



**MPN HORIZONS**  
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7<sup>th</sup> INTERNATIONAL CONFERENCE  
FOR ORGANISATIONS REPRESENTING  
PATIENTS WITH MPN

**MPN** Advocates Network

HYBRID MEETING • NETANYA • ISRAEL • 18.-20.11.2022.

# Updated guidelines in MPN

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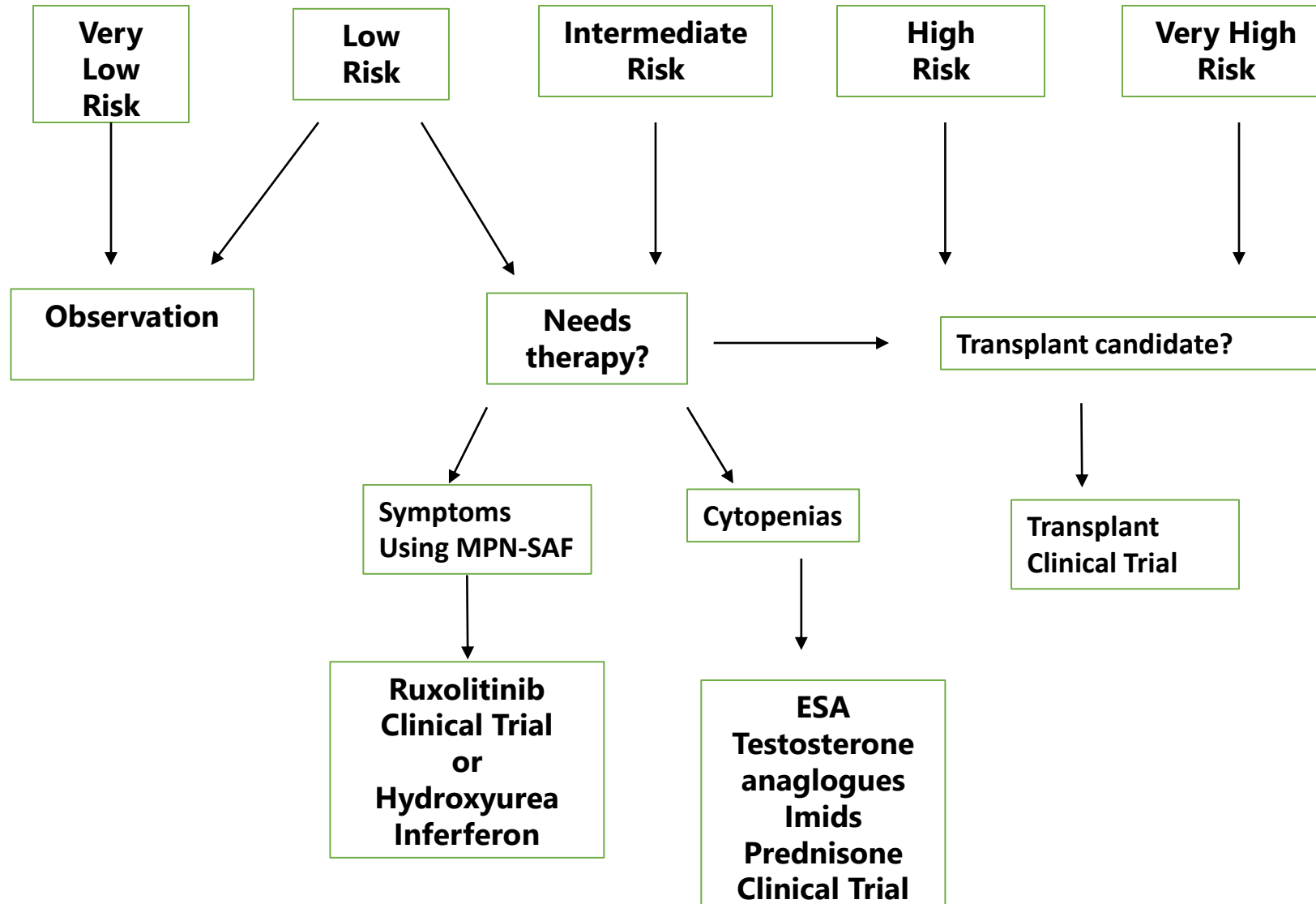
# Outline

- Myelofibrosis treatment approach
- Approved JAK inhibitors
- Update to MF guidelines – NCCN
- Polycythemia vera treatment approach
- Update to PV guidelines NCCN and ELN
- Ropeginterferon

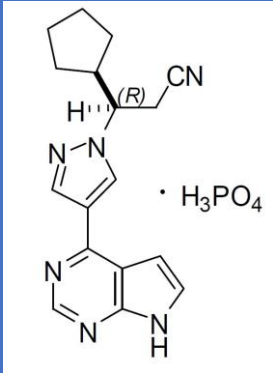
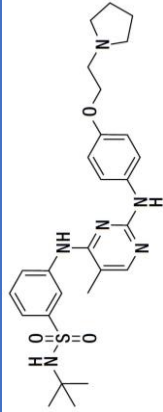
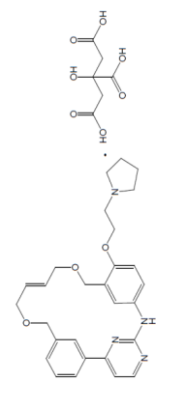
# Guidelines

- National Cancer Care Network (NCCN) in the USA
- European Leukemia Net (ELN) in Europe

# Myelofibrosis treatment approach

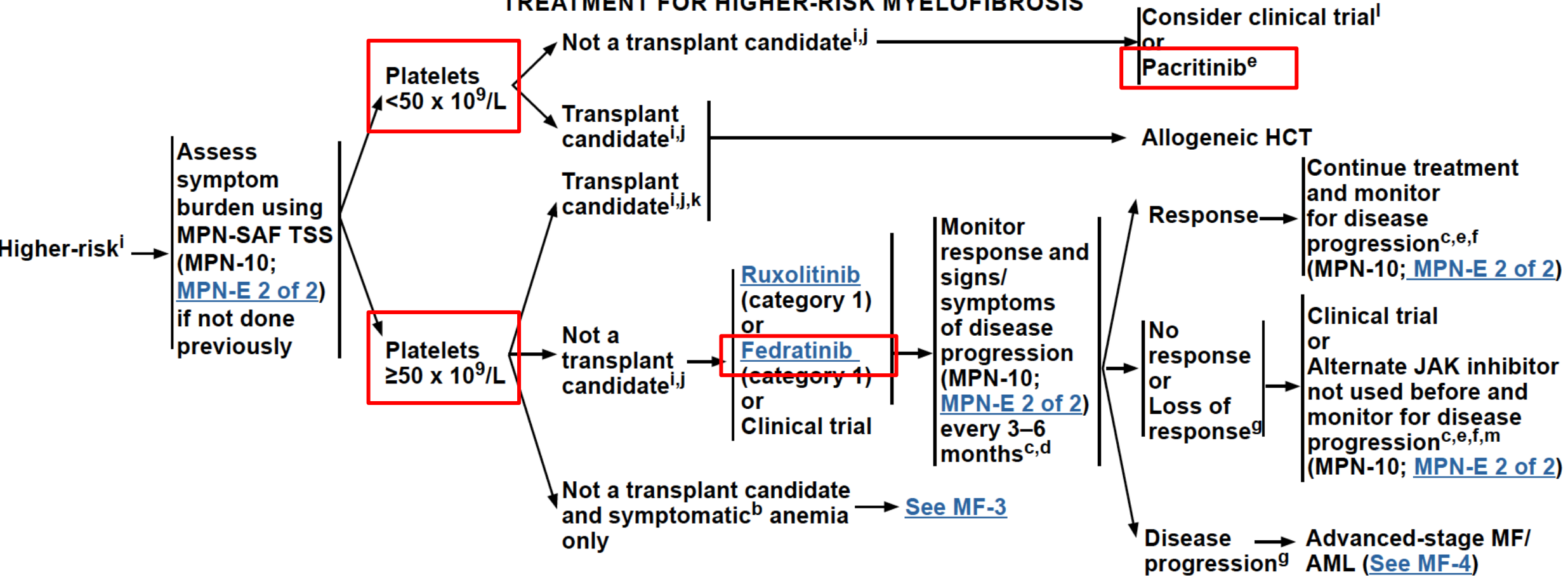


# Three approved JAK inhibitors in the USA

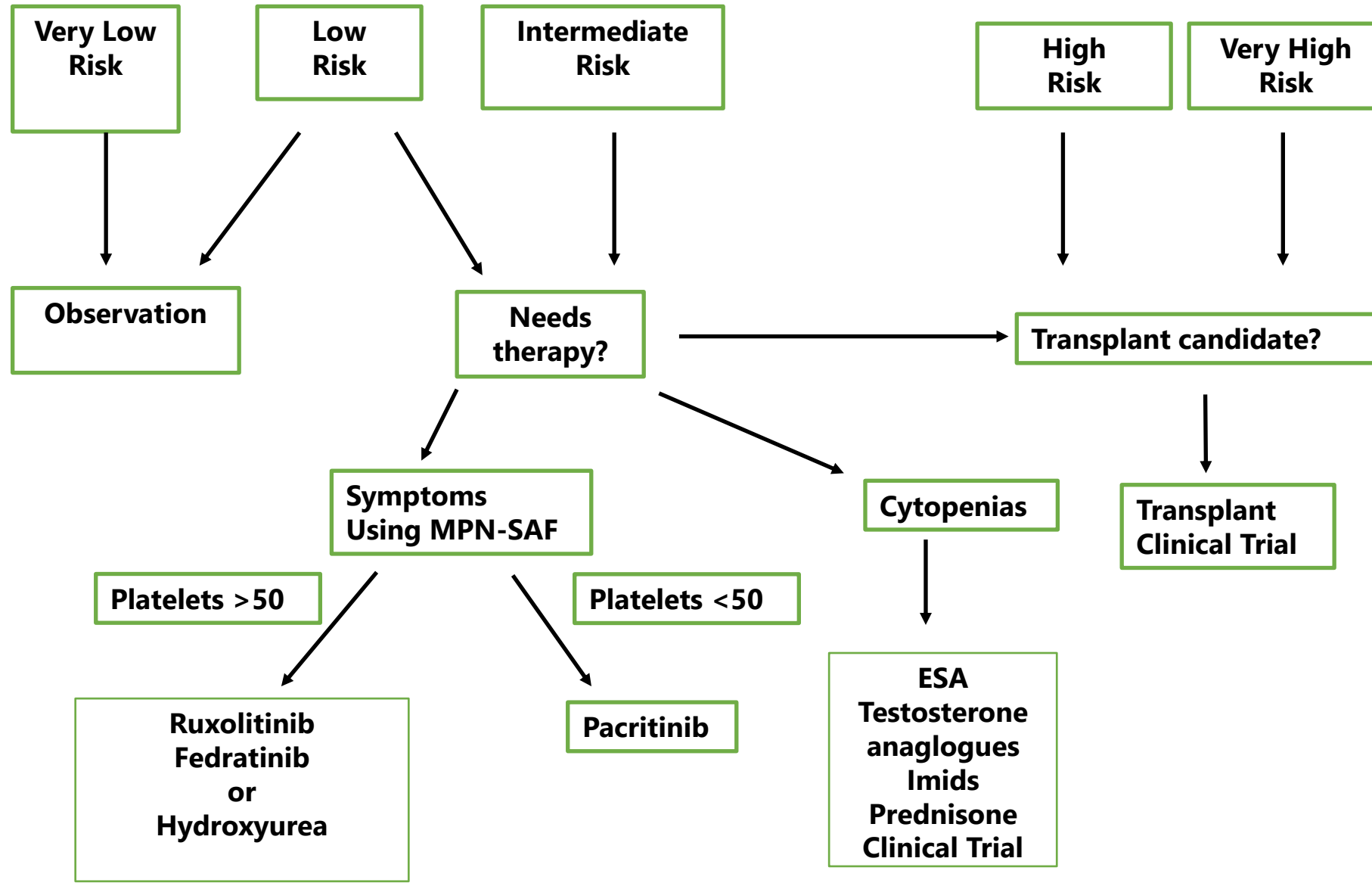
 <p>The image shows the chemical structure of Ruxolitinib phosphate. It features a central imidazole ring connected to a pyrazolo[1,5-a]pyrimidine core. A cyclopentane ring is attached to the imidazole ring, and a cyanoethyl group is attached to the cyclopentane ring. The structure is shown as a salt with a phosphate group (H<sub>3</sub>PO<sub>4</sub>).</p>	 <p>The image shows the chemical structure of Fedratinib. It features a central pyrimidine ring with a methyl group at position 2 and a sulfonamide group at position 4. A piperidine ring is attached to the pyrimidine ring via a methylene chain, and a benzamide group is attached to the piperidine ring via a methylene chain.</p>	 <p>The image shows the chemical structure of Pacritinib. It features a central pyrimidine ring with a methyl group at position 2 and a sulfonamide group at position 4. A piperidine ring is attached to the pyrimidine ring via a methylene chain, and a benzamide group is attached to the piperidine ring via a methylene chain.</p>
<b>Ruxolitinib</b> <ul style="list-style-type: none"><li>• 2011</li><li>• JAK1/2</li></ul>	<b>Fedratinib</b> <ul style="list-style-type: none"><li>• 2019</li><li>• JAK2, FLT3</li></ul>	<b>Pacritinib</b> <ul style="list-style-type: none"><li>• 2022</li><li>• JAK2, IRAK1</li></ul>

# New JAK Inhibitors added to NCCN

## TREATMENT FOR HIGHER-RISK MYELOFIBROSIS



# Updated treatment approach to Myelofibrosis



# Fedratinib

- Approved in USA in 2019, EU in 2021
- JAK2, FLT3 Inhibitor
- Approved in first or second line for int>2 or greater MF in patients with platelets  $> 50 \times 10^9/L$
- FDA hold for Wernicke's encephalopathy
- Check/replete thiamine
- GI side effects – consider concomitant antiemetics at treatment start
- 400 mg daily



# Pacritinib

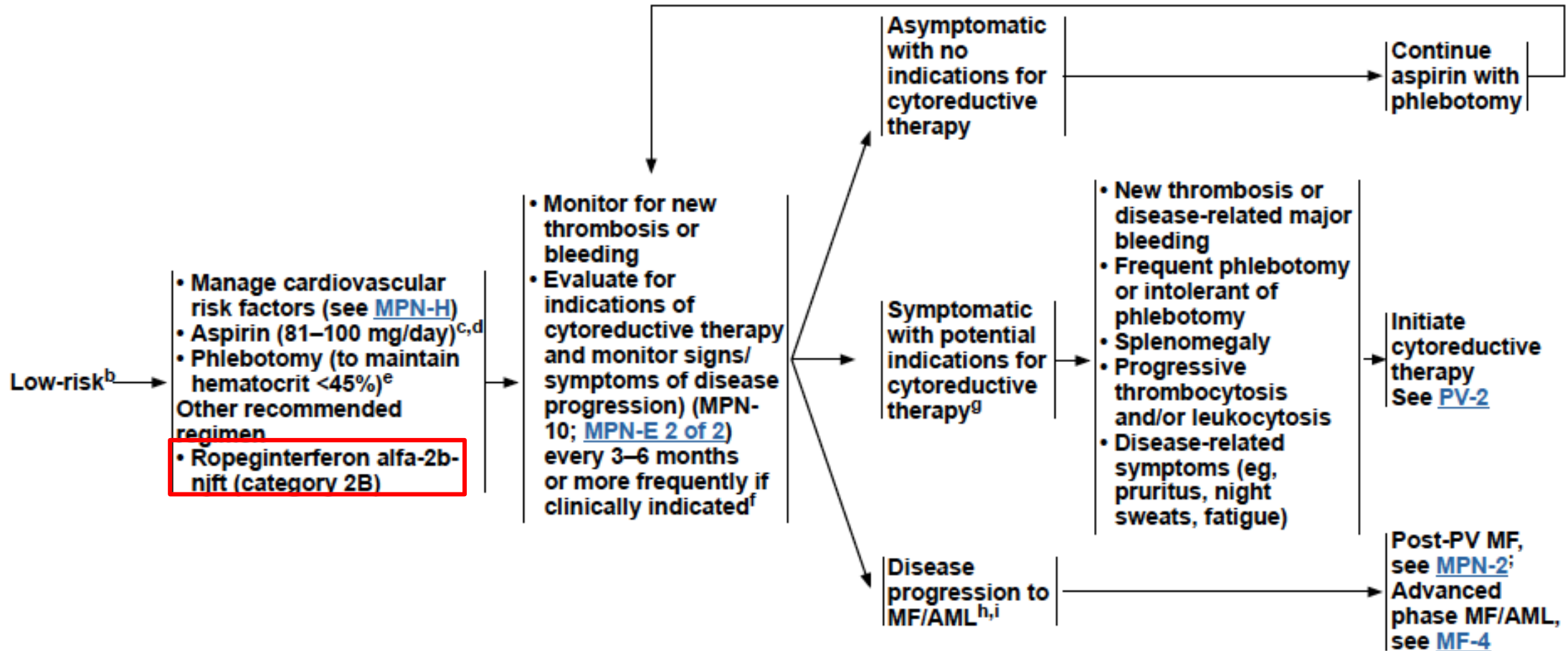
- Approved in USA in 2022
- JAK2, FLT3, IRAK1 inhibitor
- Less myelosuppressive
- Main side effect- GI and cardiac events
- Was on hold by FDA for bleeding episodes in Phase III trials

# PV treatment algorithm

Risk Categories	
Low-risk (Age<60 and no blood clot history)	Aspirin + Phlebotomy Ropeginterferon
High-risk (age >60 OR blood clot history)	Aspirin + phlebotomy + cytoreduction (hydroxyurea, interferon)
High-risk and refractory to hydroxyurea	Ruxolitinib (or hydroxyurea/interferon if not used previously)

# Ropeginterferon added for low-risk PV

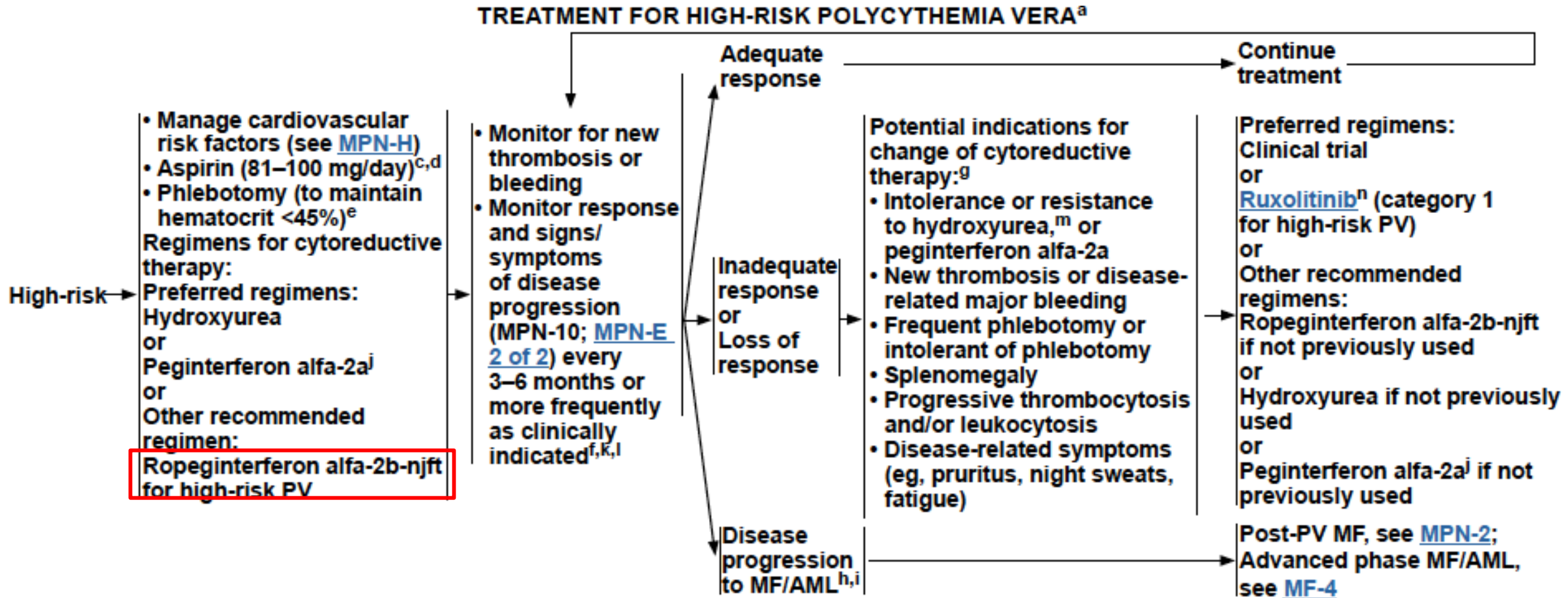
## TREATMENT FOR LOW-RISK POLYCYTHEMIA VERA<sup>a</sup>



# ELN update 2021 for low-risk PV

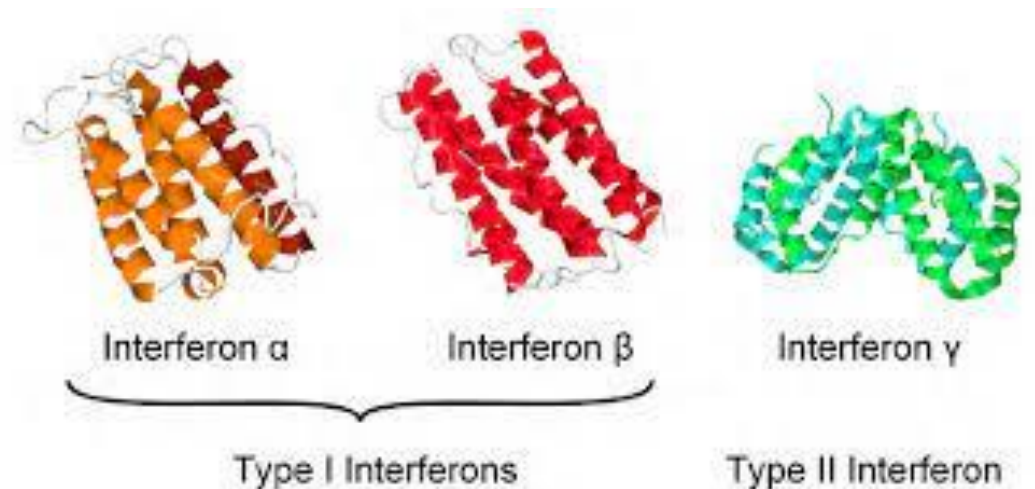
- Cytoreduction for low-risk patients if:
  - Phlebotomy intolerance (or >6 phlebotomies a year)
  - Progressive splenomegaly (MF ruled out)
  - Persistent leukocytosis  $>20 \times 10^9$  or 100% increase in WBC if baseline  $<10 \times 10^9$
  - Platelets  $>1500 \times 10^9/L$  with bleeding
  - Symptomatic patients
  - Consider for persistent CV risk despite medical management
- Ropeginterferon and other interferons recommended in first line

# Ropeginterferon added to high risk PV



# Interferon

- Recombinant  $\text{INF}\alpha$  has been used for >3 decades in MPN
- Type I Interferons in use:
  - Intron A (standard  $\text{INF}\alpha$ -2b)
  - Pegylated  $\text{INF}\alpha$  (pegasys)
  - Pegylated  $\text{INF}\alpha$ -2b (PegIntron)
  - Ropeginterferon  $\alpha$ -2b (Besremi)



# Interferon in clinical practice

Benefits	Downsides
Reduces blood clots	Flu like symptoms
Improves MPN-related symptoms	LFT abnormalities
Normalizes blood counts	Autoimmune effects (mainly thyroid)
Reduces mutation level	Depression
Non-chemo intervention	Subcutaneous injection

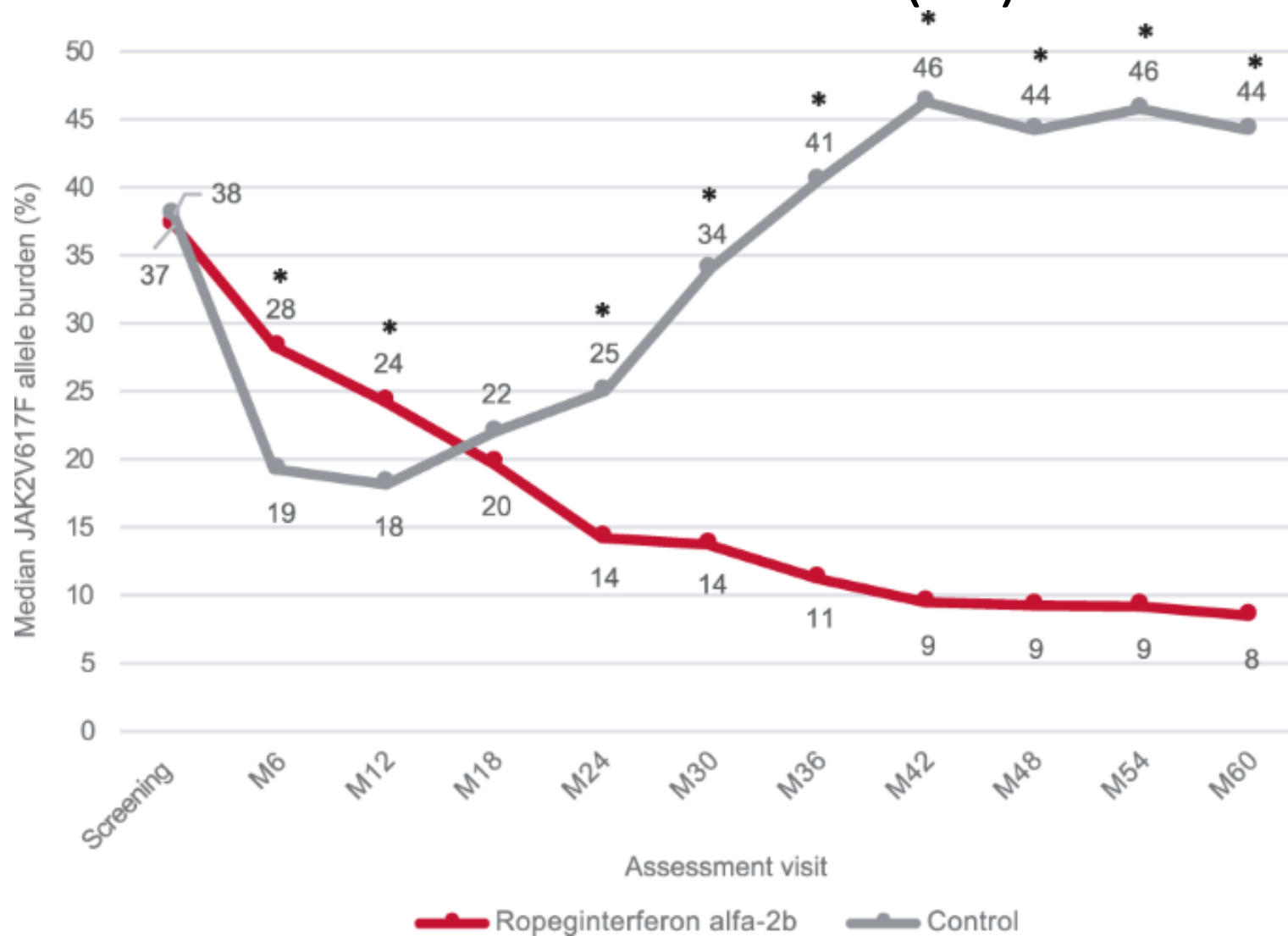
# Ropeginterferon

- Monopegylated  $\text{INF}\alpha$
- Administration is every 2 weeks (with a monthly maintenance schedule)





# Median JAK2V617F burden (%)



# Biggest unknowns

- **Does reduction in mutant allele burden (JAK2 levels) lead to decreased rates of myelofibrosis and leukemia?**
- **Does long term use lead to improved overall survival?**
- **Should Interferon be used in early PV?**
- **Is there a difference between the interferons?**
- **Should interferon be used for all young patients?**

# Upcoming changes

- JAK inhibitors: Momelotinib awaiting approval
- Luspatercept likely to be approved both alone and in combination with ruxolitinib.
- Multiple add on drugs being studied:
  - BET inhibitors
  - Navitoclax
  - PI3K inhibitors
  - LSD1 inhibitors
- How will we use these drugs with and without JAK inhibitors?

# תודה רבה לך

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