2023 Myelodysplastic Syndrome (9989/3)
- 2024 Myelodysplastic neoplasm with multilineage dysplasia (9985/3)



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Chronic/Acute Rules M8-M13 Scenario 1

- Patient present for bone marrow biopsy (1/12/2024)
  - Pathology Report:
    - Myelodysplastic syndrome
  - Genetic Testing:
    - Mutated RUNX1
  - Oncologist states the patient has myelodysplastic syndrome with 5q deletion and acute myelogenous leukemia with mutated RUNX1.

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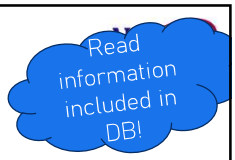
Scenario 1



- Step 1
  - Assign provisional histology using Heme Database
    - 9986/3 Myelodysplastic syndrome with 5q deletion
    - 9896/3 Acute myeloid leukemia, t(8;21)(q22;q22.1); RUNX1-RUNX1T1
- Step 2 Review Multiple Primary Rules
  - Rules M1-M7 do not apply
    - Single primary per rule M8
      - Diagnosed simultaneously from a single sample
      - Assign histology to 9896/3 (code the acute neoplasm)

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Scenario 2

- Patient present for a bone marrow biopsy on 1/12/2024
  - Pathology shows *myelodysplastic syndrome*
  - Fluorescence in situ hybridization (FISH) shows deletion of the long arm of chromosome 5 (5q Deletion)
  - Patient is treated with Lenalidomide
- Patient presents for second bone marrow biopsy (7/23/2024)
  - Pathology Report:
    - Acute myelogenous leukemia
  - Genetic Testing:
    - t(8;21)(q22;q22.1) resulting in RUNX1-TUNX1T1
  - Physician states the patient has *myelodysplastic syndrome with 5q deletion* and *acute myelogenous leukemia with mutated RUNX1.*

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Scenario 2

- Myelodysplastic syndrome with 5q deletion
- Acute myelogenous leukemia with mutated RUNX1
  - t(8;21)(q22;q22.1)

Pay attention to transform section in DB!

- Step 1
  - Assign provisional histology using Heme Database
    - 9986/3 Myelodysplastic syndrome with 5q deletion
    - 9896/3 Acute myeloid leukemia, t(8;21)(q22;q22.1); RUNX1-RUNX1T1
- Step 2 Review Multiple Primary Rules
  - Rules M1-M8 do not apply
  - Rule M10 (acute more than 21 days after chronic)
    - Two primaries per rule M10

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Scenario 3

- Patient presents for a bone marrow biopsy (1/12/2024)
  - Pathology Report:
    - Acute myelogenous leukemia
  - The patient refused any further work-up or treatment.
- Patient present for a second bone marrow biopsy on 7/23/2024
  - Pathology shows Myelodysplastic syndrome
  - Fluorescence in situ hybridization (FISH) shows deletion of the long arm of chromosome 5 (5q Deletion)

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Scenario 3

- Acute myelogenous leukemia with mutated RUNX1
- Myelodysplastic syndrome with 5q deletion

What if patient had tx between dx?

- Step 1
  - Assign provisional histology using Heme Database
    - 9861/3 Acute myeloid leukemia
    - 9986/3 Myelodysplastic syndrome with 5q deletion

Acute and Chronic…acute dx'd first

- Step 2
  - Review Multiple Primary Rules
  - Rules M1-M11 do not apply
  - Rule M12 is the first that applies.
- Single primary per rule M12
  - Assign histology 9861/3

No treatment between dx.

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Scenario 4

- During an admission for metastatic breast cancer, a bone marrow biopsy was done for which the diagnosis was MDS with excessive blasts versus AML
- Multiple consults, but none that derived anything more than MDS with excessive blasts versus AML, except for one medonc consult .
  - The consult impression stated "likely MDS transformed to AML".

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Scenario 4

- Acute myelogenous leukemia Myelodysplastic syndrome with 5q deletion

- Step 1
  - Assign provisional histology using Heme Database
    - 9861/3 Acute myeloid leukemia
    - 9986/3 Myelodysplastic syndrome with 5q deletion
- Step 2
  - Review Multiple Primary Rules
  - Rule M8 is the first that applies
- Single primary per rule M8
  - Assign histology 9861/3

Dx based on single sample

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Rule M15

- Some registrars are using this rule incorrectly
- If you have two or more histologies, DON'T go to the multiple primaries' calculator first
  - ONLY use the database to determine your histology(ies), find out specific information about your histology(ies) or determine if the histologies are the same primary (listed under same primaries)
- You must go through the rules
- Using the multiple primaries calculator could potentially give you the wrong number of primaries (happens more with lymphomas then leukemias)

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Rule M15-used incorrectly

- Bone marrow biopsy
  - Myelodysplastic syndrome (neoplasm*) with evidence of progression to AML
  - If you put MDS and AML into the Multiple Primaries calculator (as some registrars have done), it would be two primaries
  - HOWEVER, following the rules (M8) this would be one primary
- *Myelodysplastic syndrome is now called myelodysplastic neoplasm

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Rule M15–used correctly

- 1/24: Patient diagnosed with *Chronic myeloid leukemia, Chronic phase*
- 10/24: Patient diagnosed with *Acute B-lymphoblastic leukemia*, transformation from *Chronic Myelogenous leukemia*
  - From registrar: In the Heme DB neither of these histologies are listed under the Transformation TO and FROM
  - Note: Not all "transformations" are listed in the Heme DB, only the most common ones. If your documentation states transformation, yet it is not listed in the Heme DB, go through the rules
- Rules M1-M14 do not apply. Rule M15 applies which is use the multiple primaries calculator
- This would be two primaries

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Rule M15–used correctly

- Patient diagnosed 2004 with T-Acute lymphoblastic leukemia. Presents in 2024 with multiple subcutaneous skin nodules and right eye conjunctiva lesion, both biopsied and positive for myeloid sarcoma
- From registrar: per note under Myeloid Sarcoma, if myeloid sarcoma occurs simultaneously or after an acute myeloid leukemia, see M3 and Module 5:PH10. I think based on this it would be 1 primary.
- This is two primaries based on Rule M15
- Rule M3 does not apply. This is a lymphoid leukemia and Myeloid Sarcoma, not a myeloid leukemia and Myeloid sarcoma

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When determining single vs multiple primaries…

- A single histology is always a single primary (exception)
- Use the hematopoietic DB to assign provisional histologies (especially when working with more than one histology)
- Review information included in the database
  - Hodgkin/Non-Hodgkin
  - Chronic/Acute Transform from/to
  - Same primaries
  - Abstractor notes
- Pay attention to basic lineage (myeloid vs lymphoid)
- Follow the rules in order!

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MYELODYSPLASTIC SYNDROME AND MYELOPROLIFERATIVE NEOPLASMS

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INITIAL EVALUATION FOR MDS

History & Physical Exam (Document transfusion history)

Test
- Complete Blood Count (CBC)
- Platelets
- Reticulocyte Count
- Serum EPO (Prior to transfusion)
- Serum folate & B12
- Thyroid Stimulating Hormone
- Lactase Dehydrogenase
- HIV if indicated
- Serum ferritin/iron

Consider
- Genetic Testing
- Molecular testing (especially if < 50 years)
- Evaluation for copper deficiency
- Severe malnutrition
- Gastric malabsorption
- Distinction from congenital sideroblastic anemia

Perform
- Peripheral blood smear
- Bone marrow bx w/ iron stain & cytogenetics by standard karyotyping

Dx criteria for MDS met based on morphologic, cytogenic, & clinical criteria

Dx criteria for MDS not met but cytopenia present

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MYELODYSPLASTIC SYNDROMES (MDS)

Per the HPDB:

"IF the characteristics of a particular subtype of MDS develop later in the disease course, change the histology to reflect the more specific diagnosis".

Principal Sites:
- Bone Marrow (Includes Peripheral Blood)
- MDS is typically a *clinical* diagnosis.
- MDS is often treated with supportive care:
  - *Active Surveillance*
  - *Blood Transfusions* for anemia

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MYELODYSPLASTIC SYNDROMES (MDS)

Term	Definition
Myelodysplastic syndrome with single lineage dysplasia	One blood cell type — white blood cells, red blood cells or platelets — is low in number and appears abnormal under the microscope.
Myelodysplastic syndrome with multilineage dysplasia	In this subtype, two or three blood cell types are abnormal.
Myelodysplastic syndrome with ring sideroblasts	This subtype involves a low number of one or more blood cell types. A characteristic feature is that existing red blood cells in the bone marrow contain rings of excess iron.
Myelodysplastic syndrome with isolated del(5q) chromosome abnormality	People with this subtype have low numbers of red blood cells, and the cells have a specific mutation in their DNA.
Myelodysplastic syndrome with excess blasts	In this subtype, any of the three types of blood cells — red blood cells, white blood cells or platelets — might be low and appear abnormal under a microscope. Very immature blood cells (blasts) are found in the blood and bone marrow
Myelodysplastic syndrome, unclassifiable	This type of MDS is uncommon. The findings in the blood and bone marrow don't fit any other type of MDS

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5th edition

- Released as beta version in 2022
- Pathologists started using beta version in 2022
- Cancer Surveillance Community cannot make changes until a WHO Blue Book is finalized and available in print
- And then, changes can only occur on a yearly basis

- *Note: There are* ***no new ICD-O-3 histology codes****, only new terms*

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5th edition

- 5th edition became available to purchase in September 2024 (2 ½ years after beta released!)
- Changes must now be reviewed and submitted to two leadership groups for approval
- Planning for 2026 implementation
- Heme Manual/DB cannot be updated until changes approved

"BloodCellState 213" by Sarbasst Braian is available in the Public Domain

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MYELODYSPLASTIC SYNDROMES (MDS): 5TH EDITION

ICD-O-3	Histology Term
9982/3	Myelodysplastic/myeloproliferative neoplasm with low blasts and SF381 mutation* Myelodysplastic neoplasm (MDS) with low blasts and ring sideroblasts Myelodysplastic/myeloproliferative neoplasm (MDS/MPN) with SF3B1 mutation and thrombocytosis* Myelodysplastic/myeloproliferative neoplasm (MDS/MPN) with ring sideroblasts and thrombocytosis

*MDS with the SF381 mutation is the most aggressive MDS. If there are two diagnosis of MDS and this is one of them, this will be the one that is priority

Reminder: All MDS diagnoses are the same primary

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MYELODYSPLASTIC SYNDROMES (MDS): 5TH EDITIONS

ICD-O-3	Histology Term
9983/3	Myelodysplastic syndrome with increased* blasts (MDS-IB) Refractory anemia with excess blasts (NOS, 1, 2) (RAEB, RAEB-1, RAEB-2) Childhood myelodysplastic neoplasm with increased blasts

*Myelodysplastic syndrome now uses "increased" while Refractory anemia uses the "excess" blasts

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MYELODYSPLASTIC SYNDROMES (MDS): 5TH EDITION

ICD-O-3	Histology Term
9985/3	Myelodysplastic neoplasm with low blasts and multilineage dysplasia Myelodysplastic neoplasm with biallelic TP53 mutation Myelodysplastic neoplasm with multi-hit TP53 inactivation Myelodysplastic neoplasm with low blasts Myelodysplastic neoplasm, hypoplastic Childhood myelodysplastic neoplasm with low blasts (cMDS-LB) Childhood myelodysplastic neoplasm with low blasts, hypocellular

*WHO moving towards "myelodysplastic neoplasm" instead of "myelodysplastic syndrome." They are the same thing

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INTERNATIONAL PROGNOSTIC SCORING SYSTEM (IPSS)

https://pmc.ncbi.nlm.nih.gov/articles/PMC3611898/

Risk Factor	Point(s)
Age > 65 Years	1
Hemoglobin < 10 g/dL	1
White Blood Count > $25x10^9$ /1	1
Circulating Blasts ≥ 1%	1
Constitutional Symptoms • Weight Loss > 10% of baseline value in preceding year • Unexplained/persistent fever • Unexplained/persistent sweating	1

Low: 0 Points
Intermediate-1: 1 Points
Intermediate 2: 2 Points
High: 3 or more points

"CV System-Platelet 1" by Laboratoires Servier available via CC BY-SA 3.0 License

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LOWER-RISK DISEASE

IPSS-R VERY LOW, LOW, INTERMEDIATE-RISK DISEASE

- Does the patient have clinically symptomatic cytopenias?
- Does the patient have symptomatic anemia?
- Does the patient have clinically relevant thrombocytopenia or neutropenia?

Yes / No

- Does the patient have a del(5q) ± one other cytogenetic abnormality?
- Does the patient have a mIDH1 mutation?

Yes / No

- Is there disease progression?
- Is there no response?
- Is there a relapse?

Yes / No

OPTIONS:
- Supportive care
- Clinical trial
- Azacitidine or Decitabine
- Decitabine & cedazuridine
- Immunosuppressive therapy
- IDH1 inhibitor
- Allogenic stem cell transplant

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HIGHER-RISK DISEASE

IPSS-R INTERMEDIATE, HIGH, VERY HIGH RISK DISEASE

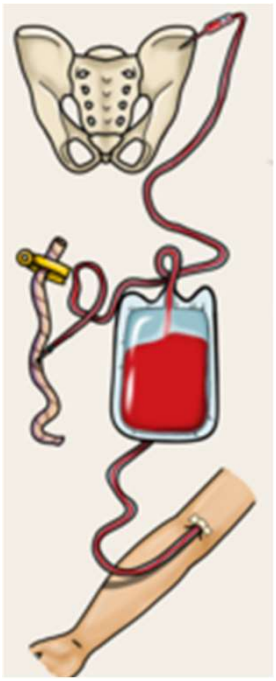
- Is the patient a transplant candidate?

Yes

- Allogenic stem cell transplant (SCT)
- Azacitadine & Ivosidenib (if mIDH1) followed by SCT
- Clinical trial followed by allogenic SCT
- Chemo regimen (Examples: Azacitadine ± venetoclax; Decitabine ± venitoclax)
- High intensity chemo

No

- PREFERRED: Azacitadine ± venetoclax
- Decitabine ± venetoclax
- Decitabine and cedazuridine ± venetoclax
- Ivosidenib ± azacitadine (if mIDH1)
- Olutasidenib ± azacitadine (if mIDH1)



"Stem Cell Transplant" by MariaCisnerosMartin is available under CC BY SA-4.0 license

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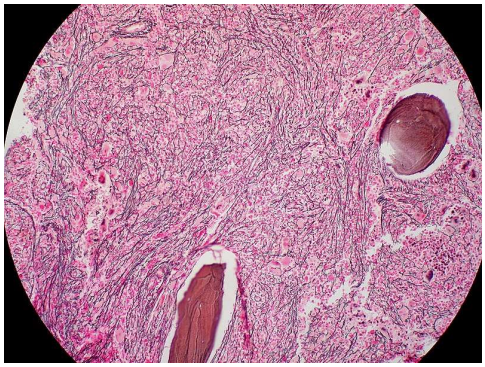
MYELOPROLIFERATIVE NEOPLASMS (MPN)



"Myelofibrosis, Reticullin Stain" by Ed Uthman available via CC BY 2.0 License

Myelofibrosis Risk — Primary v. Secondary

Mutation-Enhanced IPSS (< 70 years old)
Measures mutations in various genes, symptoms, grade of fibrosis, circulating blasts, hemoglobin, and the number of leukocytes.

Dynamic IPSS
Measures age, hemoglobin, blasts, & constitutional symptoms.

MYSEC-PM
Measures risk for secondary MF.

PV Risk — Based on age (< 60=good) & prior history of thrombosis.

ET Risk — Based on age (< 60=good), JAK-2 mutation status, and history of thrombosis.

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MYELOPROLIFERATIVE NEOPLASMS: 5TH EDITION

ICD-O-3	Histology Term
9945/3	Myelodysplastic chronic myelomonocytic leukemia (MD-CMML) Myeloproliferative chronic myelomonocytic leukemia (MP-CMML)
9946/3	PTPNI1-mutated JMML NRAS-mutated JMML KRAS-mutated JMML JMML in neurofibromatosis type 1 JMML in children with CBL syndrome* JMML-like disorders in children with Noonan syndrome

*Casitas B-Lineage lymphoma

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ACUTE MYELOID LEUKEMIA

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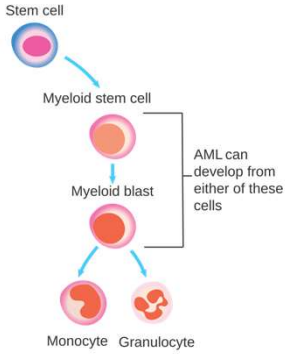
AML QUICK FACTS

There are four main types of leukemia, classified by:

1. The rate of progression
   a. Acute leukemias grow quickly
   b. Chronic leukemias progress over time
2. The blood cells affected
   a. Lymphocytes
   b. Myelocytes

The defining criterion for AML is the presence of greater than or equal to 20% myeloid blasts in the peripheral blood or bone marrow.

- Most common age at diagnosis: 65-74
- Risk Factors: Prior chemo/radiation exposure, and smoking
- 4.2 New Cases per 100,000 (2017-2021 cases)
- Death Rate: 2.7 per 100,000 (2017-2021 cases)
- 5 Year Relative Survival: 31.9% (2014-2020)



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Transformations to

None

Transformations from

9875/3 Chronic myeloid leukemia, BCR-ABL1-positive
9920/3 Therapy-related myeloid neoplasms
9945/3 Chronic myelomonocytic leukemia
9950/3 Polycythemia vera
9960/3 Myeloproliferative neoplasm, NOS
9961/3 Primary myelofibrosis
9962/3 Essential thrombocythemia
9963/3 Chronic neutrophilic leukemia
9964/3 Chronic eosinophilic leukemia, NOS
9975/3 Myelodysplastic/myeloproliferative neoplasm, unclassifiable
9980/3 Myelodysplastic syndrome with single lineage dysplasia
9982/3 Myelodysplastic syndrome with ring sideroblasts and single lineage dysplasia
9983/3 Myelodysplastic syndrome with excess blasts
9984/3 Refractory anemia with excess blasts in transformation
9985/3 Myelodysplastic syndrome with multilineage dysplasia
9986/3 Myelodysplastic syndrome with isolated del(5q)
9987/3 Therapy-related myelodysplastic syndrome, NOS
9989/3 Myelodysplastic syndrome, unclassifiable
9991/3 Refractory neutropenia
9992/3 Refractory thrombocytopenia
9993/3 Myelodysplastic syndrome with ring sideroblasts and multilineage dysplasia

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AML HISTOLOGIES WITH DEFINING GENETIC ABNORMALITIES: 5TH ED

ICD-O-3	Histology Term
9866/3	Acute promyelocytic leukemia with PML::RARA fusion Acute promyelocytic leukemia with a variant RARA translocation
9896/3	AML with ***RUNX1*::*RUNX1T1*** fusion
9871/3	AML with *CBFB::MYH22* fusion
9865/3	AML with *DEK::NUP214* fusion
9911/3	AML with *RBM15::MRTFA* fusion
9912/3	AML with *BCR::ABL1* fusion
9897/3	AML with *KMT2A* rearrangement
9869/3	AML with *MECOM* rearrangement
9861/3	AML with *NUP98* rearrangement
9877/3	AML with *CEBPA* rearrangement
9895/3	AML, myelodysplasia-related

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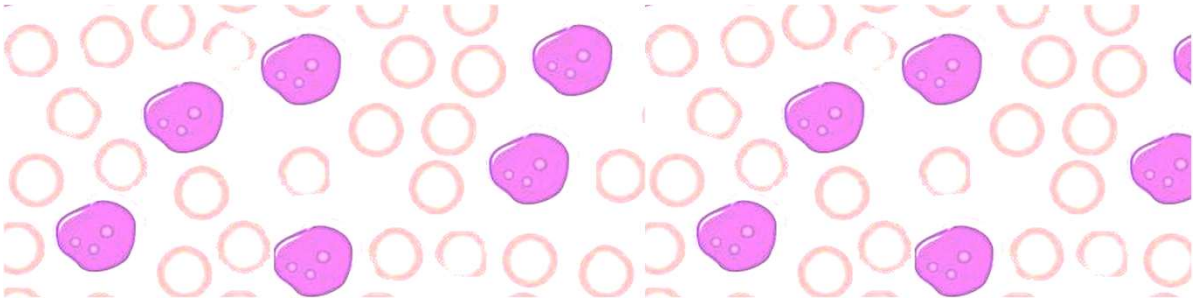
AML HISTOLOGIES WITH DEFINING GENETIC ABNORMALITIES: 5TH ED

ICD-O-3	Histology Term
9861/3	AML with other defined genetic alterations AML with *CBFA2T3::GLIS2* fusion AML with *KAT61::CREBBP* fusion AML with *FUS::ERG* fusion AML with *MNX1::ETV6* fusion AML with *NPM1::MLF1* fusion



"Schematic showing the appearance of AML" is available in the Public Domain

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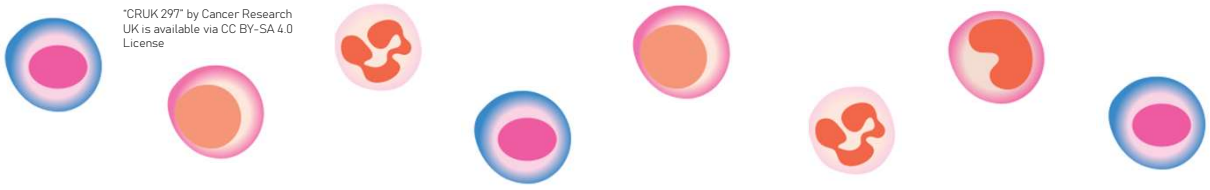
AML HISTOLOGIES DEFINED BY DIFFERENTIATION: 5TH ED

ICD-O-3	Histology Term
9872/3	AML with minimal differentiation
9873/3	AML without maturation
9874/3	AML with maturation
9870/3	Acute basophilic leukemia
9867/3	Acute myelomonocytic leukemia
9891/3	Acute monocytic leukemia
9840/3	Acute erythroid leukemia
9910/3	Acute megakaryoblastic leukemia



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Acute myeloid leukemia: 9920/3

- Reminder of the two notes regarding 9920/3
  - DO NOT code therapy-related myeloid neoplasm simply because the patient has a history of radiation therapy or chemotherapy. There must be a physician's statement that says this is a therapy related neoplasm (acute myeloid leukemia, MDS, MPN, or MDS/MPN.)
  - If a specific myeloid neoplasm that is described with a different specific histology term is also stated to be therapy related, code 9920/3 to capture the fact that this disease was therapy related. Document the other specific histology term in the text part of the abstract.
- These notes are found in the Hematopoietic database

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Therapy Related Neoplasms

- In the Heme DB, review Histology 9920/3 and familiarize yourself with it's meaning and the rules regarding it
- Notes for 9920/3 (found under **Abstractor Notes**)
  - DO NOT code therapy-related myeloid neoplasm simply because the patient has a history of radiation therapy or chemotherapy. *There must be a physician's statement that says this is a therapy-related neoplasm (acute myeloid leukemia, MDS, MPN, or MDS/MPN.)*
  - If a specific myeloid neoplasm that is described with a different specific histology term is also stated to be therapy related, code *9920/3* to capture the fact that this disease was therapy related. Document the other specific histology term in the text part of the abstract.
- *The pathologist/physician must state "therapy-related" to use this code*

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Therapy Related Neoplasm-Example 1

- 4/8/24 Bone marrow bx: Extensive involvement by Acute Myeloid Leukemia (AML). Likely therapy related. Based on flow cytometry and morphologic findings, it is better sub classification of AML as AML with minimal differentiation (AML-M0), or otherwise called therapy related AML according to pt's history. Final synoptic dx - 1. Therapy related myeloid neoplasms (MDS/AML). 2. AML with minimal differentiation

- Per the note in the Heme DB for 9920/3
  - Code histology 9920/3
  - Record "AML with minimal differentiation" in your histology text field, along with the therapy related myeloid leukemia

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Therapy Related Neoplasm-Example 2

- Findings are *consistent with* myelodysplastic syndrome secondary to previously treated MPN, which may be best classified as myelodysplastic syndrome post cytotoxic therapy (MDS-pCT) according to new WHO classification."

- This is a therapy related neoplasm, 9920/3
- "Myelodysplastic syndrome post cytotoxic therapy" is new terminology for 9920/3

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Therapy Related Neoplasm–Example 3

- I have a patient with metastatic breast cancer who underwent bone marrow bx with diagnosis of refractory anemia. Pt being treated with chemotherapy. Is this considered a new primary? I am unable to find this answer.

- This would be a second primary, refractory anemia (9980/3)
- Note: This would not be a "therapy related" neoplasm since there is no documentation in the pathology report that this is therapy related
- Do not assign therapy related (9920/3.) just because the patient had a previous cancer and was treated. The pathologist or the physician must state that the neoplasm is therapy related

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Fabulous Prizes

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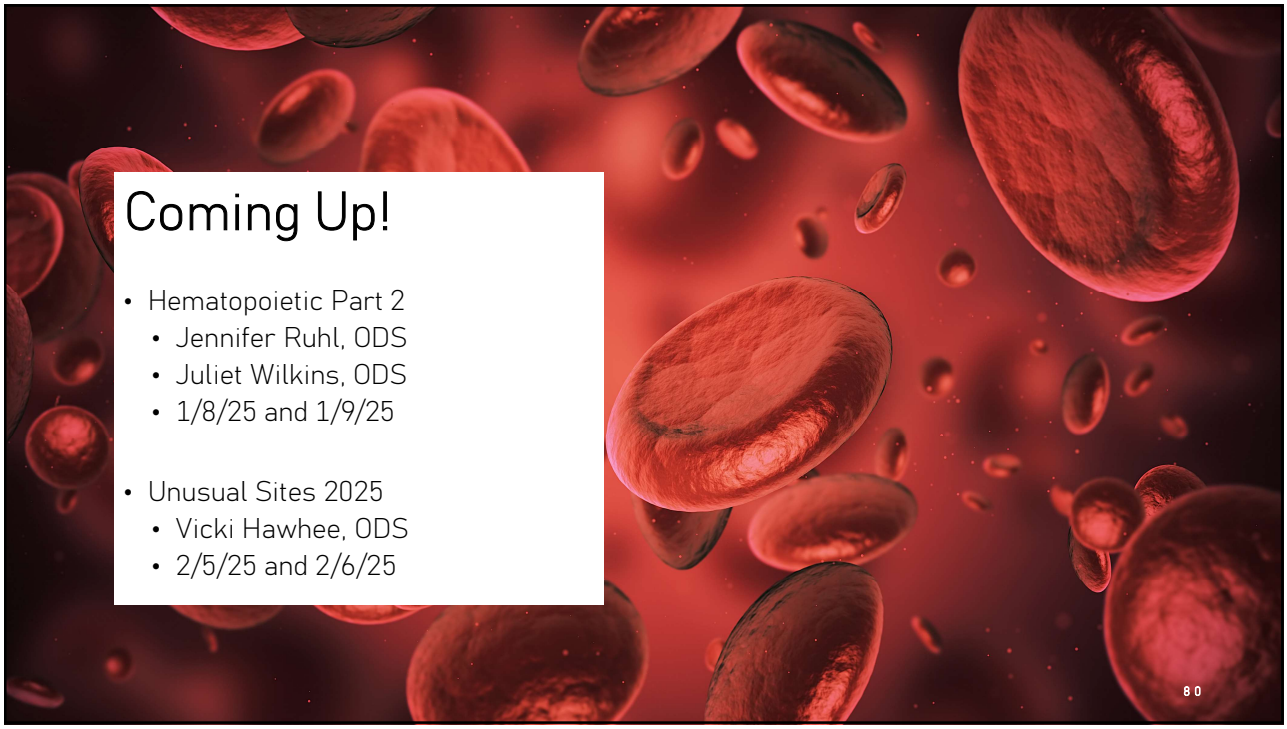

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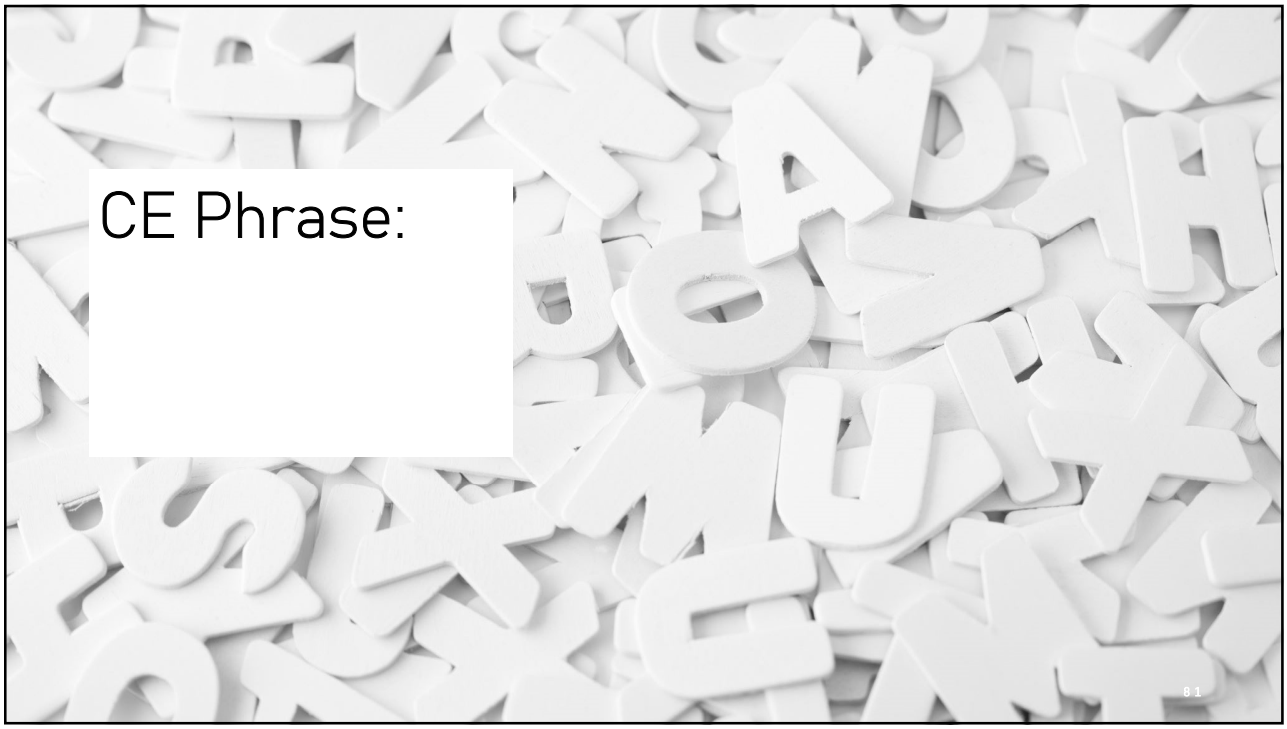

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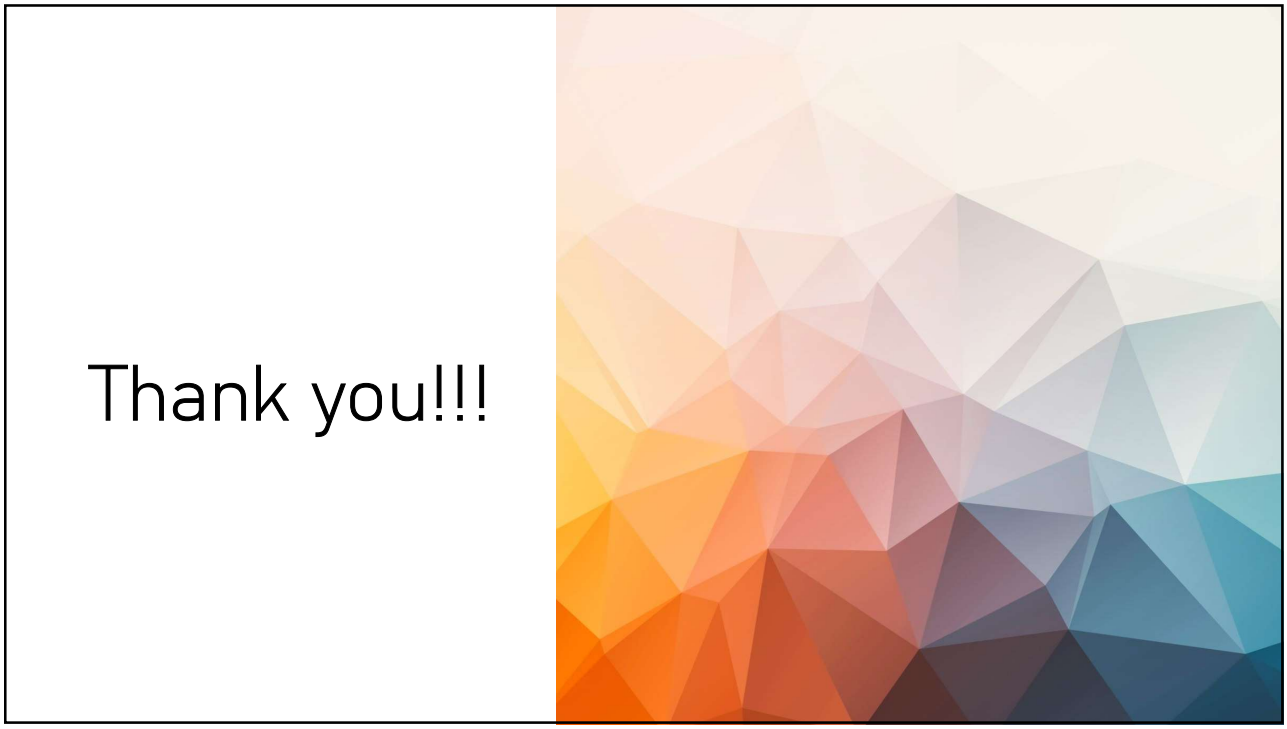

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