What Should We Expect From MPN Therapy?

Ruben A. Mesa, MD
Professor & Chairman, Division of Hematology & Medical Oncology
Deputy Director, Mayo Clinic Cancer Center
Mayo Clinic – Arizona, USA
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
Assessing MPN Burden

WHO Diagnosis Does Not Tell Whole Story

**Baseline Health**

AGE/ Medicines

Comorbidities

**Vascular Events**
- PV/ET > MF
- Counts matter
- Can be unrecognized

**Cytopenias**
- MF > ET/PV
- Anemia
  - MF 75%
  - TX Dep 25%
- TPN 30%

**Progression**
- PV/ET to MF
- PV/ET to AML
- MF to AML
- ? 2nd MDS

**Splenomegaly**
- MF > ET/PV
- Pain not always a function of size

**MPN Symptoms**
- MF>PV>ET
- Multifactorial
- Some ET/PV > MF
- Cytoreductive rx frequently not effective

©2011 MFMER | 3133089-3
10. Understand that not all MPN patients are impacted the same

9. Understand the spectrum of symptoms MPN patients face
Evolution of MPN Symptom Assessment Tools

MPN–SAF Languages
- English
- French
- German
- Spanish
- Dutch
- Swedish
- Italian
- Portuguese
- Mandarin
- Japanese
- Hebrew

MPN–SAF
2011
(27 items)
Blood 2011

MPN–SAF TSS
(10 items 2012)
JCO 2013

- Vascular and Ψ Sx
  9 Items
- Constitutional Sx
  5 Items
- Spleen Sx
  4 Items
- Brief Fatigue Inventory (BFI) – 9 Items
- QOL 1 Item
Symptoms from 2089 MPN Patients Using the MPN-SAF TSS (MPN10)

- Worst fatigue
- Early satiety
- Abdominal discomfort
- Inactivity
- Concentration
- Night sweats
- Itching
- Bone pain
- Fever
- Weight loss

Prevalence of Symptoms (%)

ET (N=874)
PV (N=729)
MF (N=486)
MPN Total (N=2089)
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same

9. Understand the spectrum of symptoms MPN patients face

8. Understand impact of symptom clusters, and gender effect on MPN patients
MPN Symptom Burden by Quartiles
1858 MPN- SAF Respondents

Quartile 1 (Q1): 0-24%
Quartile 2 (Q2): 25-49%
Quartile 3 (Q3): 50-74%
Quartile 4 (Q4): 75-100%

Scherber et al. ASH 2013
<table>
<thead>
<tr>
<th>Parameter</th>
<th>P value of Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.24</td>
</tr>
<tr>
<td>Gender F&gt;M</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MPN Diagnosis</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subtype of MF</td>
<td>0.86</td>
</tr>
<tr>
<td>IPSET (ET Risk)</td>
<td>0.18</td>
</tr>
<tr>
<td>PV Risk (PV)</td>
<td>0.30</td>
</tr>
<tr>
<td>DIPSS (MF Risk)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Results

**Females**
- Lower rate of thrombocytopenia (8% vs 14%, p<0.001).
- Higher TSS (adjusted mean 23.9 vs 20.6; p<0.001)
- Higher symptom scores for 15/18 items
- Prominent symptoms: *fatigue, bone pain, abdominal discomfort, and microvascular related*

**Males**
- Higher mean age than females (mean 60.7 yrs [SD 12.6] vs 59.3 yrs [SD 14.4]; p=0.02)
- Higher rate of requirement for red blood cell transfusion (7% vs 5%, p=0.02)
- Higher mean white blood cell count (mean 9.5x10^9/L [SD 8.2 x10^9/L] vs mean 8.5 x10^9/L [SD 6.1x10^9/L]; p=0.004)

**Females demonstrate…**
- Higher levels of fatigue
  - Younger
  - Lower red blood counts
  - Lower transfusion rates
- More Abdominal Symptoms
  - Male=female abdominal thrombosis rates
- Microvascular symptoms
  - Previous reports show more macrovascular symptoms
- Higher Symptom Scores
  - Individual SS and TSS
  - Male=female QOL score
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
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-SA F (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 (≥ 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-SA F, MPN10 scores all correlated with increased depressive symptoms (p<0.0001)

Scherber R et al. 2014, ASH: abstract 3173
MPN Fatigue Project

• Three part project:

PHASE I
Evaluate strategies to reduce fatigue burden

PHASE II
Determine strategy efficacy and comorbidities

PHASE III
Home-based prospective online trial to employ fatigue-related interventions

N=1748 MPN pts (718 PV, 625 ET, 420 MF, 29 other)
## Fatigue Project

<table>
<thead>
<tr>
<th>Strategies To Cope with Fatigue Related to MPN</th>
<th>BFI - Mean (SD), N</th>
<th>BFI - Mean (SD), N</th>
<th>Δ</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postponing non-essential activities</td>
<td>5.0 (2.1), 981</td>
<td>3.2 (2.3), 365</td>
<td>1.8</td>
<td>(1.6, 2.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Setting priorities</td>
<td>4.9 (2.2), 1015</td>
<td>3.2 (2.3), 365</td>
<td>1.7</td>
<td>(1.4, 1.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Medication psychostimulants</td>
<td>3.0 (2.4), 665</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>4.9 (2.2), 682</td>
<td>3.2 (2.3), 365</td>
<td>1.7</td>
<td>(1.4, 1.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Delegation</td>
<td>3.0 (2.4), 1015</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Scheduling of activities to times of peak energy</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Naps</td>
<td>5.0 (2.1), 827</td>
<td>3.2 (2.3), 365</td>
<td>1.8</td>
<td>(1.6, 2.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Labor-saving devices</td>
<td>4.9 (2.2), 493</td>
<td>3.2 (2.3), 365</td>
<td>1.7</td>
<td>(1.4, 1.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Structured daily routines</td>
<td>3.0 (2.4), 665</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Socializing with family or friends</td>
<td>3.0 (2.4), 853</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Support groups</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Pacing</td>
<td>4.9 (2.2), 772</td>
<td>3.2 (2.3), 365</td>
<td>1.7</td>
<td>(1.4, 1.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Reading</td>
<td>4.8 (2.2), 820</td>
<td>3.2 (2.3), 365</td>
<td>1.6</td>
<td>(1.4, 1.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Sleep therapy</td>
<td>3.0 (2.4), 853</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Music</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Church or spiritual activities</td>
<td>3.0 (2.4), 499</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Nutrition</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Steroids</td>
<td>4.9 (2.2), 493</td>
<td>3.2 (2.3), 365</td>
<td>1.7</td>
<td>(1.4, 1.9)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Meditation, quiet time, or cognitive re-framing</td>
<td>4.2 (2.4), 841</td>
<td>3.2 (2.3), 365</td>
<td>1.0</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>New activities/ diversions</td>
<td>4.4 (2.2), 853</td>
<td>3.2 (2.3), 365</td>
<td>1.2</td>
<td>(0.9, 1.5)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Relaxation, including yoga</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Walking/sitting in a natural environment</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Gardening</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Volunteer activities</td>
<td>3.0 (2.4), 282</td>
<td>3.2 (2.3), 365</td>
<td>0.1</td>
<td>(0.8, 1.3)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Exercise</td>
<td>4.4 (2.3), 1009</td>
<td>4.7 (2.5), 377</td>
<td>-0.4</td>
<td>(-0.6, -0.1)</td>
<td>0.01</td>
</tr>
</tbody>
</table>
ANY MPN Patient
- Survey online
- MPN Forum
- MPN Advocacy
- MPN Research Foundation
- CMPD Ed Foundation

Register/Online Consent

Online Survey
- Demographics
- MPN History
- MPN-SAF (MPN10)
- Impact on QoL
- Impact on Employment
- Impact on ADLs

Patients
- 813 MPN Patients
  - MF (207)/ PV (380), ET (226)
  - INT/High Risk
    - MF (94%)
    - PV (78%)
    - ET (74%)

Symptom Burden
- Anxious about their MPN
  - MF (91%)
  - PV (78%)
  - ET (74%)
- MPN Symptoms decrease my QoL
  - MF (81%)
  - PV (66%)
  - ET (57%)

Impact
- ≥1 sick day in last month
  - MF (33%), PV (23%), ET (22%)
- ≥1 cancelled activity in last month
  - MF (46%), PV (35%), ET (34%)

Mesa R et al. 2014, ASH: abstract 3183
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
6. Understand complex assessment of MPN “risk”, and comorbidities
## Monitoring MPNs

### Evolving MPN prognostic scales

<table>
<thead>
<tr>
<th></th>
<th>IPSET (ET—3 groups) Survival thrombosis risk</th>
<th>PV Risk (4 groups) Survival leukemia rates</th>
<th>DIPSS (PMF—4 groups) Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>≥ 60 (2 pts) vs &lt; 60</td>
<td>≥ 67 (5 pts)</td>
<td>≥ 65 (1 pt) vs &lt; 65</td>
</tr>
<tr>
<td></td>
<td>57-66 (2 pts), &lt; 60</td>
<td>≥ 67 (5 pts)</td>
<td></td>
</tr>
<tr>
<td><strong>Leukocytes</strong></td>
<td>≥ 11 (1 pt) vs &lt; 11 x 10⁹/L</td>
<td>≥ 15 (1 point) vs &lt; 15 x 10⁹/L</td>
<td>&gt; 25 (1 pt) vs ≤ 25 x 10⁹/L</td>
</tr>
<tr>
<td><strong>Hemoglobin</strong></td>
<td></td>
<td>&lt; 10 (2 pts) vs ≥ 10 g/dL</td>
<td></td>
</tr>
<tr>
<td><strong>Constitutional symptoms</strong></td>
<td></td>
<td>Presenta (1pt) vs absent</td>
<td></td>
</tr>
<tr>
<td><strong>Blasts</strong></td>
<td></td>
<td></td>
<td>≥ 1% (1pt) vs &lt; 1%</td>
</tr>
<tr>
<td><strong>Prior thrombosis</strong></td>
<td>Yes (1 point) vs No</td>
<td>Yes (1 Point) vs No</td>
<td></td>
</tr>
<tr>
<td><strong>Risk group point cutoffs</strong></td>
<td>0; 1-2; 3-4 pts</td>
<td>0; 1-2; 3; 4 pts</td>
<td>0; 1-2; 3-4; ≥ 4 pts</td>
</tr>
</tbody>
</table>

---

*Passamonti Blood 2012*  
*Tefferi Leuk 2014*  
*Passamonti Blood 2010*

---

* 10% weight loss over prior 6 months, night sweats, unexplained fever.
**MIPSS: Molecular International Prognostic Score System**

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

Vannucchi et. al. ASH 2014
Development of the MIPSS Score in the Learning Cohort

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Score</th>
<th>% of pts</th>
<th>OS (y)</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0-0.5</td>
<td>27</td>
<td>26.4</td>
<td>1</td>
</tr>
<tr>
<td>Int-1</td>
<td>1-1.5</td>
<td>14</td>
<td>9.7</td>
<td>4.7</td>
</tr>
<tr>
<td>Int-2</td>
<td>2-3.5</td>
<td>46</td>
<td>6.4</td>
<td>9.9</td>
</tr>
<tr>
<td>High</td>
<td>&gt;4</td>
<td>13</td>
<td>1.9</td>
<td>36.5</td>
</tr>
</tbody>
</table>

Vannucchi et al. ASH 2014
MIPSS Permits to Refine Prognostic Stratification Within the IPSS Categories

**IPSS - LOW**

- Low: 24.9y
- > Low: 15.3y

**IPSS - INT-1**

- < Int-1: 17.7y
- > Int-1: 8.1y

**IPSS - INT-2**

- < Int-2: 6.2y
- > Int-2: 1.9y

*Estimated

*, IPSS Median Survival

Vannucchi et al. ASH 2014
## FATIGUE Trial – Co-morbidities in 1676 MPN Patients

<table>
<thead>
<tr>
<th>Fatigue-related Category</th>
<th>Percent Respondents (N=1676)</th>
<th>Correlation with fatigue score (P-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Illness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>12.9%</td>
<td></td>
</tr>
<tr>
<td>Restless leg syndrome</td>
<td>7.0%</td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>6.1%</td>
<td></td>
</tr>
<tr>
<td>Obstructive sleep apnea</td>
<td>4.0%</td>
<td></td>
</tr>
<tr>
<td>Rheumatologic disease</td>
<td>3.8%</td>
<td></td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>3.6%</td>
<td></td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>1.7%</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td>Liver failure</td>
<td>0.6%</td>
<td></td>
</tr>
<tr>
<td><strong>Current Medication Use Categories</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td>32.1%</td>
<td>NS*</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>16.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>16.0%</td>
<td>0.0276</td>
</tr>
<tr>
<td>Anti-anxiety</td>
<td>10.1%</td>
<td>0.0357</td>
</tr>
<tr>
<td>Prescription pain</td>
<td>7.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Steroids</td>
<td>3.4%</td>
<td>NS*</td>
</tr>
<tr>
<td>Cough or cold medications</td>
<td>1.8%</td>
<td>NS*</td>
</tr>
</tbody>
</table>
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
6. Understand complex assessment of MPN “risk”, and comorbidities
5. Understand new response criteria, and need for their validation
### Response Criteria for MPNs 2014 (All ≥ 12 Weeks)

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

- **Complete Remission**
  - Resolve ET Signs
  - ≥ 10 pt. MPN10 ↓
  - Near normal counts
  - No Prog. or Vascular
  - BM rem & ≤Gr 1 MF

- **Partial Remission**
  - Resolve ET Signs
  - ≥ 10 pt. MPN10 ↓
  - Near normal counts
  - No Prog. or Vascular

- **Clinical Improvement**
  - Resolve ET Signs
  - ≥ 10 pt. MPN10 ↓
  - Near normal counts
  - No Prog. or Vascular

- **Other**
  - Peripheral Blood Granulocytes
    - CR – Eradicated mutation
    - PR - ≥50% ↓, ≥ 20% baseline

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

- **Complete Remission**
  - Resolve ET Signs
  - ≥ 10 pt. MPN10 ↓
  - Near normal counts
  - No Prog. or Vascular
  - BM rem & ≤Gr 1 MF

- **Partial Remission**
  - Resolve ET Signs
  - ≥ 10 pt. MPN10 ↓
  - Near normal counts
  - No Prog. or Vascular

- **Clinical Improvement**
  - Resolve ET Signs
  - ≥ 10 pt. MPN10 ↓
  - Near normal counts
  - No Prog. or Vascular

- **Other**
  - Peripheral Blood Granulocytes
    - CR – Eradicated mutation
    - PR - ≥50% ↓, ≥ 20% baseline

#### Other Criteria

- **Peripheral Blood Granulocytes**
  - CR – Eradicated mutation
  - PR - ≥50% ↓, ≥ 20% baseline

- **Bone Marrow**
  - BM CR but
  - Hb (between 85 and 100 g/L)
  - PLT (between 50-100 x 10(9)/L)
  - Symptoms (≥ 50% ↓)

- **Molecular (ET/PV Criteria)**
  - CR – Normal
  - PR - ≥ 50% ↓

- **Cytogenetic**
  - CR – Normal
  - PR - ≥ 50% ↓

---

**N.B.** ET/PV – Progression is MF/MDS/ or AML
MF – Progression based on spleen growth or AML
“Clinically Meaningful” – What is Valid?

(Example – Spleen Reduction)

> 50% reduction of Palpable Length

IWG-MRT 2006
Blood 2006

> 35% Volume Reduction by MRI

COMFORT 1 & 2
NEJM 2012

> 10% Volume Reduction by MRI
- Better Survival and PGIC

Pooled CI/CII
Blood 2013
What Should We Expect From MPN Therapy?
Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
6. Understand complex assessment of MPN “risk”, and comorbidities
5. Understand new response criteria, and need for their validation
4. Optimizing the timing and utilization of stem cell transplant
Stem Cell Transplant Use in MPNs

Baseline Assumptions/ Caveats
- SCT almost exclusively for MF/ MPN-BP
- In MF evolving risk/benefit analysis for use

Question 1
Timing?
- Urgent
- Delayed
- Never

Question 2
Pre Transplant Therapy?
- JAK Inhibition?
- Cytoreduction?
- Iron chelation?

“Problematic” MF & SCT Eligible

Allo SCT

Question 3
Post Transplant Therapy?
- JAK Inhibition?
- Interferon?
- other?
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
6. Understand complex assessment of MPN “risk”, and comorbidities
5. Understand new response criteria, and need for their validation
4. Optimizing the timing and utilization of stem cell transplant
3. Optimizing the utilization of current available agents
Proposed Algorithm of Therapy of ET/PV in 2015

**Diagnosis of PV or ET**

- Assess MPN Risk Score (Table 1)
- Assess MPN Symptoms (MPN 10)
- Control of Hematocrit (<45%) in PV (? In ET)
- Low dose aspirin in appropriate patients

**JAK2 Inhibitor (Experimental Indication)**
- Ruxolitinib
- Other Clinical Trial JAK2 Inhib

**Front Line Cytoreduction**
- HU, or HU vs INF Clinical Trial

**Consider Ruxolitinib (PV)/ ET (2nd line or Trial) or INF (Trial)/HU if not previously received**

- Decide on need for concurrent cytoreduction based on Risk and Symptoms
  - **YES**
    - Worsening symptom burden
    - Vascular event, progression
    - HU Resistance/Intolerance
  - **NO**
    - Monitor for symptom burden, vascular events, progression

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

- Low dose aspirin in appropriate patients
Proposed Algorithm of Therapy of MPN-MF in 2015

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

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

- **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)**
- **Proceed to ALLO (Possible JAK2 Inhib Prior) (Trial)**
- **JAK2 Inhibitor**
  - *Unless anemia/cytopenias main problem*

- **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

- **JAK2 Inhibitors**
  - Ruxolitinib (Jakafi/Jakavi)
  - (Approved for MF)
  - Clinical Trial JAK2 Inhib

- **Anemia Rx**
  - Clinical Trials
  - IMID/Androgens/EPO
  - Splenectomy

- **Possible Role Of JAK2 Inhib (Trial) or INF (Trial)**
- **Proceed to ALLO (Possible JAK2 Inhib Prior) (Trial)**
- **JAK2 Inhibitor**
  - *Unless anemia/cytopenias main problem*

- **Clinical Trials**
  - Ruxo Combination
  - Non Ruxo JAK2
  - New Targets

- **N.B.**
  - Consider Rx for Prevention of Vascular Events in Appropriate Patients (Aspirin & Cytoreduction)
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
6. Understand complex assessment of MPN “risk”, and comorbidities
5. Understand new response criteria, and need for their validation
4. Optimizing the timing and utilization of stem cell transplant
3. Optimizing the utilization of current available agents
2. Thoughtful analysis of combination MPN therapeutic approaches
Myelofibrosis – Rx Opportunities

Clinical Status

- Dx of MF
  - MF on JAK Inhibitor
    - Survival
    - MF Symptoms
    - Spleen

- Time

- Molecular Response
  - Anemia/Thrombocytopenia
  - Fibrosis
Interferons in MPNs – Evolving Footprint

**Peginterferon alpha-2a**

**MPD – RC 112**

*PEG IFN vs HU (Front Line)*
High Risk ET/PV
NCT01258856

**MPD-RC 111**

*PEG IFN (2nd Line)*
High Risk ET/PV - SVT
NCT01259817

**Pegylated P Interferon alpha-2b**

AOP 2014 P1101

**PROUD - PV**

AOP2014/P1101 vs HU (Front Line)
High Risk PV
NCT01949805
Different phenotypes in setting of JAK inhibition

Primary anemia phenotype

Proliferative phenotype

Good ruxolitinib response

Ruxolitinib response with anemia a problem
What Should We Expect From MPN Therapy?

Top 10 ways we better match therapy and patients

10. Understand that not all MPN patients are impacted the same
9. Understand the spectrum of symptoms MPN patients face
8. Understand impact of symptom clusters, and gender effect on MPN patients
7. Understand the complex issue of MPN fatigue, and possible mood disorders
6. Understand complex assessment of MPN “risk”, and comorbidities
5. Understand new response criteria, and need for their validation
4. Optimizing the timing and utilization of stem cell transplant
3. Optimizing the utilization of current available agents
2. Thoughtful analysis of combination MPN therapeutic approaches
1. Never lose the forest through the trees
Medicine Wheel of Health
“Integrative Medicine”
Being a Blood Disease Survivor

Top 10 List

10. Learn about your disease
9. Make friends with facing a similar challenge
8. Be your own best advocate
7. Capture what is discussed at doctors visits (friends/ recorder)
6. Take care of your caregiver
5. Take care of the rest of your health
4. Eat in a healthy way (most of the time😊)
3. Exercise
2. Live every moment
1. Focus on relationships
Quotes from Erma Bombeck
Written as she was dying from Cancer

• If I had my life to live over I would...

• Have gone to bed when I was sick instead of pretending the earth would go into a holding pattern if I weren’t there for a day
I would have...

• Burned the pink candle sculpted like a rose before it melted in storage
I would have...

• Sat on the lawn with my grass stains
I would have...

• Talked less and listened more
I would have...

• Invited friends over to dinner even if the carpet was stained or the sofa faded
I would have...

- Shared more of the responsibility carried by my husband
I would have...

• Never have insisted the car windows be rolled up on a summer day because my hair had just been teased and sprayed
I would have...

- Don’t worry about who doesn’t like you, who has more or who is doing what. Instead, cherish the relationships we have with those who do love us.
I would have...

- Never have bought anything just because it was practical, wouldn’t show soil, or was guaranteed to last a lifetime
I would have...

• Instead of wishing away nine months of pregnancy, I’d have cherished every moment and realized that the wonderment growing inside me was the only chance in life to assist God in a miracle
I would have...

- Taken the time to listen to my grandfather ramble about his youth
I would have...

• Cried and laughed less while watching TV and more while watching 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.
Mayo Clinic
Myeloproliferative Neoplasm (MPN) Team
Arizona, USA
Acknowledgements

Argentina
Ana Clara Kneese, MD
Federico Sackmann, MD

Australia
David M Ross MBBS, PhD
Cecily Forsyth
John Seymour, MBBS, PhD
Karen Hall, MD
Kate Burbury MD
Tam Constantine, MD

Canada
Lynda Foltz, MD
Vikas Gupta, MD

China
Hsin-An Hou, MD
Huan-Chau Lin,
MD Hung Chang, MD
Ming-Shen Dai, MD
Yuan-Bin Yu, MD
Yung-Chen Su, MD
Zhijian Xiao, MD

Denmark
Christen Lykkegaard Andersen, MD
Hans Hasselbalch, MD

France
Brigitte Dupriez, MD
Jean-Jacques Kiladjian, MD
Jean-Loup Demory MD
Magali Demilly, PhD

Germany
Heike L. Pahl, PhD

Ireland
Mary Francis McMullen, MD

Israel
Martin Ellis, MD

Italy
Alessandro M. Vannucchi, MD
Francesco Passamonti, MD
Giovanni Barosi, MD
Tiziano Barbui, MD

Netherlands
Harry Schouten, MD, PhD
Jan Jacques Michiels, MD
Karin Klauke, MD
Peter te Boekhorst, MD
Sonja Zweegman, MD PhD
Stephanie Slot, MD
Suzan Commandeur, MD

New Zealand
Hilary Blacklock, MD

Panama
Francis Guerra, MD

Singapore
Wee Joo Chng, MB ChB

Spain
Ana Kerguelen Fuentes, MD
Carlos Besses, MD
Francisco Cervantes, MD
Dolores Fernandez-Casados

Sweden
Andreasson Bjorn, MD
Elisabeth Ejerblad, MD
Gunnar Birgegard, MD
Jan Samuelsson, MD
Johanna Ablesson, MD
Peter Johansson, MD

UK
Anthony Green, MD
Claire N. Harrison, MD
Deepi Radia, MD

Uruguay
Pablo Muxi, MD

USA
Alison Moliterno, MD
Brady Stein, MD MHS
Casey O’Connell
Catriona Jamieson
Daniel Rubin, ND
Elizabth Hexner
Hala Simm
Jason Gotlib, MD
Jeff Sloan, PhD
Jessica Altman, MD
Joseph Prchal, MD
Kimberly Hickman
Martin Tallman, MD
Mike Boxer, MD
Olatoyosi Odenike, MD
Richard T Silver, MD
Ross Levine, MD
Soo Jin Kim
Srdan Verstovsek, MD
Thanks to MPN Patients, and their loved ones, for Their Contributions to MPN Research

Courtesy of C. Harrison and UK MPN Patient