

# Setting the stage for Transplant in MPN

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# *Setting the Stage*

What will be covered

What is a bone marrow transplant?

When to start thinking about bone  
marrow transplant

Timing of transplant

Understanding disease risk

# Bone marrow transplantation

- Involves high dose/intermediate dose chemotherapy followed by hematopoietic stem cell infusion.
  - Chemotherapy helps reduce disease + suppress immune system
  - New blood system works better
  - New stem cells fight off underlying disease 'graft versus myelofibrosis'
- Autologous: uses patients own stem cells, allows use of high dose chemotherapy
- Allogeneic : uses donor stem cells, either related or unrelated

# Alternative names

- Alternative names:
  - Peripheral blood stem cell transplant
  - Hematopoietic stem cell transplant
  - Bone marrow transplant
- Bone marrow vs peripheral blood
  - Refers to how the hematopoietic stem cells are collected:
    - Bone marrow: through bone marrow harvest, a procedure performed in the OR
    - Peripheral blood collection: collected after giving neupogen via leukopheresis

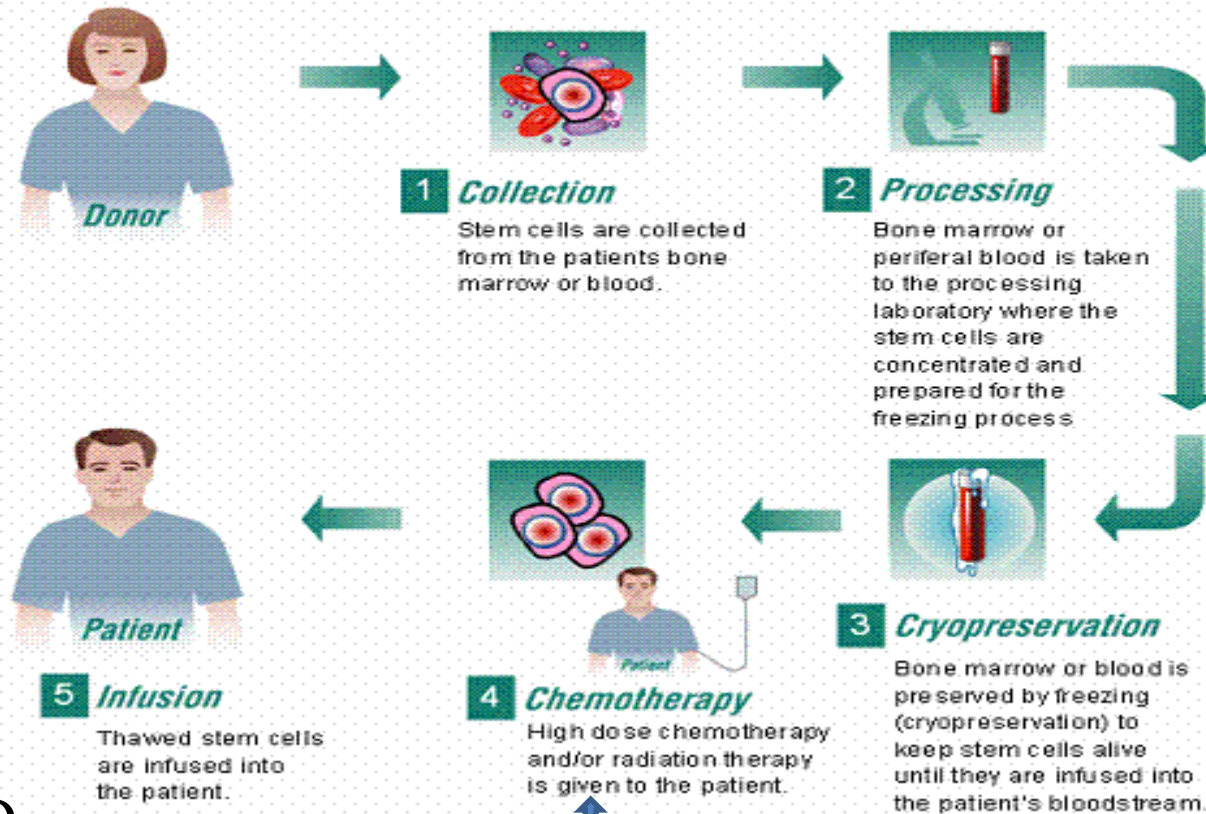


# Leukopheresis



# How does transplant work

## The Allogeneic Transplant Process

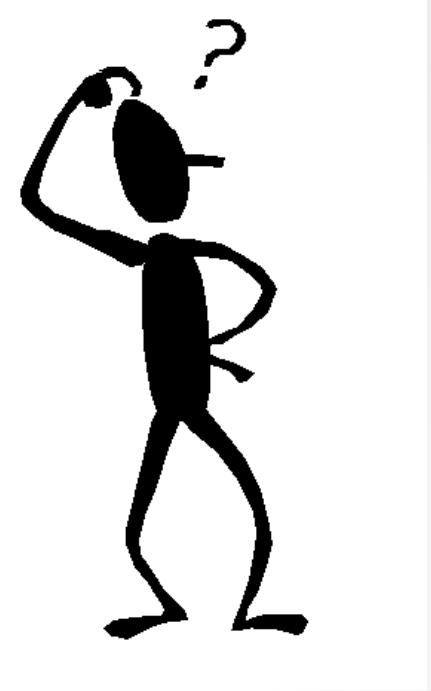


Conditioning

[http://biomed.brown.edu/Courses/BI108/BI108\\_2007\\_Groups/group07/stemcells/img/Allogenic\\_big.gif](http://biomed.brown.edu/Courses/BI108/BI108_2007_Groups/group07/stemcells/img/Allogenic_big.gif)



WHY WOULD I WANT TO DO THIS TO  
MYSELF?



SHOULD I PURSUE A CLINICAL TRIAL  
INSTEAD?

# What are common concerns about transplant?

- Survey done on patients with MPN
- Less than half the patients were referred for transplant
- Of those who saw a transplant specialist, less than half planned on proceeding with transplant due to the following concerns
  - Quality of life
  - Financial implications
  - Caregiver
  - Graft versus host disease
- WHY??
  - Further studies ongoing to understand the thought process around transplant



# Other considerations

- Physicians are human and have biases as well
  - Transplant physicians
  - Hematologists
- Blogs
  - Everyone experiences transplant differently
  - People like to share their experiences

# Clinical trials and medical treatment

- There are good clinical trials and treatments in MF
  - No curative options yet
- This is a very individualized decision

# When do I see a transplant specialist?

- Important to see a transplant specialist early in the disease course— even if you aren't sure whether you will proceed with transplant or not
  - Understand and plan for the different resources needed for transplant
    - Caregiver
    - Financial
    - Lodging
  - Understand the process of transplant
  - Have time to **process** all the information related to transplant

# Who should I see?

- Helpful to see a transplant specialist who has knowledge regarding transplants for MF
  - The timing of transplant is a **SHARED** decision making process
  - There is no one answer that is correct for anyone
- Even if you don't get a transplant at the center, good to have the discussion/opinion



# What to expect during a bone marrow transplant consultation

- Bring a family member/friend
- Be prepared to be scared
- If you can, record the consultation
- If you have any doubts get a second opinion



# So, when should I get a transplant?

- Generally transplant is reserved for higher risk patients
- It is important to KNOW YOUR RISK
- Can be dependent on life events

# HOW DO WE DEFINE RISK?



# Dynamic International Prognostic Scoring System

DIPSS scores/risk:

- 0 pts: low risk
- 1-2 pts: Intermediate – 1
- 3-4 pts: Intermediate – 2
- 5-6 pts: High risk

DIPSS	DIPSS plus
Anemia (hgb <10) (2 pts)	DIPSS score
WBC >25	Platelets <100
Blasts >1%	Transfusion dependant
Constitutional symptoms	poor risk cytogenetics: complex karyotype or any sole or two abnormalities including +8, -7/7q-, -5/5q-, inv(3), i(17q), 12p-, 11q23 rearrangement
Age >60	

DIPSS plus scores/risk

- 0 pts: low risk
- 1 pt: intermediate-1
- 2-3 pts: intermediate-2
- 4-6 pts: high risk

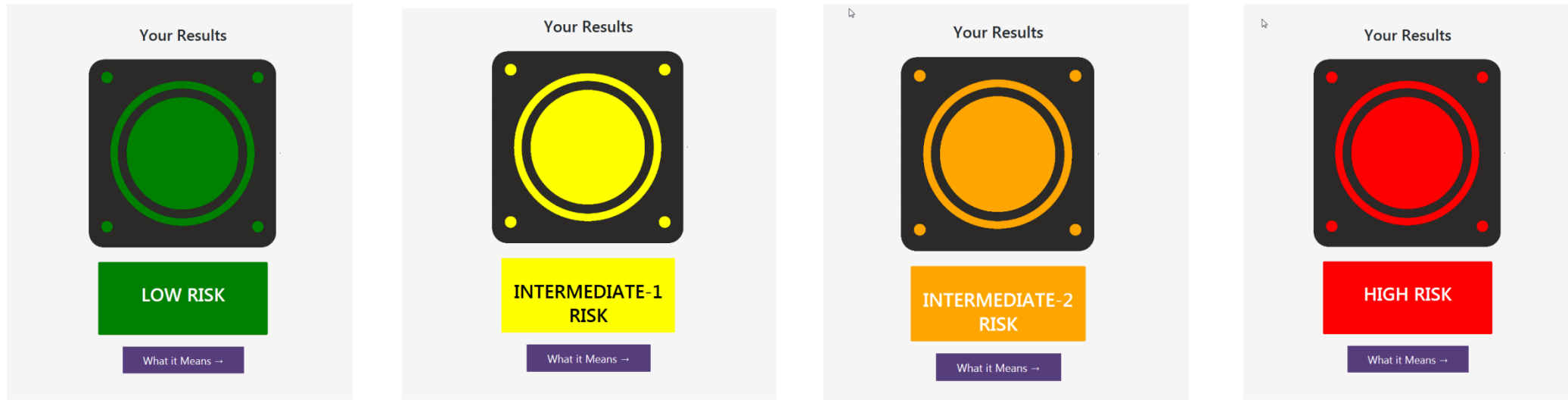


# Clarification of risks

- Anemia—low red blood cell count. Hemoglobin (hgb) is consistently less than 10
- Thrombocytopenia- low platelet (plt) count, less than 100.
- Leukocytosis – high white blood cell count (WBC), consistently greater than 25
- Blasts – immature white blood cells
  - Note this does not mean you have leukemia unless blast % greater than 20%
- Abnormal karyotype
- Constitutional symptoms- fatigue, weight loss, decreased appetite, night sweats

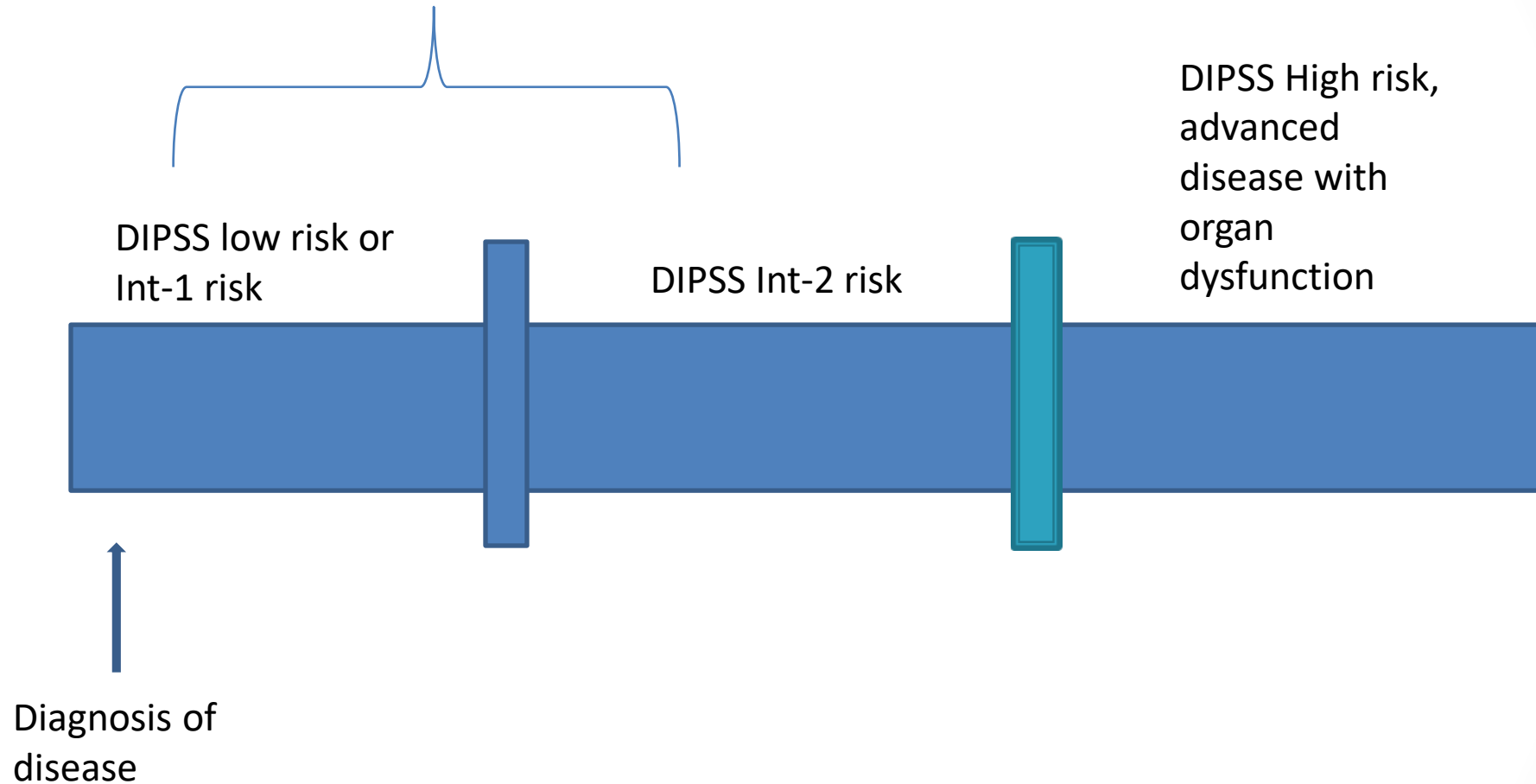
# Stem cell transplant spectrum timing tool

- This tool uses DIPSS score to give a sense of when a transplant should be considered

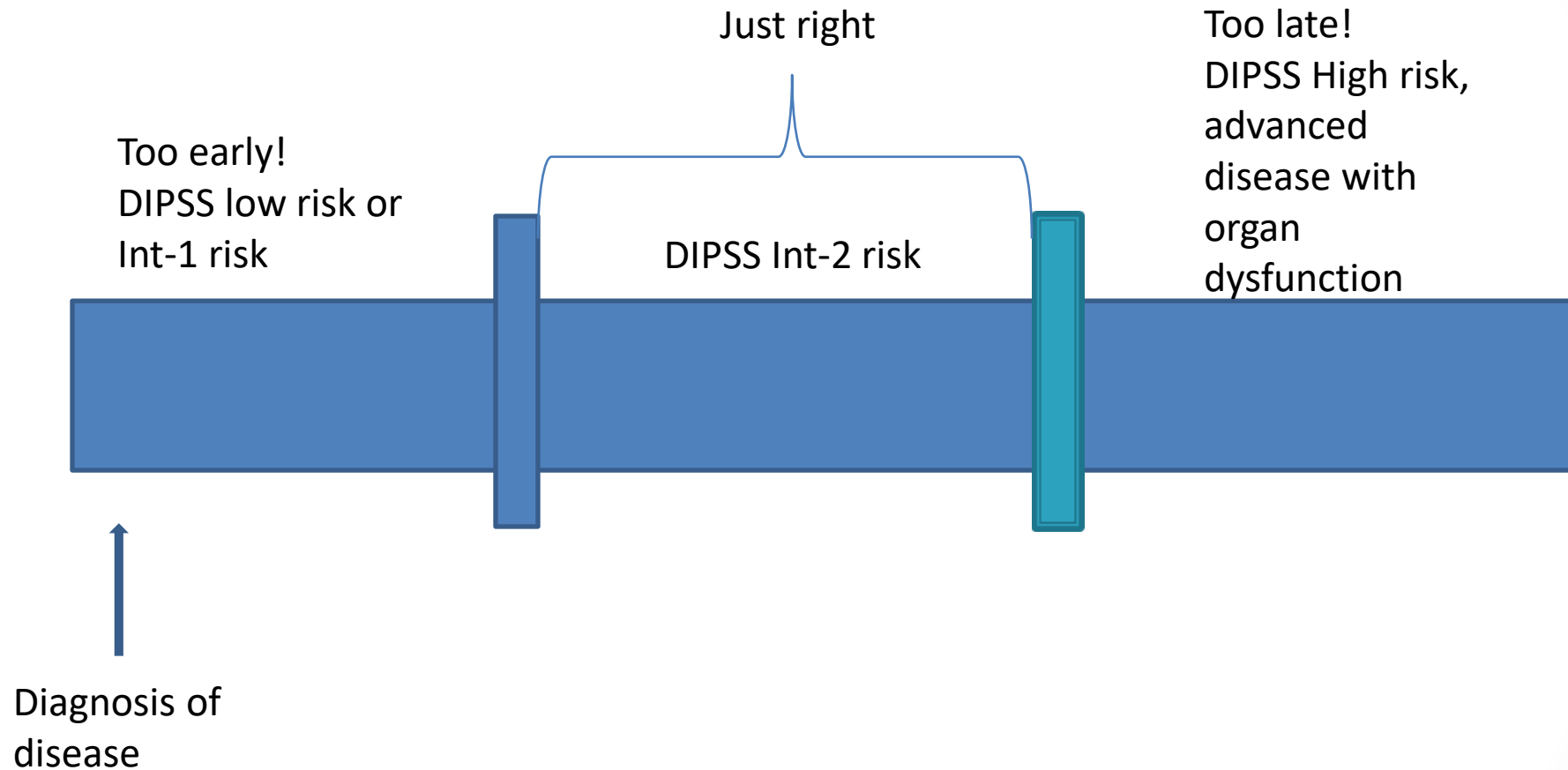


- Even in the case of low risk disease- good to start the conversation
- <http://www.mpntransplant.com/>

# When to **think about** a transplant



# When to **do** transplant



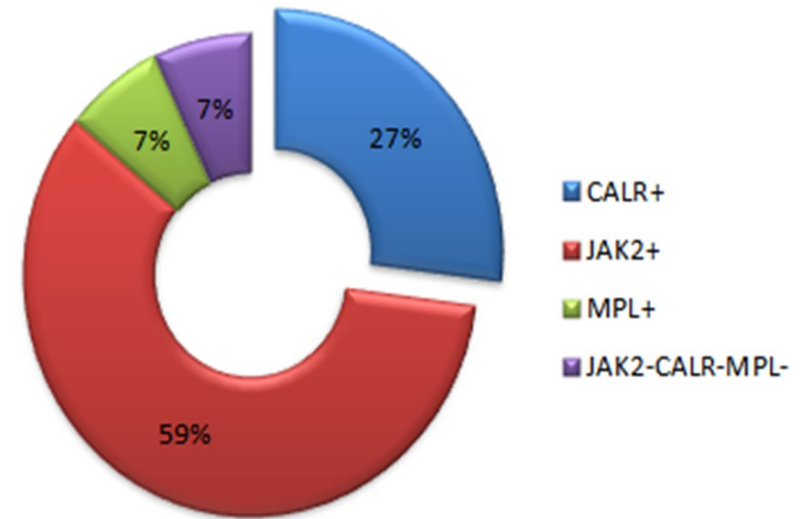


# Other factors that contribute to risk

- Driver mutation
- Cytogenetics
- Molecular mutations

# Driver mutation

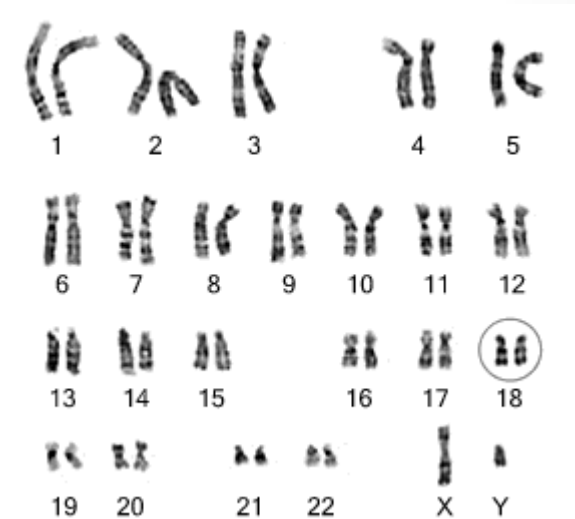
- Mutations that CAUSE the disease
  - JAK-2
  - MPL
  - CAL-R
- CAL-R is GOOD
- No mutations is unfavorable



# Cytogenetics

- Cytogenetics (abnormal chromosomes found in your bone marrow)
  - complex karyotype (3 or more abnormalities) or sole or 2 abnormalities that include +8, -7/7q-, i(17q), inv(3), -5/5q-, 12p-, or 11q23 rearrangement

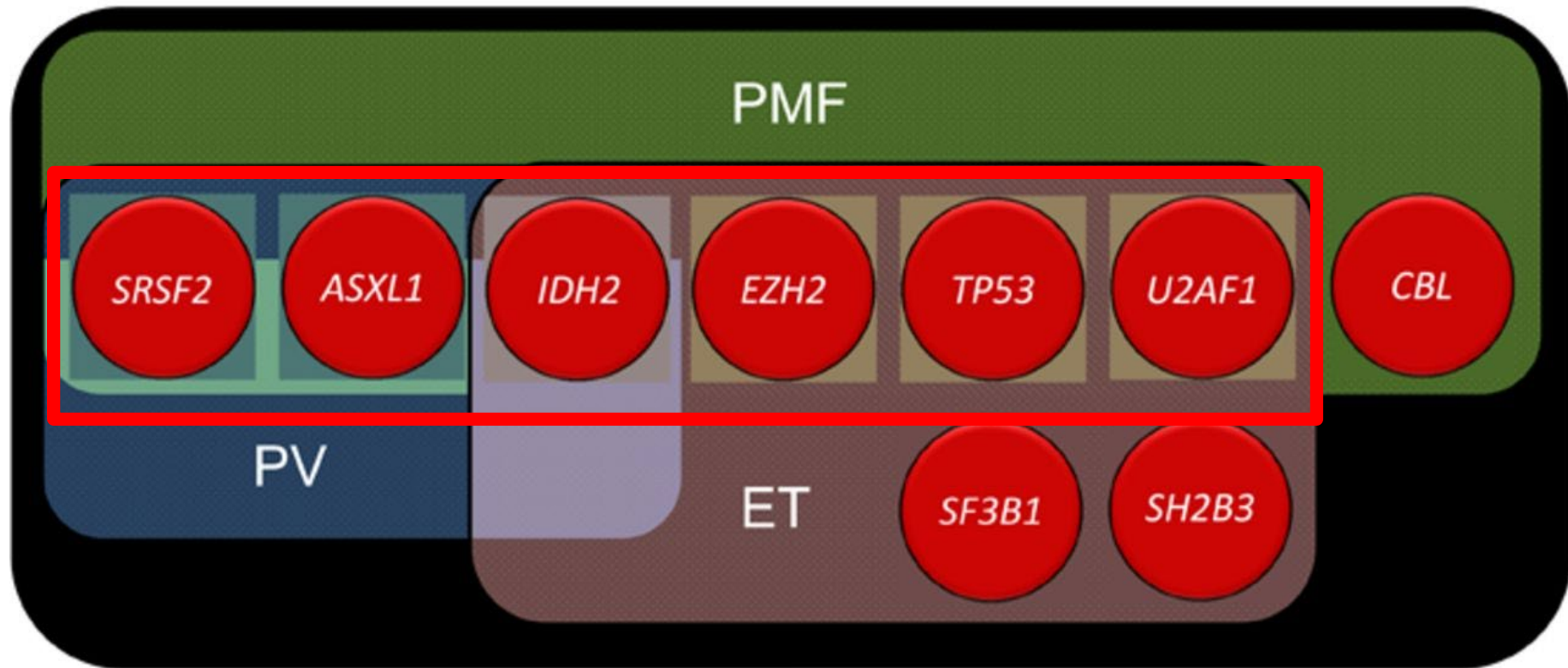
*These are not inherited...  
they are changes that occur only in disease cells*



# Molecular mutations

## “next generation sequencing”

Prognostically important genes, other than *JAK2/CALR/MPL*, in essential thrombocythemia (ET), polycythemia vera (PV) and primary myelofibrosis (PMF)

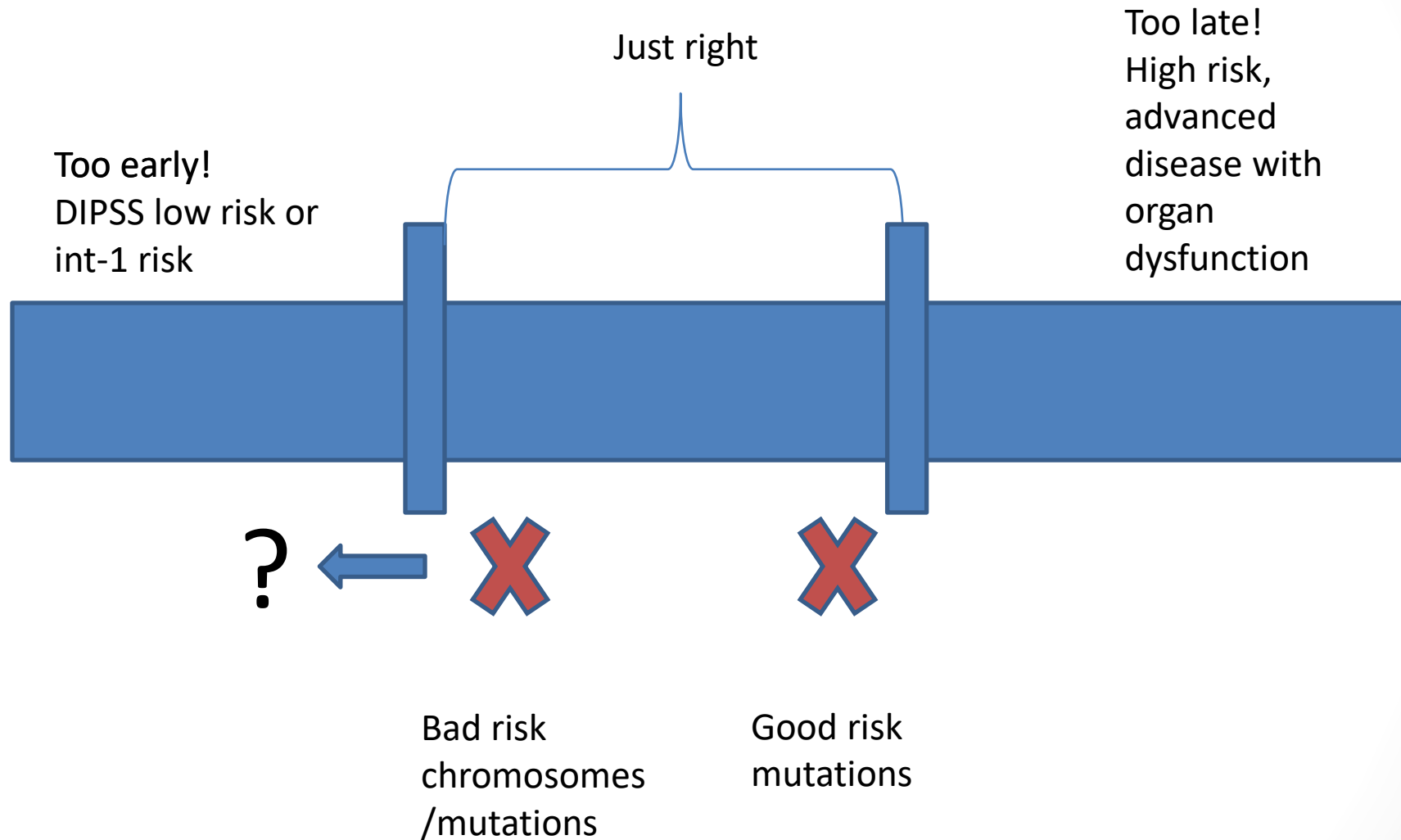




# Good news

- The disadvantages of high risk disease are usually overcome with transplant!!

# When to **do** transplant



# Other considerations

- Symptom burden
- Ruxolitinib (Jakafi®)
- Transfusion dependence
- What gives you points??

# Example #1

- 64 year old patient with primary myelofibrosis
- CAL-R positive
- On 1/5/19 WBC 23K, 2% blasts, hgb 9.7, platelets 115 (DIPSS: 3)
- On 2/5/19 WBC 26K, 0 blasts, hgb 10.2, platelets 150 (DIPSS: 1)
- Would this change if JAK2 positive?
- ASXL1 positive?

## Example #2

- Patient is 58 year old female with post-essential thrombocythemia myelofibrosis
- MPL positive
- Hgb 7, requires transfusion every month, WBC 6.7, Blasts 0 DIPSS: 2

## Example #3

- 65 year old male with primary myelofibrosis
- JAK2 positive
- Hgb 9.5, WBC 7.2, blasts 0, platelets 165 DIPSS: 3

# Summary

- Bone marrow transplant is a curative option for myelofibrosis
- When the best time to undergo transplant is still under investigation
- Know your risk! The risk of disease as characterized by cytogenetics, molecular mutations etc



# Survivors

