Novel Therapies in MPN Clinical Trials - Beyond JAK Inhibitors

MPN Advocacy & Education
International Cleveland MPN Patient Program

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Disclosures/COI

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  – Samus
  – MustangBio

• I will discuss off-label, off-protocol & investigational therapies in the course of this talk
Ruxolitinib Failure: Occurs in Different Ways

- **“Primary resistance”** – refractoriness
  - no clinical response within 28 days after RX initiation

- **Suboptimal response**
  - failure to achieve a minimum clinical improvement within 12 weeks / mixed response (dose reduction or treatment interruptions due to AEs)

- **Secondary resistance - relapse**
  - loss of a previously confirmed clinical response (≥CI)

- **Progression → post-MPN AML**
  * leukemic transformation

- **Treatment related toxicities/infections/cytopenias**

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Identification & Management of RUX Failure: How to best define? How can we build consensus?

- **REASON for RUX failure**
  * primary / secondary
  * cytopenias / progression / AEs

- **CLINICAL picture**

- **INDIVIDUAL risks**
  * age, performance status

- **DISEASE risks**
  * molecular, cytogenetic

**SCT candidate?**
**SCT = only curative therapy for MF**

- **Anemia Thrombocytopenia**
  - Rule out other causes
  - Observe vs treat (PRBC)
  - ADD EPO, danazol, IMIDS

- **MPN symptoms Spleen**
  - Optimize RUX dose
  - Alternative RX: JAK inh., cl trial
  - Supportive measures
  - Splenectomy?

- **Proliferation (↑ WBC)**
  - Rule out other causes
  - ADD cytoreductive RX (hydrea)

- **AP/BP progression (↑ blasts)**
  - ADD HMA
  - vs induction CHT

Modified from Dr Lucia Masarova, MD, Pemmaraju, Verstovsek SOHO 19
Fedratinib: FDA approved Aug 2019

- A highly selective, potent inhibitor against wild-type and mutant JAK2, also FLT3 and BRD4

- 08/2019 FDA approved for int-2 or higher MF
- 1L vs 2L (?): 400 mg once daily
- ↓ 200 mg daily with strong CYP3A4 inh OR severe renal insufficiency

*** measure and replace THIAMINE levels ***

Wernicke’s encephalopathy [ataxia, AMS, ophthalmoplegia] 8 / 806 cases (1.3%)

Platelet baseline level: The recommended dosage of INREBIC® is 400 mg taken orally once daily for patients with a baseline platelet count of $\geq 50 \times 10^9/L$ (Package insert)
Beyond Ruxo: Other JAK Inhibitors in Active Development

**Approved**
- Fedratinib
  - ≥ Int-2 MF, 1/2 L
  - Ph 2, PAC203, dose-finding study, MF pts preRX RUX (enrolled 150)
  - * awaiting results late 2019
  - **PLAN** Ph 3, PACIFICA: PACR vs BAT in MF pts with plt < 50K (Q3 2019)

**In Development**
- Pacritinib
- Momelotinib
  - **PLAN** Ph 3, MOMENTUM: MMB vs danazol in MF pts with anemia and preRX RUX (Q4 2019)

**Inactive**
- NS–018 ?

**Notes**
- XL-019, BMS -911543, AZD-1480, LY-2784544

Dr Lucia Masarova, MD SOHO 19
Transplant Superior In DIPSS Int-2 And High Risk Disease But Inferior In Low Risk Disease

Nicolaus Kröger et al. Blood 2015;125:3347-3350
Although the use of molecular risk classification for the identification of candidates for alloSCT among intermediate-1 patients deserves clinical validation, patients with intermediate-1 risk category who are triple negative (ie, JAK2 V617F, CALR, and MPL negative) or ASXL1-positive should be considered for alloSCT.
RUX: moving beyond MPN: acute GVHD

- Rux now approved for: steroid-refractory acute GVHD (aGVHD)
  - FDA approval date for this indication: May 24, 2019; 3rd FDA approval RUX
  - Ages 12 and up

- Study INCB 18424-271 (NCT02953678): REACH1, pivotal ph 2
  - Open-label, single-arm, multi-center
  - n=49 with steroid-refractory aGVHD grades II-IV s/p SCT
  - Primary endpoint = day 28 ORR = CR, vgPR, PR by CIBMTR criteria & response duration
  - Day 28 ORR in n=49 refractory to steroids alone was 57%; CR rate of 31%
  - Day-28 ORR → 100% grade 2; 40.7% grade 3; 44.4% grade 4 GVHD
  - Median response duration → 16 days; median time from day 28 response to death or new therapy → 173 days

- Most common toxicities RUX in aGVHD:
  - >50%: Anemia, thrombocytopenia, neutropenia; infections & edema

- Recommended start dose for RUX in aGVHD:
  - Rux 5 mg po BID

https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/202192s017lbl.pdf
Outcomes in patients with relapsed/refractory myelofibrosis (MF) are generally poor (~14-16 months).

No approved therapies beyond JAK inhibitor class of treatment for patients with MF.

In setting of thrombocytopenia, difficult or contraindicated to administer JAK inhibitors.

Kaplan-Meier analysis of survival of PMF patients stratified according to their driver mutation.


©2014 by American Society of Hematology
MIPSS70 and MIPSS70-Plus

http://mipss70score.it

Key Elements

- Hb <10 g/dL
- WBC >25 x 10^9/L
- PLT <100 x 10^9/L
- Blasts ≥2%
- Fibrosis > grade 1
- Constitutional symptoms
- Absence of type 1-like CALR
- HMR
  - ASXL1
  - EZH2
  - SRSF2
  - IDH1/2
- Two or more HMR
- Unfavorable karyotype
Comprehensive Clinical-Molecular Transplant Scoring System for MF Undergoing Stem Cell Transplantation

Combinations: JAKi + another agent/ “add-back strategy” for MF: Future roles in other MPNs?

- **RUXO + AZA** – frontline (MF)
  - MDACC : MF (Masarova et al BLOOD 2018)
- **RUXO + HSP90i** (MF)
  - ClinicalTrials.gov Identifier: NCT03373877
- **RUXO + BCL-xLi** (MF)
  - ClinicalTrials.gov Identifier: NCT03222609
- **RUXO + PI3Ki** (MF)
  - ClinicalTrials.gov Identifier: NCT01730248
- **RUXO + THAL** (MF) - frontline & R/R
  - ClinicalTrials.gov Identifier: NCT03069326
- **RUXO + HDACi (Pracinostat)** (MF) – frontline
- **RUXO + IFN** (2 ongoing clinical trials – Europe)

Hypomethylating Agents: MPNs

- 5-azacitidine monotherapy in **Myelofibrosis**
  - ORR 24%, Few sustained responses (Quintas-Cardama et al, Leukemia 2008)

- HMA monotherapy in **High-risk or Blast Phase MPN**
  - Retrospective data (n=54). ORR 52%, 24% CR rate. (Thepot et al., Blood 2010)
  - Retrospective data (n=21). 29% with ORR, Median duration was 7months. (Badar, et al., Leukemia Research 2015)

- In **High-risk or Blast Phase MPN**
  - Phase I Myeloproliferative Research Consortium Study.
    - Decitabine + Ruxolitinib
    - N=20. ORR 53%. Median OS 7.9 months (Rampal et al., Blood Advances 2018)
    - RP2D = 25mg BID of Ruxolitinib for 1st cycle, 10mg BID subsequently + 20mg of Decitabine

- In Int 1, Int 2, HR **Myelofibrosis**
  - Phase II Study from MD Anderson
    - Ruxolitinib + Azacitidine (Masarova et al., Blood 2018)
    - No prior therapy with Ruxolitinib or HMA
    - N=46
    - HMA introduced cycle 4

Modified from Dr Laura Michaelis, MD
Ruxolitinib + Interferon in patients with MF

- **IFN monotherapy in early MF**: Silver et al: Early Tx with IFN alpha in patients without High risk molecular mutations (Silver RT et al Cancer 2017)

- Currently two ongoing clinical trials – both in Europe
  - COMBI – Phase II
    - N=18 pts with low/int I risk MF
    - Preliminary safety established, Remissions noted, Decline in JAK2v617F allele burden noted
  - RUXOPEG Phase I/II
    - Has concludes Phase I, no DLTs observed
    - Phase II outcomes include allele burden decline

Image: Data from RUXOPEG preliminary analysis and presentation -- J Kiladjian, Oral Presentation EHA 2019; Silver RT Cancer 2017, slide modified from Dr L Michaelis
Novel Therapies In MPNs: Moving Beyond JAK Inhibition in 2019

• Promotion of Apoptosis
  – SMAC mimetics/IAP antagonists (LCL161; ph2; NCT02098161): n=44, 30% ORR R/R MF
  – BCL-xL inhibition (Navitoclax; ph2; NCT03222609)

• Targeting of Hematopoietic stem cell/micro-environment
  – CD123 inhibition (SL-401; ph2; NCT02268253)
  – HSP90 inhibition (PU-H71; ph 1; NCT03373877)

• Activation of TP53 pathway
  – MDM2 inhibition (Idasanutlin, ph 2 (PV); NCT03287245)

• Targeting Fibrosis, Cytokines, Epigenetics,other pathways
  – Pentraxin (PRM-151; ph 2; NCT01981850)
  – TGF-β modulation, Sotatercept/Luspatercept
  – Aurora Kinase A inhibition : Alisertib ph I (n=24, Gangat/Crispino, CCR 2019)
  – Bromodomain inhibition (CPI-0610, NCT02158858)
  – LSD1 inhibition

• Telomerase inhibition : Imetelstat ph 2 results 9.4 mg/kg iv q3wks n=107; median OS in 9.4 mg/kg arm has not been reached (R/R MF)

LCL161, an Oral Smac Mimetic/IAP Antagonist for Patients with Myelofibrosis (MF): Novel Translational Findings Among Long-Term Responders in a Phase 2 Clinical Trial

Naveen Pemmaraju, Bing Z Carter, Hagop Kantarjian, Jorge Cortes, Tapan Kadia, Guillermo Garcia-Manero, Courtney DiNardo, Prithviraj Bose, Naval Daver, Marina Konopleva, Maro Ohanian, Sherry Pierce, Lingsha Zhou, Zeev Estrov, Gautam Borthakur, Karina Salinas, Po Yee Mak, Nitin Jain, Elias Jabbour, Srdan Verstovsek

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LCL161 in MF: Background

- **Second mitochondrial activator of caspases (Smac)** mimetics
  - Binds to cIAP1, cIAP2, and XIAP and triggers cytokine- and caspase-mediated apoptotic cell death

- Overexpression of TNF-α & cytokines in patients with MF

- **Study rationale:** Inhibition of tumor activity in MF by LCL161 in high TNF-α expressing environment

References:
LCL161 in MF: Conclusions

• ORR = 32% (14/44 patients)
  – Median response duration (months): 5.5 [3-31.5+]
  – Long-term responders: N=7 for ≥1 year

• Correlatives and Translational Findings:
  – On-target cIAP1 inhibition observed in responders
  – Ongoing translational studies: high baseline levels of XIAP and/or XIAP increase during therapy may contribute to resistance/progression

• Grade 2 fatigue syndrome & dose reductions

• Future directions include:
  – LCL161 combinations
  – Further investigation: cytokines & symptom burden, TNF-α, tumor microenvironment, anemia responders
Tagraxofusp (SL-401): Novel Targeted Therapy Directed to the IL-3 Receptor (IL-3Rα / CD123)

- IL-3Rα/CD123 overexpressed on BPDCN and many other hematologic cancers
- Tagraxofusp (SL-401) is a targeted therapy directed to CD123
- Tagraxofusp potent vs BPDCN cells in vitro and in vivo
- Previous Phase 1 study
  - Major responses in 7/9 patients (78%):
    5 CR, 2 PR (Frankel et al. Blood, 2014)

Jordan CT, Upchurch D, Szilvassy SJ, Guzman ML et al: Leukemia 2000 : 1777-84
Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm

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Anthony S. Stein, M.D., Sumithira Vasu, M.D., William Blum, M.D.,
David A. Rizzieri, M.D., Eunice S. Wang, M.D., Madeleine Duvic, M.D.,
J. Mark Sloan, M.D., Sharon Spence, M.S., Shay Shemesh, M.S.,
Christopher L. Brooks, Ph.D., John Balser, Ph.D., Ivan Bergstein, M.D.,
Jeffrey E. Lancet, M.D., Hagop M. Kantarjian, M.D.,
and Marina Konopleva, M.D., Ph.D.
Tagraxofusp, Mechanism of Action, and Rationale

CMML and MF overlap

- ~50% of CMML presents with myeloproliferative features (MP-CMML), e.g. splenomegaly, etc. (similar to MF); associated with poor prognosis
- ~10-20% of MF presents with monocytosis (similar to CMML); associated with poor prognosis
  - Monocytes share a common progenitor with CD123+ plasmacytoid dendritic cells (pDCs)

CD123 Expression in MF

- CD123+ pDCs in MF tumor microenvironment

CD123 (red) and TCF4 (brown) immunohistochemistry double staining of MF bone marrow at baseline

CD123+ staining in MF bone marrow

CD123+ TCF4+ pDCs are indicated by arrows

- In MF, monocytosis (>1x10^9/L monocytes) is associated with an accelerated disease phase and poor prognosis
- Monocytes share a common precursor cell with pDCs and express CD123


Conclusions: Tagraxofusp (SL-401)

• 57% of evaluable patients, with baseline spleen size ≥5cm, had reduction in baseline splenomegaly
  - 21% had reduction by ≥45%
• 100% of evaluable patients with monocytosis and baseline spleen size ≥5cm, had reduction in baseline splenomegaly
  - 80% had reduction by ≥29%; 40% had reduction by ≥45%
• 6 patients with spleen response had treatment duration of 6+ months; 5 patients ongoing
  • 5 patients with baseline thrombocytopenia (platelet count <100K) had treatment duration of 6+ months; 4 patients ongoing
  • 3 patients with baseline monocytosis (>1x10⁹/L) had treatment duration of 8+ months; 2 patients ongoing

• Most common treatment-related adverse events (TRAEs) include headache and hypoalbuminemia (each 22%), and alanine aminotransferase increased and thrombocytopenia (each 17%). The most common TRAE, grade 3+, was thrombocytopenia (8%)
Background: P53/MDM2

- P53 regulates cell cycle, apoptosis, DNA repair, and senescence
- Wild type P53 seen in chronic phase MPN and mutated P53 in advanced phase
- Down regulation of P53 by MDM2 overexpression
  - Promotes proteosomal degradation
  - Inhibits P53 transcription
  - Inhibits transactivation
  - Facilitates export from nucleus
- Nutlins Block the MDM2:P53 interaction and activate the p53 pathway

MDM2 and PV and MF

• PV CD34+ cells contain higher levels of MDM2 compared to normal CD34+ cells

• Low doses of a Nutlin and Peg-IFNα 2a increase p21 and PUMA protein levels in PV CD34+ cells and promote apoptosis

• Treatment with low doses of a Nutlin and Peg-IFNα 2a reduce the numbers of JAK2V617F-positive cells transplanted in NOD/SCID mice

Of interest, there are several ongoing clinical trials in MPNs investigating MDM2 targeted agents:

1. Ph 2: KRT-232 vs RUXO: phlebotomy-dependent PV
3. Ph 2: Idasanutlin: Hydrea-intol/resistant PV


J Mascarenhas R Hoffman, MD et al
Monocyte-derived Fibrocytes and Inhibition of Marrow Fibrosis

- Tissue fibrosis in many diseases → monocyte-derived fibrocytes

- Do fibrocytes play a role in the initiation of bone marrow fibrosis in patients with MF?

- Marrow from patients with MF → increased amount of clonal, neoplastic collagen & fibronectin–producing fibrocytes

- pDX: Treatment with fibrocyte inhibitor SAP (pentraxin-2) led to significantly increased prolonged survival / decreased marrow fibrosis

- Fibrocytes of neoplastic origin, such as those in patients with MF, can contribute to induction of marrow fibrosis; and that inhibition of fibrocytes with SAP (PRM-151) can interfere with fibrotic formation/development processes

PRM-151: Recombinant Human Pentraxin-2 (PTX-2)

- PTX-2 (郿) is an endogenous regulator of tissue repair
- PTX-2 binds to damaged tissue (郿) and monocytes/macrophages
- PTX-2 prevents and reverses fibrosis in pre-clinical models
- PTX-2 levels are low in MF patients
  - Also low in patients with renal, pulmonary and liver fibrosis

**Hypothesis:**
Reduction of bone marrow fibrosis will restore hematopoiesis and improve cytopenias

Verstovsek S et al
Imetelstat: First in Class Telomerase Inhibitor

**Imetelstat binds to RNA template preventing maintenance of telomeres**

- **Proprietary:** 13-mer thio-phosphorodiamidate oligonucleotide complementary to hTR, with covalently-bound lipid tail to increase cell permeability/tissue distribution
- **Long half-life** in bone marrow, spleen, liver (estimated human t½ = 41 hr with doses 7.5 – 11.7 mg/kg);
- **Potent competitive inhibitor of telomerase:** IC50 = 0.5-10 nM (cell-free)
- **Target:** malignant progenitor cell proliferation

**Mascarenhas J et al ASH 2018**
Overall Survival (ITT) for Imetelstat at Different Dose Levels

Median follow-up: 27.4 months

Median survival:
- 19.9 months (95% CI, 17.1, NE) in 4.7 mg/kg
- 29.9 months (95% CI, 22.8, NE) in 9.4 mg/kg

Multiple sensitivity analyses were performed (including data censoring at time of dose escalation, censoring at subsequent JAKi or stem cell transplant and excluding patients who were dose escalated or randomized after closure of the 4.7 mg/kg arm), all generating similar results.
SOTATERCEPT MECHANISM OF ACTION AND STUDY RATIONALE

- Sequesters ligands of TGF-β superfamily secreted by bone marrow stromal cells, especially GDF11
- Removal of GDF11 relieves suppression of terminal erythropoiesis
- Improves erythropoiesis in preclinical models of β-thalassemia, Diamond Blackfan anemia, and in hepcidin transgenic mice
- Effective against anemia of lower risk MDS

Bose et al. Sotatercept in MF

LSD1 is a key regulator of hematopoietic differentiation

- LSD1 (Lysine-specific demethylase 1) is a histone demethylase specific for H3K4
- Is essential for differentiation of megakaryocyte-erythroid progenitors (MEPs) to mature megakaryocytes\(^1\)
  - In part, through interaction with GFI1b
- Is required for normal megakaryocyte function including platelet production\(^1\)
- Overexpressed in MPN\(^2\)

Slide courtesy: Dr Kristen Petit EHA 2019
Preliminary Efficacy Analysis: LSD1 inhibitor

- n = 9
- Data collected after 12 weeks on therapy

Patient Responses:
- 6 had reduction or stabilization in spleen volume (none met 35% SVR threshold)
- All had some degree of symptom reduction, and 5 had a >50% reduction in MPN TSS
- 2 had at least 1 grade improvement in BM fibrosis

Mean duration at goal dose 26 days (84-day cycle)

Slide courtesy: Dr Kristen Petit EHA 2019
LSD1 Inhibitor: IMG-7289

- IMG-7289 (LSD1 inhibitor): a novel epigenetic therapy in MF; oral once daily

- Safe/well tolerated; n=6/16 had taste changes

- Prelim, ongoing analysis: spleen reduction in 66% of evaluable patients and 56% had TSS reduction of 50% or greater

- Aug 2019 → FDA granted fast track designation for IMG-7289 for patients with MF

- This study has now been expanded to a phase IIb study: NCT03136185 (US, UK, EU)
RNAi Screen Identifies Brd4 as a Therapeutic Target in Acute Myeloid Leukemia


MLL-AF9 and Nras\(^{G12D}\) model
Pemigatinib (INCB054828): oral FGFR inhibitor

- Myeloid/Lymphoid Neoplasms with FGFR1 re-arrangement
- 8p11
- Eosinophilia-associated: FGFR1, PDGFRα, PDGFRβ
- ORR ~85% ongoing pivotal clinical study: FIGHT203 (Verstovsek et al, ASH 2018)

ClinicalTrials.gov Identifier: NCT03011372
Avapritinib (BLU-285): Mutant KIT inhibitor for patients with aggressive SM

- Selective, oral TKI targeted to KIT mutation
- Most cases SM driven by D816V KIT mutation
- ORR ~77% in phase I (EXPLORER) study (Radia EHA 2019)
- Phase 2 clinical trial (PATHFINDER) now ongoing in patients with advanced SM

ClinicalTrials.gov Identifier: NCT03580655
CLINICAL TRIALS AND OBSERVATIONS

Aggressive B-cell lymphomas in patients with myelofibrosis receiving JAK1/2 inhibitor therapy

Edith Pospačić,1,* Sabrina Tripolt,2,* Andrea Hoelbl-Kovacic,2,† Bettina Gisslinger,1 Zsuzsanna Bago-Horvath,2,3 Emilio Casanova-Hevia,4,5 Emmanuelle Clappier,6,6 Thomas Decker,9 Sabine Fajmann,2 Daniela A. Fux,2 Georg Greiner,10 Sinan Gueltekin,1 Gerwin Heller,11 Harald Herkner,12 Gregor Hoermann,10,13,14 Jean-Jacques Kiladjian,15 Thomas Kolbe,16,17 Christoph Kornauth,3 Maria-Theresa Krauth,1 Robert Kralovics,10,18 Leonhard Muellauer,3 Mathias Mueller,19 Michaela Prchal-Murphy,2 Eva Maria Putz,2 Emmanuel Raffoux,20 Ana-Iris Schiefer,3 Klaus Schmetterer,19 Christine Schneckenleithner,2 Ingrid Simonitsch-Klupp,3 Cathrin Skrabs,1 Wolfgang R. Sperr,1,13 Philipp Bernhard Staber,1 Birgit Strobl,19 Peter Valent,1,13 Ulrich Jaeger,1,13,† Heinz Gisslinger,1,† and Veronika Sexl2,†

Letter to Blood

TO THE EDITOR:

Characteristics of patients with myeloproliferative neoplasms with lymphoma, with or without JAK inhibitor therapy

Naveen Pemmaraju,1 Hagop Kantarjian,1 Loretta Nastoupil,2 Megan Dupuis,1 Lisa Zhou,1 Sherry Pierce,1 Keyur P. Patel,3 Lucia Masarova,1 Jorge Cortes,1 and Srdan Verstovsek1

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MPN, JAK inhibitors, and Lymphoma?

- **Porpaczy et al BLOOD 2018**
  - N= 626 with MPN; n=69 with MF receiving JAKi
  - B-cell lymphomas → 4 (5.8%) of 69 patients receiving JAKi compared with 2 (0.36%) of 557 with standard/other treatments (16-fold increased risk)
  - A similar 15-fold increase was observed in an independent cohort of 929 patients with MPN
  - The Lymphomas occurring during JAKi therapy were preceded by a preexisting B-cell clone in all 3 patients that were evaluated

- **Pemmaraju et al BLOOD 2019**
  - 2,500 + MPN patients
  - n=9 total had lymphoma ; n=6 after JAKi, n=3 without JAKi (p=value not significant)
  - No statistically significant difference in cases of lymphoma after JAKi vs no JAKi

- **Rumi & Zibellini: Accompanying editorial in Blood 2019; 133:2251-2253**
  - Noted the debate and need for ongoing confirmatory studies
  - Pre-existing IGVH gene rearrangements / lymphoma pre-disposition?
  - Extended, long-term monitoring

Porpaczy, et al BLOOD 2018; Pemmaraju et al BLOOD Feb 2019
Conclusions: Novel therapies and SCT in MPNs in 2019

- **RUXO:** now 3 approved indications:
  - MF: int-risk/High-risk: dosing based on plts/package insert
  - PV: intolerant/resistant to HU: 10 mg PO BID
  - aGVHD: ages 12 and up: 5 mg PO BID
  - Monitor infections, non-melanoma skin cancers

- **Fedratinib:** 2nd JAKi now recently approved
  - Broad indication in MF, does not specify frontline vs R/R
  - Monitor for encephalopathy syndromes, thiamine, GI N/V/D

- **Novel therapies in MPNs:**
  - JAKi combinations: “add-back” and frontline combos
  - Moving Beyond JAKi with novel agents

- **SCT in MF**
  - Intermediate/high risk patients (int-1 with high risk)
  - New scoring systems SCT consideration specific
Thank you: MPN community

• Please email me npemmaraju@mdanderson.org or call me 713-792-4956 if you have any questions

• #MPNSM: Twitter/social media; @doctorpemm

• Serge Verstovsek
• Alison Moliterno
• Jerry Spivak
• Laura Michaelis
• Richard Silver
• Ruben Mesa
• John Mascarenhas
• Brady Stein
• Aaron Gerds
• Angela Fleischman
• Robyn Scherber
• Hagop Kantarjian
• Jorge Cortes
• Marina Konopleva
• Jean-Jacques Kiladjian
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• Mike Thompson
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• Steve Oh
• Betty Hamilton