

# State of the Art Care of MPNs

New Drugs in Hematology - Bologna 2016

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# Disclosures

- Consultancy: Novartis, Shire, Ariad
- Research Funding: Incyte, Gilead, CTI, Genentech, Promedior, NS Pharma, Pfizer, Pharmessentia

## **Session I: Classical Ph1-neg myeloproliferative neoplasms**

*Chairmen: F. Passamonti, A.M. Vannucchi*

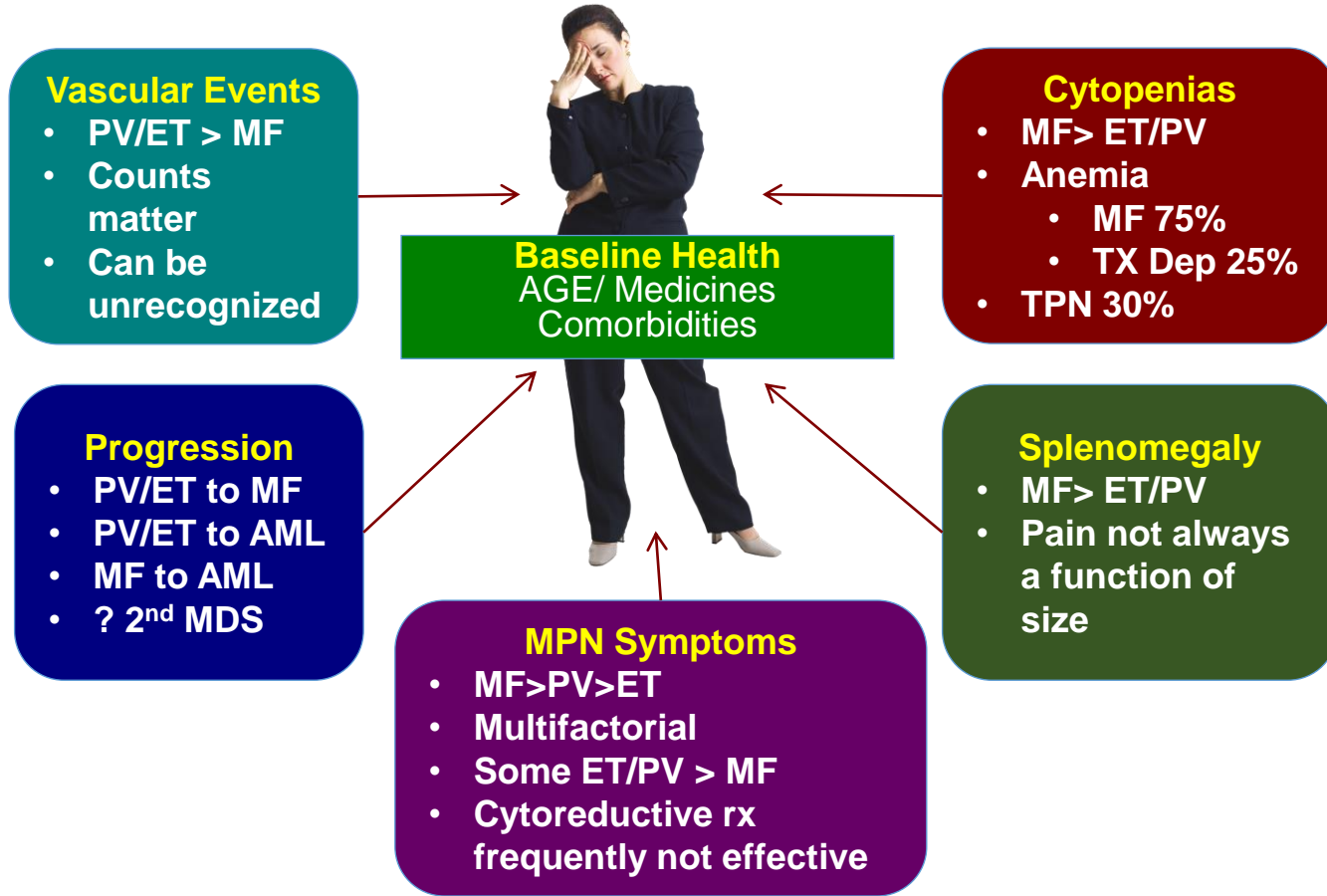
- 11.00 a.m.** Status of the art of treatment - *R.A. Mesa*
- 11.25 a.m.** Ruxolitinib in myelofibrosis - *F. Passamonti*
- 11.40 a.m.** Ruxolitinib in polycitemia vera - *A.M. Vannucchi*
- 11.55 a.m.** New JAK2 inhibitors in MPNs and combination therapy - *F. Cervantes*
- 12.10 p.m.** Interferons in MPNs - *H.C. Hasselbalch*
- 12.25 p.m.** Newer drugs for myelofibrosis - *G. Barosi*

# “State of the Art” Care of MPN Patients

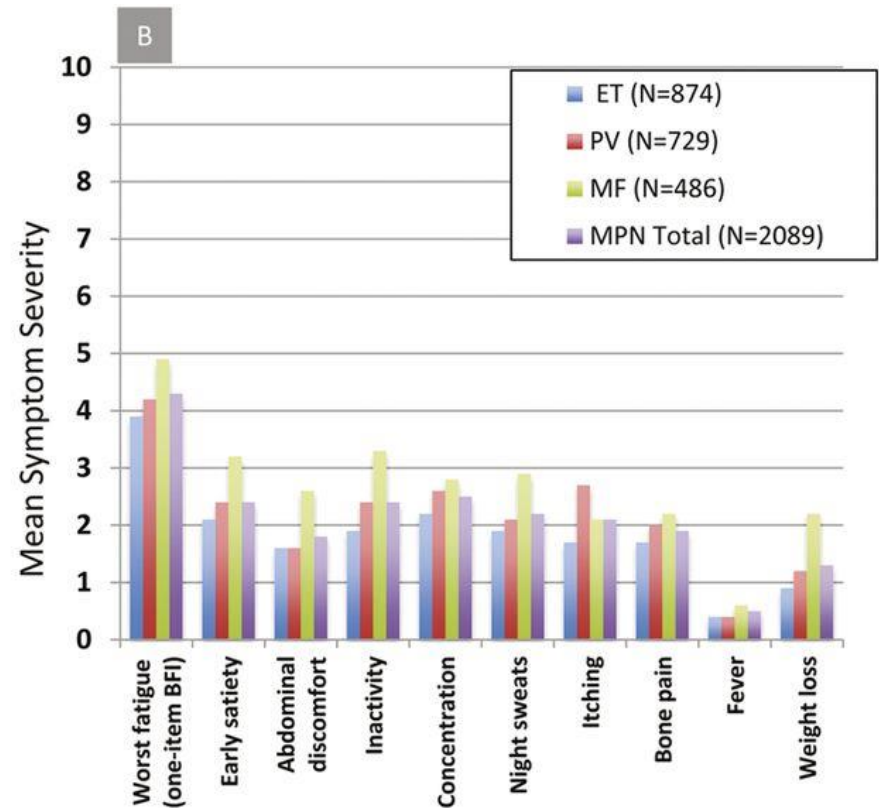
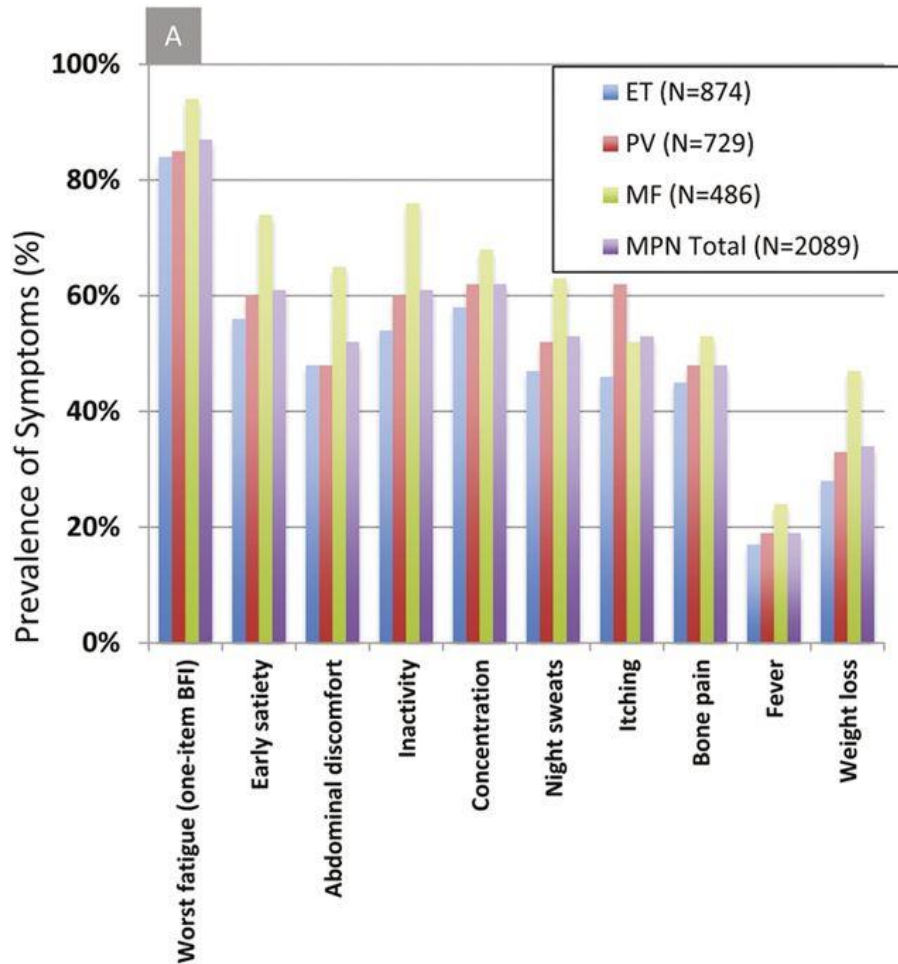
- What is your patients disease burden?
- What is your patients risk?
- What are your treatment goals?
- What are the unmet needs “new drugs” in hematology need to address?
- Who is a clinical trial patient in MPNs in 2016 vs. standard therapy?
- Future directions

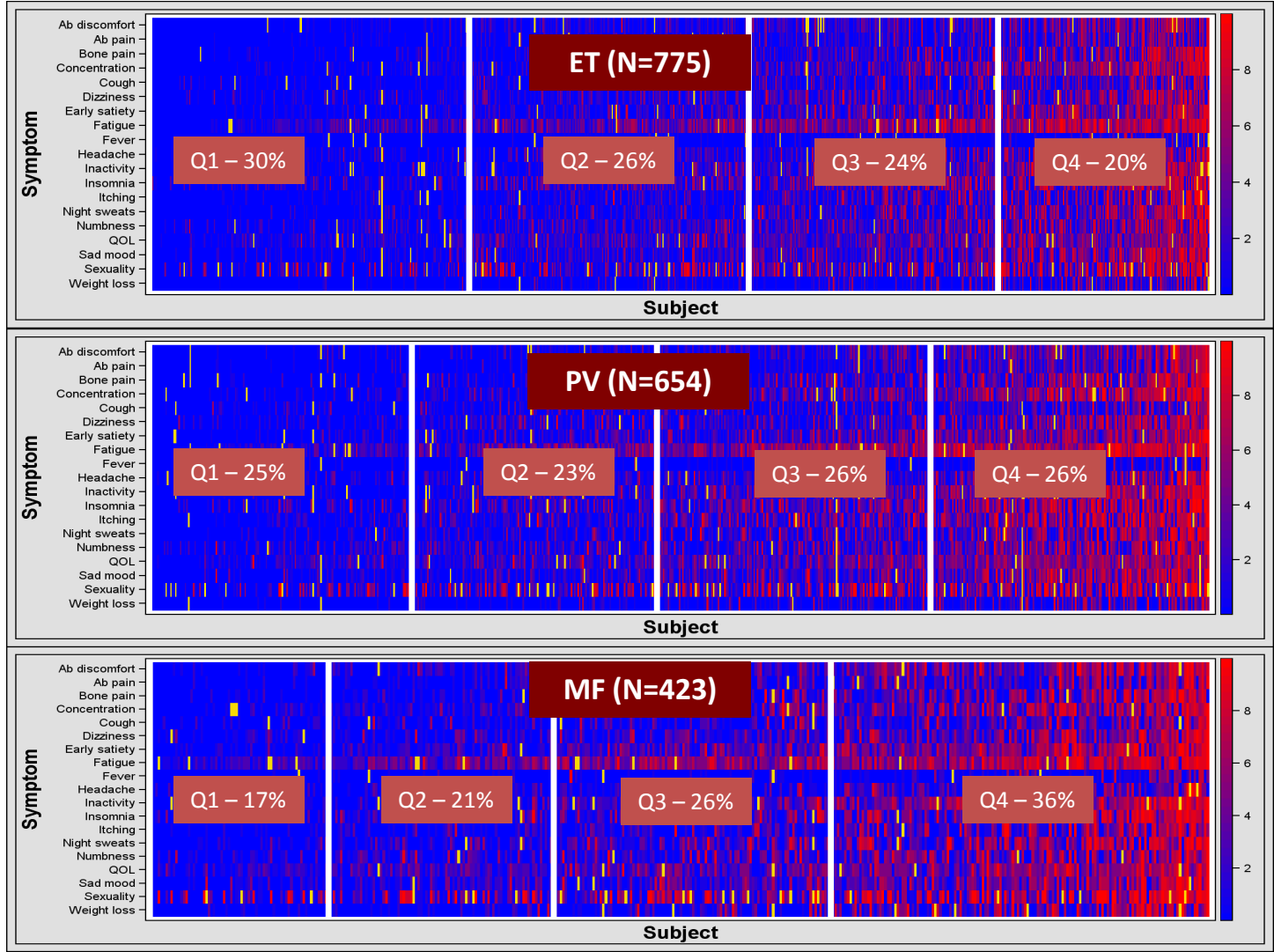
# Assessing MPN Burden

*WHO Diagnosis Does Not Tell Whole Story*

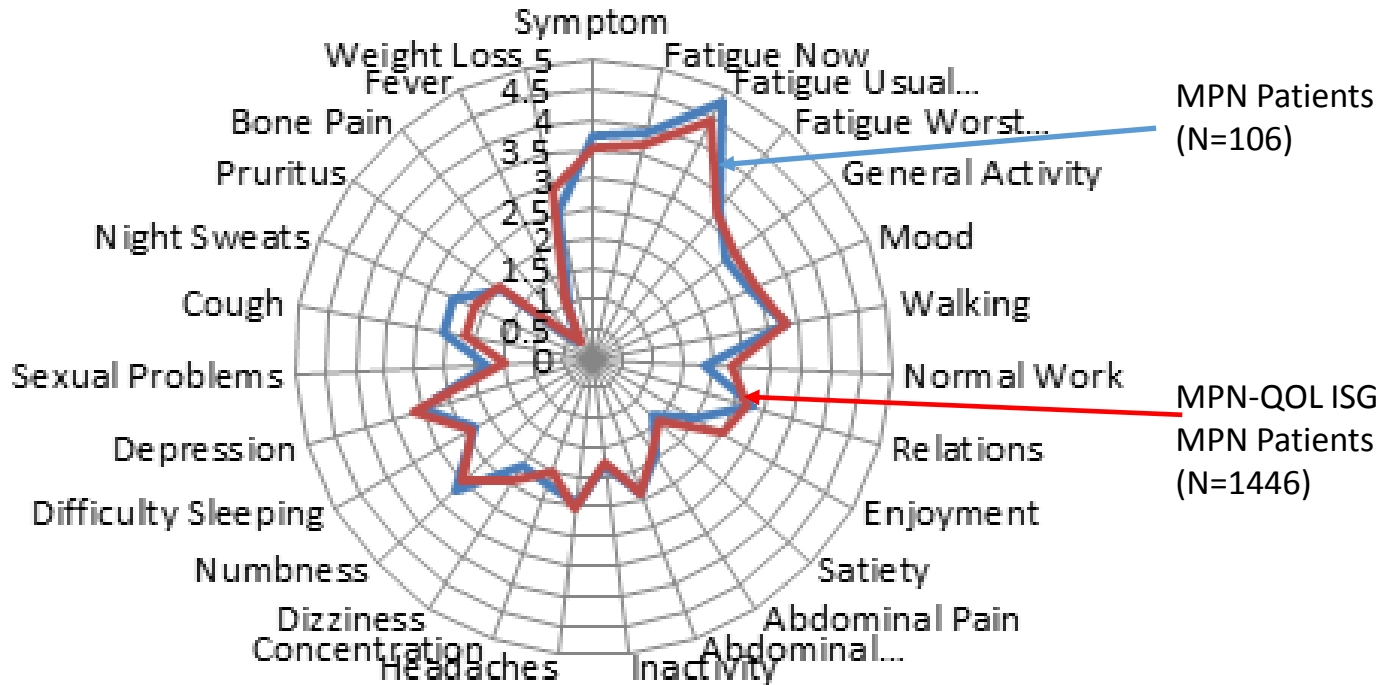


# Classic Signs and Symptoms of MPN





## What is MPN Symptom Burden in Patients vs. General Population? MOSAICC Population Vs. MPN-QOL ISG



Anderson et. al. ASH 2015



# MPN Symptom Burden is Significant, and Worse Than General Population

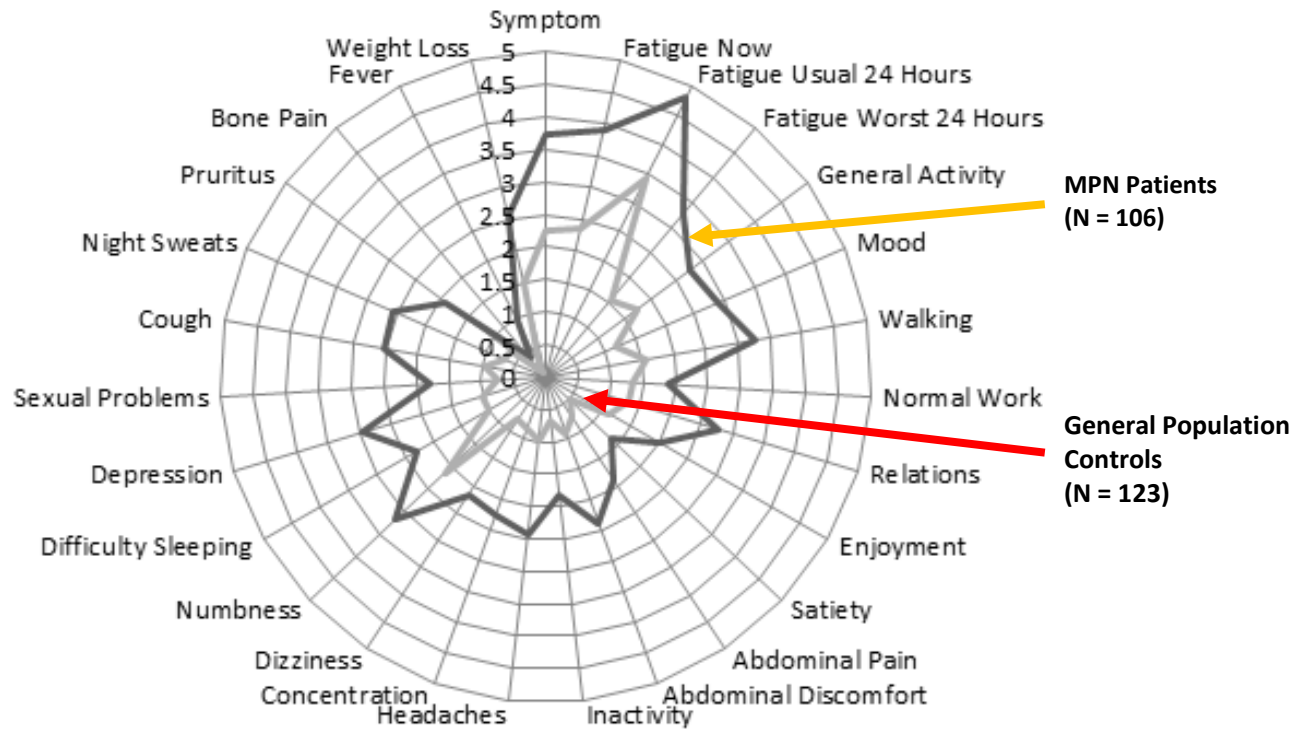


Image courtesy of Ruben A. Mesa, MD

# Definitions

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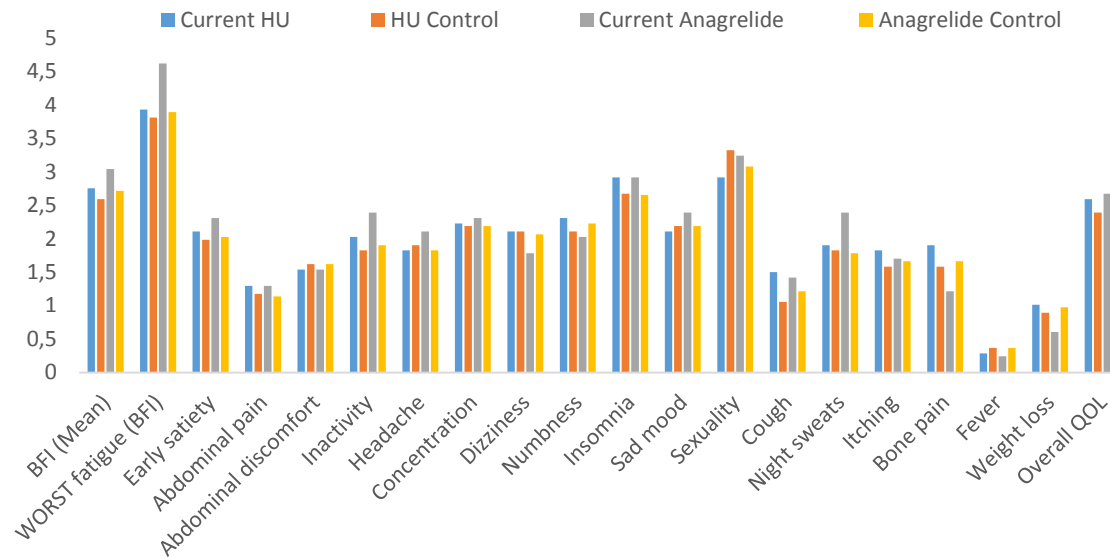
## HRQOL in MPNs?

Σ

- MPN related symptoms
- Medication related toxicities
- Problems from prior MPN complications
- Stressors from having their MPN
  - Financial
  - Emotional
  - Intrapersonal
- Co-morbidities
- Hassle of medical care

## Lesson 1 MPN Symptoms ASH 2015: Current ET Therapies Seem to Have Minimal Impact on Symptom Burden

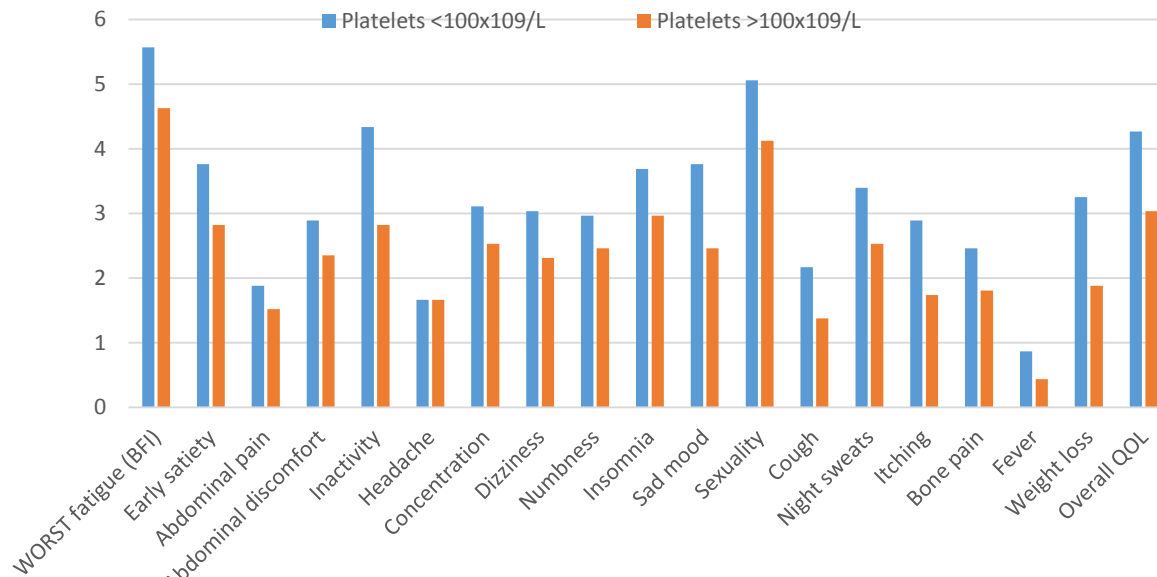
- ET Patients (N = 843)
  - Impact HU or anagrelide on symptom burden
  - In non-randomized assessment similar symptom burden despite HU or anagrelide



Geyer HL, et al. *Blood*. 2015;126 abstract xx.

## Lesson 2 MPN Symptoms ASH 2015: *MF Patients with Thrombocytopenia Have Worse Prognosis and Symptom Burden*

- MF Patients (N = 418)
  - Symptom burden stratified by platelets
  - Much higher symptom burden in those with platelets  $<100 \times 10^9/L$



Geyer HL, et al. *Blood*. 2015;126 abstract xx.

## Lesson 3 MPN Symptoms ASH 2015: Duration of MPN Has a Significant Impact on Symptom Burden

Item Mean (SD)	Early (N = 757)	Middle (N = 353)	Late (N = 333)	Total (N = 1443)	P Value
<b>BFI (Mean)</b>	<b>3.1 (2.29)</b>	<b>3.3 (2.29)</b>	<b>3.5 (2.36)</b>	<b>3.2 (2.31)</b>	<b>.04</b>
WORST Fatigue (BFI)	4.3 (2.83)	4.5 (2.76)	4.7 (2.84)	4.4 (2.82)	-
Early satiety	2.4 (2.80)	2.5 (2.77)	2.7 (2.63)	2.5 (2.76)	-
Abdominal pain	1.4 (2.24)	1.5 (2.33)	1.5 (2.24)	1.5 (2.26)	-
Abdominal discomfort	1.8 (2.37)	1.9 (2.53)	2.0 (2.49)	1.8 (2.44)	-
Inactivity	2.3 (2.70)	2.4 (2.62)	2.5 (2.73)	2.4 (2.69)	-
Headache	1.8 (2.48)	1.8 (2.45)	1.5 (2.21)	1.8 (2.42)	-
<b>Concentration</b>	<b>2.3 (2.71)</b>	<b>2.8 (2.83)</b>	<b>2.8 (2.84)</b>	<b>2.5 (2.78)</b>	<b>.007</b>
Dizziness	2.0 (2.54)	2.1 (2.62)	2.0 (2.46)	2.0 (2.54)	-
Numbness	2.5 (2.79)	2.6 (2.77)	2.4 (2.73)	2.5 (2.77)	-
<b>Insomnia</b>	<b>2.8 (3.02)</b>	<b>3.2 (3.11)</b>	<b>3.3 (3.05)</b>	<b>3.0 (3.05)</b>	<b>.02</b>
Sad mood	2.3 (2.70)	2.4 (2.72)	2.5 (2.70)	2.4 (2.70)	-
<b>Sexuality</b>	<b>2.9 (3.37)</b>	<b>3.2 (3.53)</b>	<b>3.7 (3.70)</b>	<b>3.2 (3.50)</b>	<b>.002</b>
<b>Cough</b>	<b>1.4 (2.18)</b>	<b>1.5 (2.41)</b>	<b>1.8 (2.40)</b>	<b>1.5 (2.29)</b>	<b>.03</b>
<b>Night sweats</b>	<b>1.9 (2.76)</b>	<b>2.4 (2.97)</b>	<b>2.5 (2.82)</b>	<b>2.2 (2.84)</b>	<b>.002</b>
<b>Itching</b>	<b>2.0 (2.87)</b>	<b>2.3 (2.85)</b>	<b>2.5 (3.09)</b>	<b>2.2 (2.92)</b>	<b>.02</b>
Bone pain	1.9 (2.72)	1.8 (2.60)	2.2 (2.93)	2.0 (2.75)	-
Fever	0.3 (1.06)	0.4 (1.25)	0.4 (1.16)	0.4 (1.13)	-
Weight loss	1.1 (2.25)	1.0 (2.10)	1.2 (2.35)	1.1 (2.24)	-
<b>Overall QOL</b>	<b>2.7 (2.45)</b>	<b>3.1 (2.54)</b>	<b>3.0 (2.44)</b>	<b>2.9 (2.47)</b>	<b>.03</b>
<b>MPN-SAF TSS</b>	<b>20.3 (16.32)</b>	<b>21.6 (15.95)</b>	<b>23.7 (16.31)</b>	<b>21.4 (16.27)</b>	<b>.008</b>

**Early: 0-5 y**  
**Middle: 6-10 y**  
**Late: ≥11 y**

P values calculated via ANOVA F-Test

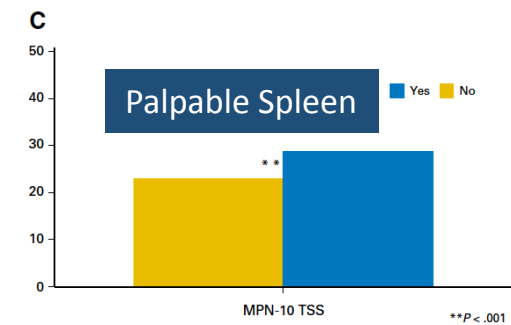
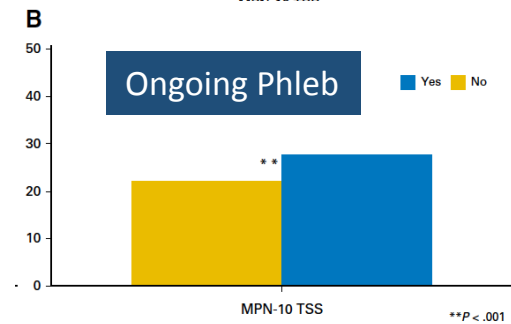
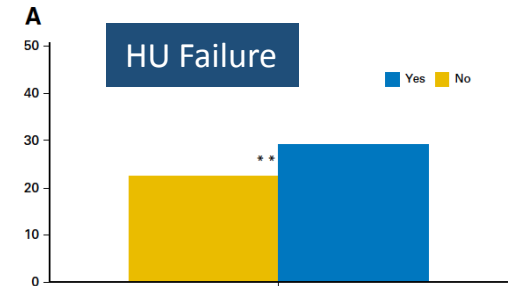
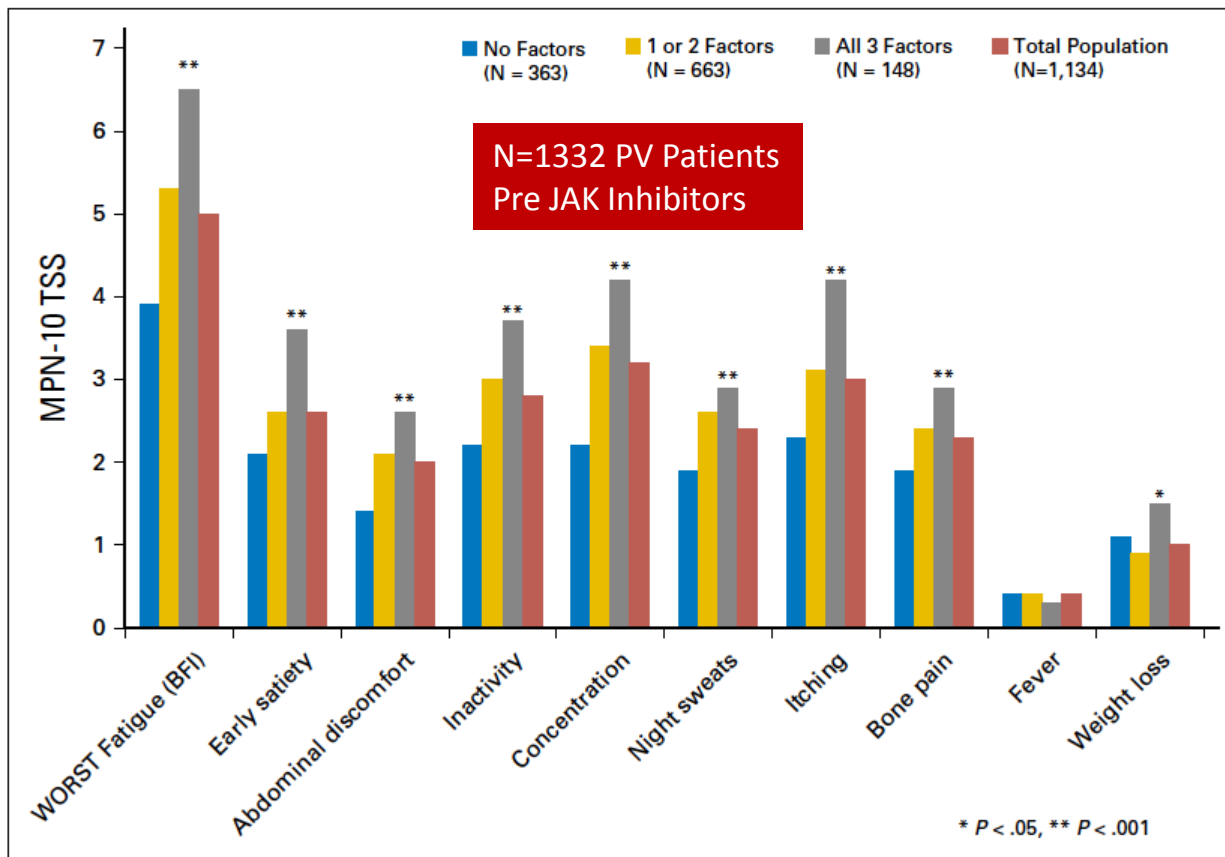
Scherber R, et al. *Blood (Annual Meeting Abstracts)*. 2015;126 abstract 4073.

# Symptomatic Profiles of Patients With Polycythemia Vera: Implications of Inadequately Controlled Disease

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Geyer et. al.  
JCO 2015



# State of the Art MPNs - Concept 1

1. An accurate and serial assessment of MPN symptom burden is important

# “State of the Art” Care of MPN Patients

- What is your patients disease burden?
- **What is your patients risk?**
- What are your treatment goals?
- What are the unmet needs “new drugs” in hematology need to address?
- Who is a clinical trial patient in MPNs in 2016 vs. standard therapy?
- Future directions



# 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>
<b>Age, years</b>	≥ 60 (2 pts) vs < 60	≥ 67 (5 pts) 57-66 (2 pts), < 60 (0)	≥ 65 (1 pt) vs < 65
<b>Leukocytes</b>	≥ 11 (1 pt) vs < 11 x 10 <sup>9</sup> /L	≥ 15 (1 point) vs < 15 x 10 <sup>9</sup> /L	> 25 (1 pt) vs ≤ 25 x 10 <sup>9</sup> /L
<b>Hemoglobin</b>			< 10 (2 pts) vs ≥ 10 g/dL
<b>Constitutional symptoms</b>			Present <sup>a</sup> (1pt) vs absent
<b>Blasts</b>			≥ 1% (1pt) vs < 1%
<b>Prior thrombosis</b>	Yes (1 point) vs No	Yes (1 Point) vs No	
<b>Risk group point cutoffs</b>	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*

<sup>a</sup> 10% weight loss over prior 6 months, night sweats, unexplained fever.

# Next Generation Sequencing Hematologic Neoplasms

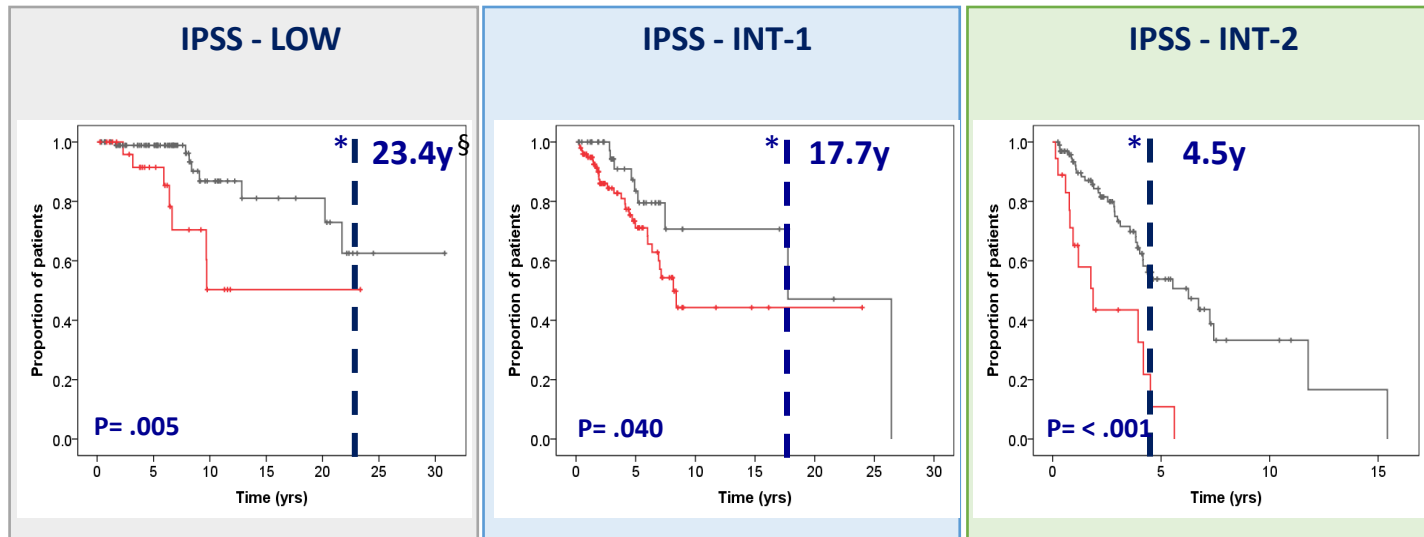
GENE	EXONS	GENE	EXONS	GENE	EXONS
<i>ASXL1</i>	11-14	<i>GATA2</i>	4-8	<i>PTPN11</i>	3, 4, 12, 13
<i>BCOR</i>	5-16	<i>IDH1</i>	4	<i>RUNX1</i>	4-10
<i>BRAF</i>	15	<i>IDH2</i>	4	<i>SETBP1</i>	6 – partial
<i>CALR</i>	9	<i>JAK2</i>	12-16	<i>SF3B1</i>	14-17
<i>CBL</i>	8,9*	<i>KIT</i>	8-11, 17	<i>SRSF2</i>	1, 2
<i>CEBPA</i>	1	<i>KRAS</i>	2, 3	<i>TERT</i>	2-16
<i>CSF3R</i>	14, 17	<i>MPL</i>	10, 11	<i>TET2</i>	3-11
<i>DNMT3A</i>	8-23	<i>MYD88</i>	5	<i>TP53</i>	4-9
<i>ETV6</i>	3-8	<i>NOTCH1</i>	26, 27, 34	<i>U2AF1</i>	2, 7, 9
<i>EZH2</i>	3-21	<i>NPM1</i>	9, 11, 12	<i>WT1</i>	1-11
<i>FLT3</i>	14-20	<i>NRAS</i>	2, 3	<i>ZRSR2</i>	1-11
<i>GATA1</i>	2, 4	<i>PHF6</i>	2-10		

# MIPSS: Molecular International Prognostic Score System

MULTIVARIATE ANALYSIS			Weighted value
Variables	HR (95% CI)	P	
Age >60yrs	3.8 (2.60-5.51)	<0.0001	1.5
Hb <100g/L	1.4 (1.01-1.99)	0.04	0.5
Constitutional Symptoms	1.5 (1.13-2.16)	0.007	0.5
PLT <200x10 <sup>9</sup> /L	2.5 (1.77-3.42)	<0.0001	1.0
Triple Negativity	3.9 (2.20-6.80)	<0.0001	1.5
JAK2/MPL mutation	1.8 (1.11-2.90)	0.016	0.5
ASXL1 mutation	1.4 (1.06-1.99)	0.02	0.5
SRSF2 mutation	1.7 (1.08-2.58)	0.02	0.5

Vannucchi et. al. ASH 2014

# MIPSS Permits to Refine Prognostic Stratification Within the IPSS Categories



Low 24.9y §  
 > Low 15.3y §

≤ Int-1 17.7y  
 > Int-1 8.1y

≤ Int-2 6.2y  
 > Int-2 1.9y

§Estimated

\*, IPSS Median Survival — — — —

**MIPSS**

Vannucchi et. al. ASH 2014

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

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

# State of the Art MPNs - Concept 2

1. An accurate and serial assessment of MPN symptom burden is important
2. Risk, of thrombosis and mortality, is assessed by combination of clinical and molecular features (evolving)

# “State of the Art” Care of MPN Patients

- What is your patients disease burden?
- What is your patients risk?
- **What are your treatment goals?**
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## Response Criteria for MPNs 2014 (All ≥ 12 Weeks)

ET/PV – ELN (Barosi et. al. *Blood* 2013)

MF – IWG-MRT (Tefferi et. al. *Blood* 2013)

	Complete Remission	Partial Remission	Clinical Improvement	Other
ET	<ul style="list-style-type: none"> <li>Resolve ET Signs</li> <li>≥ 10 pt. MPN10 ↓</li> <li>Near normal counts</li> <li>No Prog. or Vascular</li> <li>BM rem &amp; ≤Gr 1 MF</li> </ul>	<ul style="list-style-type: none"> <li>Resolve ET Signs</li> <li>≥ 10 pt. MPN10 ↓</li> <li>Near normal counts</li> <li>No Prog. or Vascular</li> </ul>		Peripheral Blood Granulocytes <ul style="list-style-type: none"> <li>CR – Eradicated mutation</li> <li>PR - ≥50% ↓, ≥ 20% baseline</li> </ul>
PV	<ul style="list-style-type: none"> <li>Resolve PV Signs</li> <li>≥ 10 pt. MPN10 ↓</li> <li>Near normal counts</li> <li>No Prog. or Vascular</li> <li>BM rem &amp; ≤Gr 1 MF</li> </ul>	<ul style="list-style-type: none"> <li>Resolve PV Signs</li> <li>≥ 10 pt. MPN10 ↓</li> <li>Near normal counts</li> <li>No Prog. or Vascular</li> </ul>		Peripheral Blood Granulocytes <ul style="list-style-type: none"> <li>CR – Eradicated mutation</li> <li>PR - ≥50% ↓, ≥ 20% baseline</li> </ul>
MF	<ul style="list-style-type: none"> <li>Resolve MF Signs</li> <li>Resolve MF symptoms</li> <li>Near normal counts</li> <li>BM rem &amp; ≤Gr 1 MF</li> </ul>	Like MF CR but <ul style="list-style-type: none"> <li>Hb (between 85 and 100 g/L)</li> <li>PLT (between 50-100 x 10<sup>9</sup>/L)</li> </ul>	<ul style="list-style-type: none"> <li>Anemia (2g/dl or T.I.)</li> <li>Spleen (Based on BL)</li> <li>Symptoms (≥ 50% ↓)</li> </ul>	Molecular (ET/PV Criteria) <ul style="list-style-type: none"> <li>Cytogenetic                             <ul style="list-style-type: none"> <li>CR – Normal</li> <li>PR - ≥ 50% ↓</li> </ul> </li> </ul>

N.B. ET/PV – Progression is MF/MDS/ or AML  
 MF – Progression based on spleen growth or AML



# 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

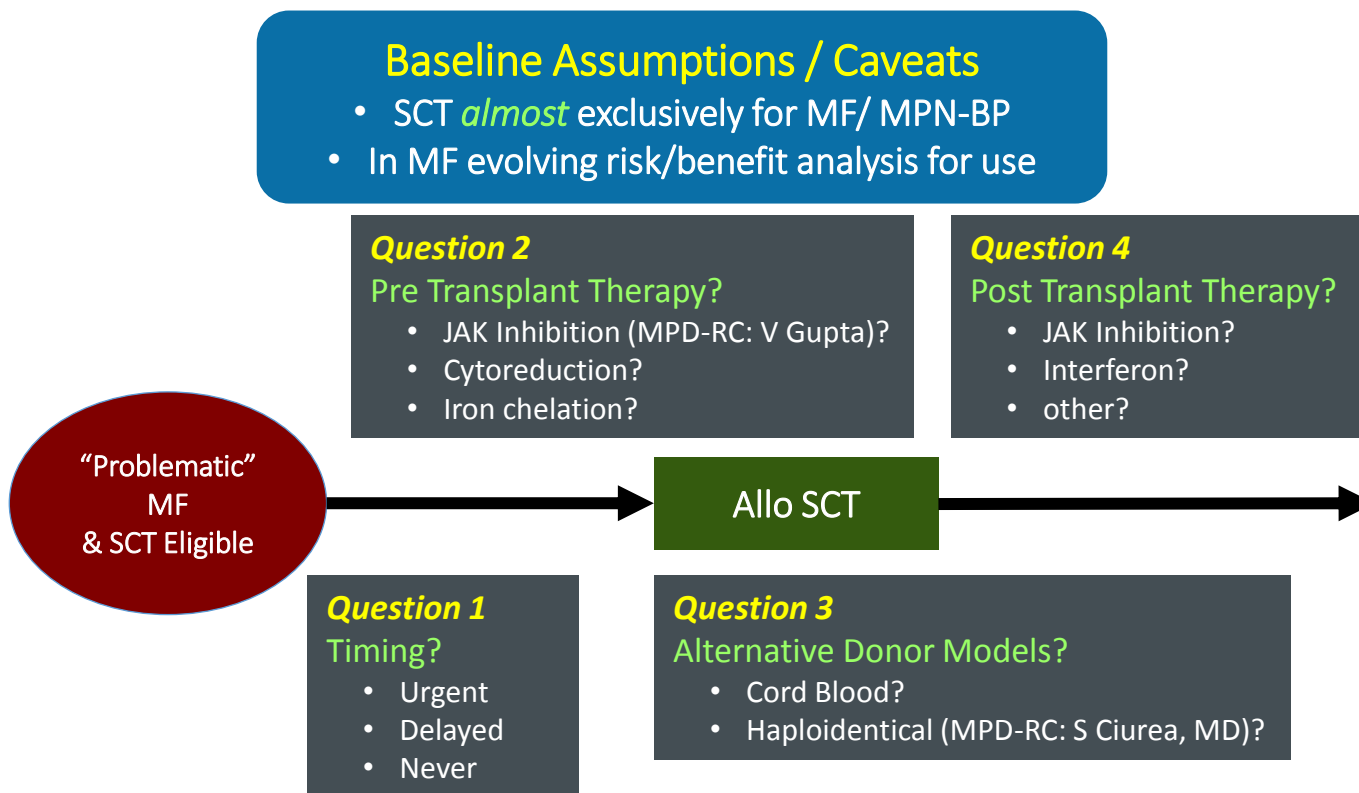
## CHRONIC Neoplasm (ET, PV, Some MF)

- 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

# “State of the Art” Care of MPN Patients

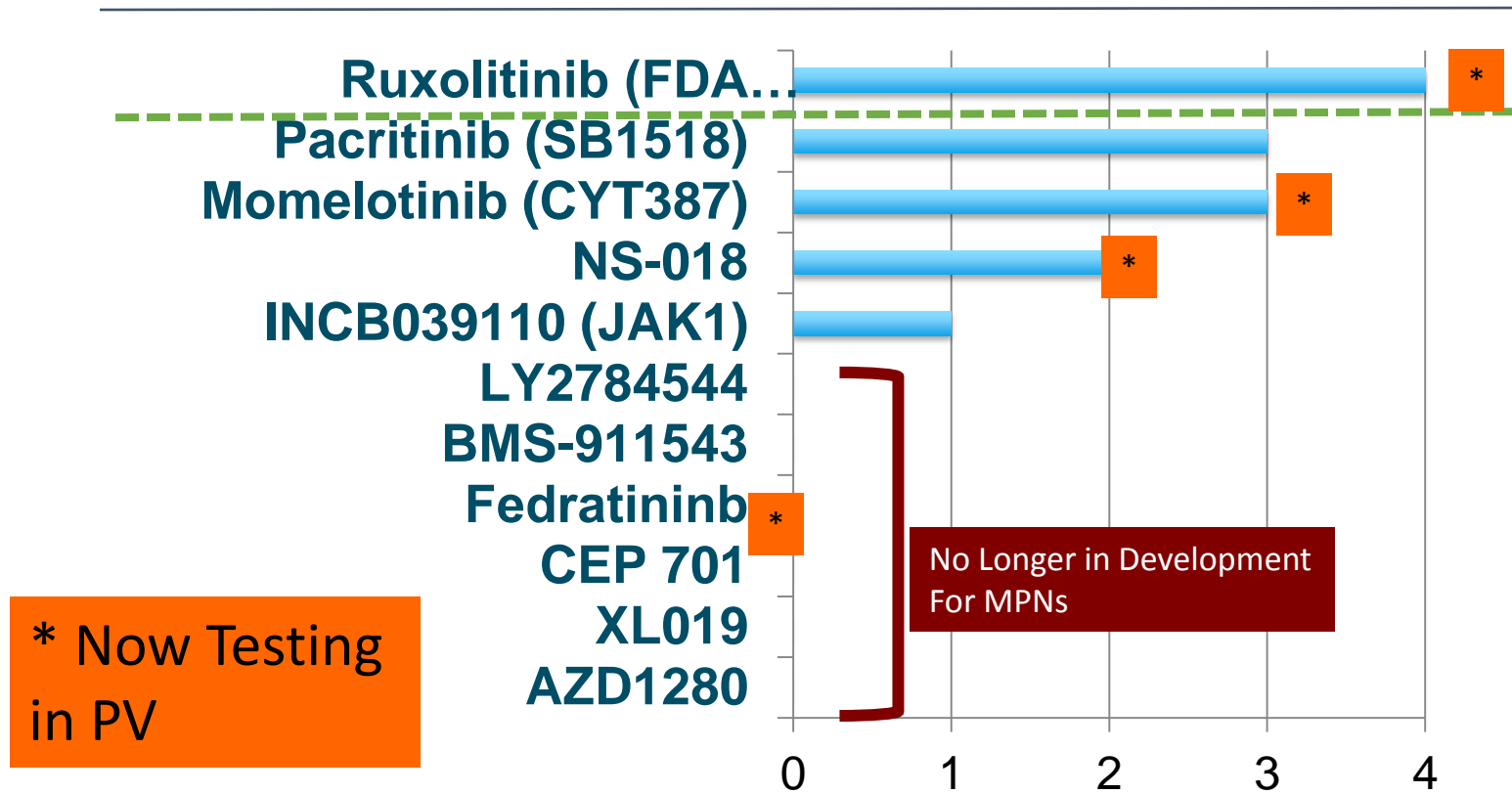
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# Evolving Stem Cell Transplant Use in Myelofibrosis



# JAK Inhibitors and Status of Development

*Myelofibrosis as lead indications*



\* Now Testing  
in PV

No Longer in Development  
For MPNs

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

# Proposed Algorithm of Therapy of MF in 2016

**N.B.**  
Consider Rx for Prevention of Vascular Events in Appropriate Patients (Aspirin & Cytoreduction)

**Symptom Quartiles by MPN 10**  
**Q1:TSS <8**      **Q3:TSS 18-31**  
**Q2:TSS 8-17**    **Q4:TSS ≥32**

Diagnosis of MPN-MF (Primary, Post ET or Post PV Myelofibrosis)

Calculate DIPSS MF Score & Assess MPN Symptoms (MPN 10)

**JAK2 Inhibitors**

- Ruxolitinib (Jakifi/Jakivi) (Approved for MF)
- Clinical Trial JAK2 Inhib

**Anemia Rx**

- Clinical Trials
- IMiD/ Androgens/ EPO
- Splenectomy

Low Risk  
Med S = 185m  
**Symptom Q1-Q2**

Low Risk  
Med S <185m  
**Symptom Q3-Q4**

Intermediate to High Risk  
Med S = 16m (H), 35m (Int 2), 78 (Int 1)  
*Assess role and timing of ALLO SCT (Donor, Risk, Candidate)*  
*ALLO – Urgent, Delayed, Never*

Observation Vs. INF (Trial)

Possible Role Of JAK2 Inhib (Trial) or INF (Trial)

Urgent ALLO  
Proceed to ALLO (Possible JAK2 Inhib Prior) (Trial)

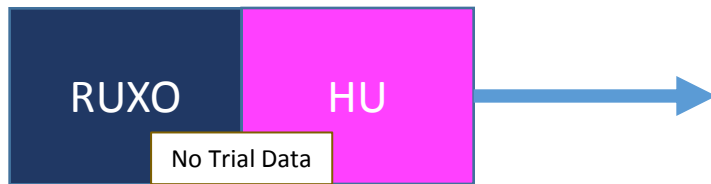
Delayed/Never ALLO  
JAK2 Inhibitor\*  
\*Unless anemia/cytopenias main problem

JAK2 Single Agent Failure Refractory Cytopenias

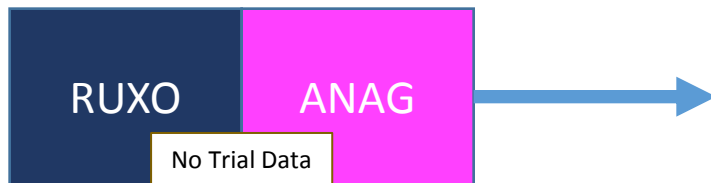
Clinical Trials

- Ruxo Combination
- Non Ruxo JAK2
- New Targets

# JAKi Combinations: ET/PV/MF - Cytoreductive



OFF Label: Can be tolerated  
For reduction of problematic leukocytosis or  
thrombocytosis



OFF Label: Can be tolerated  
For reduction of problematic thrombocytosis

# JAKi and AML Therapy

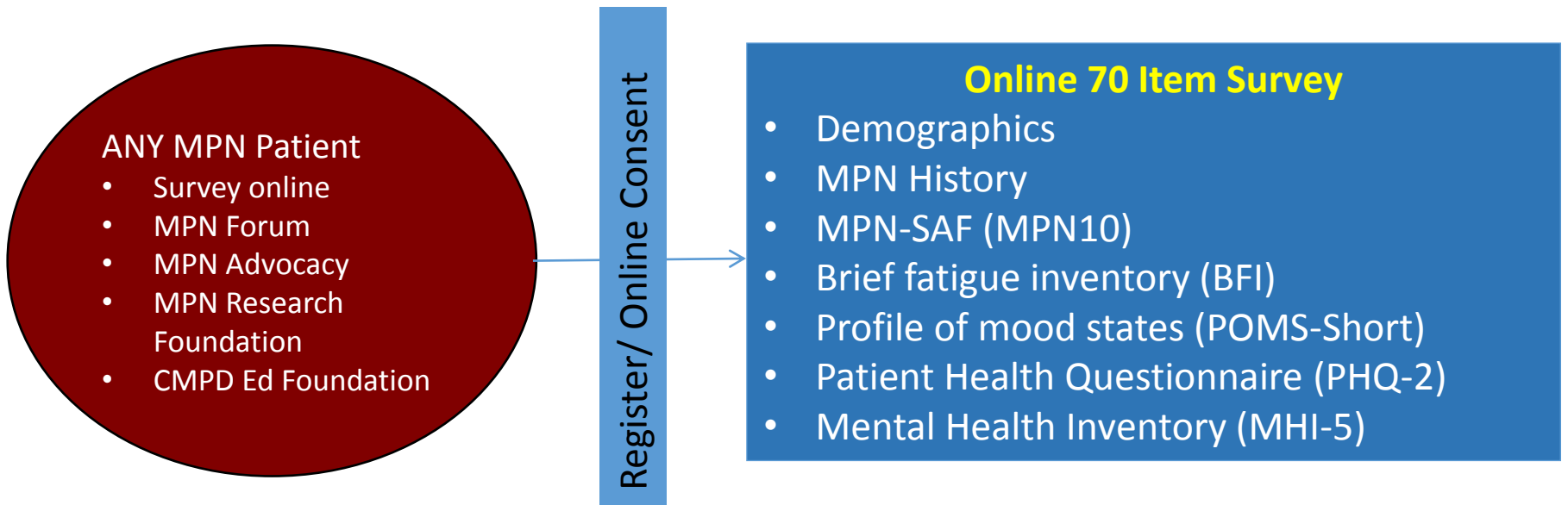
- Ruxolitinib has some activity as single agent in MF to AML, and can still alleviate splenomegaly and symptoms
- Cessation of ruxolitinib, completely, for HMA or induction has not been ideal
- Cautious, off label, combinations-sequential can be considered and has been done successfully (watch the antifungals)



# State of the Art MPNs - Concept 3

1. An accurate and serial assessment of MPN symptom burden is important
2. Risk, of thrombosis and mortality, is assessed by combination of clinical and molecular features (evolving)
3. Stem Cell Transplant (MF), Ruxolitinib (MF/PV), INF (MPN), and Cytoreductives (HU/ANAG) all can be woven together in evolving and individualized care plans

## Collaborative Internet Based Trial with MPN Forum



**ANY MPN Patient**

- Survey online
- MPN Forum
- MPN Advocacy
- MPN Research Foundation
- CMPD Ed Foundation

Register/ Online Consent

**Online 70 Item Survey**

- Demographics
- MPN History
- MPN-SAF (MPN10)
- Brief fatigue inventory (BFI)
- Profile of mood states (POMS-Short)
- Patient Health Questionnaire (PHQ-2)
- Mental Health Inventory (MHI-5)

### Patients

1788 MPN patients/ 1676 Eval.

ET 33%, PV 39%, MF 25%

68% Female, median age 59. MPN10 Score average 28.4 (range 0-83)

### Psych Comorbidity

23% high likelihood of depression ( $\geq 3$  on PHQ-2)

Prior diagnosis depression (32%), anxiety (29%), stress (26%), grief (15%)

22% on therapy for mood disorder in last 6 months

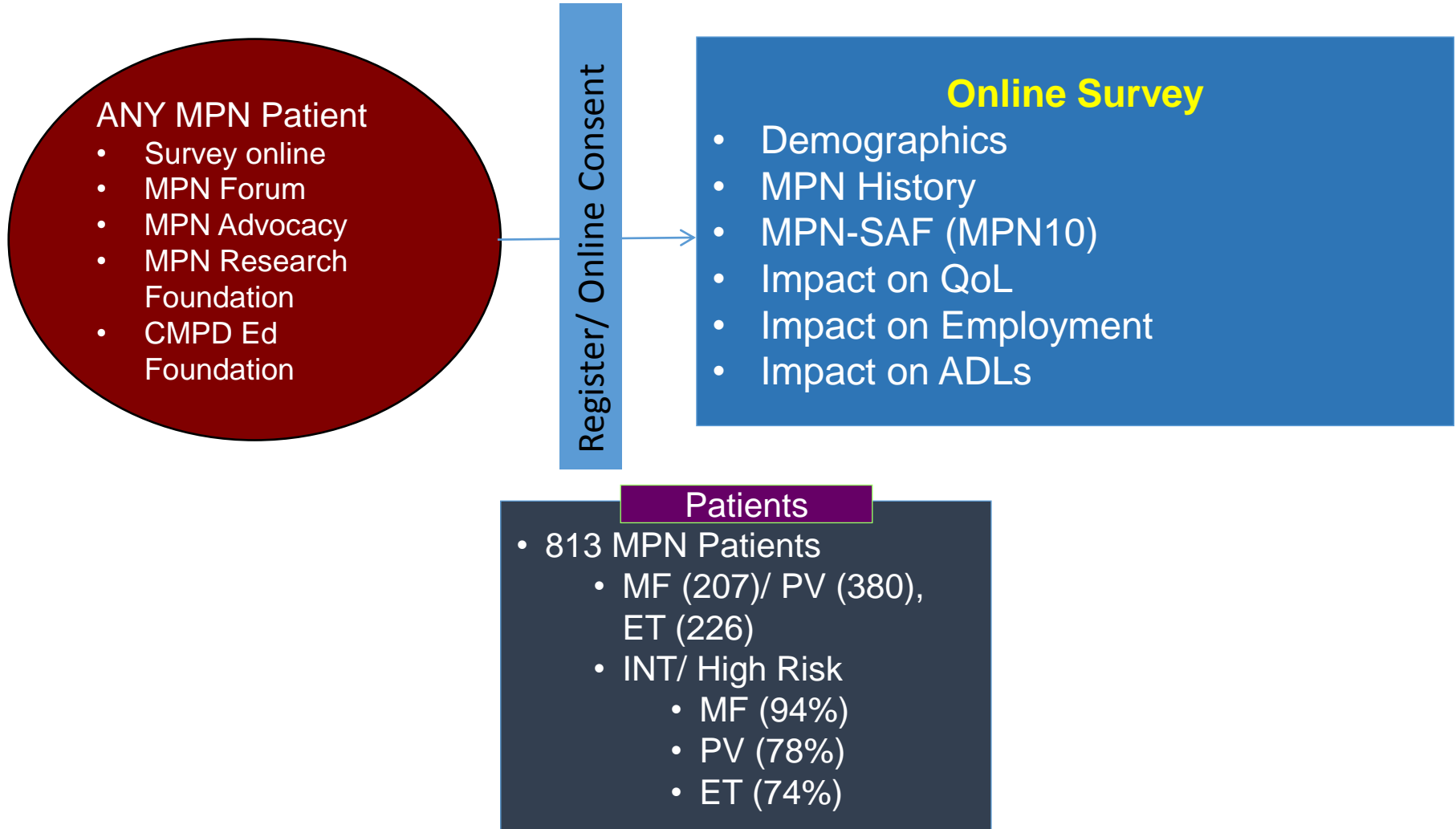
### MPN Correlation

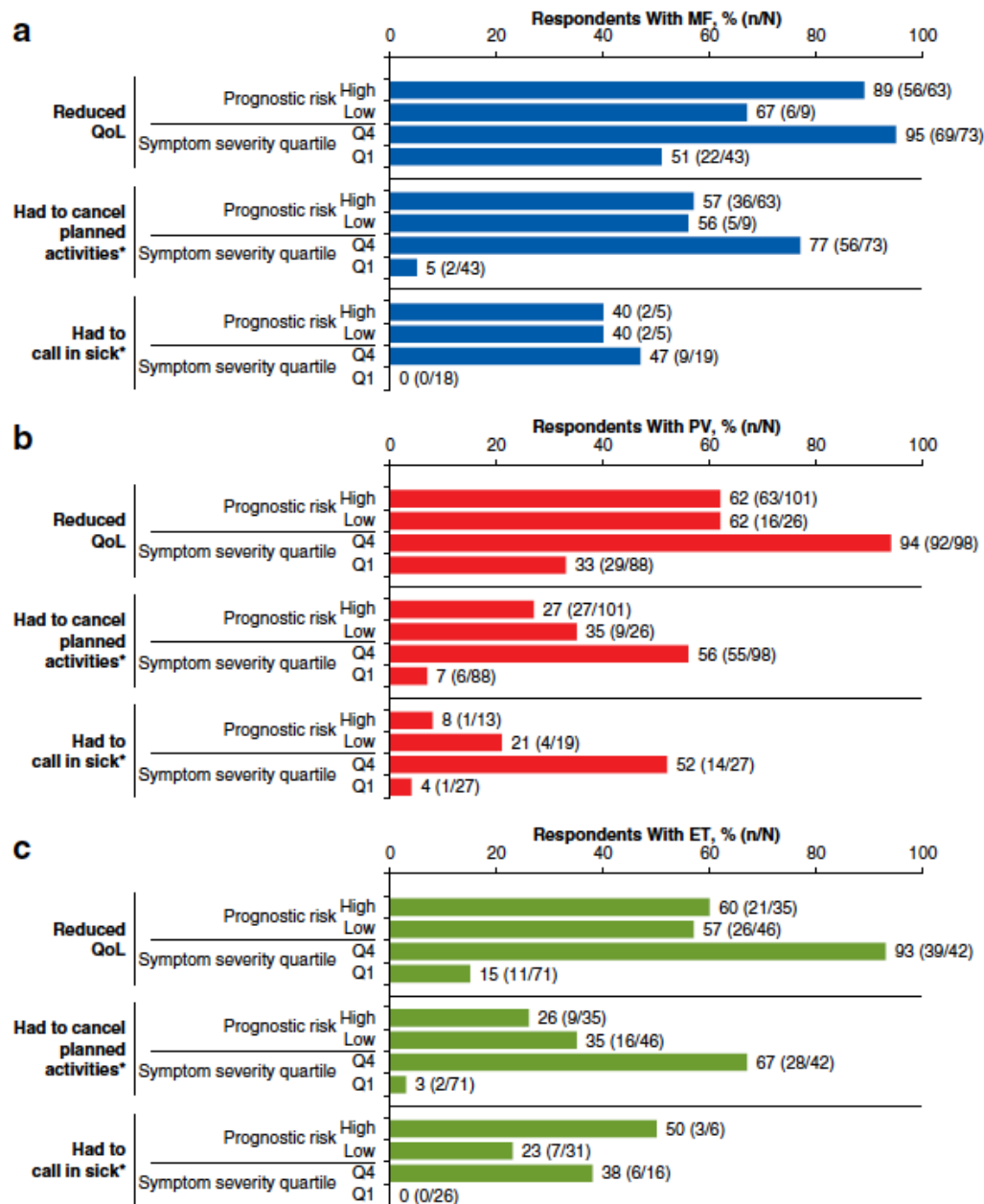
Higher BFI, MPN-SAF, MPN10 scores all correlated with increased depressive symptoms ( $p < 0.0001$ )

# MPN Patient Burden- Disease Impact

## 2014 Landmark Study

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





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

**Fig. 1** Impact of MPNs on QoL, work, and activities of daily living. MPN impact was stratified by calculated prognostic risk score and symptom severity quartile in respondents with (a) MF, (b) PV, and (c) ET. ET = essential thrombocythemia; MF = myelofibrosis; MPN = myeloproliferative neoplasm; PV = polycythemia vera; Q1 = quartile 1; Q4 = quartile 4; QoL = quality of life. \*  $\geq 1$  day in the preceding 30 days

# Symptoms ever experience by MF patients vs most heard by physicians

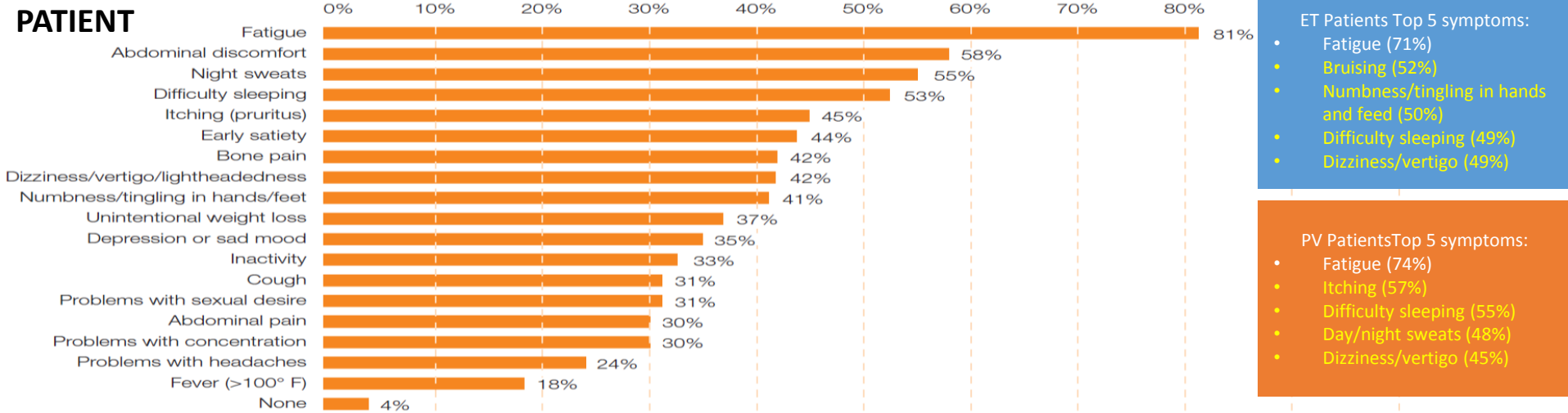


Figure 1. Question 8: Have you ever had any of the following symptoms? (n = 207)

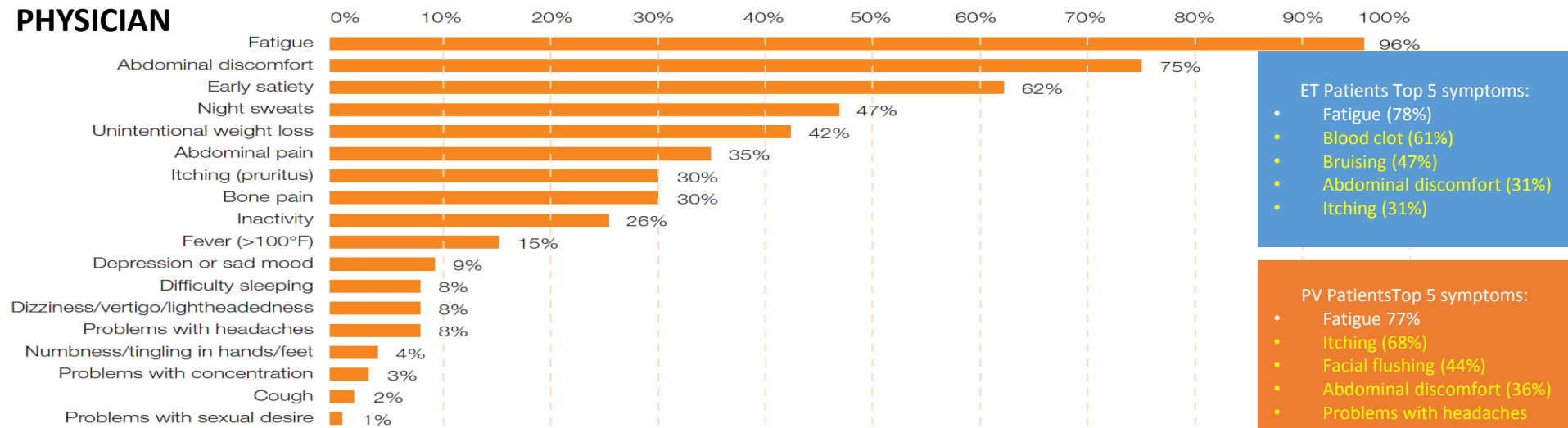


Figure 50. Question 15: What are the five symptoms of MF you most often hear about from your patients? (n = 156)

# MF Patient-reported MPN-SAF mean severity score

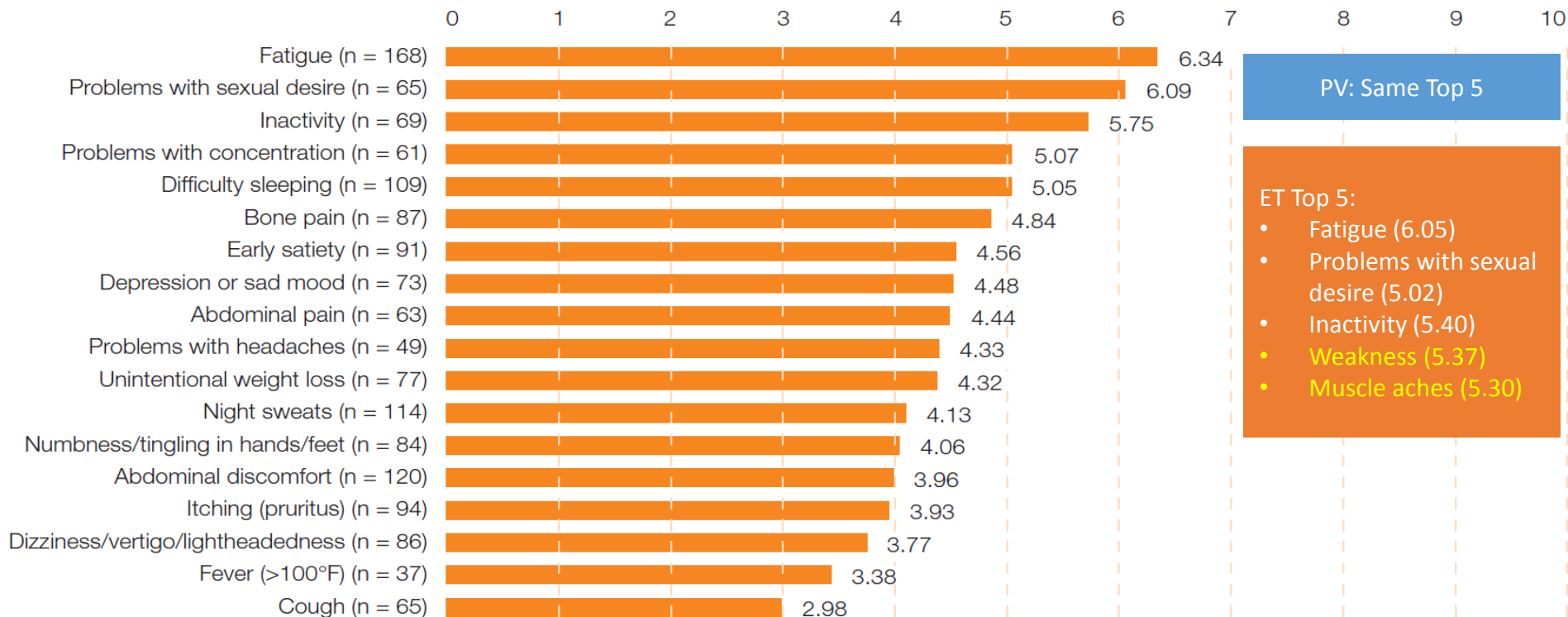
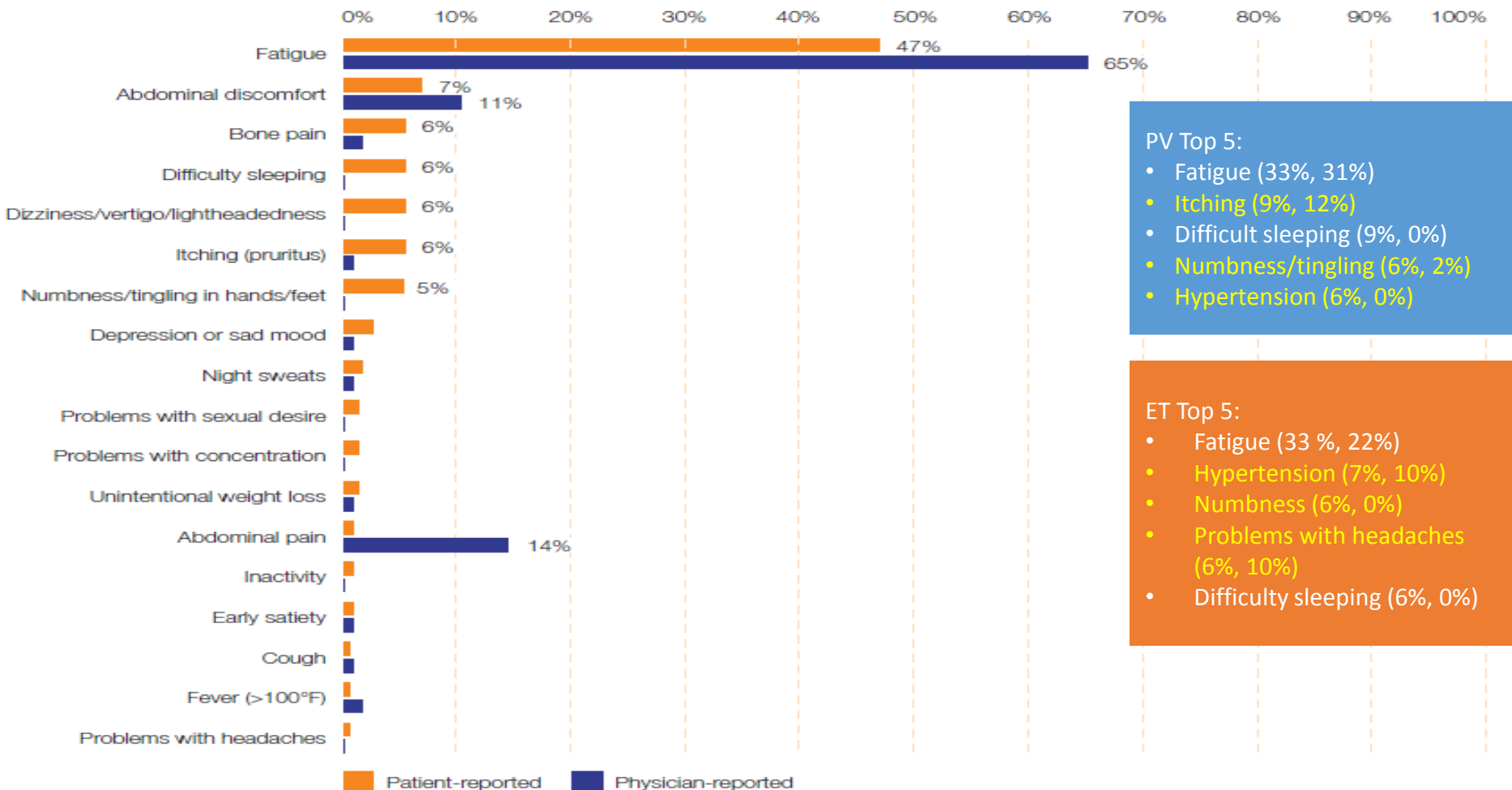


Figure 2. Question 13a-dd: How severe is [symptom]?

# MF Patient-reported first symptom they would like to resolve vs physician-reported perception

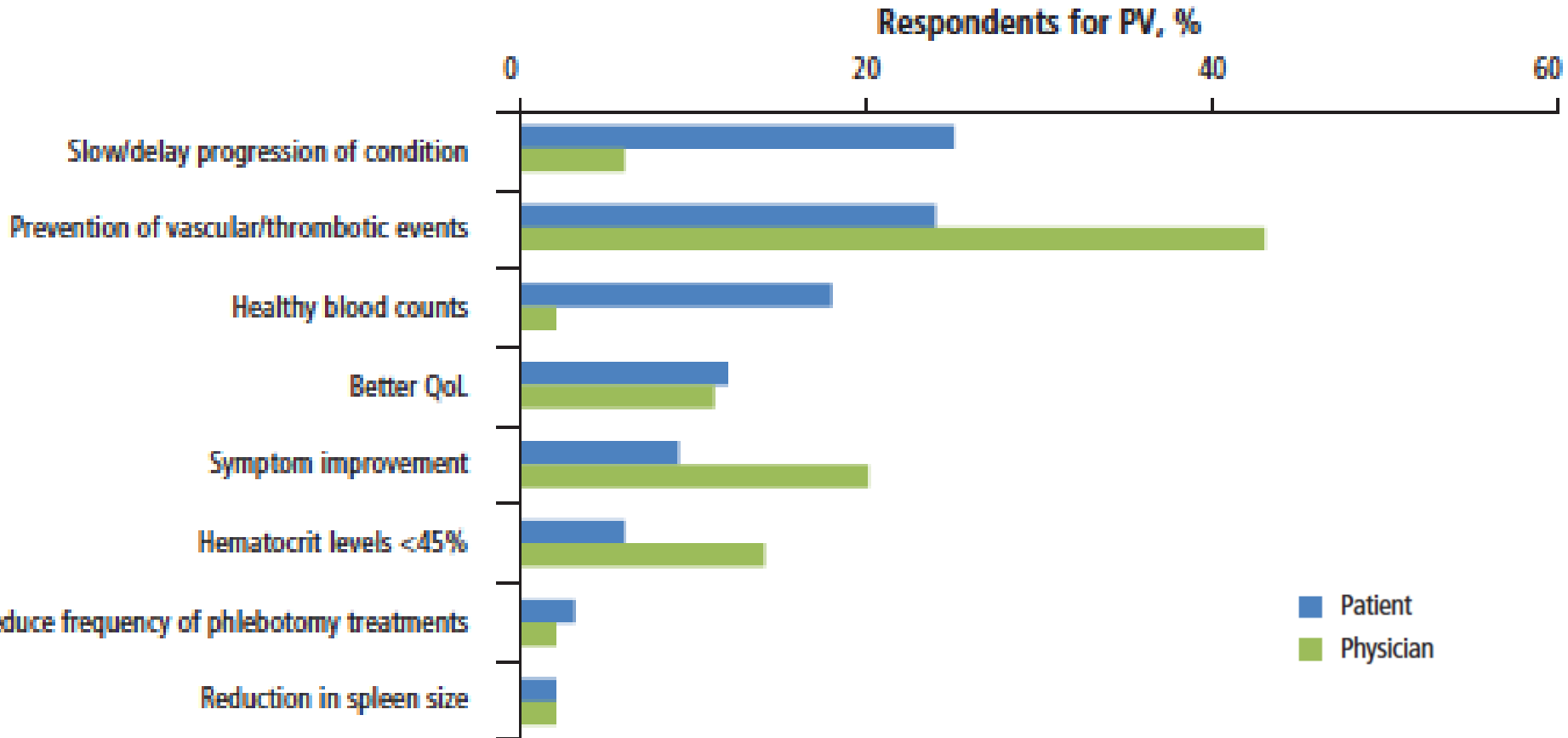


- PV Top 5:**
- Fatigue (33%, 31%)
  - Itching (9%, 12%)
  - Difficult sleeping (9%, 0%)
  - Numbness/tingling (6%, 2%)
  - Hypertension (6%, 0%)

- ET Top 5:**
- Fatigue (33%, 22%)
  - Hypertension (7%, 10%)
  - Numbness (6%, 0%)
  - Problems with headaches (6%, 10%)
  - Difficulty sleeping (6%, 0%)

Figure 52. Question 14: Of the symptoms that you are currently experiencing, which one would you most like to resolve? (n = 199)  
 Question 17: Out of all the symptoms patients experience, which single symptom do you perceive they would most want to resolve? (n = 156)  
 Note: Labels for data under 5% are not displayed.

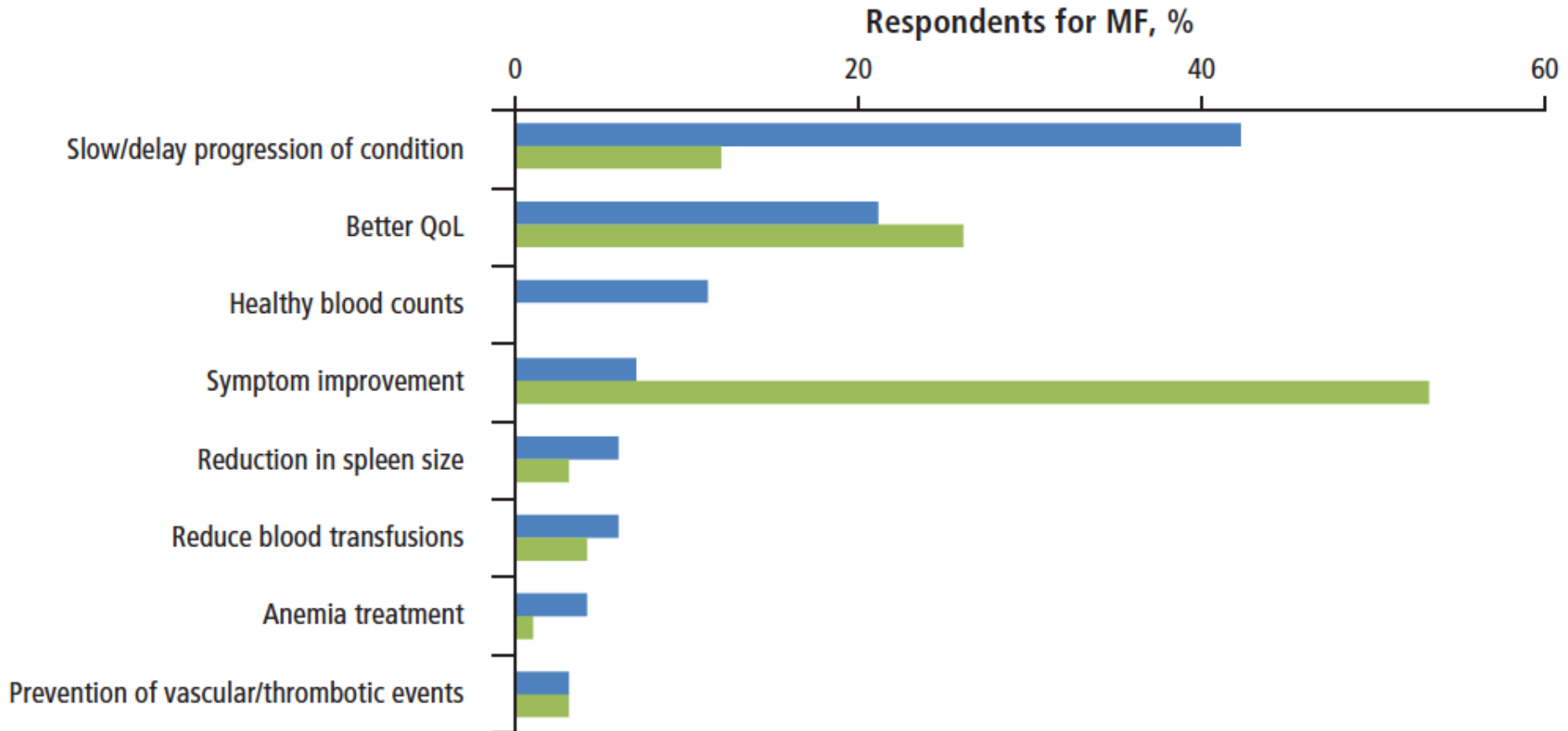
# LANDMARK Study in PV Goals (Patients (N=382) & Physicians)



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



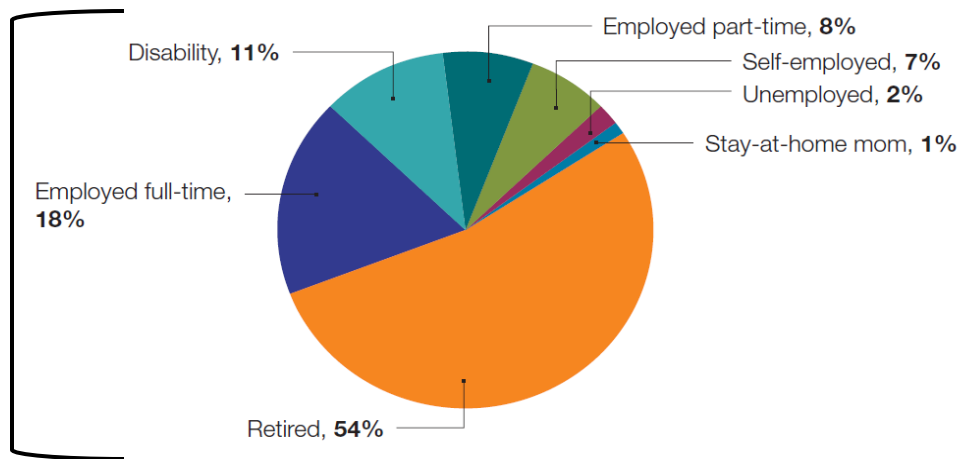
# LANDMARK Study in MF Goals (Patients (N=207) & Physicians)



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

# Employment status and MF's impact

**Respondents  
employment status**



## Impact on Employment Status as a Result of MF

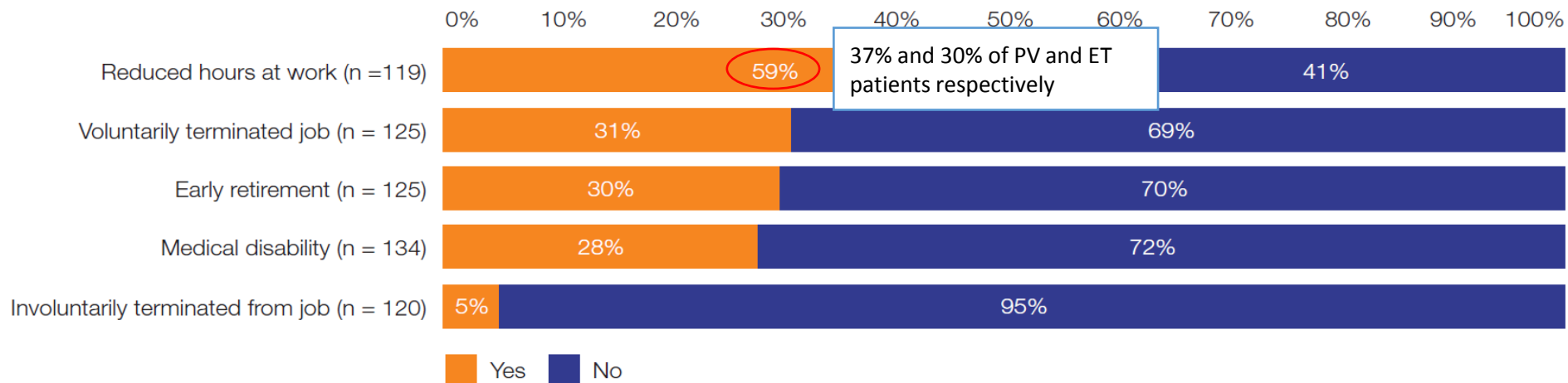


Figure 10. Q21a-e: As a result of your diagnosis have you ever...?\*

\*Note: Data excludes "Not applicable" responses. Individual values are rounded and may not total 100%.

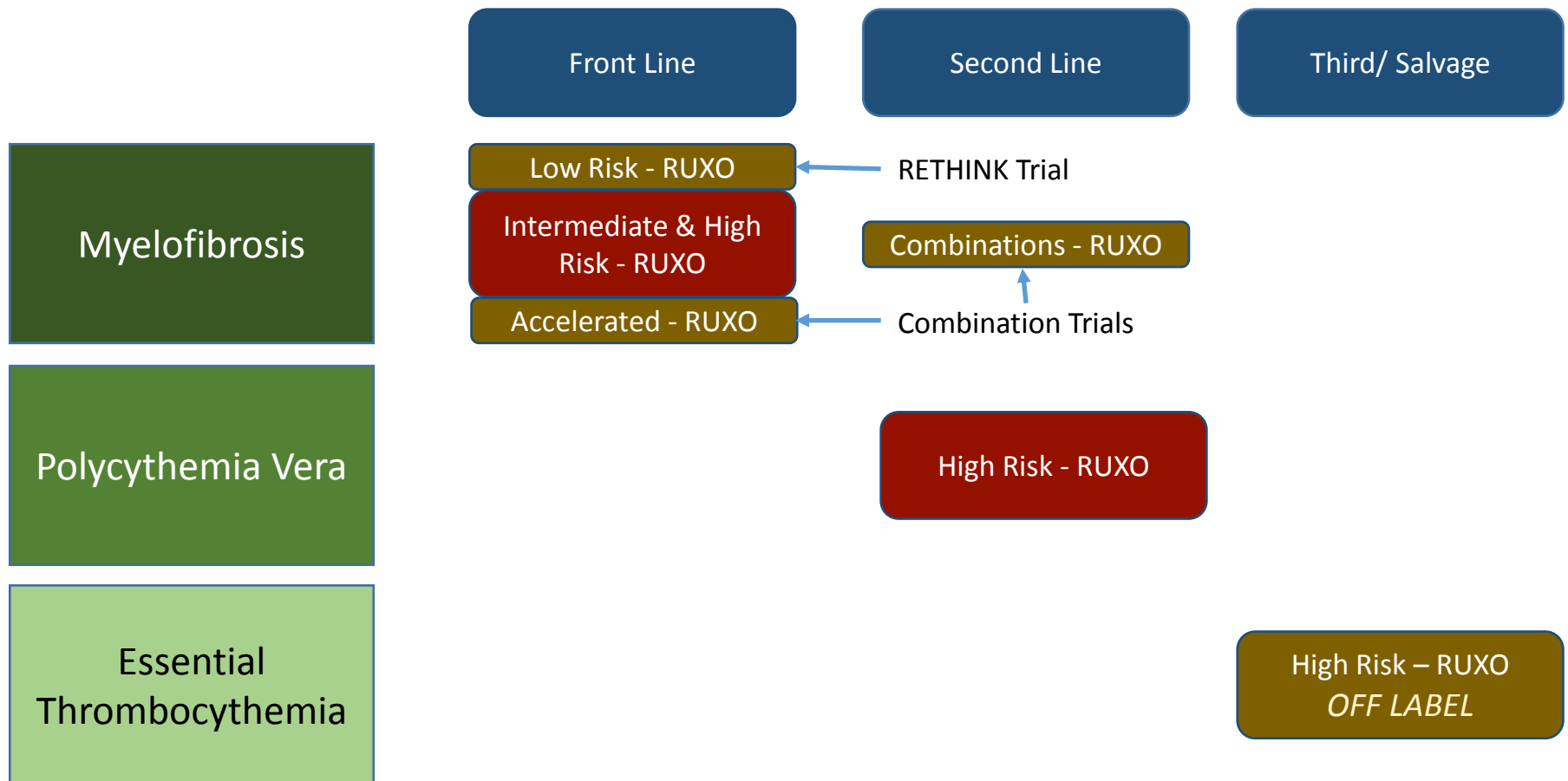
# State of the Art MPNs - Concept 4

1. An accurate and serial assessment of MPN symptom burden is important
2. Risk, of thrombosis and mortality, is assessed by combination of clinical and molecular features (evolving)
3. Stem Cell Transplant (MF), Ruxolitinib (MF/PV), INF (MPN), and Cytoreductives (HU/ANAG) all can be woven together in evolving and individualized care plans
4. Decreasing risk of progression is a major concern of patients, and surrogate markers for risk of progression an unmet scientific need

# “State of the Art” Care of MPN Patients

- What is your patients disease burden?
- What is your patients risk?
- What are your treatment goals?
- What are the unmet needs “new drugs” in hematology need to address?
- **Who is a clinical trial patient in MPNs in 2016 vs. standard therapy?**
- Future directions

# Footprint of Ruxolitinib in MPNs – Q2 2016



# New JAK Inhibitors – Possible Positioning



# Who is a clinical trial patient for ET?

## What do we do well in ET?

- Prevention of vascular events
- Front line with HU
- Second line with ANAG, perhaps INF?

## What is the unmet need in ET?

- Better symptom control in symptomatic patients
- Third line therapy
- Clear prevention of progression to MF or AML

# Who is a clinical trial patient for PV?

## What do we do well in PV?

- Prevention of vascular events
- Front line with HU, perhaps INF
- Second line with Ruxolitinib

## What is the unmet need in PV?

- Better symptom control in non JAKi patients
- Optimal management in SVT
- Third line therapy
- Clear prevention of progression to MF or AML



# Who is a clinical trial patient for MF?

## What do we do well in MF?

- Reduction of splenomegaly and symptoms with JAKi
- Some impact on survival
- Allo Transplant in good risk candidates

## What is the unmet need in MF?

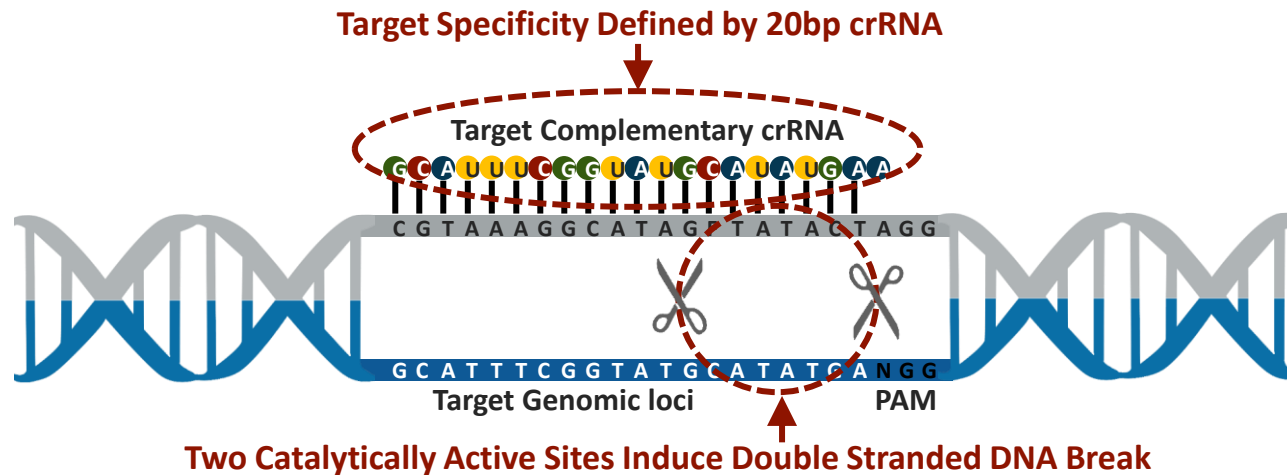
- Prevention of progression in lower risk patients
- Therapy for significant cytopenias
- Post ruxolitinib options
- Allo transplant in higher risk candidates
- Any MF patient with accelerated or blast phase disease

# “State of the Art” Care of MPN Patients

- What is your patients disease burden?
- What is your patients risk?
- What are your treatment goals?
- What are the unmet needs “new drugs” in hematology need to address?
- Who is a clinical trial patient in MPNs in 2016 vs. standard therapy?
- **Future directions**

# CRISPR: Gene Therapy Finally Coming to MPNs?

- Clustered Regularly Interspaced Short Palindromic Repeat
  - Bacterial immune response system leveraged for genome editing
  - Cas9 DNA nuclease
  - GuideRNA = CrisprRNA (crRNA) + tracrRNA



MPN forum Magazine. CRISPR/Cas9: Gene Editing with Precision.  
[www.mpnforum.com/cascade](http://www.mpnforum.com/cascade)

# M3 Trial: Myeloproliferative Neoplasm Meditative Movement Trial

## Background:

- Fatigue is major unmet need in MPNs, reduced by JAK inhibition but rarely eradicated
- Meditative movement (including yoga) well known to aid fatigue in chronic diseases

## Trial:

- Feasibility trial of an MPN specific, gentle, Yoga program (in collaboration Udaya yoga) over 12-week period done at home with computer modules
- 50 MPN patients (online screening and consent)
- Serial assessments of MPN symptoms and QoL
- Activity assessment by activity tracker (FitBit) – provided



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



# State of the Art MPNs - Concept 5

1. An accurate and serial assessment of MPN symptom burden is important
2. Risk, of thrombosis and mortality, is assessed by combination of clinical and molecular features (evolving)
3. Stem Cell Transplant (MF), Ruxolitinib (MF/PV), INF (MPN), and Cytoreductives (HU/ANAG) all can be woven together in evolving and individualized care plans
4. Decreasing risk of progression is a major concern of patients, and surrogate markers for risk of progression an unmet scientific need
5. MPN therapy pipeline robust with key unmet needs avoiding progressive disease, improving cytopenias, deeper and more durable responses



# 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

