INTRODUCTION TO CYTOGENETICS AND MOLECULAR TESTING IN MDS

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WELCOME

Welcome to London, Ontario







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OBJECTIVES

- At the conclusion of this presentation the participant will be able to:
 - Describe the Cytogenetic and Molecular testing that are performed on blood and bone marrow samples
 - 2. Understand the importance of Cytogenetic and Molecular testing in conditions such as myelodysplastic syndrome (MDS)
 - 3. Describe the potential impact of Cytogenetic and Molecular test results in conditions such as myelodysplastic syndrome (MDS)







DISCLOSURES

- Relevant conflicts of interest for current presentation in the last 3 years:
 - Participated as a consultant in advisory boards for Celgene, Novartis, Amgen, & Jansen
 - Received speakers honoraria from Celgene, Novartis, Amgen, & Jansen
- Liberal use of images from the internet for illustration and teaching purposes







SOME BASICS: BLOOD CELLS AND WHERE THEY COME FROM

Our bodies are made of cells and more cells..

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CBC

The complete blood count





CBC

The complete blood count





BLOOD

What is blood made of?







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BONE MARROW

This is the factory that makes all of our blood cells..





THE STEM CELL

In the bone marrow factory, all of our blood cells come from a stem cell. Stem cells divide and grow and eventually become these different blood cells.







BONE MARROW

This is how we take a bone marrow sample..





Because our cells are controlled by genes..

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WHERE ARE THESE GENES?

 In all cells in our body with a Nucleus, there are genetic materials called genes that controls all the actions of these cells





WHERE ARE THESE GENES?

- These genes are neatly coiled into structures called chromosomes in the Nucleus of each cell.
- We have 23 pairs of chromosomes in the Nucleus of each cell usually.





WE INHERIT THESE GENES

- We have 2 sets of genes in the Nucleus of each cell.
- 1 set comes from our father and 1 set comes from our mother.





GENETIC MUTATIONS

- Mutations in our genetic materials, genes, can be inherited or acquired.
- Inherited mutations are passed down from the genes from our father or mother.



GENETIC MUTATIONS

- Mutations in our genetic materials, genes, can be inherited or acquired.
- Acquired mutations can occur at any point in our cells after birth from many causes. Often these mutations can occur by random chance during cell division.







CYTOGENETICS

- Cytogenetics is the study of these chromosomes
- We want to know if there are any changes in the chromosome structure, location, or function



CYTOGENETICS

- Cytogenetics is the study of these chromosomes
- We want to know if there are any changes in the chromosome structure, location, or function
- Example: 5q deletion in MDS





MOLECULAR GENETICS

- Molecular genetics is the study of genetic material in chromosomes
- We want to know if there are any mutations in the genetic materials of cells



MOLECULAR GENETICS

• Example: SF3B1 is a mutation in MDS with ring sideroblasts









LET'S TALK MDS



MYELODYSPLASTIC SYNDROMES

Definition

 Myelodysplastic syndromes (MDS) form a group of clonal hematopoietic stem cell malignancies characterized by ineffective hematopoiesis in one or more cell lineages, associated peripheral cytopenias, and risk of transformation to acute myeloid leukemia

Sloand EM. Myelodysplastic syndromes: introduction. Semin Hematolo. 2008;45:1-2. Valent P, Horny HP, Bennett JM, et al. Leuk Res 2007;31:72-36.



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Dr. Robert Barr and the Ford Pinto



MYELODYSPLASTIC SYNDROMES

In other words..

- MDS is a group of blood and bone marrow disorders (cancers) where the blood cells are made with defects and don't survive as long as it should.
- This leads to low blood counts in 1 or more of the blood cells.
- It is NOT leukemia, but can be considered pre-leukemic.
- It is NOT 1 disease and behaves differently in different people.



SUMMARY

- Myelodysplastic syndromes (MDS) are a heterogenous group of bone marrow disorders or cancers of the bone marrow
- Management of MDS relies on understanding the severity of the disease by assessing the number of blasts in the bone marrow, the number of blood cells involved, cytogenetics and molecular diagnostics
- A specific example of a cytogenetic abnormality in MDS is the 5q del that may confer good response to a drug called Revlimid (lenalidomide).
- A specific example of a molecular genetic abnormality in MDS is the SF3B1 that may confer good response to a new drug called luspatercept (currently not available).





Bone marrow factory - The future Any Questions?



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APPENDICES

