Treatment

- Cytoreductive Therapy
  - Hydroxycarbamide
  - Busulfan
  - Cytarabine
- Pegylated interferon
  - Role in pregnancy
- Allogeneic bone marrow transplant
  - Only known curative treatment
  - Blast crisis or those who failed to achieve deep remission on TKI

Treatment Free Remission (TFR)

Not completely new idea

- Few case reports of a group of patient with CML treated with IFN
  - Low level BCR-ABL1 transcript detected but somehow don't progress

TFR in TKI era ~50%

- Quantifiable BCR-ABL1
- Sustained deep remission prior to TFR
- Maintain BCR-ABL1 MMR

Almost all patient regain MR4 once restart same treatment

Minimal (stop allowed):	First-line therapy, second-line if the reasons for switch were intolerance or resistance due to a mutation sensitive to another TKI.
	Typical e13a2 or e14a2 *BCR::ABL1* transcripts. In case of atypical transcripts in laboratories with a high standard of quantification.
	Duration of TKI therapy >5 years (>4 years for 2GTKI).
	Duration of DMR (MR^4 or better) >2 years.
Optimal (stop recommended for consideration):	Duration of TKI therapy >5 years.
	Duration of DMR >3 years if MR^4.
	Duration of DMR >2 years if $MR^{4.5}$.
Procedures after stop:	Molecular monitoring 6 to 8 weekly for the first 6 months, 2 monthly for months 6–12, and every 3–6 months thereafter. Monitoring should increase in frequency if there is an increase in *BCR::ABL1* transcript levels.
	Restart TKI-therapy if MMR is lost.
	If TKI-therapy is restarted monitor 4-6 weekly until MMR is regained and then every 3 months until MR^4 is regained.

2025 Euronet Guideline (page 16)

CLASSICAL MPN

Incidence

	Incidence		Estimated Prevalence**	
	International	NZ Data*	International	NZ Data*
PV	2.0/100000	0.76/100000	~1000 (17)	~380 (6.3)
PMF	1.5/100000	0.82/100000	~375 (6.3)	~200 (3.3)
ET	2.5/100000	0.99/100000	~1875 (31)	~750 (12.5)

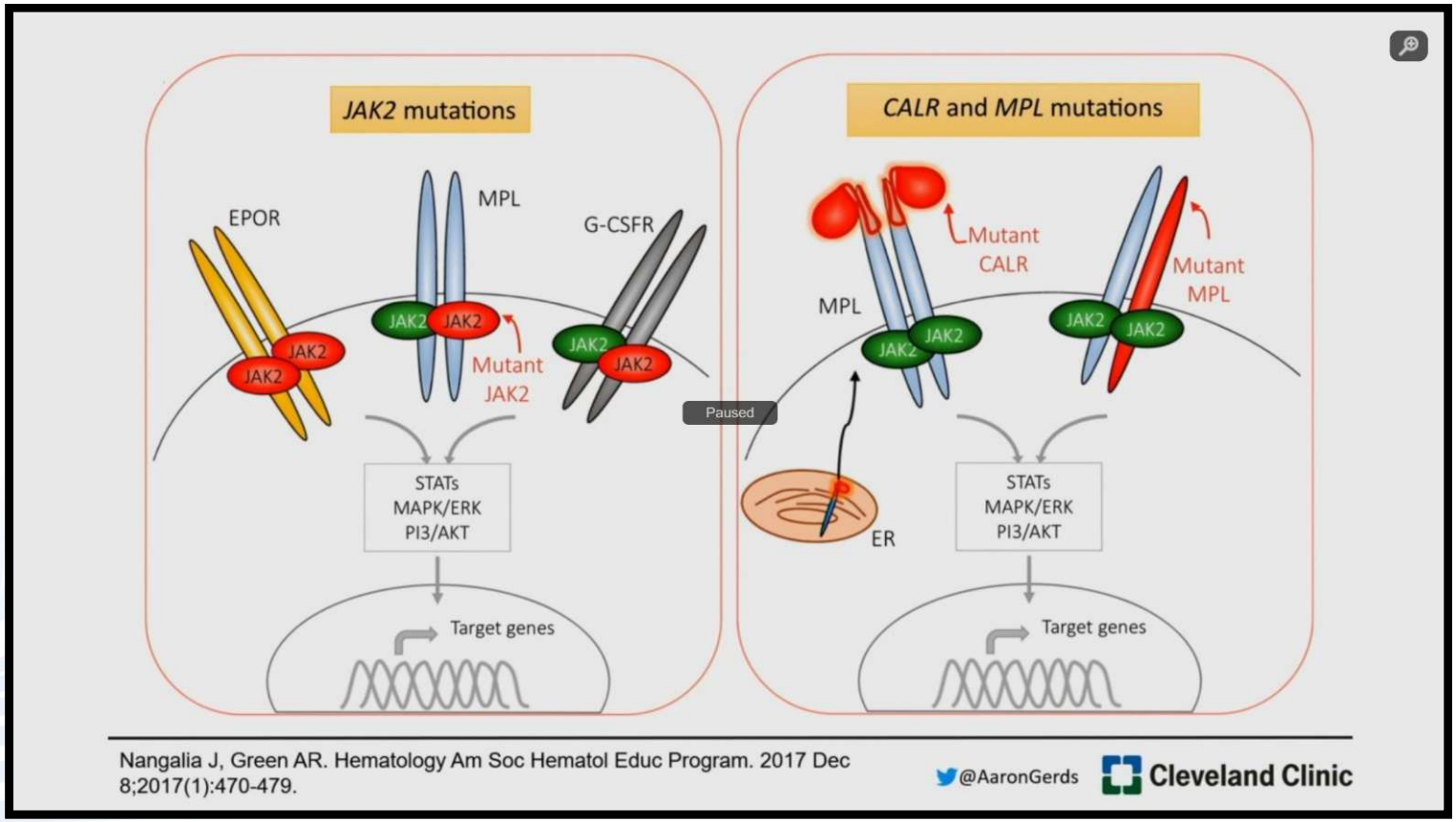
* Varghese et al. Curr Oncol. 2021 Apr 18:28(2):1544-1557
** Population 5M (Stat NZ), survival PV 10 yrs, ET 15 yrs, MF 5 yrs and 60 haematologists in NZ

Presentation

	PV	ET	MF
Epidemiology			
• Incidence (/100000)	2	2.5	1.5
• Gender (M:F)	2:1	1:2	1:1
• Median Age	60	60	67
- <40	10%	20%	5-10%
Manifestation			
• Thrombosis (/100 patient years)	5.5	1~3	2
- At diagnosis	23%	9-22%	13.2%
• Bleeding			
- At diagnosis	4%	3-37%	---
• Constitutional Symptoms	+/-	+/-	+++
• Splenomegaly	36%	35%	>90%

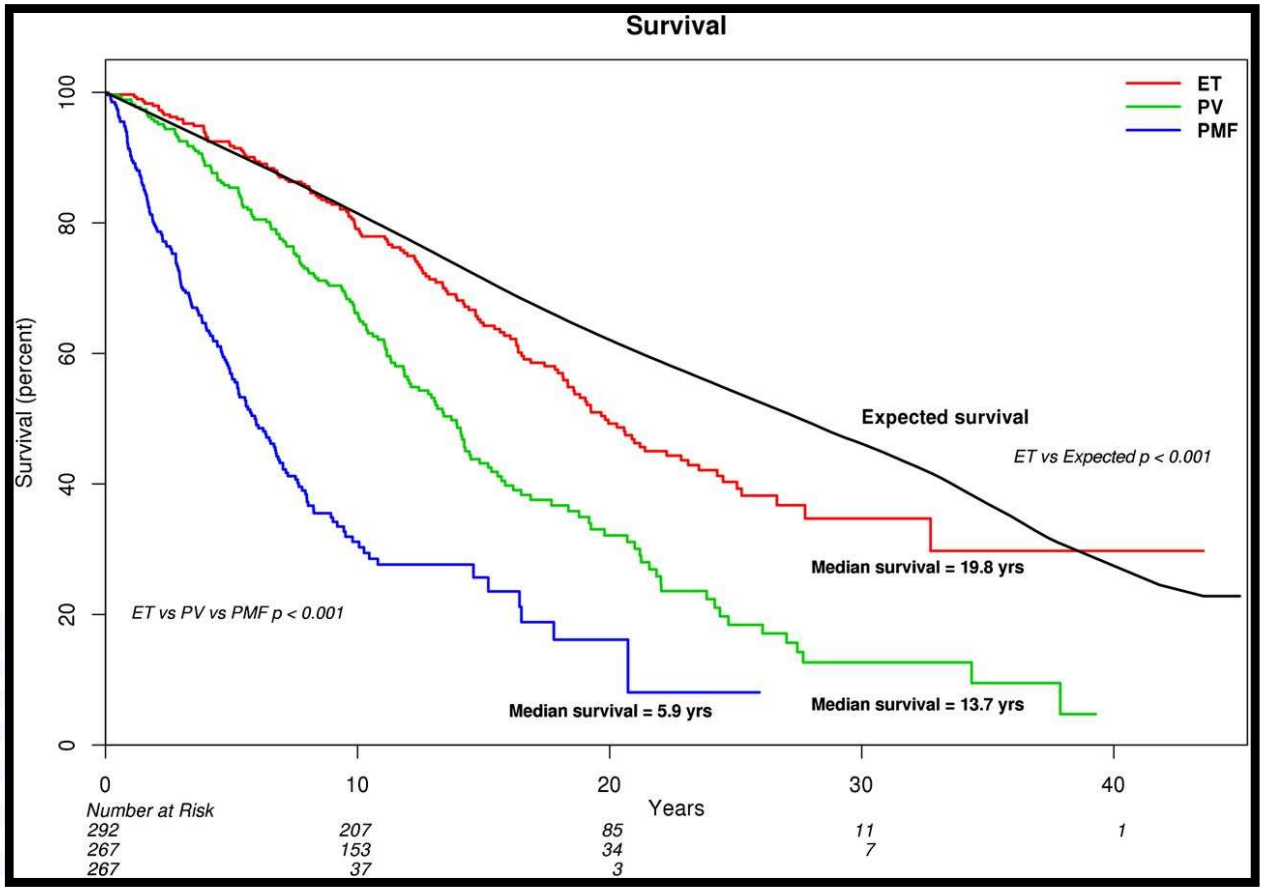
* Pruritis, erythromelalgia, vasomotor symptoms …etc.

Driver Mutations



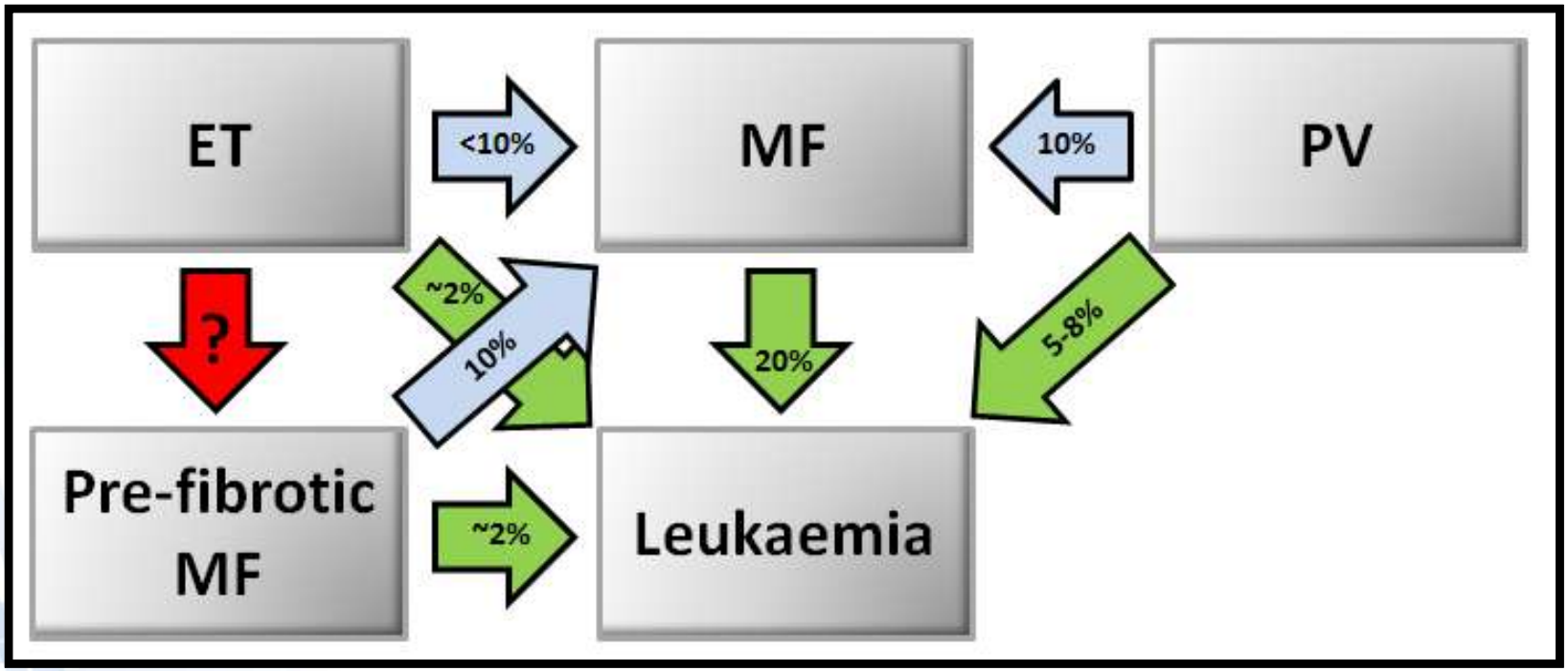
Prognosis

Tefferi et al. *Blood*. 2014 (124): 2507



Transformation

Rate of fibrotic and leukaemic transformation over 10 years



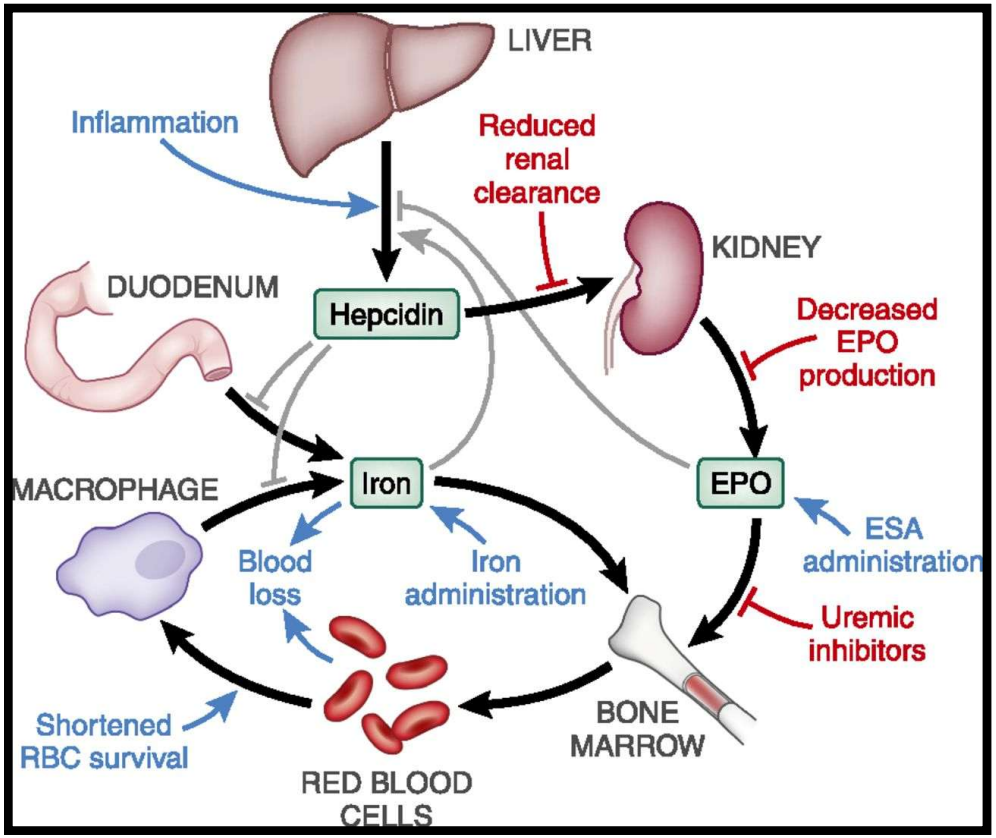
Laboratory Findings - PV

		Ref. Range
Haemoglobin	163	(115 – 155)
RBC	6.34	(3.60 – 5.60)
HCT	0.48	(0.40 – 0.46)
MCV	78	(80 – 99)
MCH	25.8	(27.0 – 33.0)
Platelets	420	(150 – 400)
WBC	8.9	(4.0 – 11.0)
Neutrophils	6.3	(1.90 – 7.50)
Lymphocytes	1.9	(1.00 – 4.00)
Monocytes	0.26	(0.20 – 1.00)
Eosinophils	0.3	(<0.51)
Basophils	0.22	(0.00 – 0.20)
Ferritin	10	(20 – 170)

- Typical Findings
  - Persistent and progressive polycythaemia
    - **With time may develop "panmyelosis"**
  - Occasionally "iron deficiency" indices
  - Blood film relatively unhelpful

Polycythaemia

- Diagnosis
  - Driver mutations
    - JAK2 V617F (90-95%)
    - JAK2 exon 12 (1-3%)
  - Serum erythropoietin
    - Should be low
    - Normal or high suggest other cause
- Manage the thrombosis risk factors (PV)
  - Venesection
  - Aspirin
  - Hydroxyurea > 60yr or with CVD RF
- Don't
  - Replace iron



Laboratory Findings - ET

	2009	2011	2014	2016	2019	Now	Ref. Range
Haemoglobin	140	143	141	148	151	150	(115 – 155)
RBC		4.80	4.87	5.40	5.3	5.22	(3.60 – 5.60)
HCT	0.43	0.45	0.42	0.47	0.47	0.46	(0.40 – 0.46)
MCV	89	90	87	87	89	88	(80 – 99)
MCH	29	29.4	29.0	27.4	28.5	28.7	(27.0 – 33.0)
Platelets	446	426	571	482	640	702	(150 – 400)
WBC	10.7	8.3	12.4	9.5	11.9	8.1	(4.0 – 11.0)
Neutrophils	7.0	5.2	8.8	6.1	7.8	5.8	(1.90 – 7.50)
Lymphocytes	2.6	2.2	2.3	2.4	2.7	1.9	(1.00 – 4.00)
Monocytes	0.9	0.6	0.8	0.6	0.7	0.2	(0.20 – 1.00)
Eosinophils	0.2	0.3	0.5	0.4	0.6	0.1	(<0.51)
Basophils	<0.1	<0.1	<0.1	<0.1	0.1	0.1	(0.00 – 0.20)

- Blood film - **increased variation in platelet size and granulation.**