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

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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

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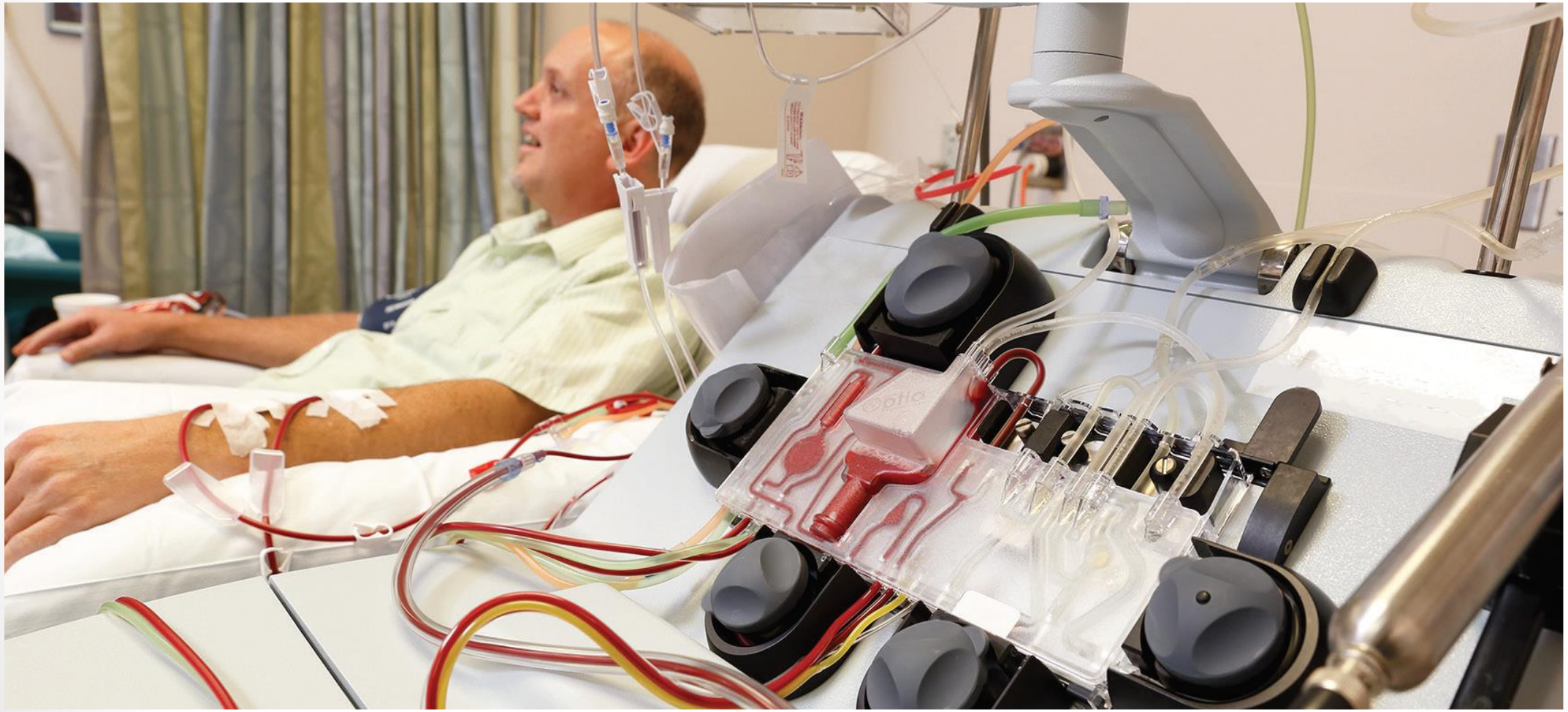
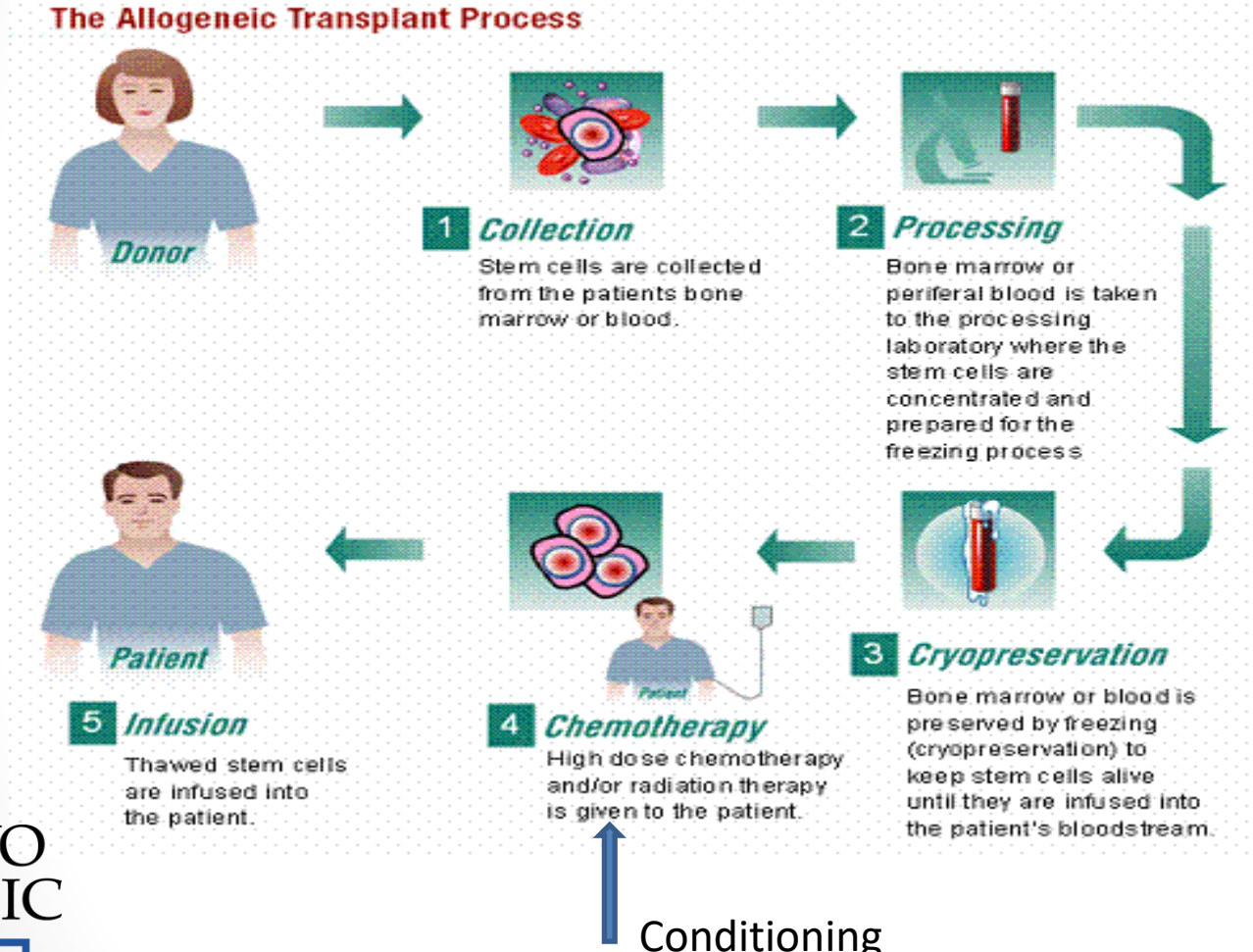
Leukopheresis



How does transplant work



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Conditioning

http://biomed.brown.edu/Courses/BI108/BI108_2007_Groups/group07/stemcells/img/Allogenic_big.gif

What needs to happen

- Live near the transplant center for 3-4 months
- 1 month in the hospital (or daily appointments at the hospital)
- Time off of work for you and your caregiver
- Risk of being really sick or even dying

WHY WOULD I WANT TO DO THIS TO MYSELF?

SHOULD I PURSUE A CLINICAL TRIAL INSTEAD?

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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

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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

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HOW DO WE DEFINE RISK?

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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

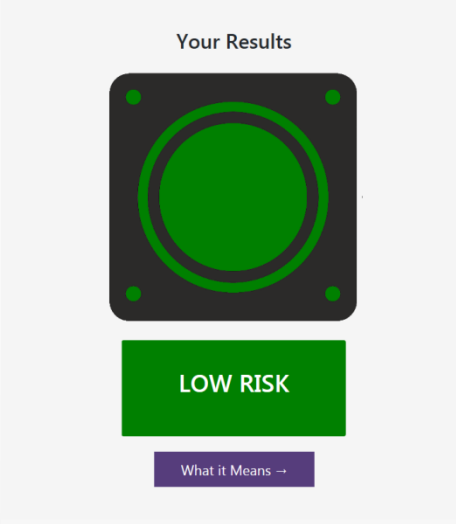
- 0 pts: low risk
- 1 pt: intermediate-1
- 2-3 pts: intermediate-2
- 4-6 pts: high risk

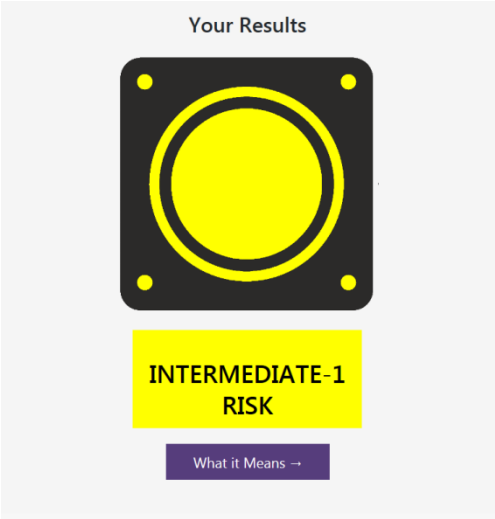
Clarification of risks

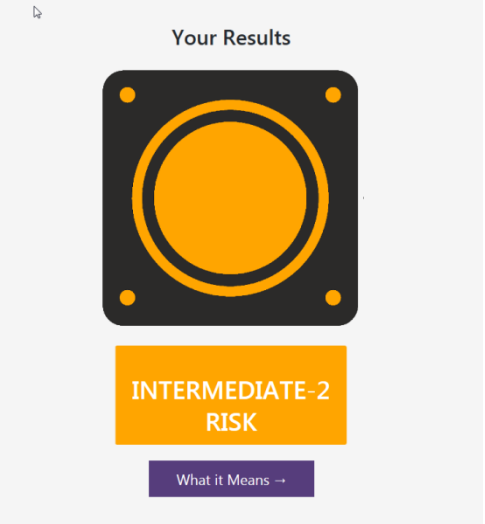
- Anemia–low red blood cell count. Hemoglobin (hgb) is consistently less than 10
- Thrombocytopenia- low platelet (plt) count, less than 100.
- Leukocytosis – high white blood cell count (WBC), consistently greater than 25
- Blasts – immature white blood cells
  - Note this does not mean you have leukemia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

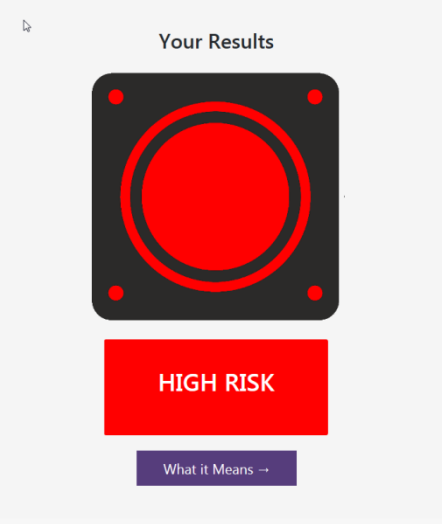
Stem cell transplant spectrum timing tool

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



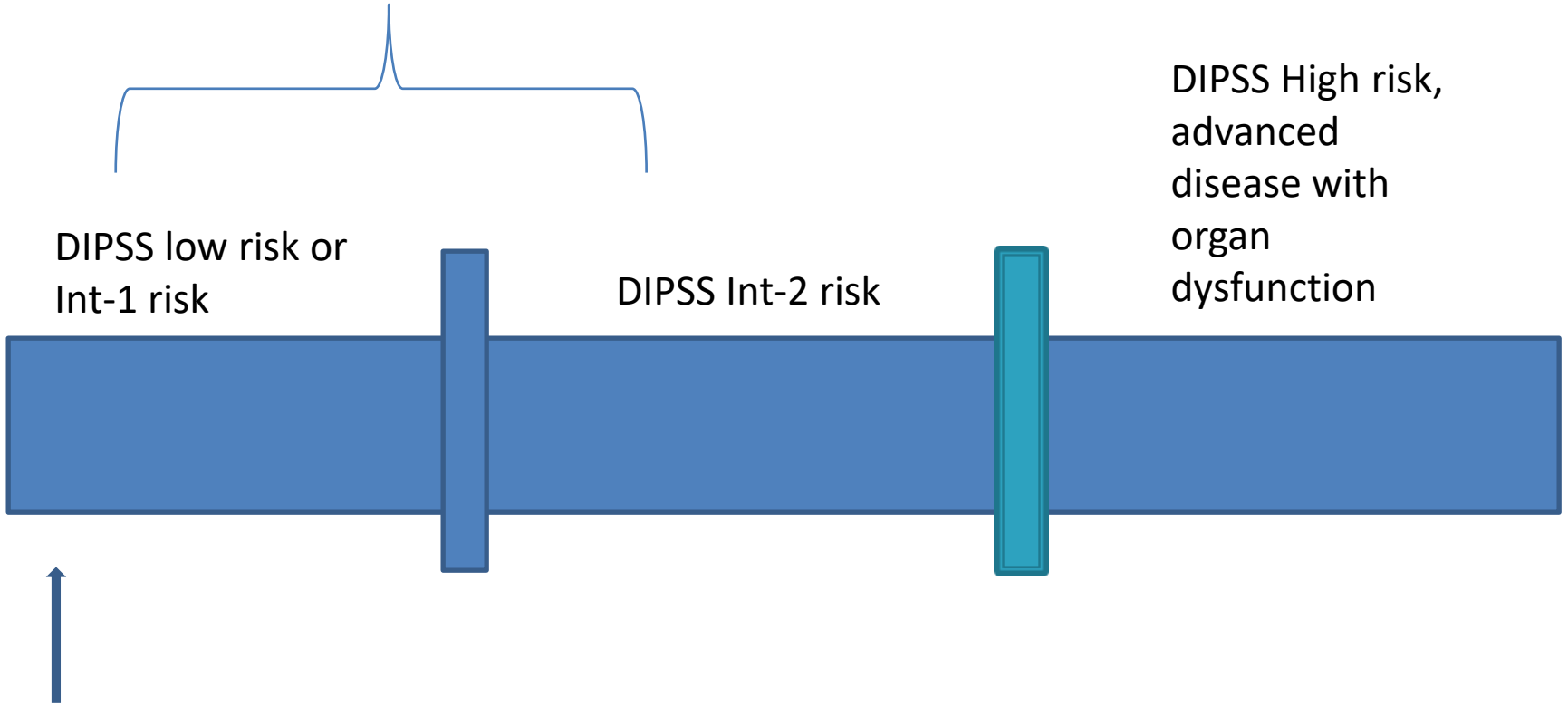






- Even in the case of low risk disease- good to start the conversation
- http://www.mpntransplant.com/

When to **think about a** transplant



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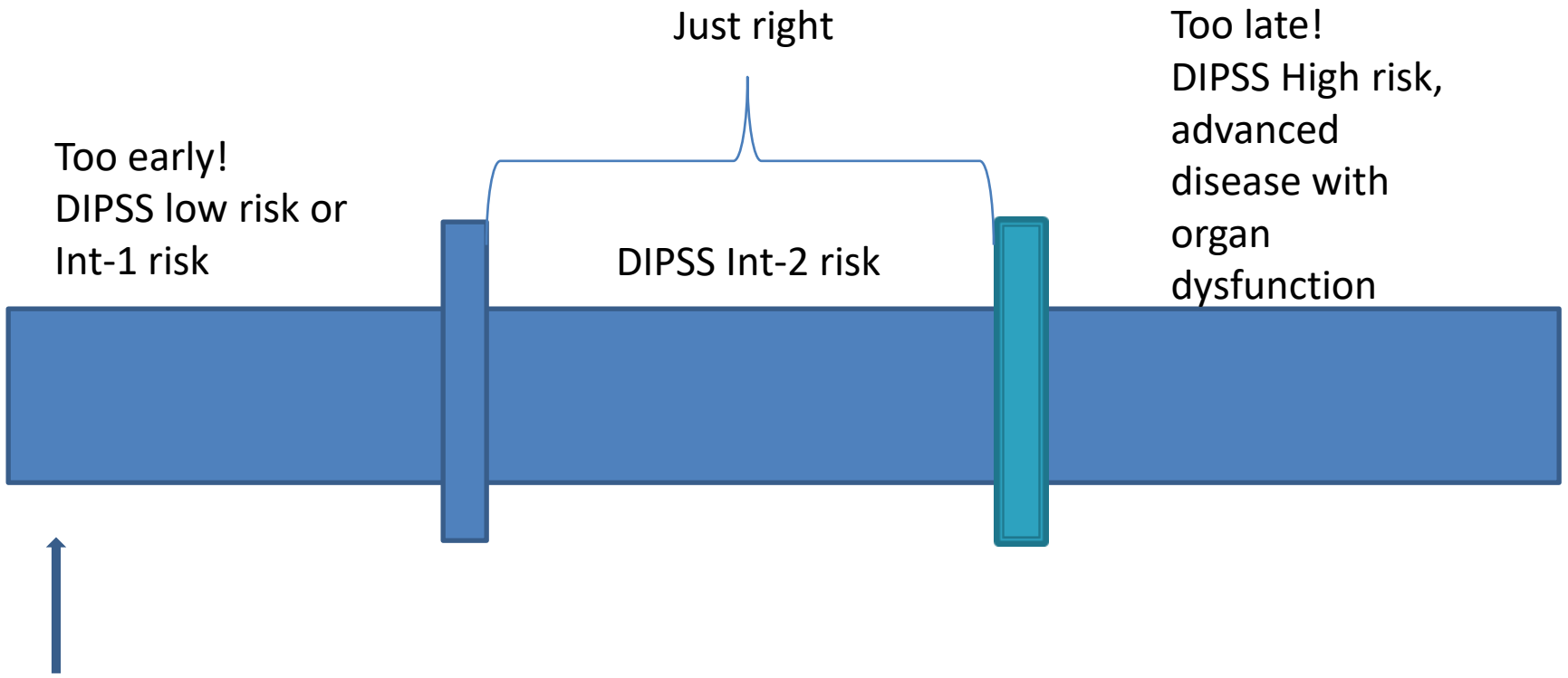
When to **do** transplant



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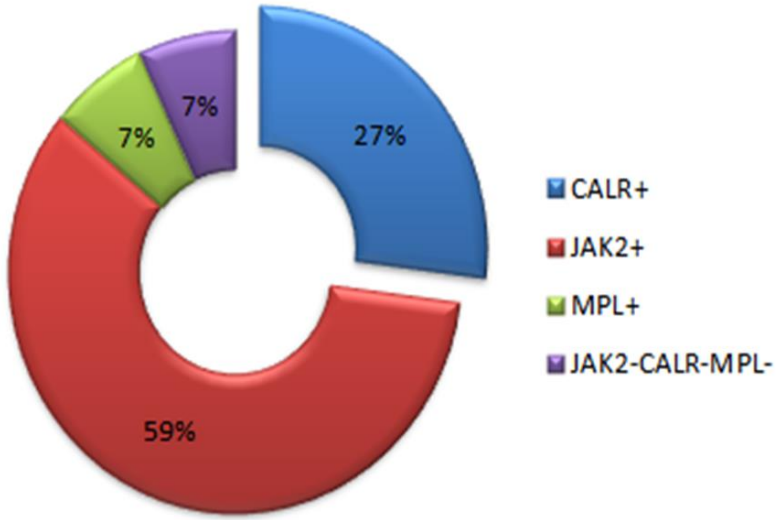
Other factors that contribute to risk

- Driver mutation
- Cytogenetics
- Molecular mutations

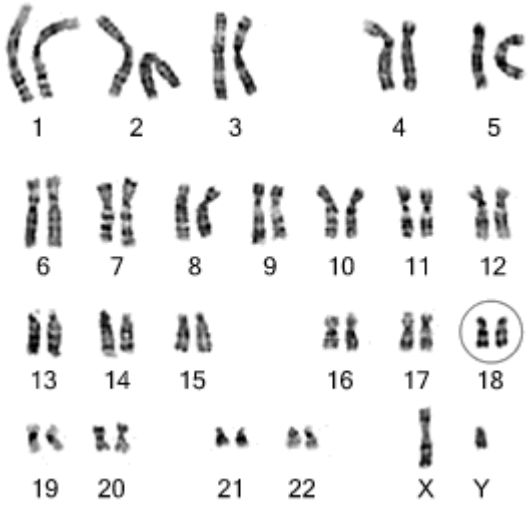
Driver mutation

- 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

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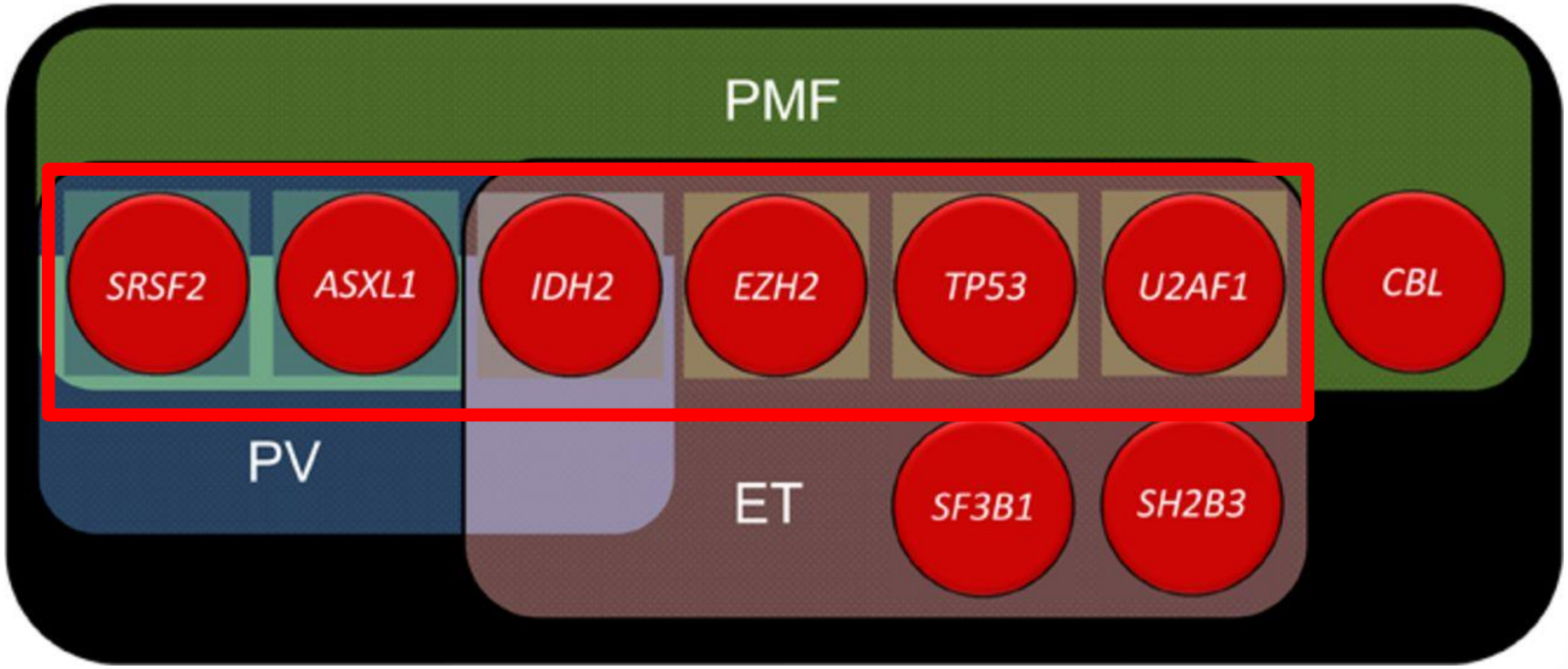
Molecular mutations
"next generation sequencing"

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



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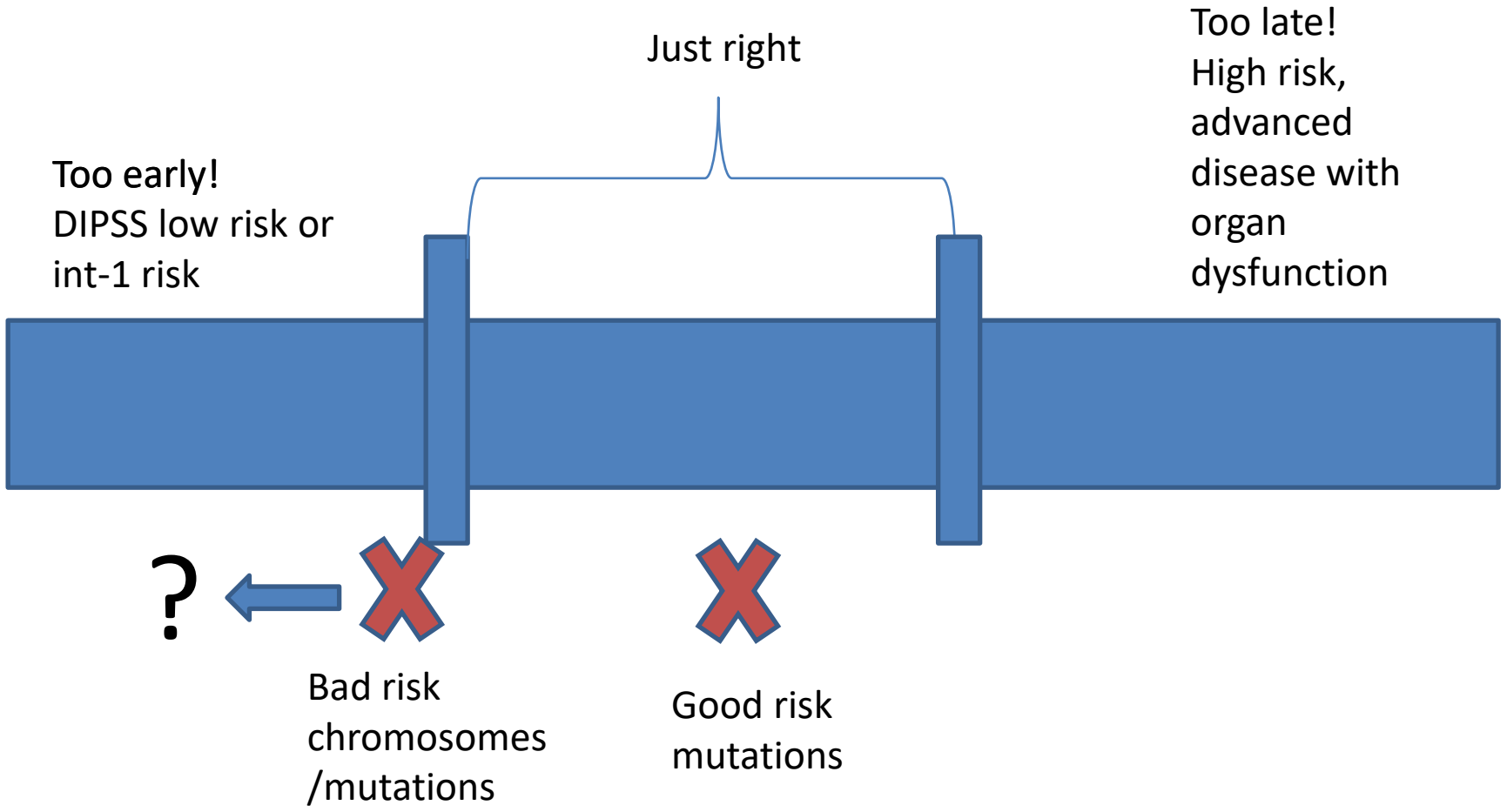
When to **do** transplant



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Other considerations

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

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Example #1

- 64 year old patient with primary myelofibrosis
- CAL-R positive
- On 1/5/20 WBC 23K, 2% blasts, hgb 9.7, platelets 115
  - (DIPSS: 3 points- Intermediate -2)
- On 2/5/20 WBC 26K, 0 blasts, hgb 10.2, platelets 150
  - (DIPSS: 1 points- Intermediate -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 points -Intermediate 1

Example #3

- 65 year old male with primary myelofibrosis
- JAK2 positive
- Hgb 9.5, WBC 7.2, blasts 0, platelets 165
  - DIPSS: 3 points- Intermediate-2

Other questions to consider

- I feel SO good on Jakafi-- should proceed with transplant??
- These newer agents in clinical trial may reduce my mutation burden and fibrosis- will these cure the disease?
- Should I do a clinical trial first, then transplant?

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