

Myeloproliferative Neoplasms 2017

Leukemia and Lymphoma Society -Northern CA
Blood Cancer Conference

Ruben A. Mesa, MD, FACP

Professor and Chair, Division of Hematology & Medical Oncology

Deputy Director, Mayo Clinic Cancer Center

Arizona, USA

mesa.ruben@mayo.edu

The Itch

I have an itch you cannot know,
not the least hint will ever show
No bump no rash no insect bite
provides a clue as to my plight
My clothes, a shower, the air I breathe
make my skin prickle and seethe
Constant reminders it provides
of the disease my body hides
Maddening tears the burning brings,
no scratch, no pills can stop the stings
Life is good,
it could be much worse
I can live with my itchy curse
I walk the dog to pass the time,
take deep breaths and clear my mind
Pruritus is a small price
for my wonderful blessed life

Paul Nudelman

Poet & PV Patient

Gurnee, IL, USA

MPNS 2017

- MPNs – spectrum of burden, risk, care needs
- Evolving Options for PV and ET
- Footprint of Ruxolitinib 4 years after MF Launch
- New JAK inhibitors
- JAKi combinations
- New Targets
- Future Directions

Acute vs. Chronic Neoplasms

ACUTE Neoplasm (AML, DLBCL, Some MF)

- Life threatening in < 2 years
- Disease eradication most critical goal
- Significant toxicity acceptable to extend life
- Quality of life frequently a casualty of therapy

CHRONIC Neoplasm (ET, PV, Some MF)

- Survival ranges from normal to diminished but at least 5 years
- Diminishment of disease morbidity a key goal
- QOL and acceptability of toxicity a key issue
- Cure a goal, but not at any price

Assessing MPN Patient Risk

	IPSET (ET—3 groups) <i>Survival thrombosis risk</i>	PV Risk (4 groups) <i>Survival leukemia rates</i>	DIPSS (PMF—4 groups) <i>Survival</i>
Age, years	≥ 60 (2 pts) vs < 60	≥ 67 (5 pts) 57-66 (2 pts), < 60 (0)	≥ 65 (1 pt) vs < 65
Leukocytes	≥ 11 (1 pt) vs < 11 x 10 ⁹ /L	≥ 15 (1 point) vs < 15 x 10 ⁹ /L	> 25 (1 pt) vs ≤ 25 x 10 ⁹ /L
Hemoglobin			< 10 (2 pts) vs ≥ 10 g/dL
Constitutional symptoms			Present ^a (1pt) vs absent
Blasts			≥ 1% (1pt) vs < 1%
Prior thrombosis	Yes (1 point) vs No	Yes (1 Point) vs No	
Risk group point cutoffs	0; 1-2; 3-4 pts	0; 1-2; 3; 4 pts	0; 1-2; 3-4; ≥ 4 pts

Blood 2012

Leuk 2014

Blood 2010

^a 10% weight loss over prior 6 months, night sweats, unexplained fever.

Test ID: NGSHM

OncoHeme Next Generation Sequencing (NGS), Hematologic Neoplasms

Testing Algorithm

This assay detects the following mutations:

ASXL1 (NM_015338.5) exons 11-14, *BCOR* (NM_001123385.1) exons 5-16, *BRAF* (NM_004333.4) exon 15, *CALR* (NM_004343.3) exon 9, *CBL* (NM_005188.3) exons 8-9, *CEBPA* (NM_004364.4) exon 1, *CSF3R* (NM_000760.3) exons 14 and 17, *DNMT3A* (NM_022552.4) exons 8-23, *ETV6* (NM_001987.4) exons 3-8, *EZH2* (NM_004456.4) exons 3-21, *FLT3* (NM_004119.2) exons 14-20, *GATA1* (NM_002049.3) exons 2 and 4, *GATA2* (NM_001145661.1) exons 4-8, *IDH1* (NM_005896.3) exon 4, *IDH2* (NM_002168.3) exon 4, *JAK2* (NM_004972.3) exons 12-16, *KIT* (NM_000222.2) exons 8-11 and 17, *KRAS* (NM_033360.3) exons 2 and 3, *MPL* (NM_005373.2) exons 10-11, *MYD88* (NM_002468.4) exon 5, *NOTCH1* (NM_017617.3) exons 26, 27, and 34, *NPM1* (NM_002520.6) exons 9, 11, and 12, *NRAS* (NM_002524.4) exons 2 and 3, *PHF6* (NM_001015877.1) exons 2-10, *PTPN11* (NM_002834.3) exons 3-4 and 12-13, *RUNX1* (NM_001001890.2) exons 4-10, *SETBP1* (NM_015559.2) partial exon 6; amino acids 400 - 950, *SF3B1* (NM_012433.2) exons 14-17, *SRSF2* (NM_003016.4) exons 1 and 2, *TERT* (NM_198253.2) exons 2-16, *TET2* (NM_001127208.2) exons 3-11, *TP53* (NM_000546.4) exons 4-9, *U2AF1* (NM_001025203.1) exons 2, 7, and 9, *WT1* (NM_024426.4) exons 1-11, and *ZRSR2* (NM_005089.3) exons 1-11.

NGS and Myeloid Mutations/ Other Prognosis

- >80% of PMF patients have a non JAK2/CALR/MPL mutation
- The greater the number the worse the prognosis
- ASXL1, CBL, RUNX1, SRSF2 have independent adverse prognostic impact

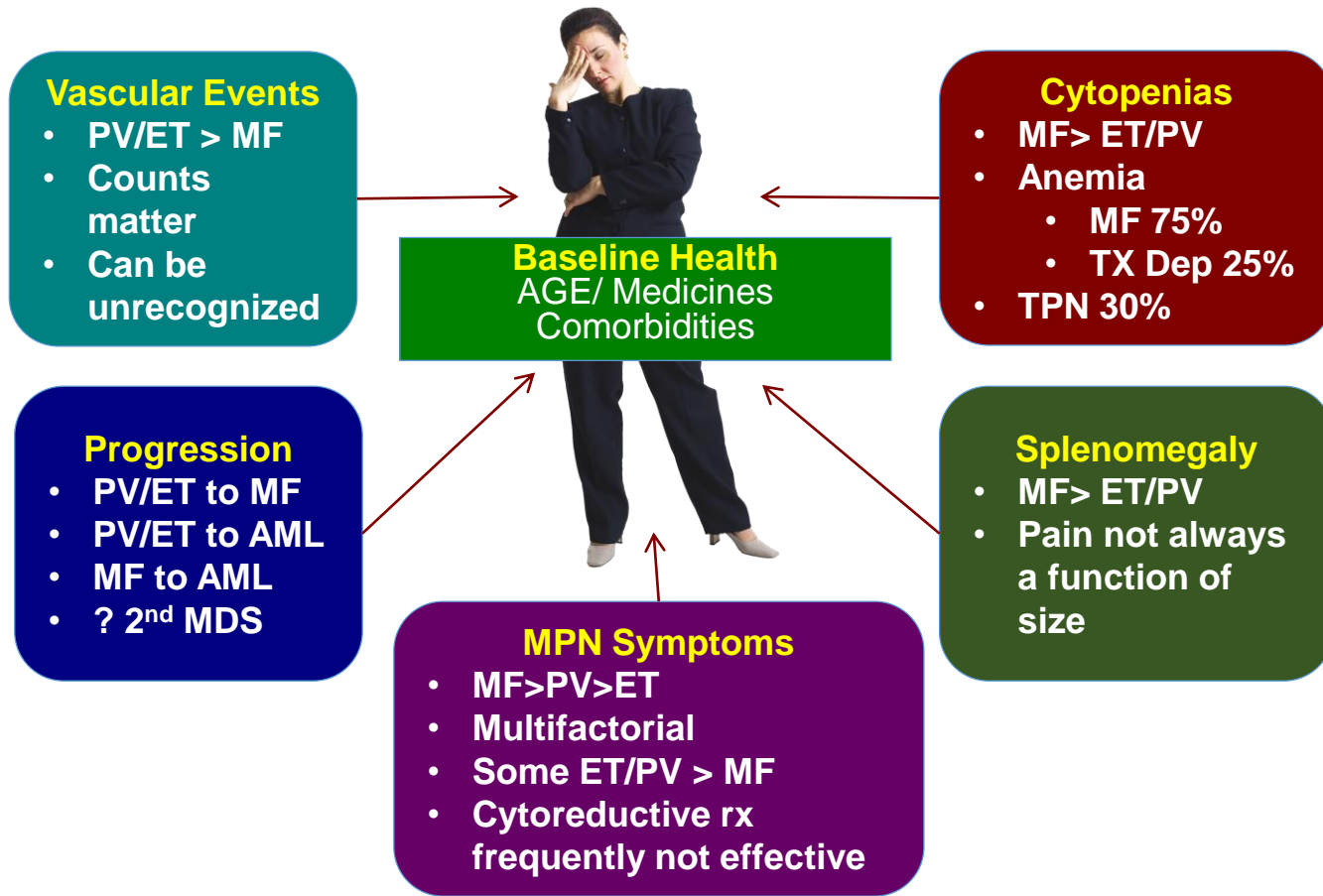
- MF grades 2 and 3 worse prognosis than 0 and 1

- With allo outcomes may improve with SRSF2, EZH2, IDH1 mutations
 - May not improve with ASXL1, U2AF1, IDH2, DNMT3A

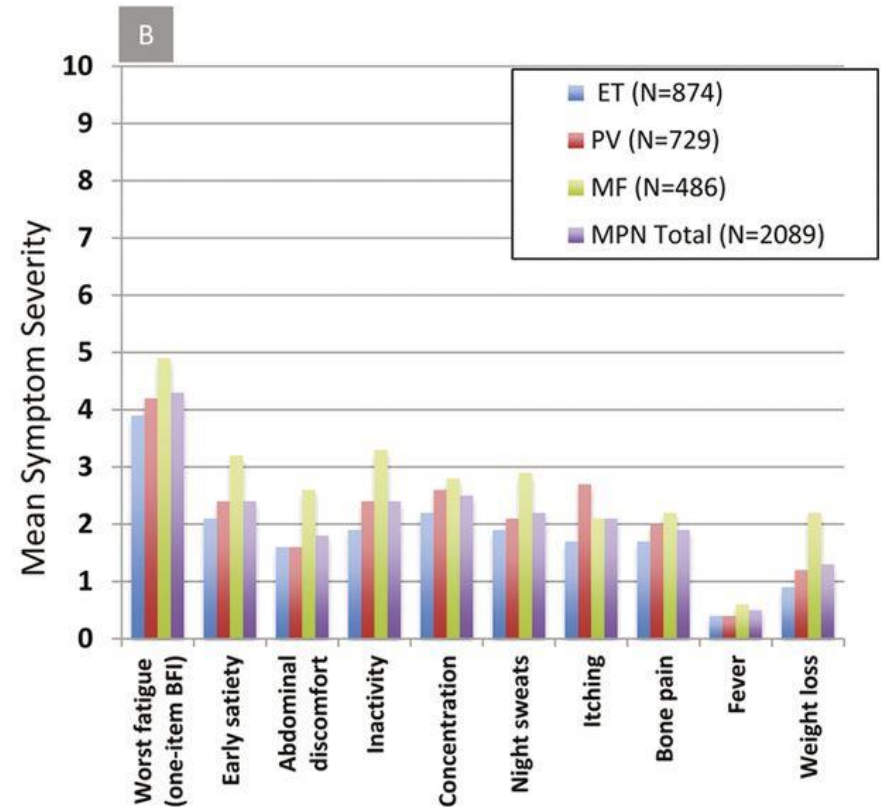
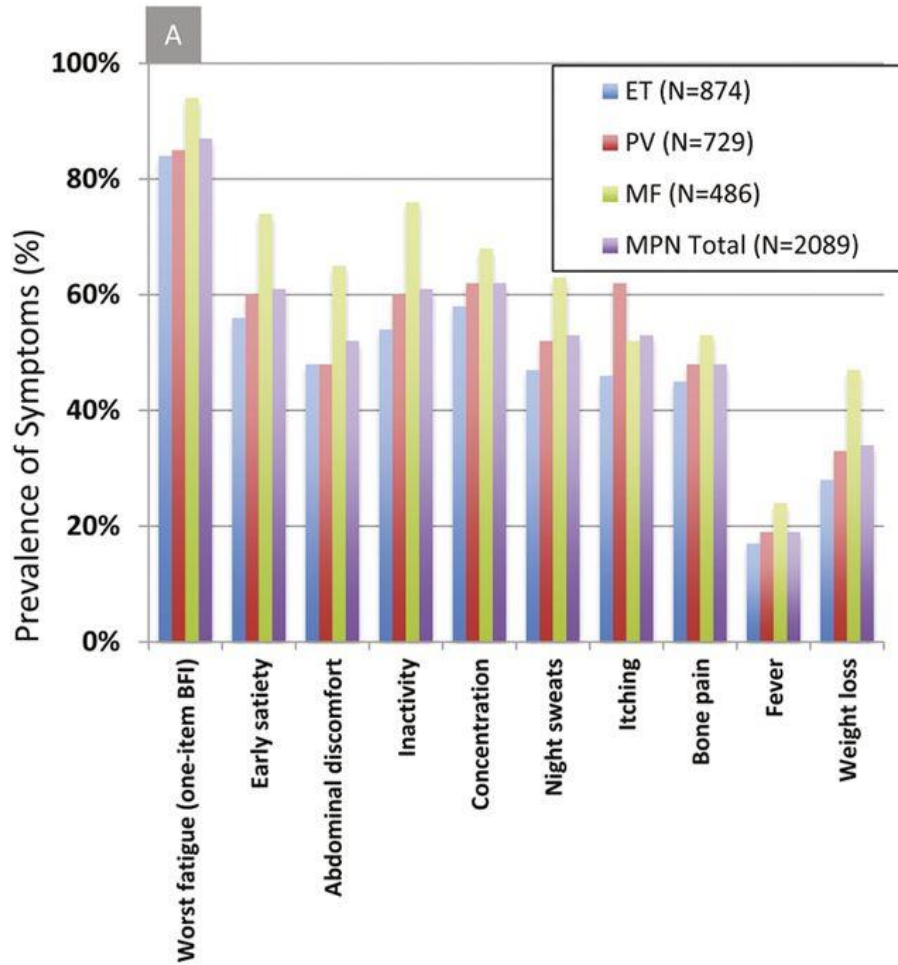
Tefferi et. al. ASH 2015; Gugliemi et. al. ASH 2015, Kroger et. al. ASH 2015

Assessing MPN Burden

WHO Diagnosis Does Not Tell Whole Story



Classic Signs and Symptoms of MPNs



MPNS 2017

- MPNs – spectrum of burden, risk, care needs
- **Evolving Options for PV and ET**
- Footprint of Ruxolitinib 4 years after MF Launch
- New JAK inhibitors
- JAKi combinations
- New Targets
- Future Directions

Diagnosis of PV/ET

Assess PV/ET Risk Score &
Assess MPN Symptoms (MPN 10)

All PV/ET Patients
Control of Hematocrit (<45%)
Low dose aspirin

Decide on need for concurrent cytoreduction based on PV Risk and Symptoms

NO

YES

Monitor for symptom
burden, vascular events,
progression

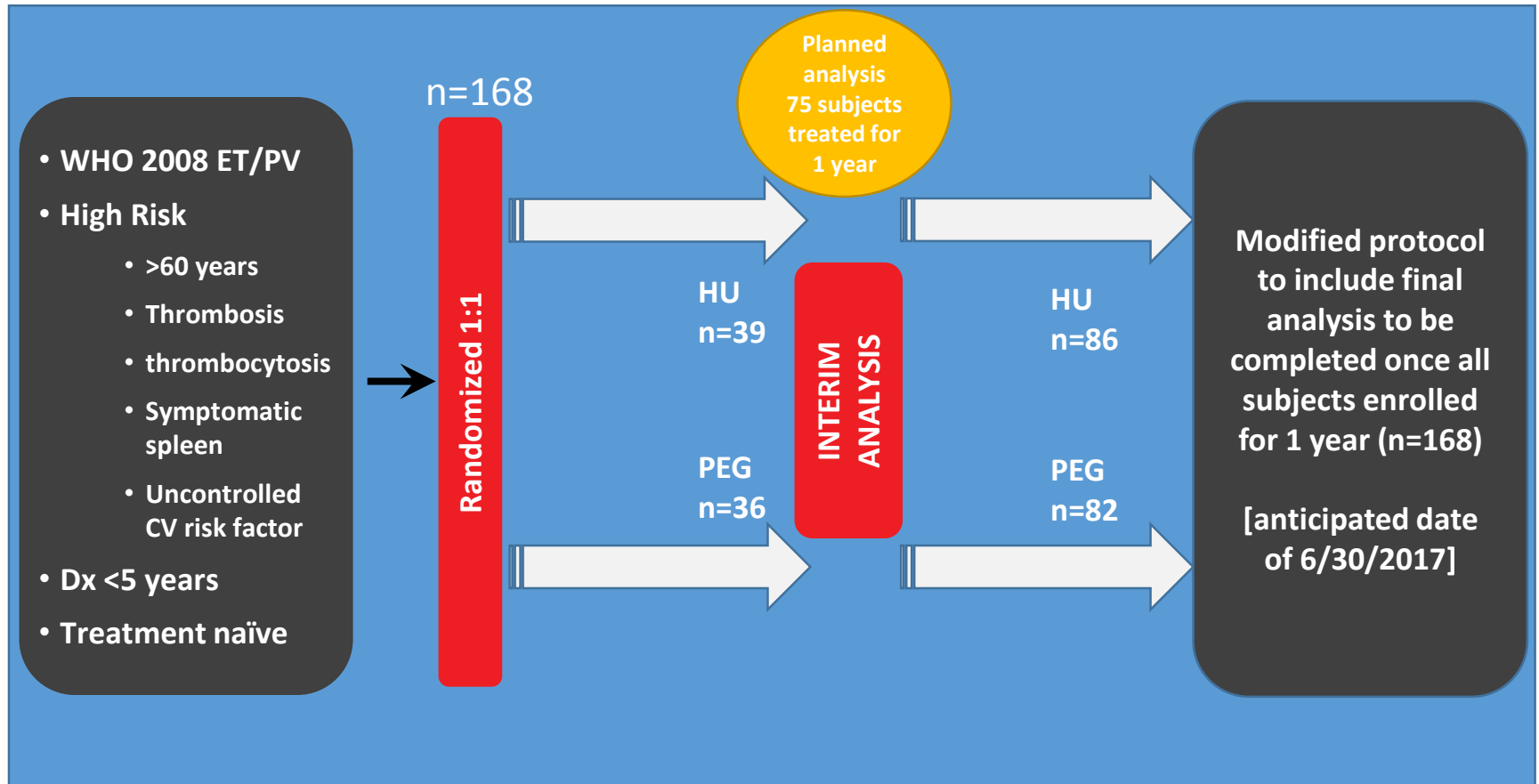
Front Line Cytoreduction
HU, or HU vs INF Clinical Trial

Worsening symptom burden
Vascular event, progression
HU Resistance/ Intolerance

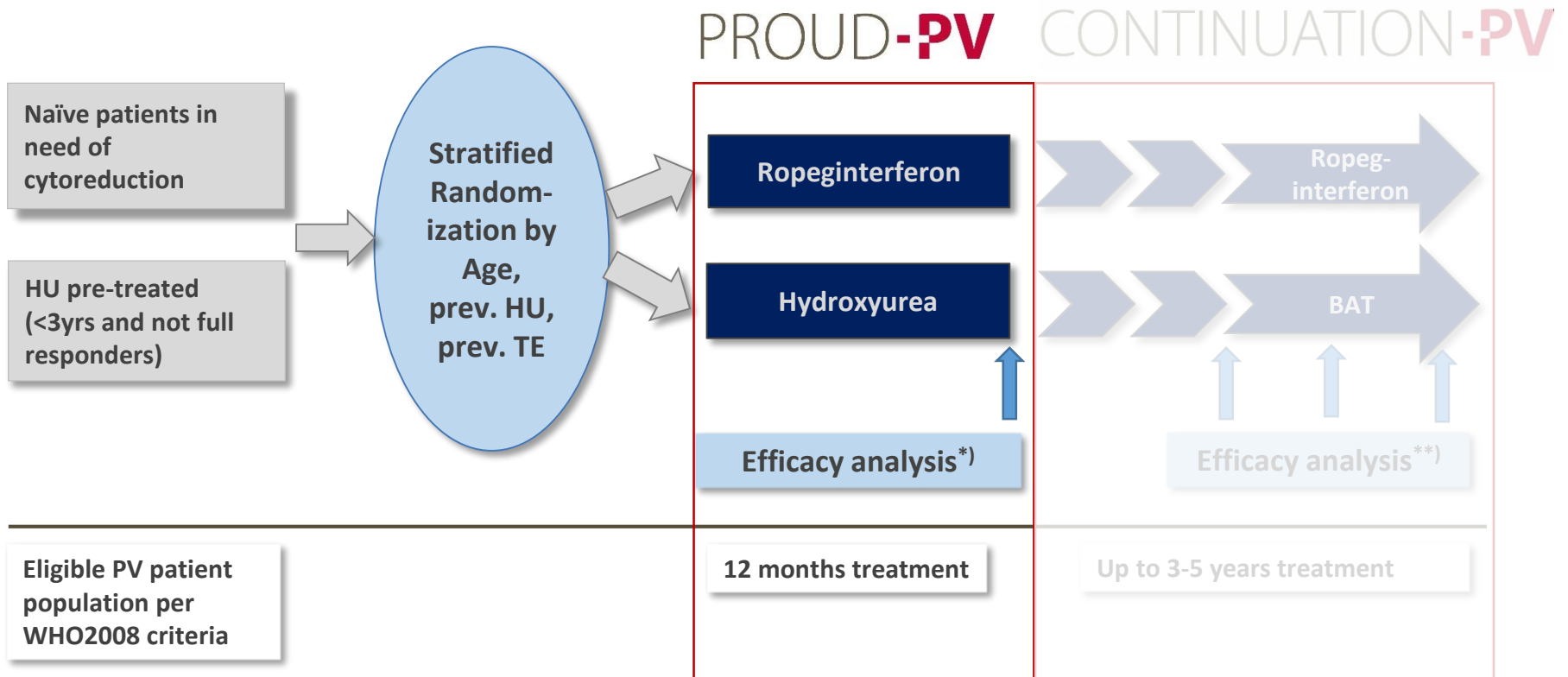
Worsening symptom burden
Vascular event, progression
Phlebotomy intolerance

Consider Ruxolitinib (PV) or
INF (Trial)/HU if not previously received

MPD-RC 112 Study Schema



Ropeginterferon alfa-2b phase III development: PROUD/CONTI-PV



Expected outcome: ^{*)} non-inferiority: Hematologic Response

^{**)} benefit: durable Hematologic Response, PFS, PV symptom relief

Summary

- Both treatments achieved robust hematologic control from week 12 on.
- Non-inferiority of Ropeginterferon vs. HU demonstrated:
12 month Complete Hematologic Response: 43.1 vs. 45.6%
($p=0.0028$).
- Safety and tolerability of Ropeginterferon showed benefits over HU.
- Five related secondary malignancies appeared in the HU cohort (long-term).

**Final results from the Phase 3 trial ARETA
comparing a novel, extended-release *anagrelide*
formulation to placebo in essential
thrombocythemia patients with defined risk status**

Heinz Gisslinger, Christoph Klade, Kudrat Abdulkadyrov, Sławomira Kyrzcz-Krzemien, Elena Karyagina, Anait Melikyan, Kryztof Warzocha, Barbara Grohmann-Izay, Juri Hodisch, Rudolf Widmann, Robert Kralovics, Petro E. Petrides, Jiri Schwarz, and Jean-Jacques Kiladjian

ARETA

Phase III, multicenter, randomised, subject- and sponsor-blinded, placebo-controlled study – early intervention in ET

Eligible patients

ET diagnosed according to WHO2008 with „at risk“ status

Stratification by JAK2 status

1:1

Randomization

Anagrelide ER
2-8 mg/day

Placebo

6 weeks
titration
weekly
visits

1 year
main study
visits every
3 months

Up to 3 years
extension period
visits every 3
months

Primary endpoint:

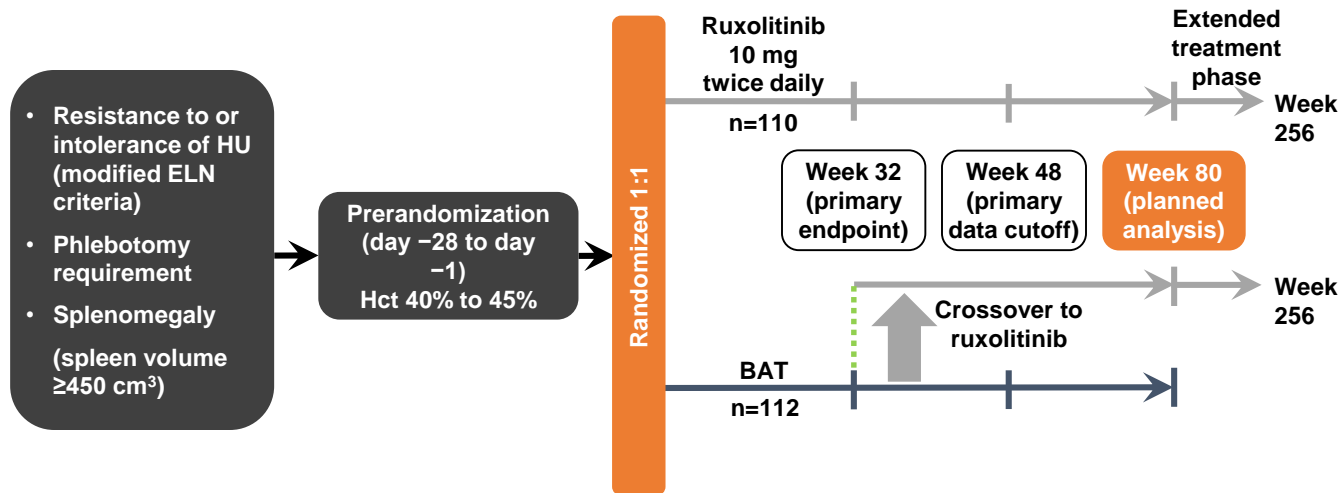
ET-related cardiovascular events (as confirmed by independent blinded Endpoint Adjudication Committee), or disease progression or disease worsening (platelet increase >1000 G/l)

SUMMARY & CONCLUSION

- Primary Endpoint time to first ET related event met ($p=0.0008$).
- Platelet count normalization and delayed progression to high risk status.
- Safety profile consistent with conventional anagrelide formulations.
- More convenient dosing schedule compared to licensed immediate release formulations confirmed.

In conclusion data from ARETA support a “treat early concept” for all ET patients where platelet count or symptom reduction is a goal

RESPONSE Study Design

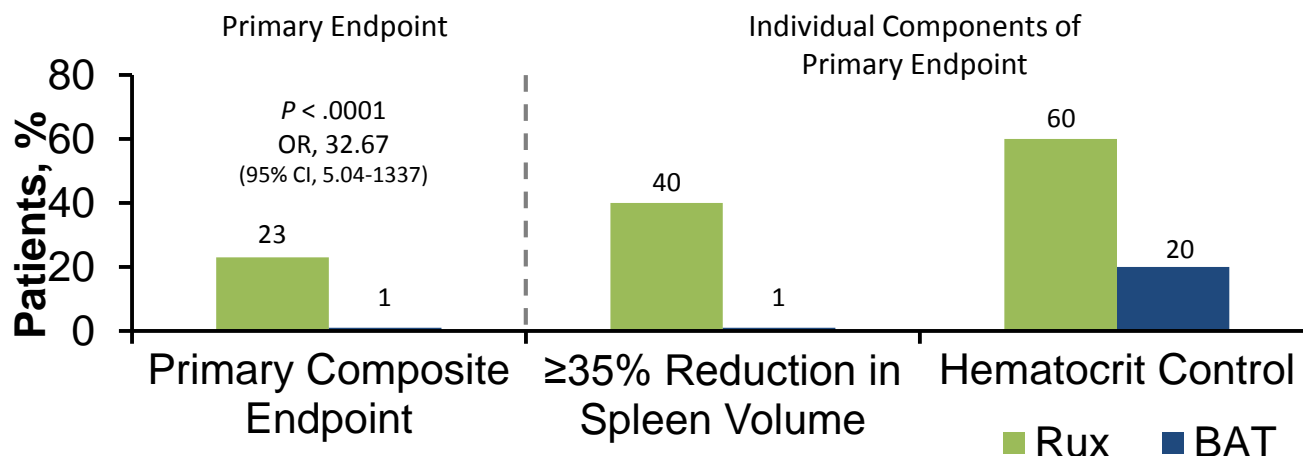


ELN=European LeukemiaNet; Hct=hematocrit

- Patients randomized to BAT were permitted to cross over to ruxolitinib at week 32 if they did not meet the primary endpoint or after week 32 in case of phlebotomy eligibility or splenomegaly progression

Vannucchi et. al. NEJM 2014
Kiladjan et. al. EHA 2015

RESPONSE Primary Analysis at Week 32

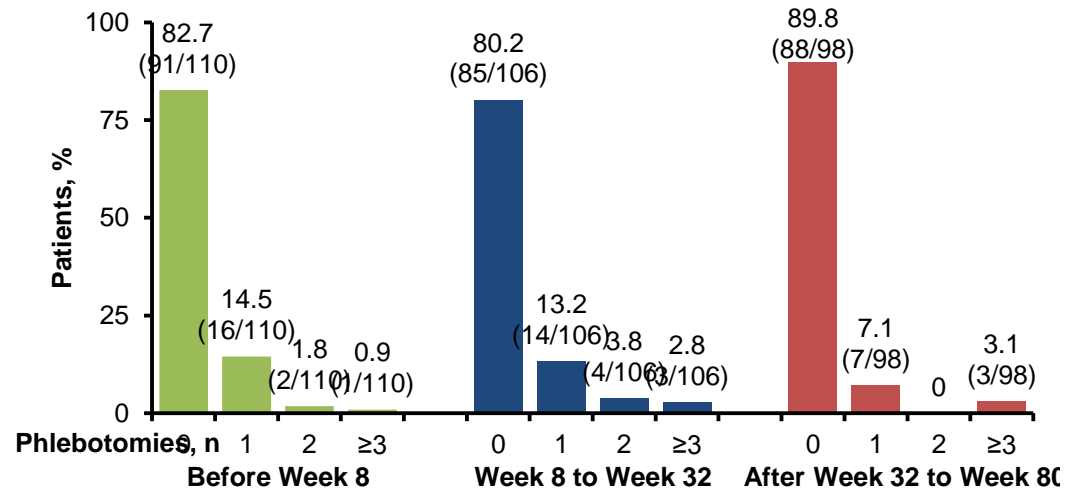


- During MRI data review for the current 80-week analysis, 2 additional patients were identified that were primary responders in the ruxolitinib arm bringing the total number (%) of primary responders to 25 (22.7%). No additional responders were identified in the BAT group

Vannucchi et. al. NEJM 2014
Kiladjian et. al. EHA 2015

9

Phlebotomy Procedures in the Ruxolitinib Arm



- Of the 98 patients who did not discontinue ruxolitinib at week 32, 88 (89.8%) had no phlebotomy between weeks 32 and 80
- Of the 109 patients randomized to BAT who did not discontinue before week 8, 68 (62%) had ≥1 phlebotomy and 22 (20%) had ≥3 phlebotomies between week 8 and 32

Vannucchi et. al. NEJM 2014
Kiladjian et. al. EHA 2015

0

Improvements in Blood Counts – Rux in PV

Changes in WBC Counts and Platelet Counts in Ruxolitinib Arm	N	Week 32 % Patients	Week 80 % Patients
WBC $\leq 10 \times 10^9/L$ in patients with baseline WBC $> 10 \times 10^9/L$	87	31.0	47.1
WBC $\leq 10 \times 10^9/L$ in patients with baseline WBC $> 15 \times 10^9/L$	64	26.6	42.2
Platelets $\leq 400 \times 10^9/L$ in patients with baseline platelet count $> 400 \times 10^9/L$	54	44.4	59.3

Vannucchi et. al. NEJM 2014
Kiladjian et. al. EHA 2015

1

Thromboembolic Adverse Events

- At the week 80 analysis, the rates of thromboembolic events per 100 patient-years of exposure were 1.8 in the ruxolitinib arm vs 8.2 in the BAT arm

Exposure, Patient-Years	Ruxolitinib (n=110) 227.7		BAT (n=111*) 73.6	
	Rate per 100 Patient-Years of Exposure	All Grades	Grade 3 or 4	All Grades
All thromboembolic events	1.8	0.9	8.2 [†]	2.7
Portal vein thrombosis	0.4	0.4	0	0
Cerebral infarction	0.4	0.4	0	0
Ischemic stroke	0.4	0	0	0
Retinal vascular thrombosis	0.4	0	0	0
Myocardial infarction	0	0	1.4	1.4
Deep vein thrombosis	0	0	2.7	1.4
Pulmonary embolism	0	0	1.4	1.4
Splenic infarction	0	0	1.4	0
Thrombophlebitis	0	0	1.4	0
Thrombosis	0	0	1.4	0

*1 patient was randomized to BAT but did not receive study treatment

[†]1 patient in the BAT arm had both pulmonary embolism and deep vein thrombosis

Vannucchi et. al. NEJM 2014
Kiladjian et. al. EHA 2015

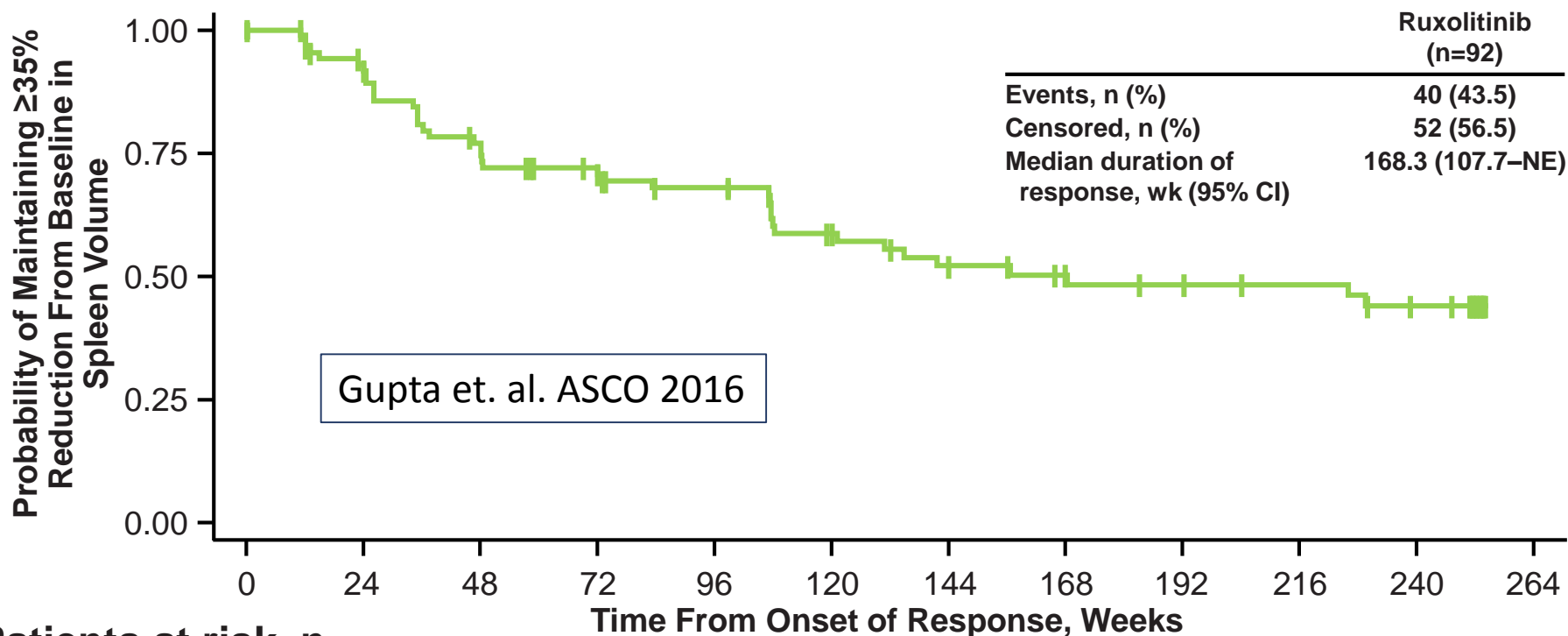
2

MPNS 2017

- MPNs – spectrum of burden, risk, care needs
- Evolving Options for PV and ET
- **Footprint of Ruxolitinib 4 years after MF Launch**
- New JAK inhibitors
- JAKi combinations
- New Targets
- Future Directions

Duration of $\geq 35\%$ Reduction From Baseline in Spleen Volume*

- In the primary analysis, 41.9% of patients randomized to ruxolitinib vs 0.7% randomized to placebo had a $\geq 35\%$ spleen volume reduction at Week 24 (odds ratio, 134.4 [95% CI, 18.0–1004.9]; $P < 0.001$)¹
- In the 5-year analysis, median duration of response was 168.3 weeks for the 92 patients who had a spleen response with ruxolitinib



Patients at risk, n

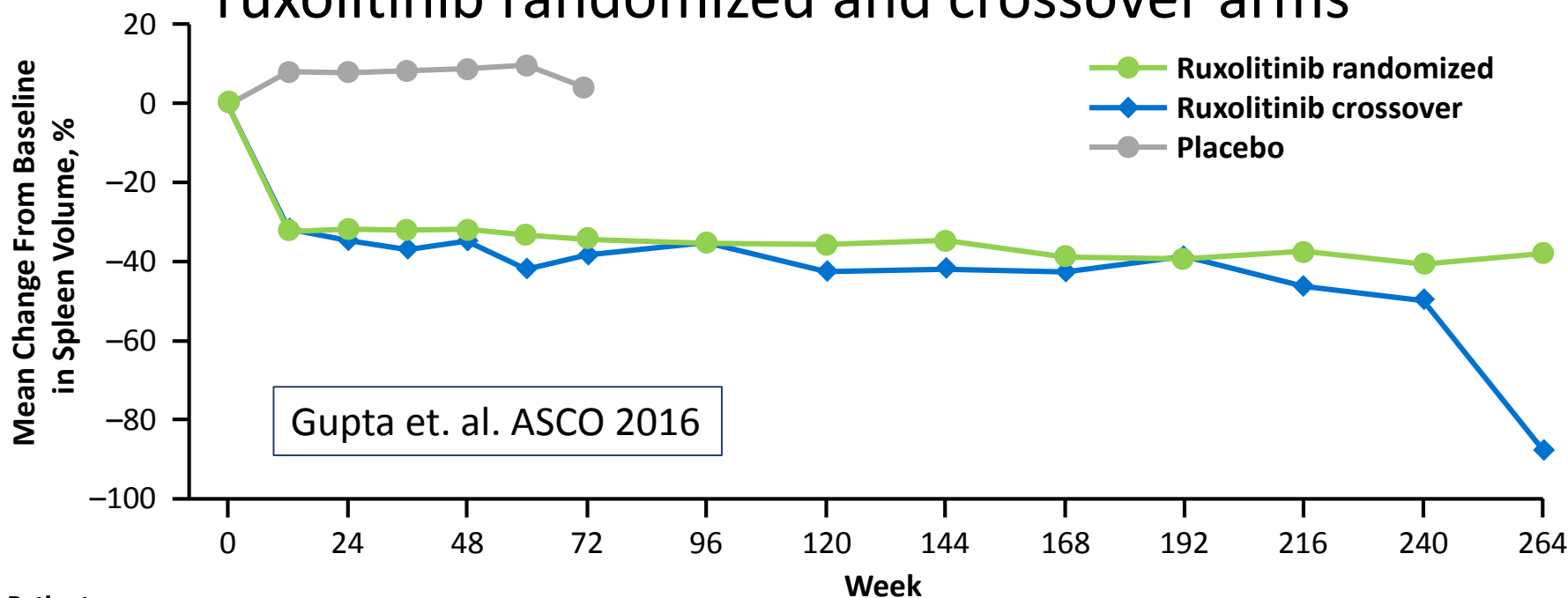
Ruxolitinib 92 77 62 54 47 37 30 26 24 22 18 1

*The median time to loss of spleen response was defined as the interval from the first spleen response to the first spleen volume that was a $< 35\%$ reduction from Baseline and a $> 25\%$ increase from the nadir

1. Gada et al. *N Engl J Med.* 2012;366(9):799-807

Mean Percentage Change From Baseline in Spleen Volume Over Time*

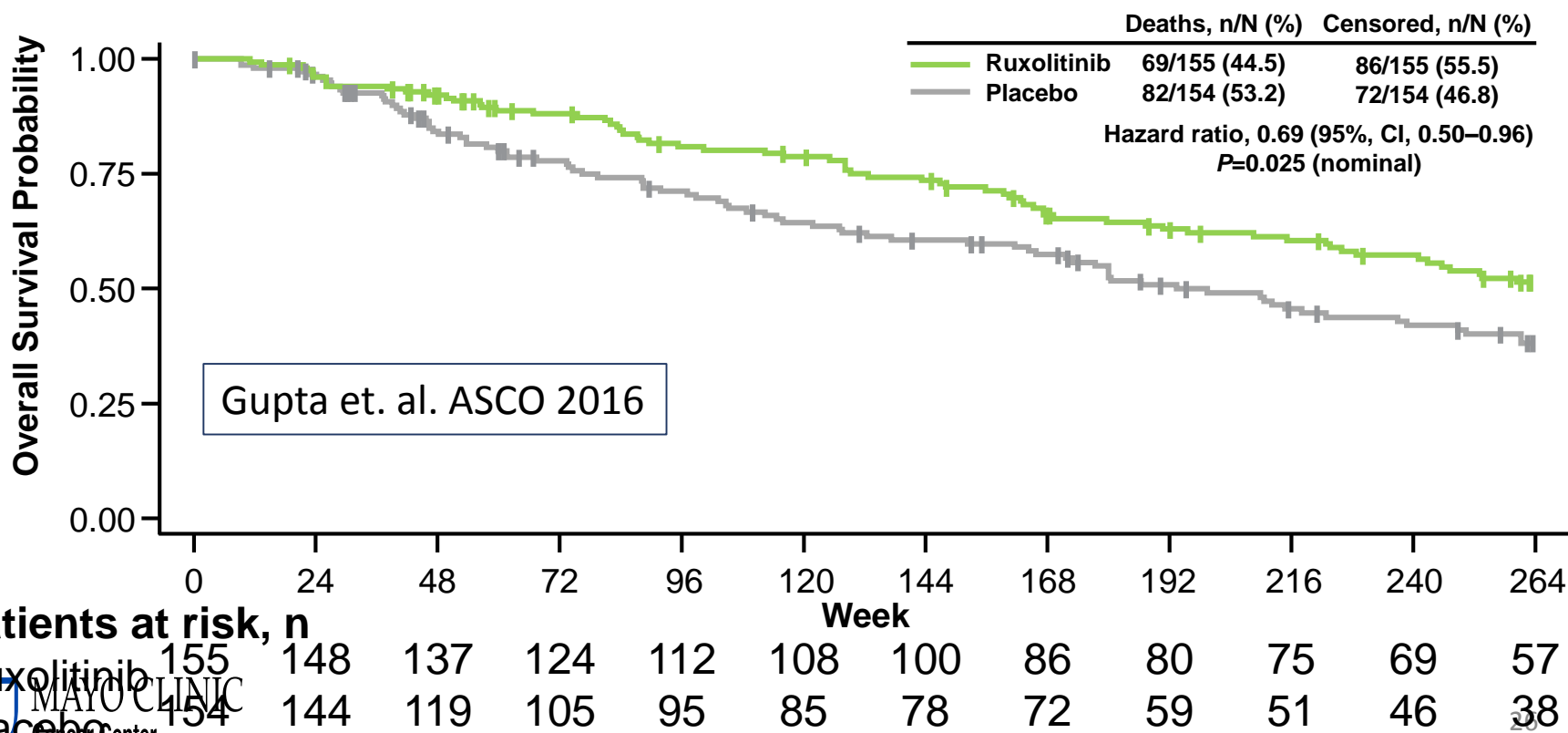
- Mean percentage reductions from Baseline in spleen volume were rapid and durable in the ruxolitinib randomized and crossover arms



	0	24	48	72	96	120	144	168	192	216	240	264
Patients, n												
Ruxolitinib randomized	155	139	120	107	100	85	76	57	55	53	50	42
Ruxolitinib crossover	111	85	44	55	63	46	41	35	33	25	9	1
Placebo	153	107	35	1								

Overall Survival as Assessed by the Kaplan-Meier Method

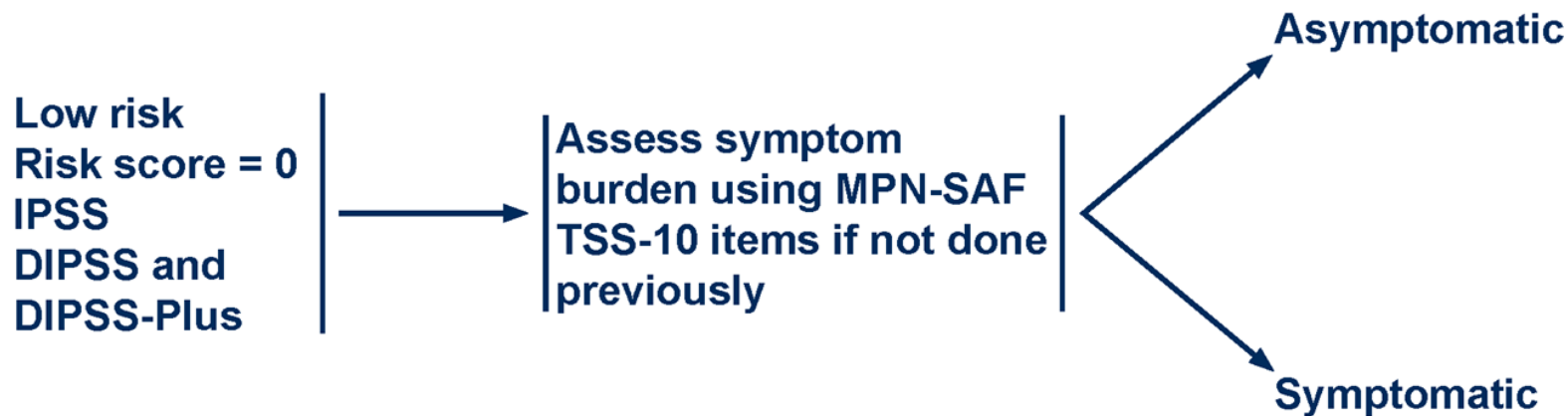
- Median follow-up was 268.4 weeks for ruxolitinib and 269.0 weeks for placebo
- Median OS was not reached for patients randomized to ruxolitinib and was 200 weeks for patients in the placebo arm
 - A sensitivity analysis censoring patients at crossover showed a median OS of 108 weeks for patients randomized to placebo





NCCN Guidelines Version 1.2017 Myeloproliferative Neoplasms

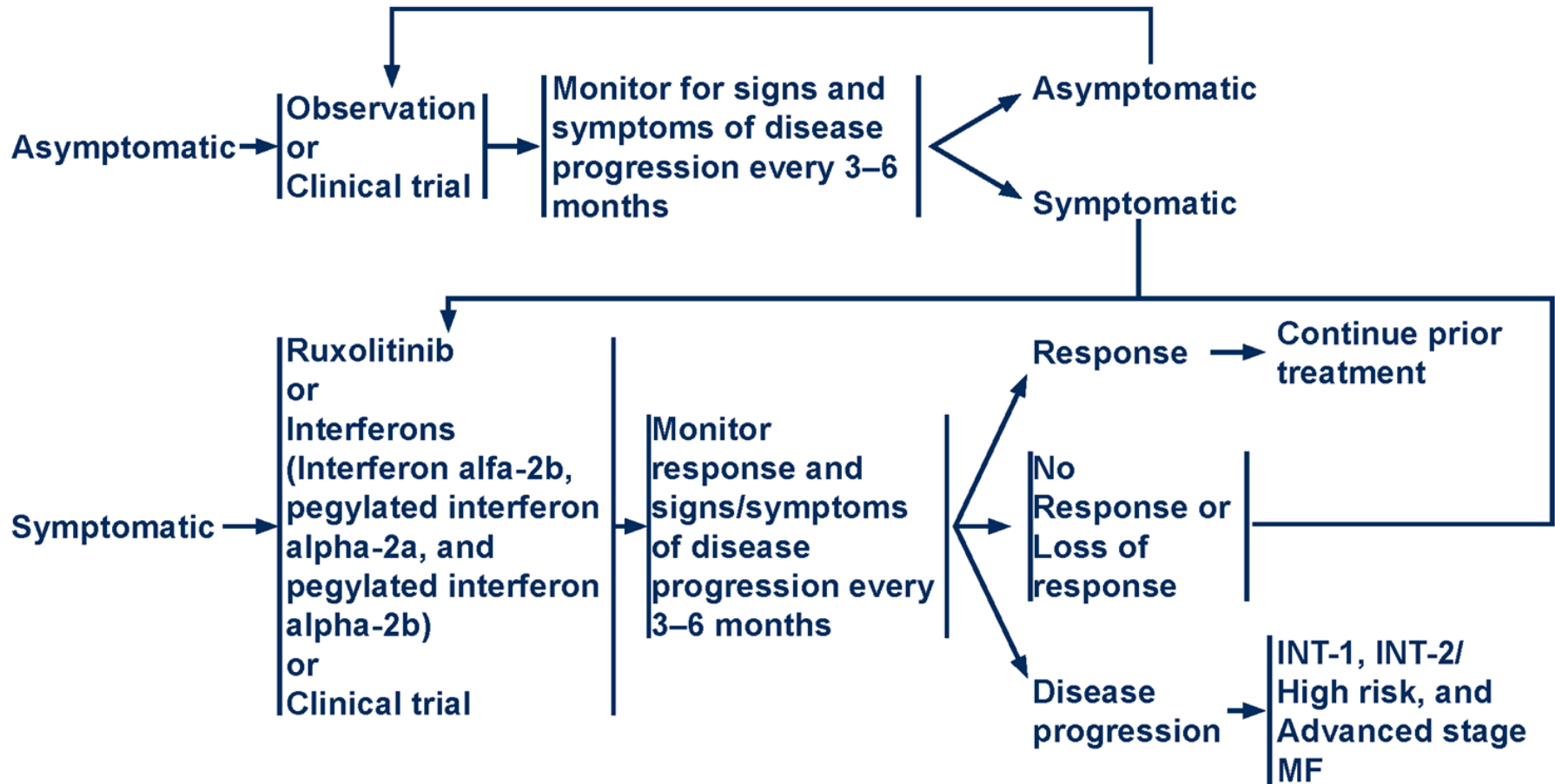
TREATMENT FOR LOW-RISK MYELOFIBROSIS





NCCN Guidelines Version 1.2017 Myeloproliferative Neoplasms

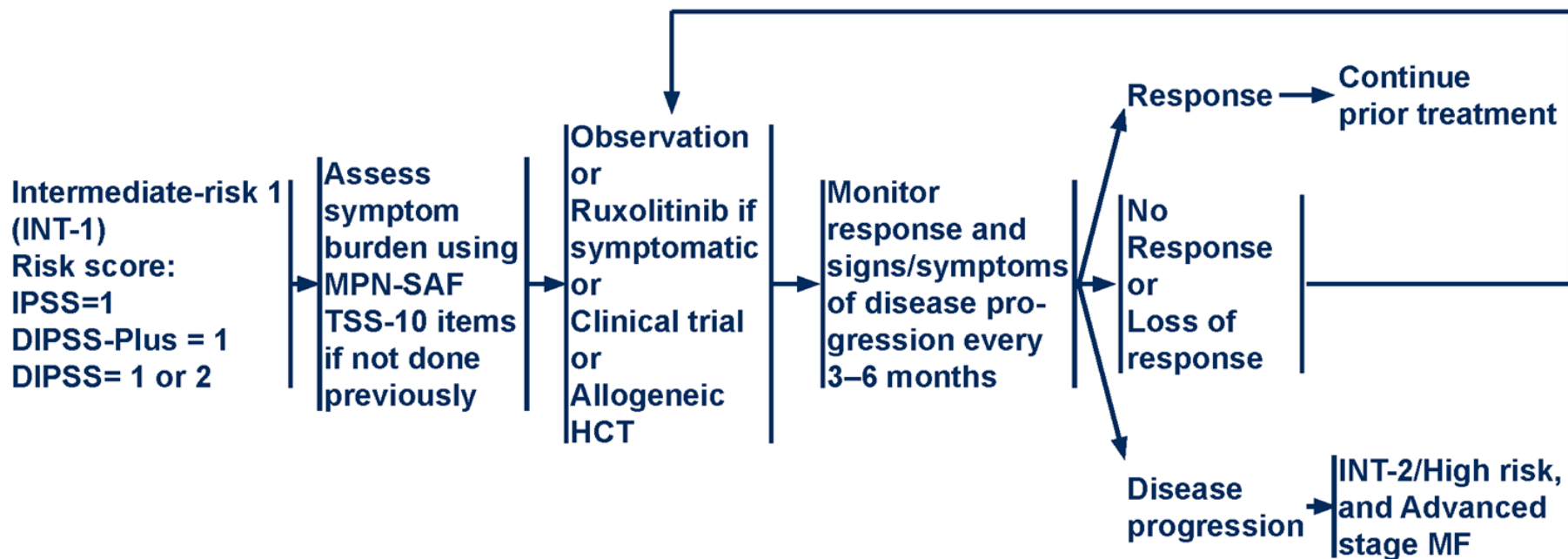
TREATMENT FOR LOW-RISK MYELOFIBROSIS





NCCN Guidelines Version 1.2017 Myeloproliferative Neoplasms

TREATMENT FOR INTERMEDIATE-RISK 1 (INT-1) MYELOFIBROSIS

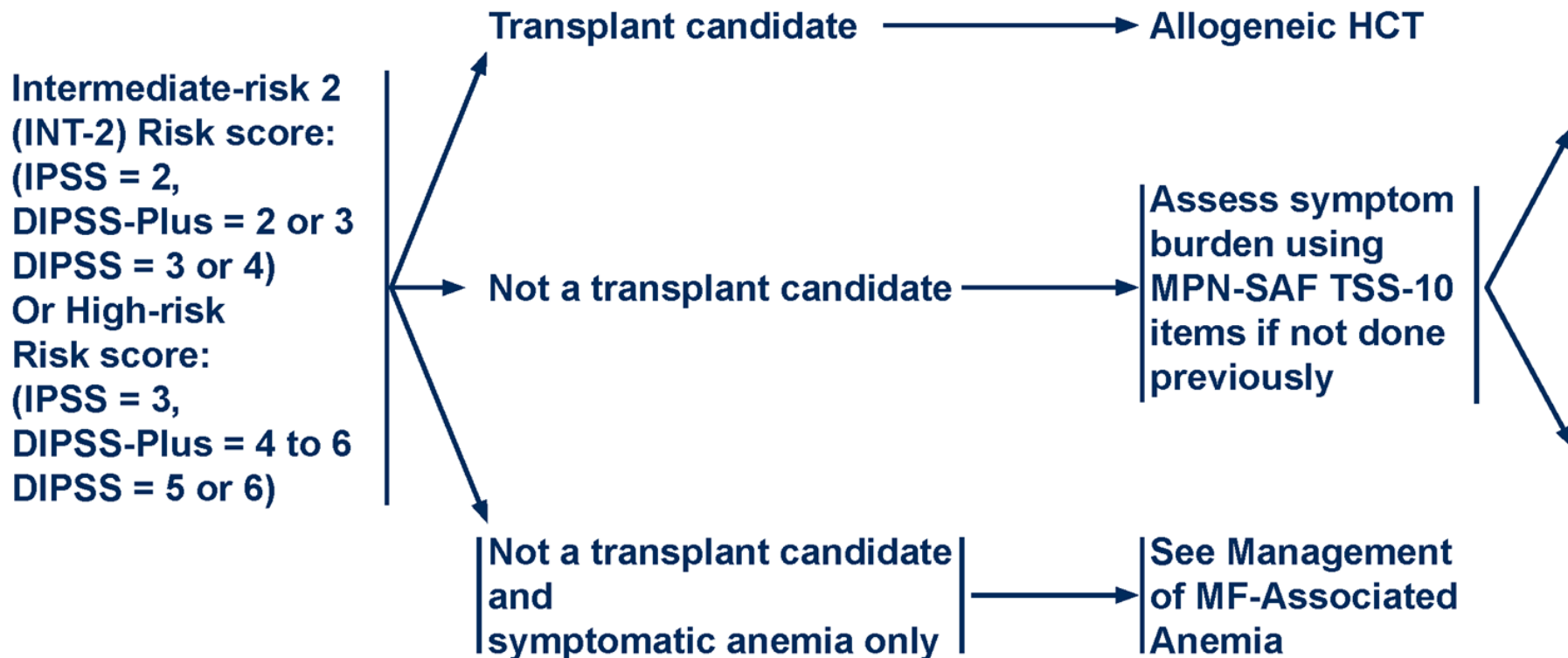


MPN-3



NCCN Guidelines Version 1.2017 Myeloproliferative Neoplasms

TREATMENT FOR INTERMEDIATE-RISK 2 (INT-2) OR HIGH-RISK MYELOFIBROSIS





NCCN Guidelines Version 1.2017 Myeloproliferative Neoplasms

TREATMENT FOR INTERMEDIATE-RISK 2 (INT-2) OR HIGH-RISK MYELOFIBROSIS

Platelets $\leq 50K$ → Consider Clinical trial

Platelets $> 50K$ → Ruxolitinib or Clinical trial

Monitor response and signs/symptoms of disease progression every 3–6 months

Response

Continue prior treatment

No Response or Loss of response

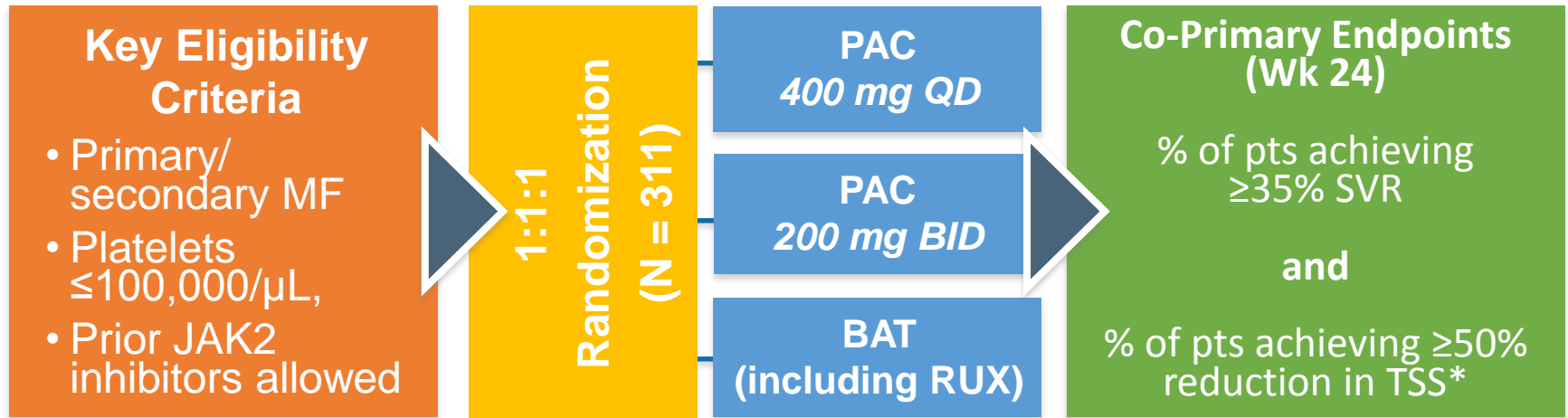
Disease progression

MPNS 2017

- MPNs – spectrum of burden, risk, care needs
- Evolving Options for PV and ET
- Footprint of Ruxolitinib 4 years after MF Launch
- **New JAK inhibitors**
- JAKi combinations
- New Targets
- Future Directions

PERSIST-2 Phase 3 Study Design

Mascarenhas et. al. ASH 2016

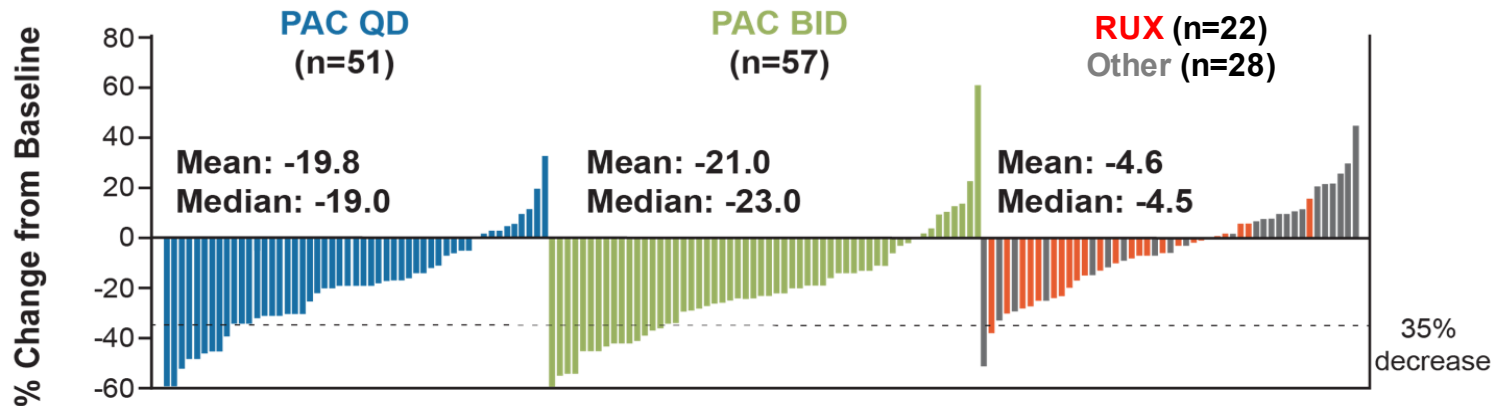


*TSS, total symptom score by MPN-SAF 2.0

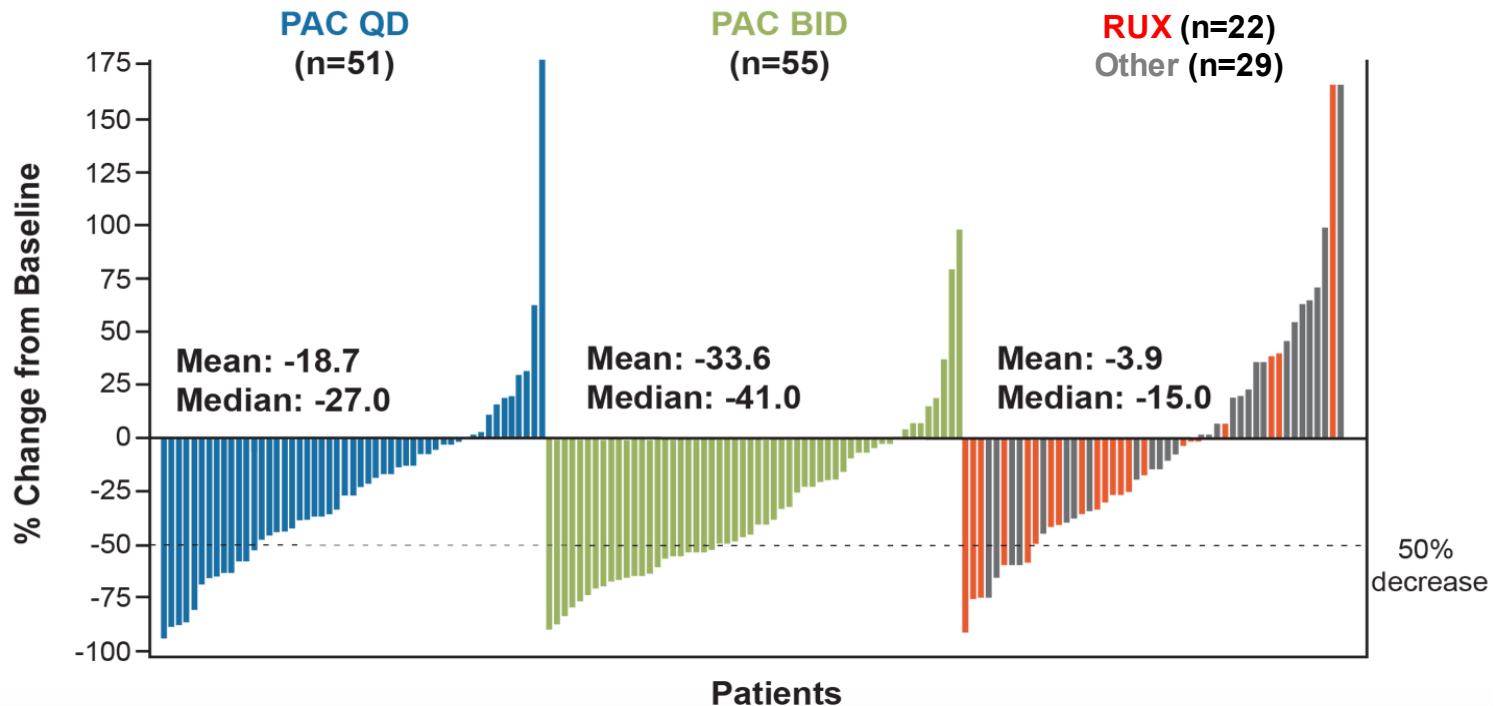
- In PK simulations, PAC 200 mg BID was predicted to have higher C_{\min} and lower C_{\max} than PAC 400 QD
- Crossover from BAT allowed after progression (any time) or at Wk 24
- **Study Objectives:**
 - Primary: efficacy of pooled QD and BID PAC vs BAT
 - Secondary: efficacy of QD PAC or BID PAC separately vs BAT

Efficacy: Analysis by Arm

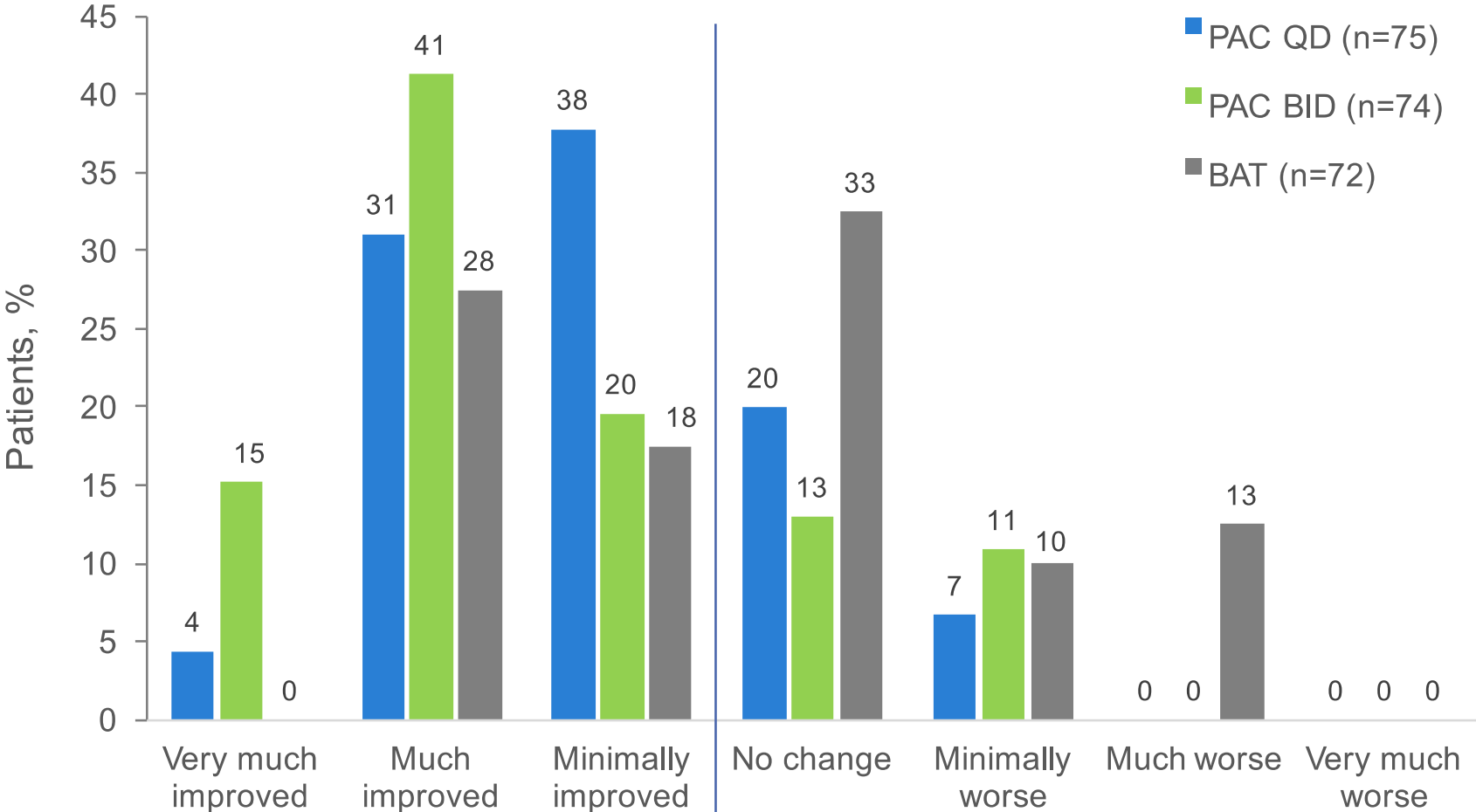
SVR



TSS



Patient Global Impression of Change Scores



Conclusions

Despite study truncation due to the clinical hold:

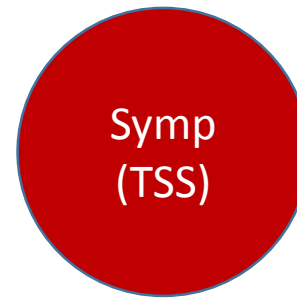
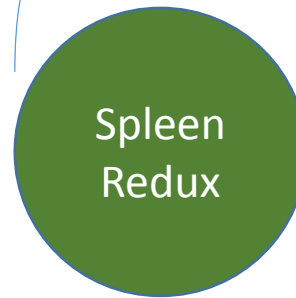
- PAC (QD+BID) was significantly more effective than BAT (including RUX) for SVR ($p=0.001$) and trended toward improved TSS ($p=0.079$)
- PAC BID appeared more effective than PAC QD versus BAT for SVR and TSS
- SVR and TSS responses to PAC BID were consistent across demographic and disease risk characteristics
- PAC BID appeared to have a better benefit/risk profile than BAT, which included RUX

Momelotinib Update 11/16/2016

Simplify 1

MOM non inferior to RUX

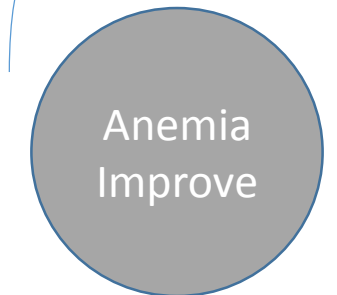
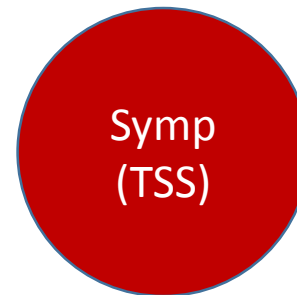
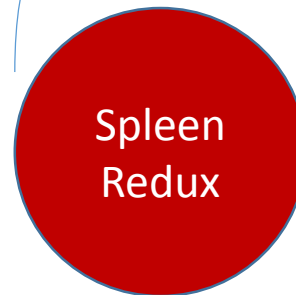
Superior



Simplify 2

MOM SUP to BAT (RUX)

Superior



MPNS 2017

- MPNs – spectrum of burden, risk, care needs
- Evolving Options for PV and ET
- Footprint of Ruxolitinib 4 years after MF Launch
- New JAK inhibitors
- **JAKi combinations**
- New Targets
- Future Directions

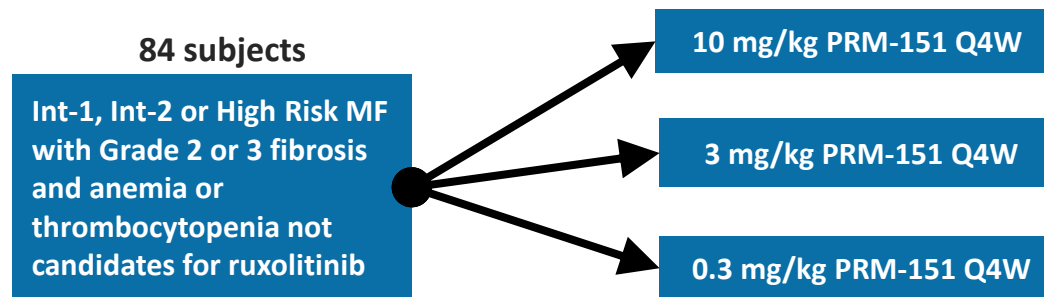
Combination + Ruxolitinib	Authors	Spleen Response	Symptom Response	PLT Impact	HB Impact	Fibrosis Response	Other
Danazol	Gowin Mascarenhas Mesa	High	High	Low	Low	Low	Low
Pomalidomide	Stegelman Dohner	High	High	Low	High	Low	Low
PEG INF a2a	Mikkelson Hasselbalch	High	High	Low	Low	Low	Low
5- AZA	Daver Verstovsek	High	High	Low	Low	Low	Low
Panobinostat (HDAC)	Harrison Ribrag	High	High	Low	Low	High	Low
BKM-120 (PI3-K)	Durrant Martinez-Lopez	High	High	Low	Low	Low	Low
LDE-225 (HH)	Gupta Heidel	High	High	Low	Low	Low	Low

MPNS 2017

- MPNs – spectrum of burden, risk, care needs
- Evolving Options for PV and ET
- Footprint of Ruxolitinib 4 years after MF Launch
- New JAK inhibitors
- JAKi combinations
- **New Targets**
- Future Directions

PRM-151 MF Stage 2 Enrolling

- A Phase 2, Prospective Study Of PRM-151 In Subjects With Primary Myelofibrosis (PMF), Post-Polycythemia Vera MF (post-PV MF), Or Post-Essential Thrombocythemia MF (post-ET MF)

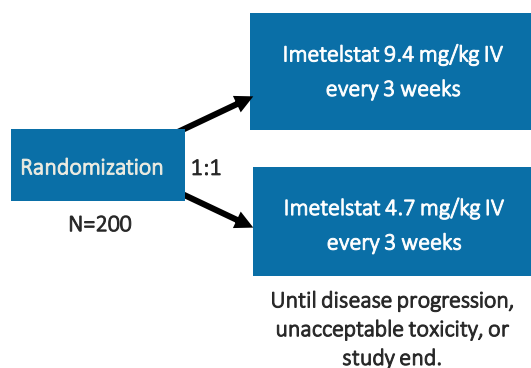


Key Eligibility:

- Int-1, Int-2, High Risk MF: Primary, Post-ET, or Post-PV
- WHO Grade 2 or 3 MF
- Not a candidate for ruxolitinib based on
- EITHER Hgb <100 g/L, requiring transfusions, and intolerant of or inadequate response to RUX
- OR Platelets <50 x 10⁹/L

Imetelstat Phase 2 MF Study – Opened for Enrollment

A Randomized, Single-Blind, Multicenter Phase 2 Study to Evaluate the Activity of 2 Dose Levels of Imetelstat in Subjects With Intermediate-2 or High-Risk Myelofibrosis (MF) Relapsed/Refractory to Janus Kinase (JAK) Inhibitor



*Not a complete list of inclusion and exclusion criteria
NCT02426086 – clinicaltrials.gov

Co - Primary End Points

- To evaluate the spleen response rate at Week 24
 - The percentage of participants who achieve $\geq 35\%$ reduction in spleen volume from baseline as measured by MRI
- To evaluate the symptom response rate at Week 24
 - The percentage of subjects who have $\geq 50\%$ reduction in total symptom score as measured by modified MFSAF v2.0.

Secondary End Points

- To measure complete remission (CR) or partial remission (PR) per modified 2013 IWG-MRT criteria
- To measure clinical improvement (CI) per modified 2013 IWG-MRT criteria
- PK profile
- Safety profile
- Overall Survival

Key Eligibility Criteria*

- 18 years of age and older
- Diagnosis of PMF; or PET-MF or PPV-MF
- DIPSS intermediate-2 or high risk MF
- Measurable splenomegaly
- Active symptoms of MF prior to study entry
- Documented progressive disease during or after JAK inhibitor
- ANC $\geq 1,500/\mu\text{l}$
- Platelets $\geq 75,000/\text{mm}^3$
- Peripheral blood and bone marrow blast count of $<10\%$

New MPN Therapies – Possible Positioning

	Front Line	Second Line	Third Line
Myelofibrosis	Ruxolitinib Momelotinib? Pacritinib?	Momelotinib? Pacritinib? PRM151? Imetelstat?	
Polycythemia Vera	HU, ? INF	Ruxolitinib	
Essential Thrombocythemia	HU, ? INF	Anagrelide	Ruxolitinib

Non Transplant Care of MPN Patients

- MPNs – spectrum of burden, risk, care needs
- Evolving Options for PV and ET
- Footprint of Ruxolitinib 4 years after MF Launch
- New JAK inhibitors
- JAKi combinations
- New Targets
- **Future Directions**

CRISPR and MPNs: Collaborations – Advocacy by Patient Groups/ Foundations and Scientists

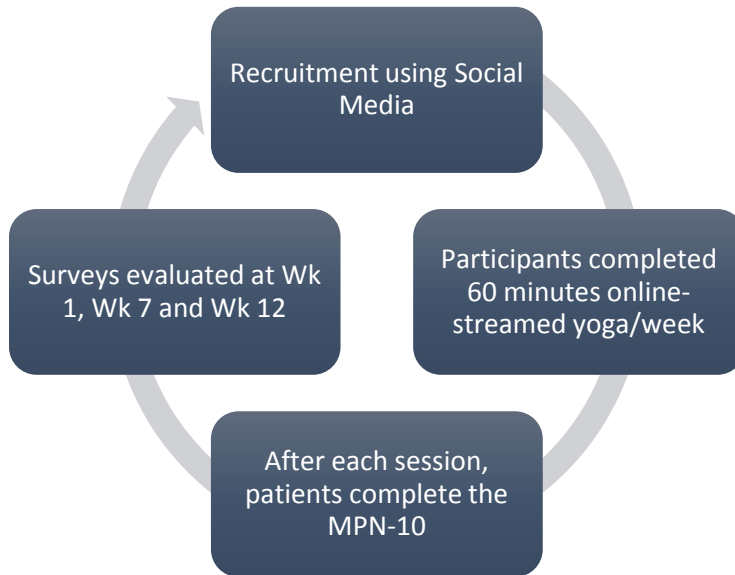
- Patient groups have been at vanguard encouraging CRISPR scientists to explore MPNs as a target genetic disease
- Clinical trials first in HIV, now in hemophilia B
- CRISPR Editing of JAK2-V617F in vitro in patient samples^a



a. Smith C, et al. *Mol Ther.* 2015;23:570-577.

The MPN Yoga Study - Feasibility 1

METHODS



RESULTS

- **38 MPN Patients participated**
 - PV (38%)
 - ET (37%)
 - MF (20%)
- **43% of participants completed >60min/wk**
- **Baseline MPN TSS: 34.6**
- *68% were satisfied (32%) or very satisfied (36%) w/ online yoga*
- *Improved MPN-10 by 4.77 points, p0.004*
- *Improved fatigue, anxiety, depression, sleep (all p=0.05)*

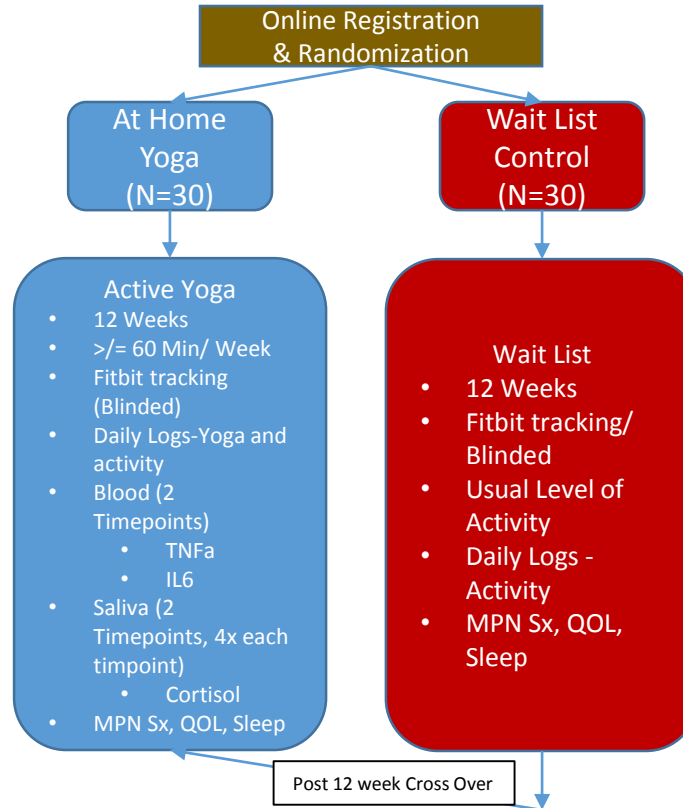


M3 Team: Mayo Clinic: R. Mesa and K. Gowin
Arizona State University: Jennifer Huberty PhD



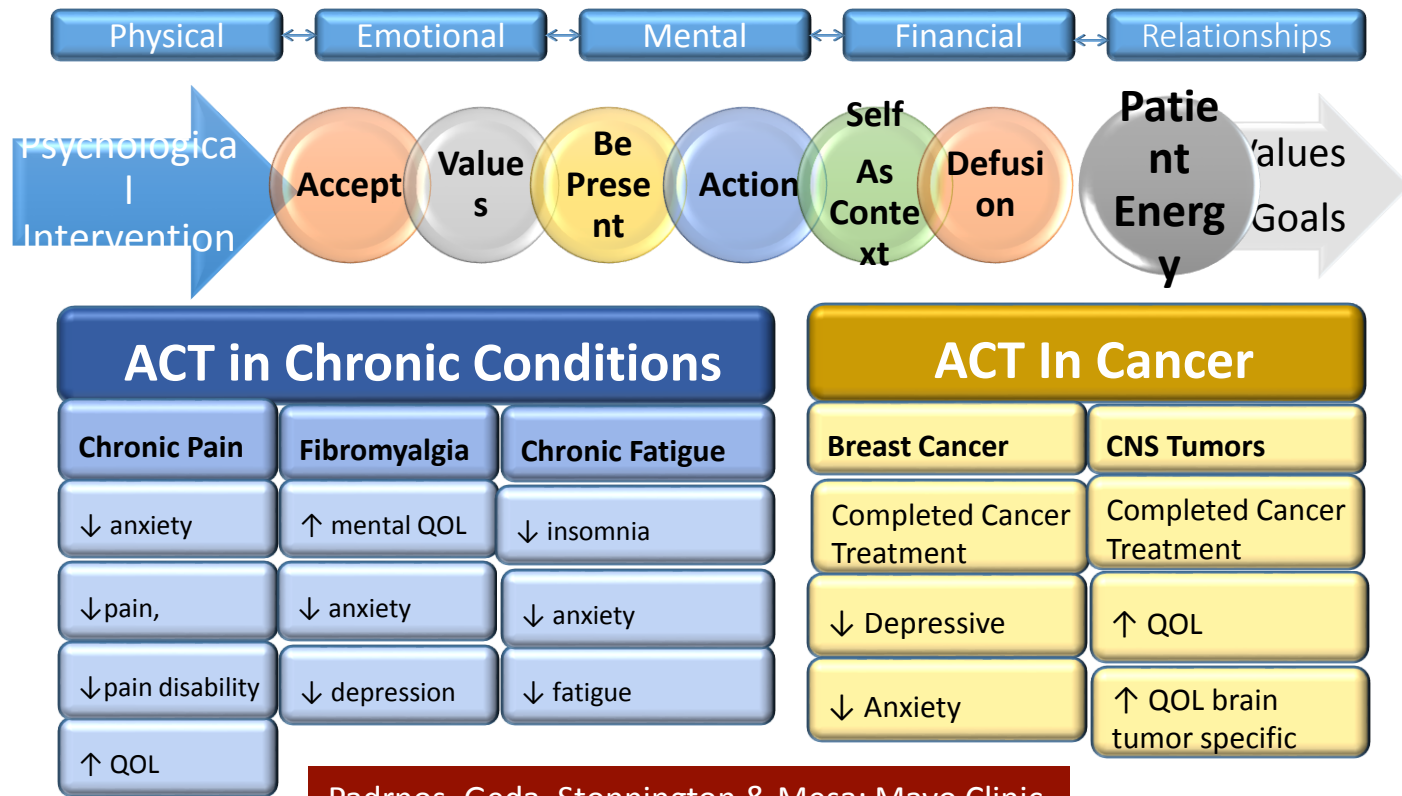
MPN Yoga II - Pilot

- Key Eligibility**
- MPN Patient
 - Not Depressed
 - PS<3
 - Not already doing yoga or Mindfulness
 - <150 Min of weekly exercise



- MPN Yoga Team:**
- Arizona State University:** Jennifer Huberty PhD
Linda Larkey, PhD
Ryan Eckert, B.S.
- Mayo Clinic Arizona**
R. Mesa, MD
Amylou Dueck, PhD
K. Gowin, MD

Acceptance and Commitment Therapy for MPNs -The Opportunity-



Padrnos, Geda, Stonnington & Mesa: Mayo Clinic

Overcoming Blood Diseases – A Partnership

Top 10 List

10. Learn about your disease

The Second

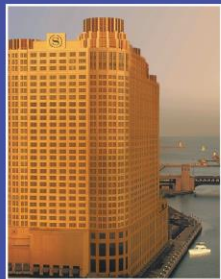
Living with a Blood Disease Symposium

A Comprehensive Workshop for Patients and Loves Ones



April 23-25, 2010

The Sheraton Chicago Hotel & Towers
Chicago, Illinois



Course Director:
Ruben Mesa, MD

Course Co-Directors:
Timothy Call, MD
Phillip Greipp, MD
Thomas Habermann, MD
Joseph Mikhael, MD
Tait Shanafelt, MD
David Steensma, MD

Mayo Clinic Hematology
Arizona | Minnesota | Florida

Capture the Moment Cancer Education Symposium

A Patient, Caregiver and
Public Education Forum



Saturday, March 12, 2016

Ritz-Carlton Orlando, Grande Lakes
4012 Central Florida Parkway
Orlando, Florida 32837

Course Directors:
Winston Tan, M.D.
Asher A. Chanan-Khan, M.D.



mcaevents@mayo.edu
REGISTER NOW

ORIGINAL RESEARCH

Quality of life and disease understanding: impact of attending a patient-centered cancer symposium

Leslie Padrnos¹, Amylou C. Dueck², Robyn Scherber¹, Pamela Glassley³, Rachel Stigge³, Donald Northfelt³, Joseph Mikhael³, Annette Aguirre³, Robert M. Bennett⁴ & Ruben A. Mesa³

¹Internal Medicine Residency Program, Mayo Clinic, Scottsdale, Arizona

²Division of Health Sciences Research, Mayo Clinic, Scottsdale, Arizona

³Division of Hematology and Medical Oncology, Mayo Clinic, Scottsdale, Arizona

⁴Paradise Valley Community College, Phoenix, Arizona

- Sense of community
- Deeper understanding of my disease
- Better understanding of resources to help me
- Decrease in stress

Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease

Precise Knowledge of Your Disease

Rest of Your
Health

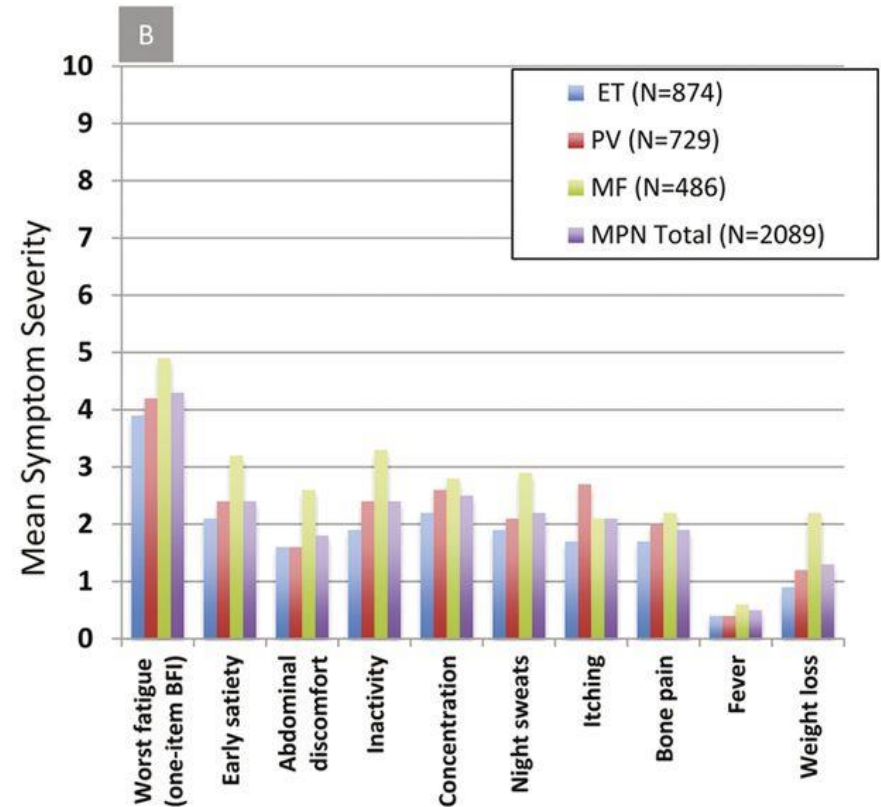
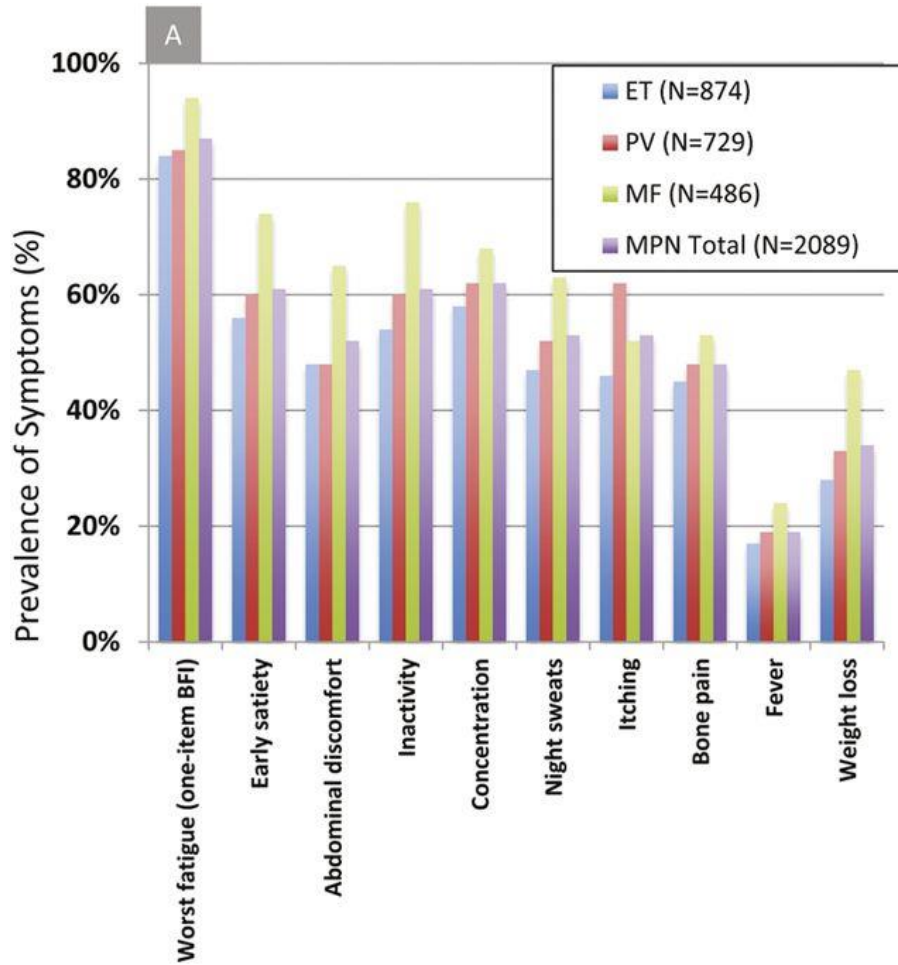
Your
Beliefs and
Choices

Biological
Features
(Genes, Proteins,
Other)

Precise
Options
(including
Clinical Trials)

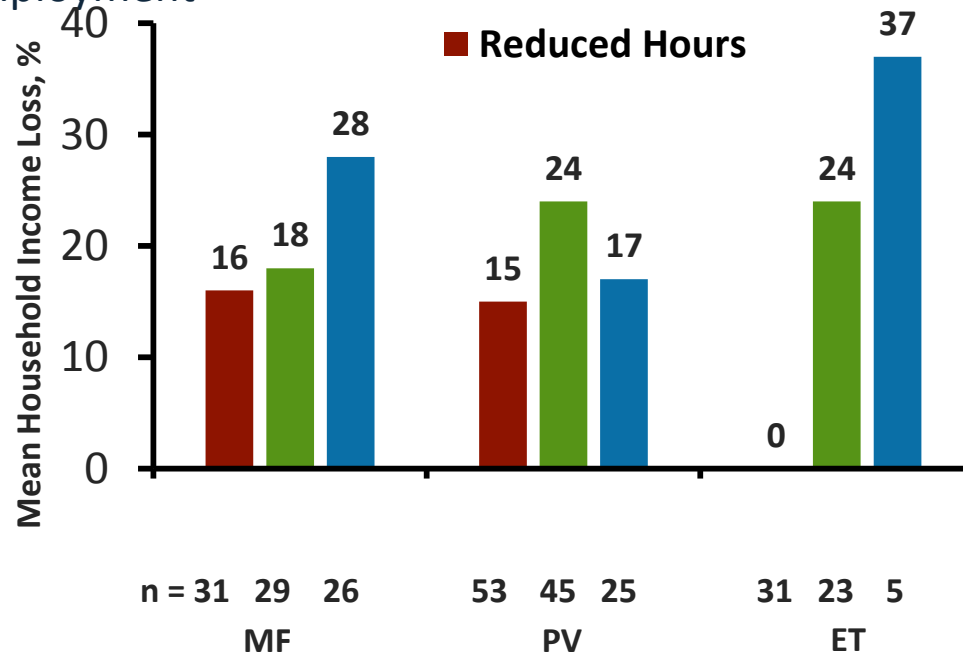
Your
Wellness

Classic Signs and Symptoms of MPNs



Lesson 4 MPN Symptoms ASH 2015: *MPNs Have A Major Impact on Employment*

- Landmark (N = 813 MPN Patients): Impact on Employment



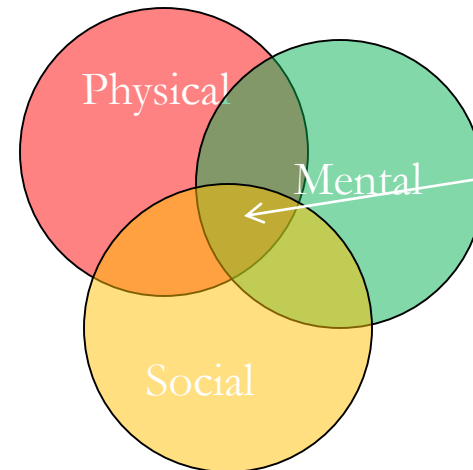
Parasuraman SV, et al. *Blood (Annual Meeting Abstracts)*. 2015;126 abstract xx.
Image courtesy of Ruben Mesa, MD.

Quality of Life (QOL)

- Definitions

- *“net consequence of life characteristics on a person’s perception of their position in life, in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns.” (WHO, Soc Sci Med 1995)*
- **Calman’s Gap:** *“the gap between one’s life expectations and actual life experiences....a good quality of life can be said to be present when the hopes of an individual are matched and fulfilled by experience.” (Calman, J Med Ethics, 1984)*

The narrower the gap the better.



Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand

What is your plan? Do you understand it?

How long till it works?

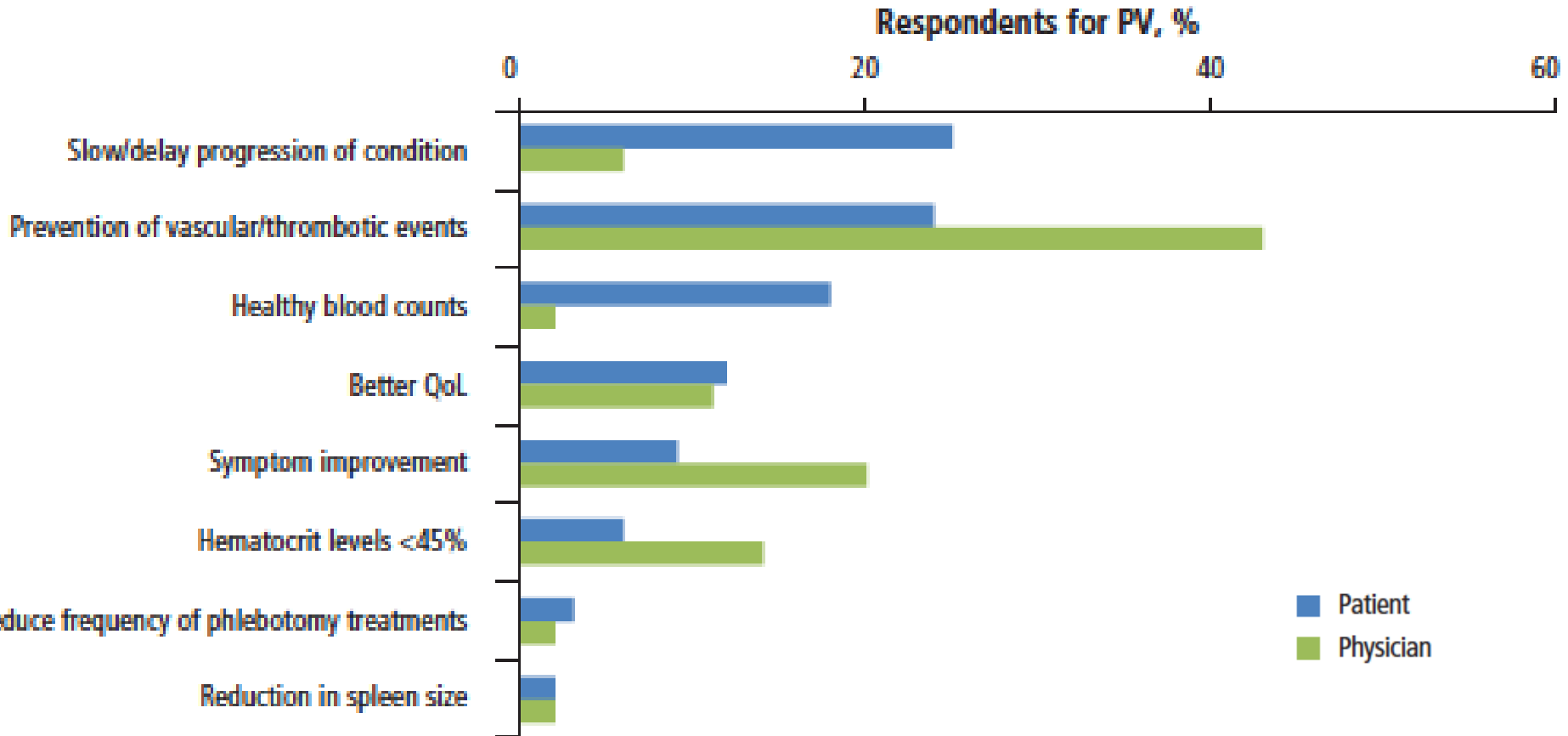
What do I do next?

My Plan?

How do we know it is working?

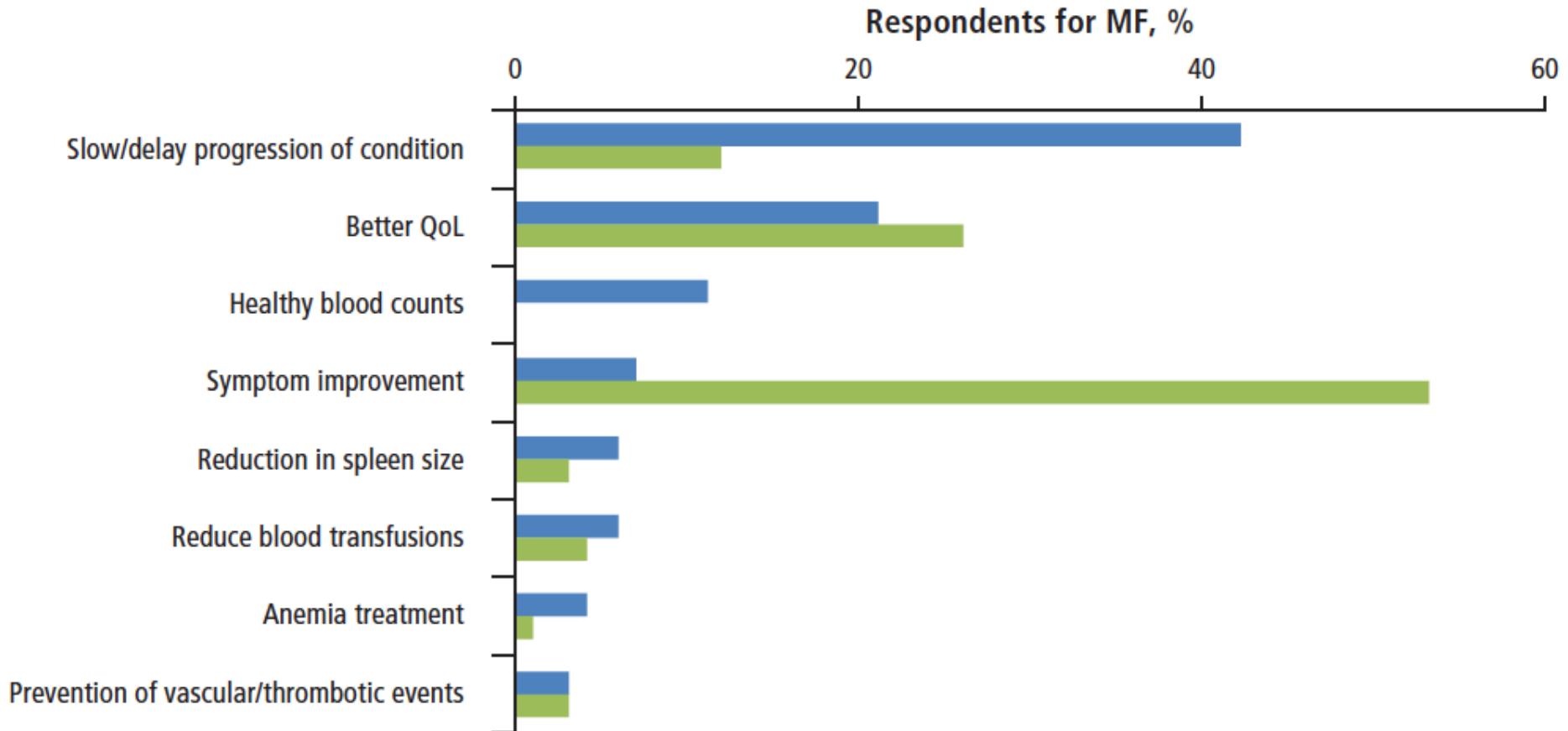
Cure or Control?

LANDMARK Study in PV Goals (Patients (N=382) & Physicians)



Mesa et. al.
BMC Cancer
2016;16:167

LANDMARK Study in MF Goals (Patients (N=207) & Physicians)



Mesa et. al.
BMC Cancer
2016;16:167

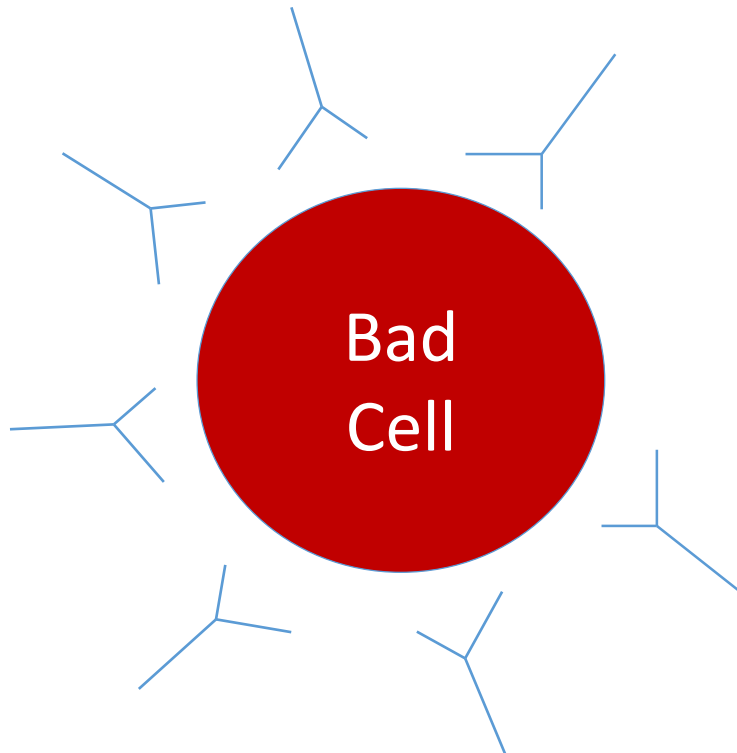
Overcoming Blood Cancers – A Partnership

Top 10 List

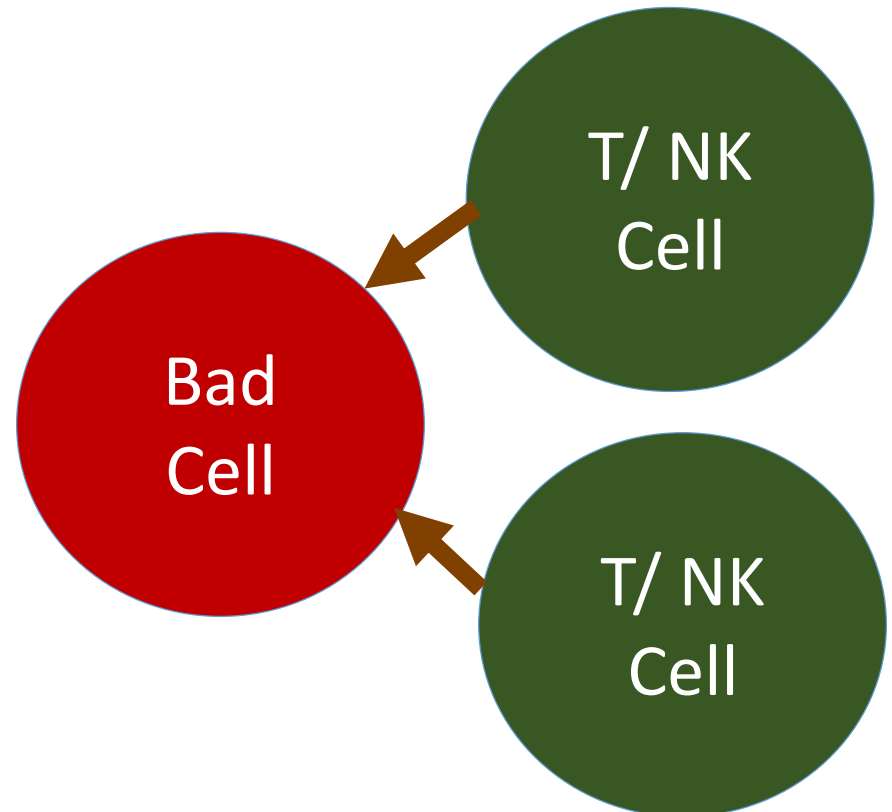
10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system

Using your immune system to treat your disease

Humoral – B Cell Immunity



Cellular – T Cell Immunity



Using your immune system to treat your disease

Humoral – B Cell Immunity “ – Mabs”

- Rituximab
- Bexxar
- Zevalin
- Blinatumomab
- Ofatumumab
- Daratumumab
- Pembrolizumab
- PRM151

Cellular – T Cell Immunity

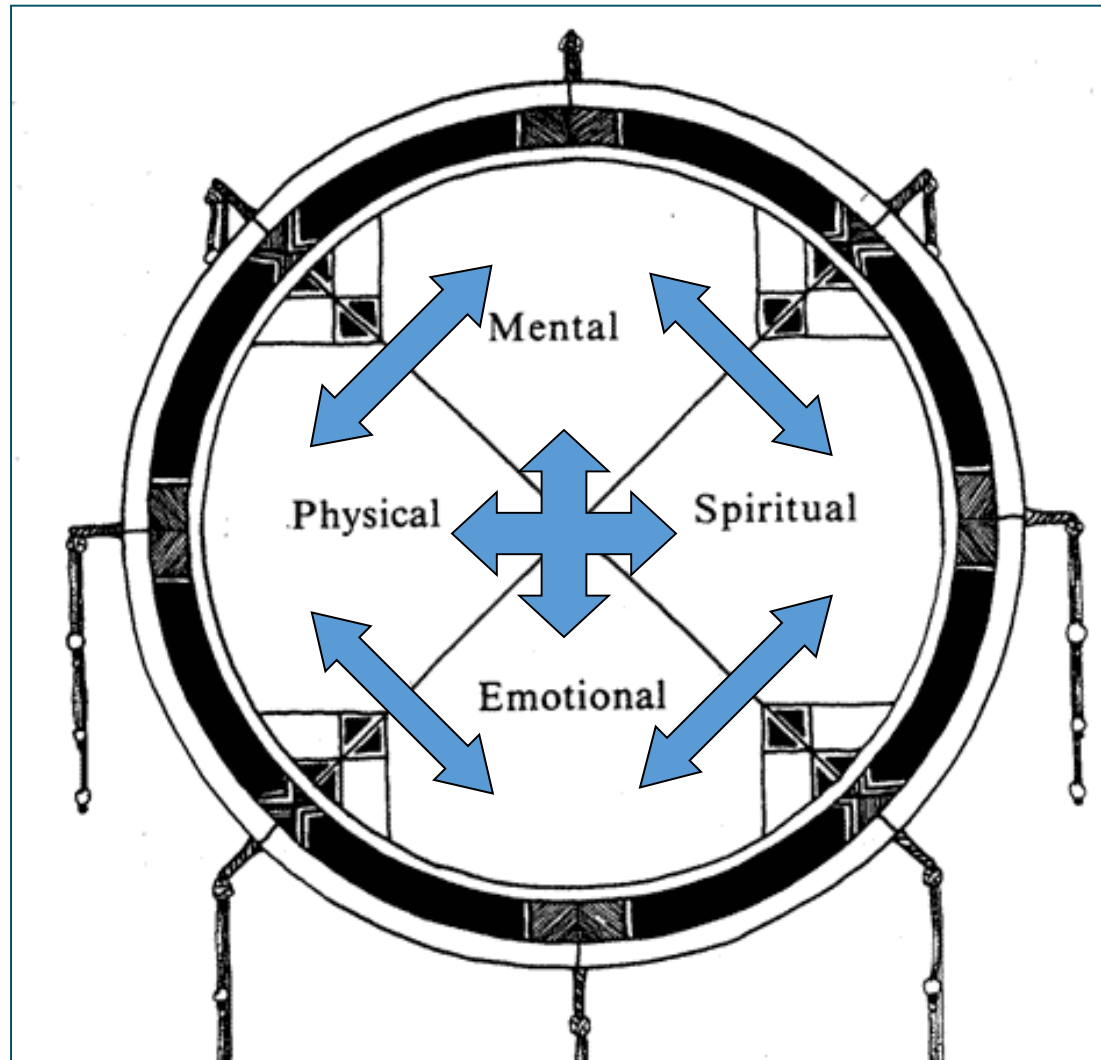
- CART
(Chimeric Antigen Receptor) T Cell Therapy
- Allogeneic Stem Cell Transplant

Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system
6. Take care of the rest of your health

Medicine Wheel of Health “Integrative Medicine”



Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system
6. Take care of the rest of your health
5. Targeting key weaknesses in blood cancer cells

Targeting the weakness in blood cancer cells

Targeted Inhibitors in Heme Cancers (Partial List) (“-nibs”)

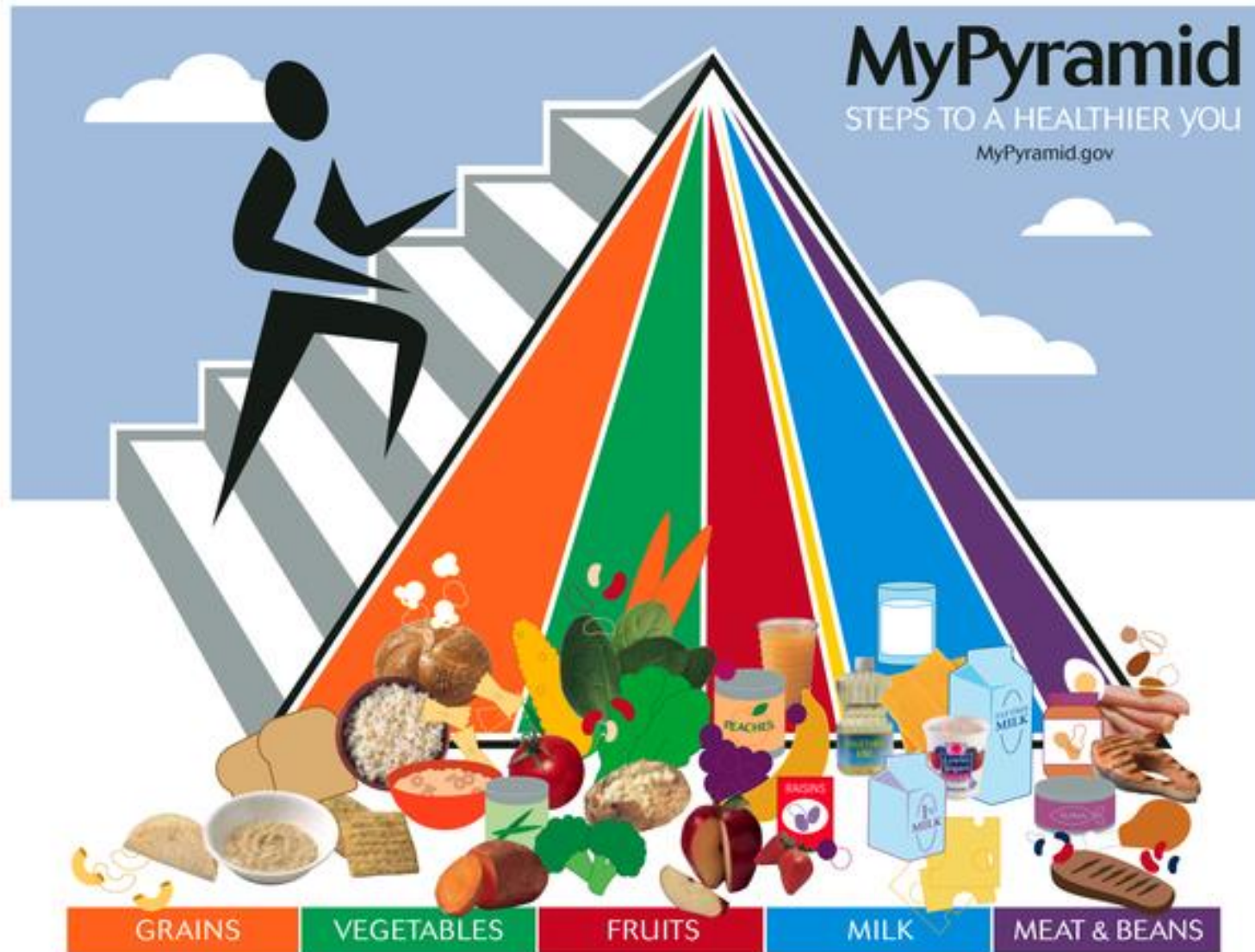
- Imatinib
- Nilotinib
- Dasatinib
- Ponatinib
- Bosutinib
- Ruxolitinib
- Pacritinib
- Momelotinib
- Fedratinib
- Ibrutinib

Overcoming Blood Cancers – A Partnership

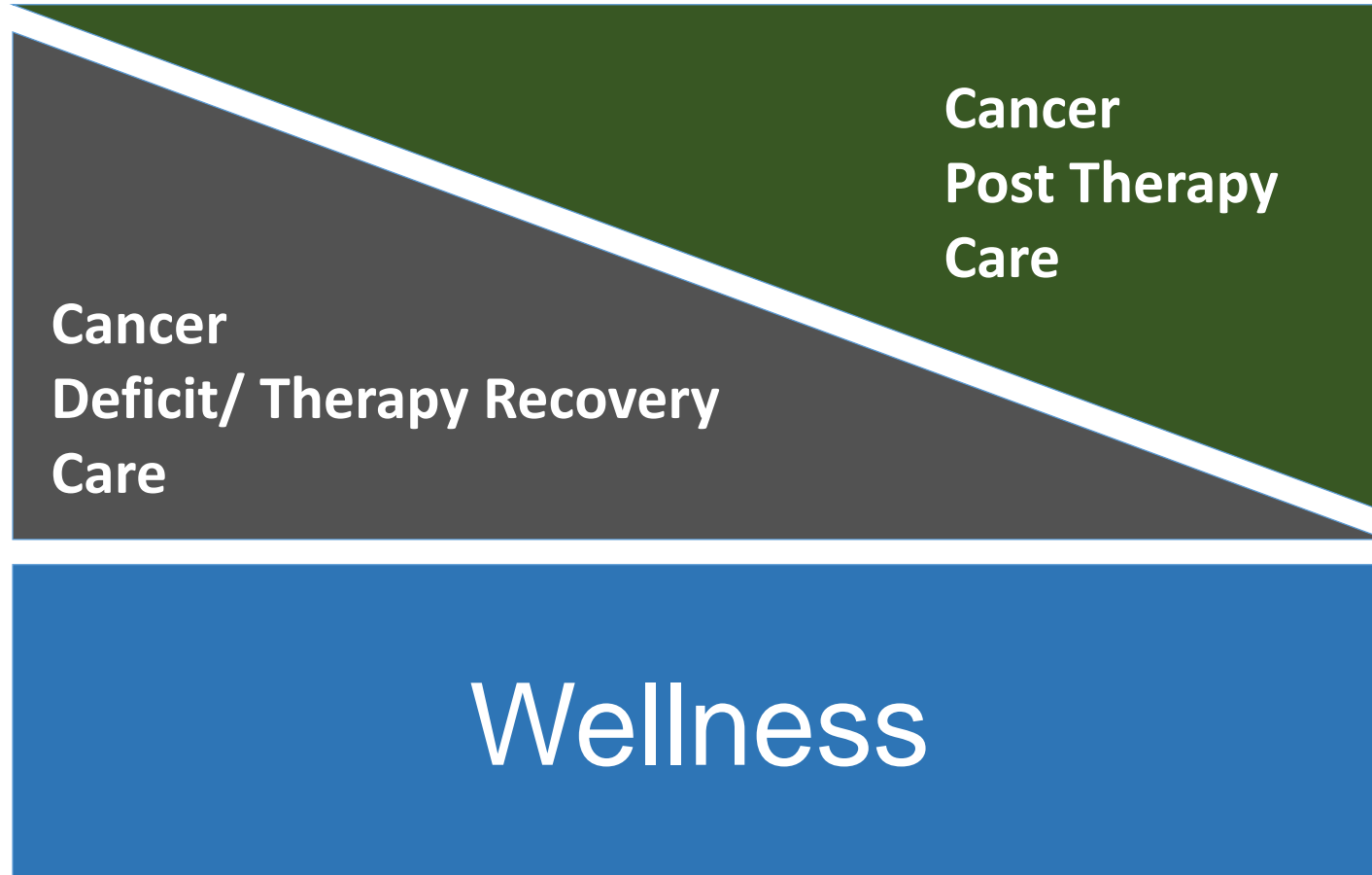
Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system
6. Take care of the rest of your health
5. Targeting key weaknesses in blood cancer cells
4. Eat in a healthy way (most of the time 😊)

Eat healthy most of the time



Mayo Clinic – Cancer Wellness Program



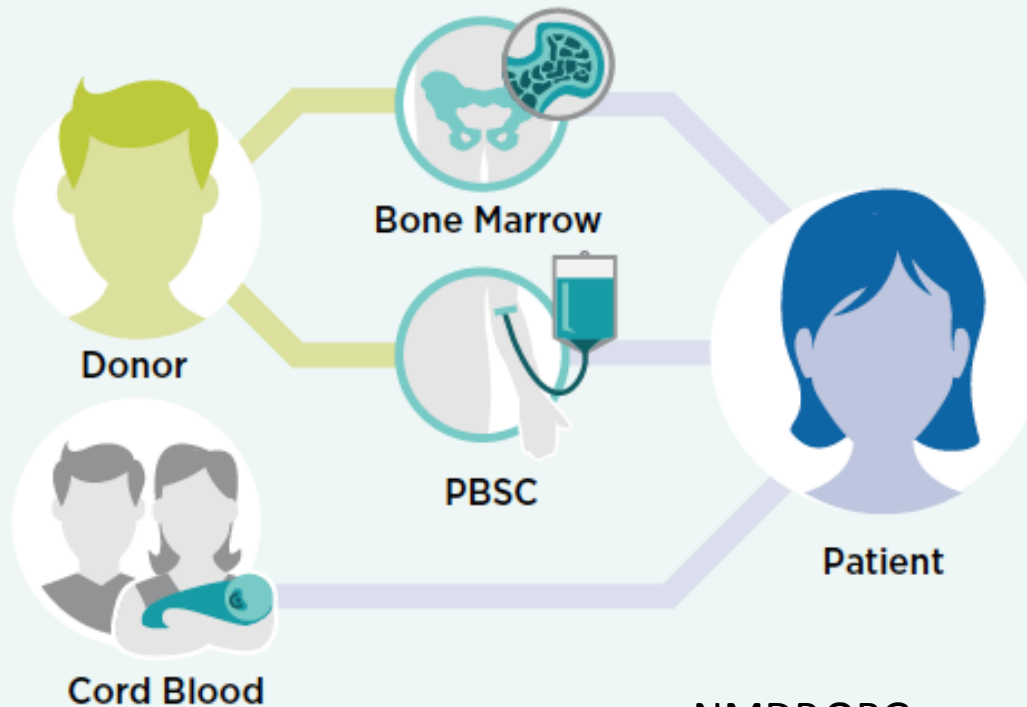
Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system
6. Take care of the rest of your health
5. Targeting key weaknesses in blood cancer cells
4. Eat in a healthy way (most of the time 😊)
3. The complex healing power of Stem Cell transplant

Complex Healing Process of Stem Cell Transplant

Allogeneic Transplant



ALLO

- AML
- ALL
- CML
- MDS
- MF

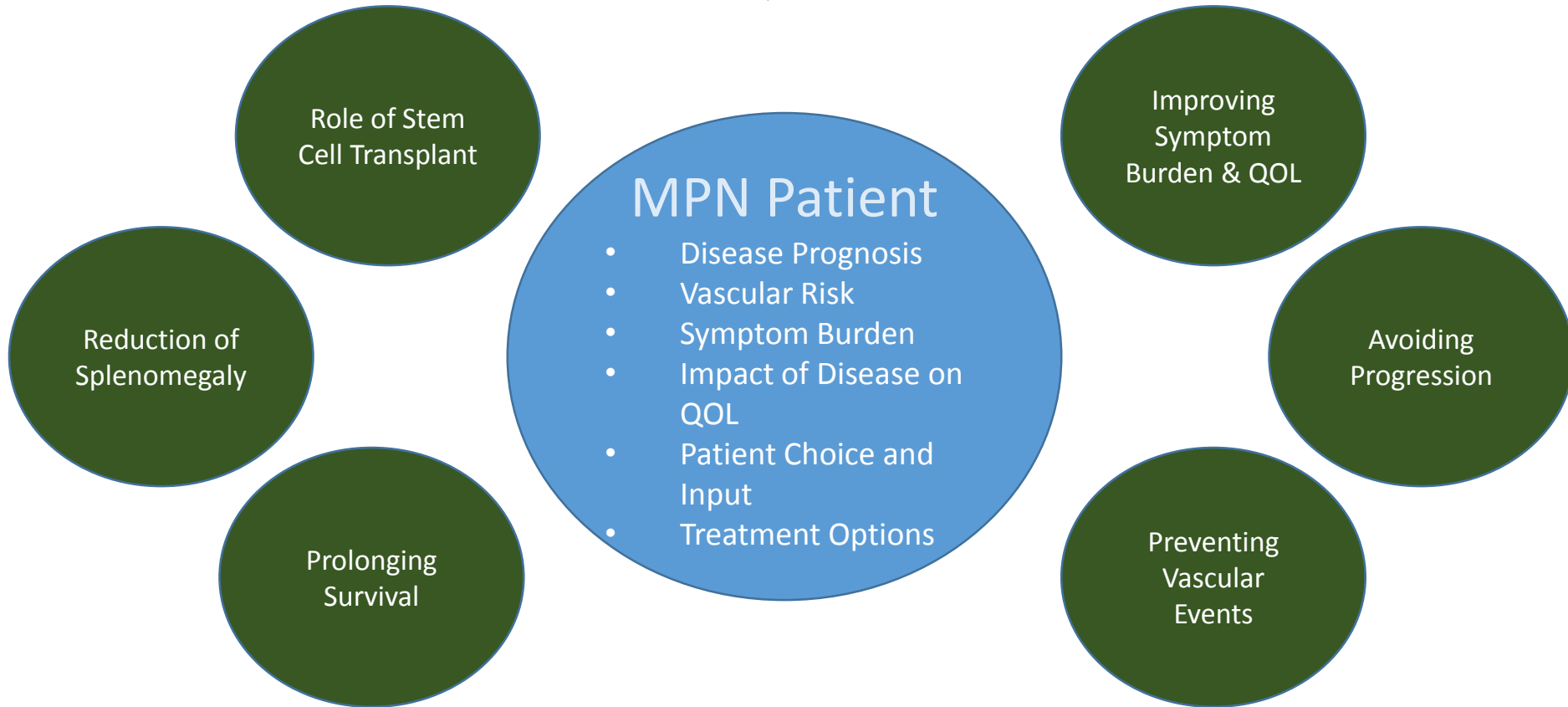
- CLL
- Myeloma
- Lymphoma

AUTO

- Myeloma
- Lymphoma
- Hodgkins
- Amyloid
- Waldenstroms

What about Autologous Stem Cell Transplant?

Putting It All Together – MPNs and QOL

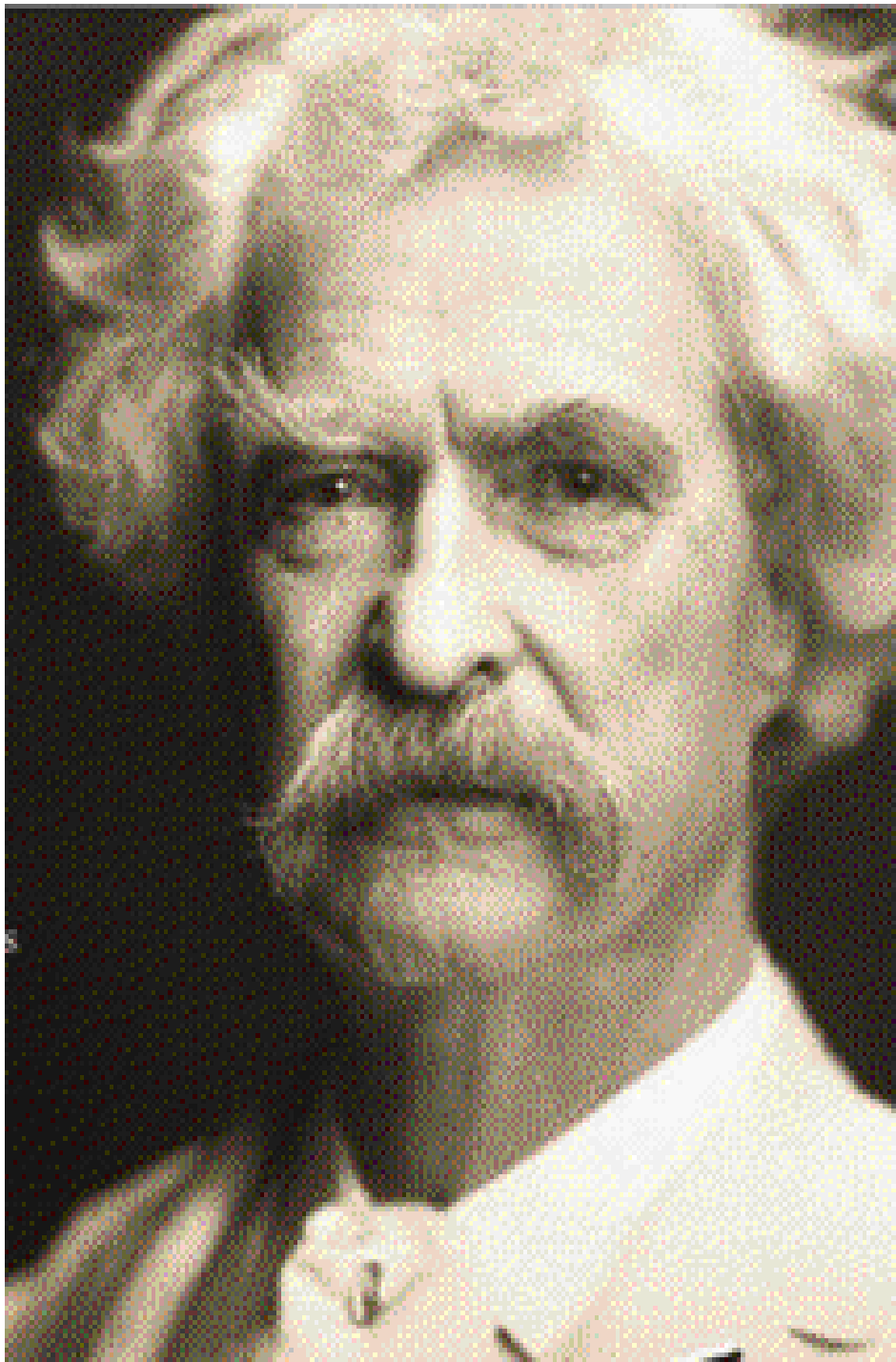


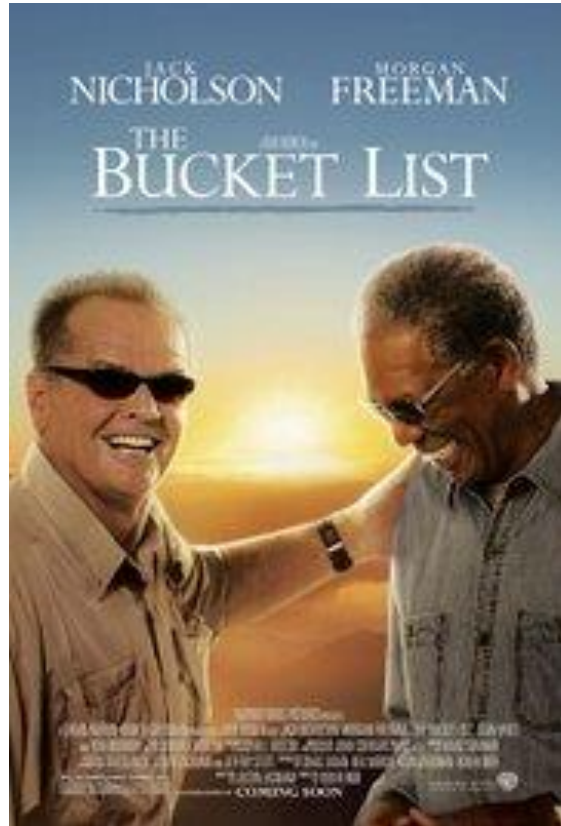
Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system
6. Take care of the rest of your health
5. Targeting key weaknesses in blood cancer cells
4. Eat in a healthy way (most of the time 😊)
3. The complex healing power of Stem Cell transplant
2. Live every moment

**“In 5 years
we will have
regrets and
remorse for
the things
we did not
do, rather
than what
we did.”**









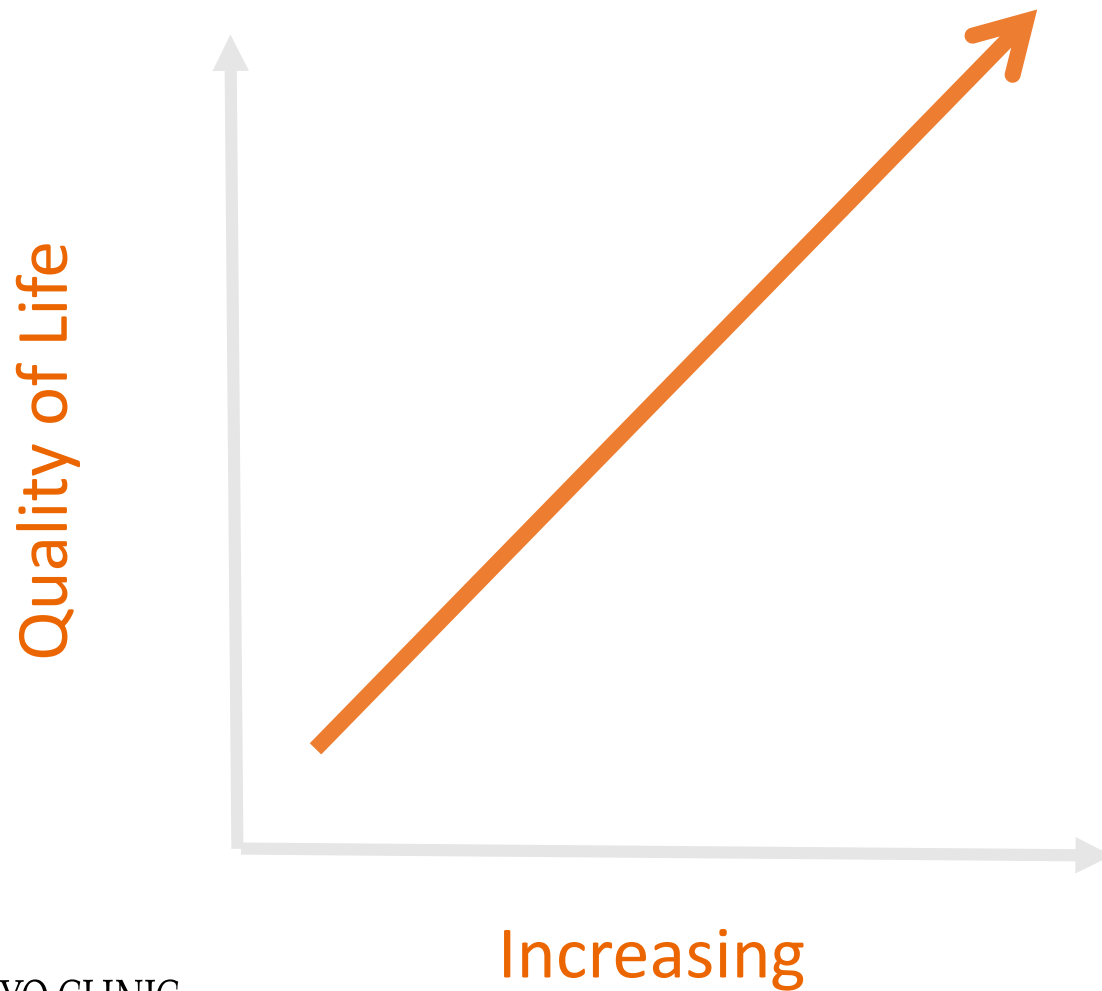
Don't wait to go to Alaska

Overcoming Blood Cancers – A Partnership

Top 10 List

10. Learn about your disease
9. Understand precisely your disease
8. Have a clear plan with your team that you understand
7. Harness the power of the immune system
6. Take care of the rest of your health
5. Targeting key weaknesses in blood cancer cells
4. Eat in a healthy way (most of the time 😊)
3. The complex healing power of Stem Cell transplant
2. Live every moment
1. **Focus on relationships**

What is quality of life



I would have...

- But mostly, given another shot at life, I would seize every minute... look at it and really see it... live it and never give it back. Stop sweating the small stuff.

Erma Bombeck
1927-1996





Myeloproliferative Neoplasms

Multi-Disciplinary Team
Mayo Clinic, Arizona, USA

MPN Burden/
Symptom/QOL
Assessment

Improving
Transplant
Outcomes

New MPN
Drug/
Genetic
Therapies

Physical
Activity/
Behavioral
Therapies



Questions?

