Clinical Trials

The Myeloproliferative Disorders Research Consortium (MPD-RC)

Ruben A. Mesa, MD

Professor of Medicine

Chair, Division of Hematology & Medical Oncology

Mayo Clinic

Arizona, USA

MPD-RC

1. Who is the MPD-RC?
2. What has been learned from prior trials?
3. Which trials are ongoing?

MPD Research Consortium

USA
Italy
UK
France
Germany
Netherlands
Sweden
Denmark
Spain
Croatia

- NIH PPG
- 6 Projects
  - 5 Lab
  - 1 Cooperative Group

- **Project 1:** (Genetic Basis of Polycythemia Vera, Principal Investigator: Josef T. Prchal)
- **Project 2:** (Mechanisms and Effects of NF-E2 and PRV-1 Overexpression in PV: Role of Jak2V617F, Principal Investigator: Heike L. Pahl)
- **Project 3:** (Animal Models of Polycythemia Vera, Principal Investigator: Jerry Spivak)
- **Project 4:** (Mouse Models of Myelofibrosis, Principal Investigator: Anna Rita Migliaccio)
- **Project 5:** (Abnormal Stem Cell Trafficking in Myelofibrosis, Principal Investigator: Ronald Hoffman)

MPD Research Consortium-Project 6

Centers-USA

Mayo Clinic Arizona
Emory University, Winship Cancer Institute

Duke University
Geisinger Cancer Center
Georgetown University Medical Center

John H. Stroger Hospital of Cook County

Johns Hopkins University School of Medicine

Mount Sinai Medical Center
Ohio State University
Roswell Park Cancer Institute
The Palo Alto Clinic
University of California at San Francisco

University of Illinois at Chicago
University of Maryland
University of Pennsylvania School of Medicine

University of Utah
Weill Cornell Medical College
Princess Margaret Medical Center

Centers-Europe

Cliniques Universitaires Saint-Luc

Hopitaux de Paris
Hopital Claude Huriez, Lille
Hopital de la Cavale Blanche, Brest
Institute Paoli-Calmettes, Marseille
Ospedali Riuniti de Bergamo
Ospedale San Martino Genova
San Matteo Hospital
Universita Cattolica del Sacro Cuore
University of Florence
VU University Medical Centre, Amsterdam

Erasmus Medical Center Rotterdam
Stockholm South Hospital, Sweden
Sahlgrenska University Hospital Hematology Section, Medical Dept.
Guy's and St Thomas' NHS Foundation Trust

Belfast City Hospital, Belfast
Royal Hallamshire Hospital, Sheffield
University of Cambridge

MAYO CLINIC

Myeloproliferative Disorders Research Consortium
MPD-RC

MPD-RC

1. Who is the MPD-RC?
2. What has been learned from prior trials?
3. Which trials are ongoing?

MPD Research Consortium

Clinical Trials

Protocol 101 -Study of Fludarabine Based Conditioning for Allogeneic Stem Cell Transplantation for Myelofibrosis

Protocol 102 (Europe Only) -Open-Label, Phase 1/2 Study of VELCADE (Bortezomib) for Injection in Subjects with Myelofibrosis with Myeloid Metaplasia (MMM)

Protocol 103 -Phase II Study of Bevacizumab (Avastin®) in Myelofibrosis

Protocol 104 -CEP-701 (Lestaurtinib) in Myelofibrosis

Allo SCT for MF

	Median Ages	TRM (1y)	OS (5y)
Full MA (N=504)	40-49	20-42%	31-61%
RIC (N=263)	50-56	0-37%	50-67%

Adapted from Alchalby et. al. CHMR 2010;5:53-61

MPD Research Consortium
MPD-RC 101 protocol:

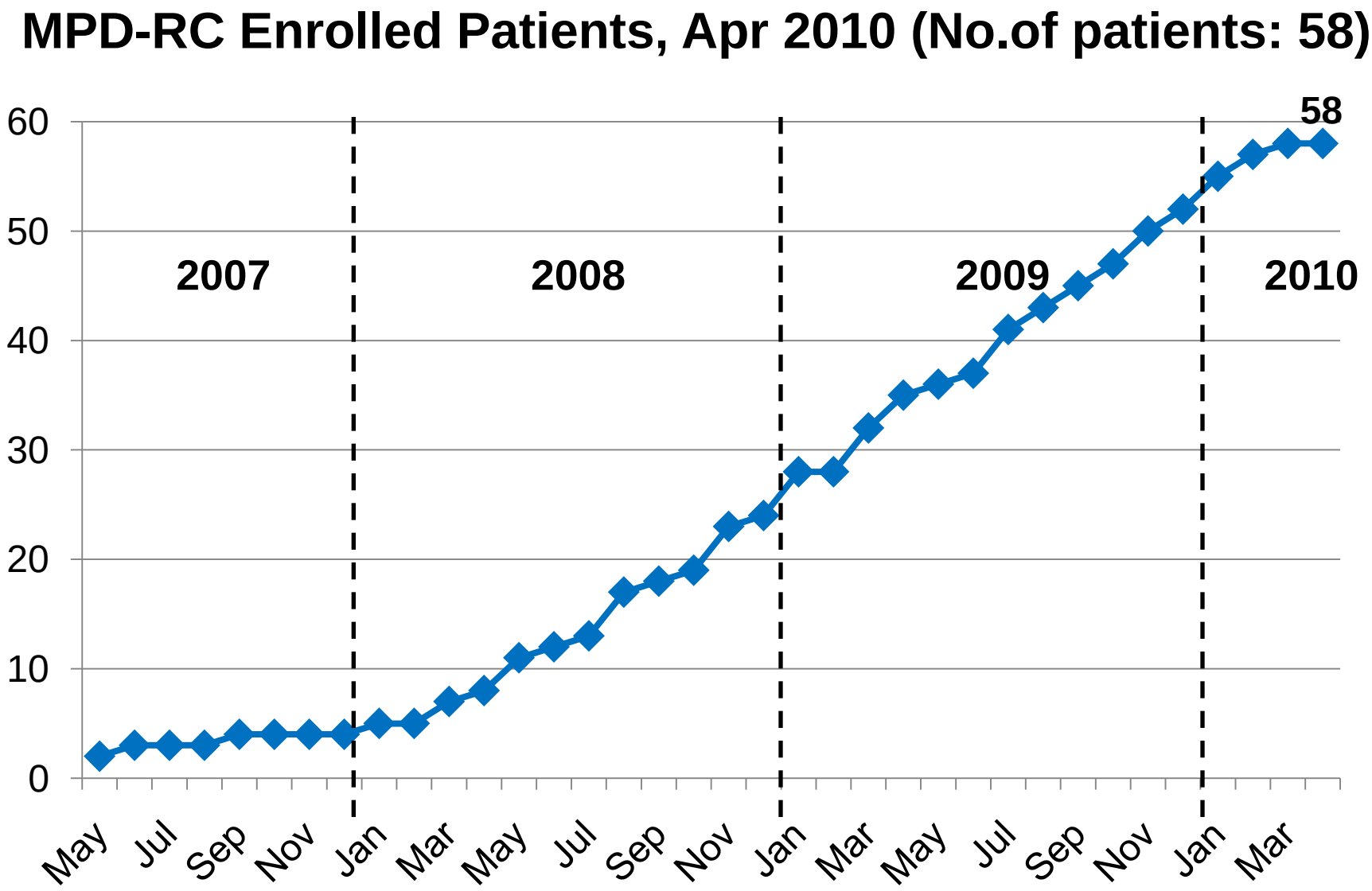
AGENT	DAY -6	-5	-4	-3	-2	-1	0
FLUDARABINE (30mg/m^2)	X	X	X	X	X		
MELPHALAN (70 mg/m^2)				X	X		
THYMOGLOBULIN* (total 4.5 mg/kg)				X	X	X	

* MUD transplants

GVHD PROPHYLAXIS:
Tacrolimus 0.03 mg/kg/d I.V. D-2; MTX (10 mg/m^2) I.V. days: 1, (5mg/m^2) 3 &6

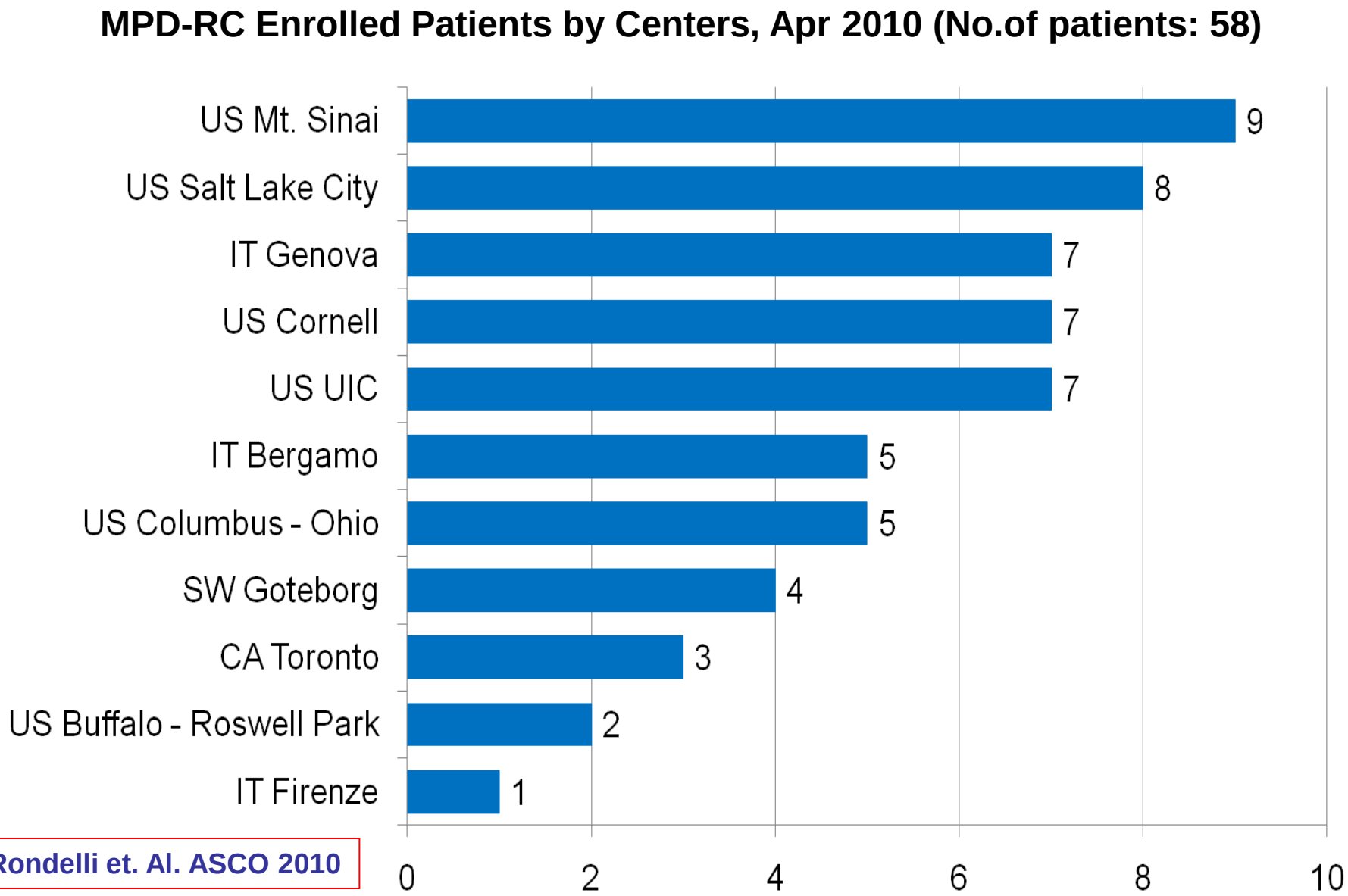
Rondelli et. Al. ASCO 2010

MPD-RC 101/107: enrollment



Rondelli et. Al. ASCO 2010

MPD-RC 101/107: Transplant Centers



Rondelli et. Al. ASCO 2010

Table 1: Patients' characteristics

	All Pts	Related	Unrelated
Total n. of patients	58	32	26
Median age (range)	55 (37-65)	55 (40-65)	55 (37-64)
Gender M/F	33/25	19/13	14/12
Inclusion Diagnosis			
PMF (%)	34 (59)	14 (44)	20 (77)
PV-MF (%)	6 (10)	3 (9.4)	3 (12)
ET-MF (%)	18 (31.0)	15 (46.9)	3 (12)
Lille score > 0 or Plt <100K(%)	58 (100)	32 (100)	26 (100)
Lille score > 0 (%)	55 (95)	29 (91)	26 (100)
Marrow Fibrosis (%)			
1	2 (4)	0 (0.0)	2 (8)
2	5 (9)	2 (6)	3 (12)
3	32 (55)	16 (50)	16 (62)
NA	19 (33)	14 (44)	5 (19)
Patient JakV617F+(%)			
Yes	21 (36)	11 (34)	10 (39)
No	19 (33)	14 (44)	5 (19)
NA	18 (31)	7 (22)	11 (42)
Spenectomy(%)	9 (16)	5 (16)	4 (15)
Splenomegaly(%)	44 (90)	22 (82)	22 (100)
Normal spleen(%)	3 (6)	3 (11)	0 (0.0)
NA(%)	2 (4)	2 (7)	0 (0.0)
Cytogenetic abnormalities(%)			
Yes	17 (29)	10 (31)	7 (27)
No	29 (50)	16 (50)	13 (50)
NA	12 (21)	6 (19)	6 (23)
Prior MPD medical treatment(%)	48 (83)	26 (81)	22 (85)

Rondelli et. Al. ASCO 2010

Table 2: Donor HLA compatibility

	All Pts	Related	Unrelated
Total n. of patients	58	32	26
Donor HLA compatibility (%)			
10/10 matched donor	50 (86)	30 (94)	20 (77)
1 Antigen mismatch class 1	3 (5)	2 (6)	1 (4)
1 Antigens mismatch class 2	2 (4)	0 (0.0)	2 (8)
1 Allele mismatch class 1	2 (4)	1 (3)	1 (4)
1 Allele mismatch class 2	6 (10)	1 (3)	5 (19)

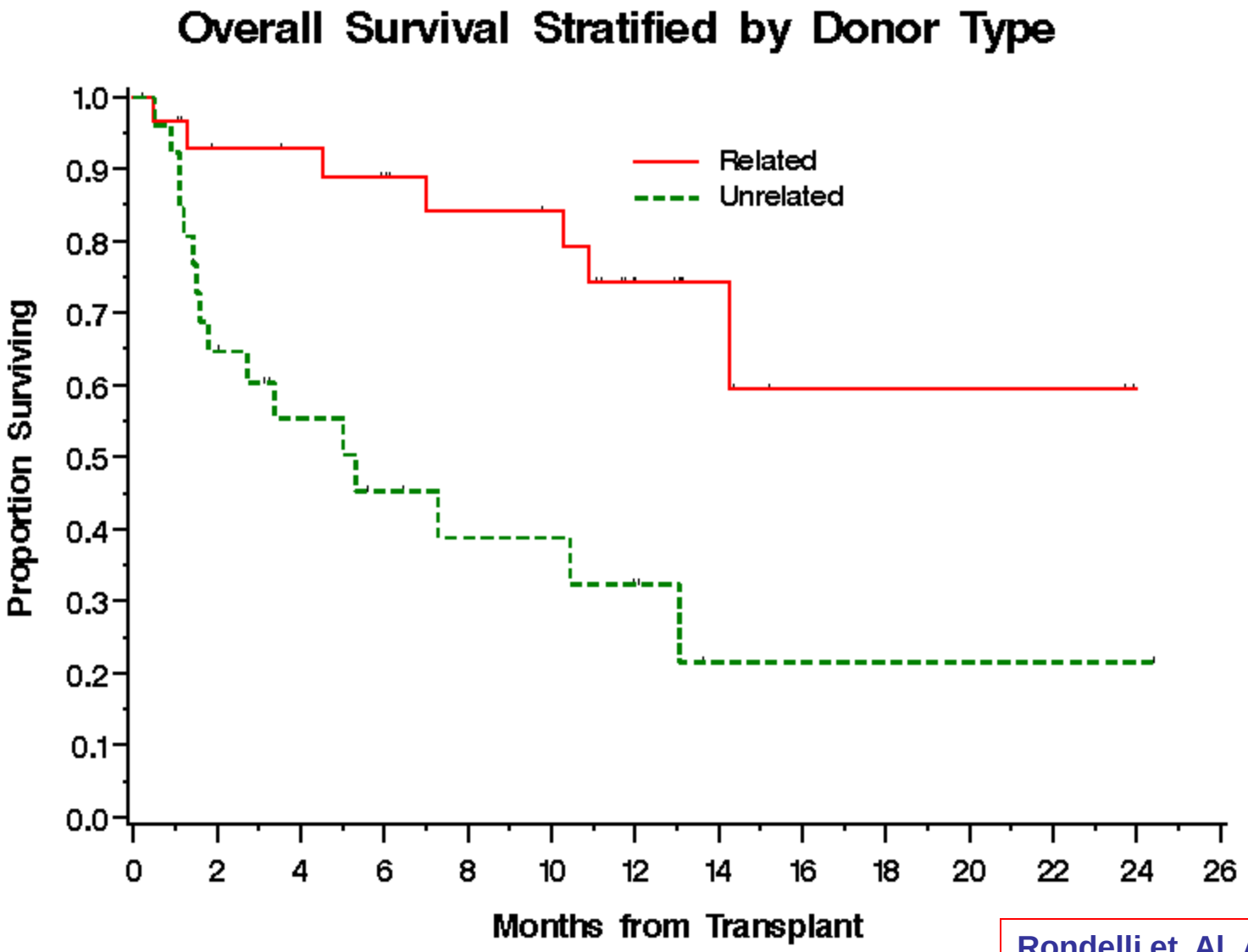
Rondelli et. Al. ASCO 2010

Table 4: Results II: Survival, causes of death

	All Pts	Related	Unrelated
Median follow-up:			
living patients (days) (range) (N=35)	190(17-749)	353 (17-736)	190 (92-749)
dead patients (days) (range) (N=23)	92(22-441)	220 (7-441)	83 (16-402)
Off-study pts (%)	28 (48)	9 (28)	19 (73)
Deaths	23 (40)	7 (22)	16 (62)
Patient's refusal	1 (2)	0 (0.0	1 (4)
Physician's decisions	3 (5)	1 (3)	2 (8)
End of study	1 (2)	1 (3)	0 (0.0)
Cause of death			
Relapse-related mortality	2 (4)	1 (3)	1 (4)
secondary cancer	1 (2)	1 (3)	0 (0.0)
Transplant–related mortality	20 (35)	5 (16)	15 (58)
Cardiac toxicity	1	1	0
Graft rejection/BM failure	3	0	3
GvHD	7	3	4
Hemorrhage	4	1	3
Renal failure	2	0	2
Respiratory failure	2	0	2
VOD	1	0	1

Rondelli et. Al. ASCO 2010

MPD-RC 101/107: Interim analysis



Rondelli et. Al. ASCO 2010

CONCLUSIONS

- Low rate of relapse
- High TRM remains
- MUD
  - Higher GVHD and TRM
  - More mismatch in Unrelated arm

Rondelli et. Al. ASCO 2010

Upcoming Transplant Trials

- Allo SCT preceded by JAK2 inhibition (Ruxolitinib) with goals of improving performance status, time to engraftment, outcomes in MF

- MUD Allo SCT trial with post transplant RAD001 to impact GVHD and decrease TRM

MPD Research Consortium

Clinical Trials

Protocol 101 -Study of Fludarabine Based Conditioning for Allogeneic Stem Cell Transplantation for Myelofibrosis

Protocol 102 -Open-Label, Phase 1/2 Study of VELCADE (Bortezomib) for Injection in Subjects with Myelofibrosis with Myeloid Metaplasia (MMM)

Protocol 103 -Phase II Study of Bevacizumab (Avastin®) in Myelofibrosis

Protocol 104 -CEP-701 (Lestaurtinib) in Myelofibrosis

Protocol 26866138-CAN-2002, VEL-04-118 (Ex Bortezomib- IM)

An Open-Label, Phase 1/2 Study of VELCADE® (Bortezomib) for Injection in Subjects with Myelofibrosis with Myeloid Metaplasia (MMM) (MPD-RC 102)

Investigational Agent Bortezomib supplied by Janssen-Cilag

Study Chair

Giovanni Barosi. Laboratory of Clinical Epidemiology/Center for the Study of Myelofibrosis. IRCCS Policlinico S. Matteo Foundation, Pavia, Italy

Study Co-chair

Tiziano Barbui. Division of Hematology. Ospedali Riuniti di Bergamo, Bergamo, Italy

Ronald Hoffman, University of Illinois Cancer Center, Chicago, USA

Data Coordinator

Roberto Marchioli. Istituto Mario Negri Sud, Santa Maria Inbaro, Chieti, Italy.

Judith D. Goldberg, New York University School of Medicine, New York

CRO

GB Pharma, Italy

Barosi et. al. Am J Hematol 2010;85(9):616-9

Rationale

- Bortezomib directly induces **tumor cell death** by degrading several intracellular protein (p53,p21)
- Inhibits degradation of IkB and blocks multifunctional transcription factor NFkB leading to **reduction of growth factors** (IL-6, TGF-beta, VEGF)
- Indirectly **inhibits angiogenesis** and prevents tumor adaptation to hypoxia by functional inhibition of HIF-1 alpha

Barosi et. al. Am J Hematol 2010;85(9):616-9

Maximum Tolerated Dose

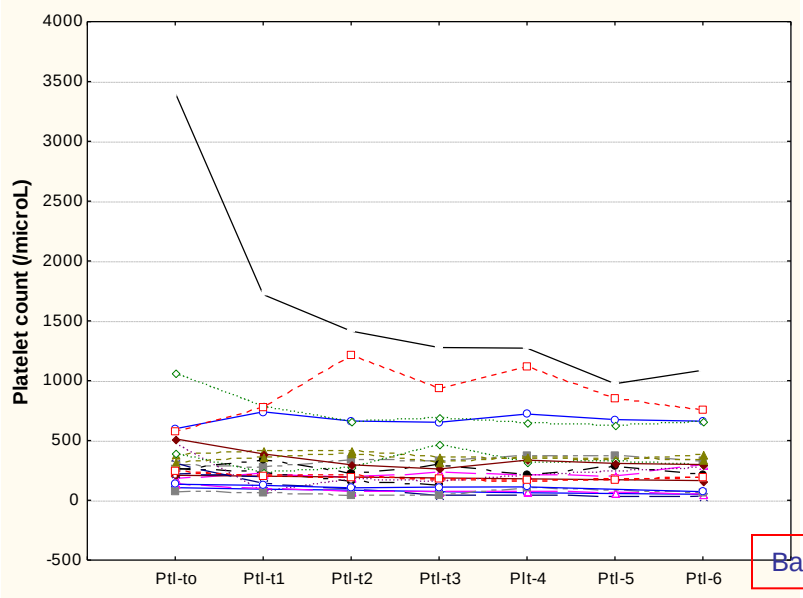
Dose Cohort	Patients Enrolled	Dose Limiting Toxicity
1 (0.8 mg/m^2/twice weekly)	3	0
2 (1 mg/m^2/twice weekly)	3	0
3 (1.3 mg/m^2/twice weekly)	6	1
Total	12	1

The MTD resulted to be 1.3 mg/m2/twice weekly

Barosi et. al. Am J Hematol 2010;85(9):616-9

Phase II: Intention to treat analysis (N=16)

Response	Number
Complete Response (complete response in anemia, splenomegaly, constitutional symptoms, platelet and leukocyte count)	**0/16**
Major response	**0/16**
Moderate response	**0/16**
Minor response (response in platelet count without progression in anemia, splenomegaly or constitutional symptoms)	**1/16**



Barosi et. al. Am J Hematol 2010;85(9):616-9

Toxicity Summary (N=22)

Event	All adverse events	Grade =>3 events
Thrombocytopenia	8 (36%)	3
Fatigue	4	0
Rush	2	0
Pyrexia	3	0
Dyspnoea with pulmonary distress syndrome	1	1
Dyspnoea with pulmonary hypertension	1	1
Cutaneous vasculitis	1	1
Peripheral neuropathy	1	0
Cutaneous infectious ulcer	1	1
Total	**22**	**7 (31.8%)**

Barosi et. al. Am J Hematol 2010;85(9):616-9

Clinico-hematological response- Conclusions

- MTD: 1.3 mg/m^2 given in 4 doses every 21 days
- The most frequently encountered toxicity: thrombocytopenia, occurring at all dose levels.
- Severe toxicities: 31.8%
- No complete to moderate clinico-hematological response. One minor response (platelet count decrease) by EUMNET criteria.
- The study was stopped after the first Simon's stage of the phase II
- 50-60% of patients had a myeloproliferative reaction (leukocytosis and increase in splenomegaly)

Barosi et. al. Am J Hematol 2010;85(9):616-9

Conclusion on cellularity, CD34%, and fibrosis of bone marrow during bortezomib

- Bortezomib produces a non statistically significant reduction in bone marrow cellularity that is some case is biologically significant.
- Few cases showed a reduction in bone marrow CD34+ cells
- Bone marrow fibrosis did not change significantly during treatment. Few cases had an increase in bone marrow fibrosis
- Plasma TGF-beta did not show any change during therapy

Barosi et. al. Am J Hematol 2010;85(9):616-9

MPD Research Consortium

Clinical Trials

Protocol 101 -Study of Fludarabine Based Conditioning for Allogeneic Stem Cell Transplantation for Myelofibrosis

Protocol 102 (Europe Only) -Open-Label, Phase 1/2 Study of VELCADE (Bortezomib) for Injection in Subjects with Myelofibrosis with Myeloid Metaplasia (MMM)

Protocol 103 -Phase II Study of Bevacizumab (Avastin®) in Myelofibrosis

Protocol 104 -CEP-701 (Lestaurtinib) in Myelofibrosis

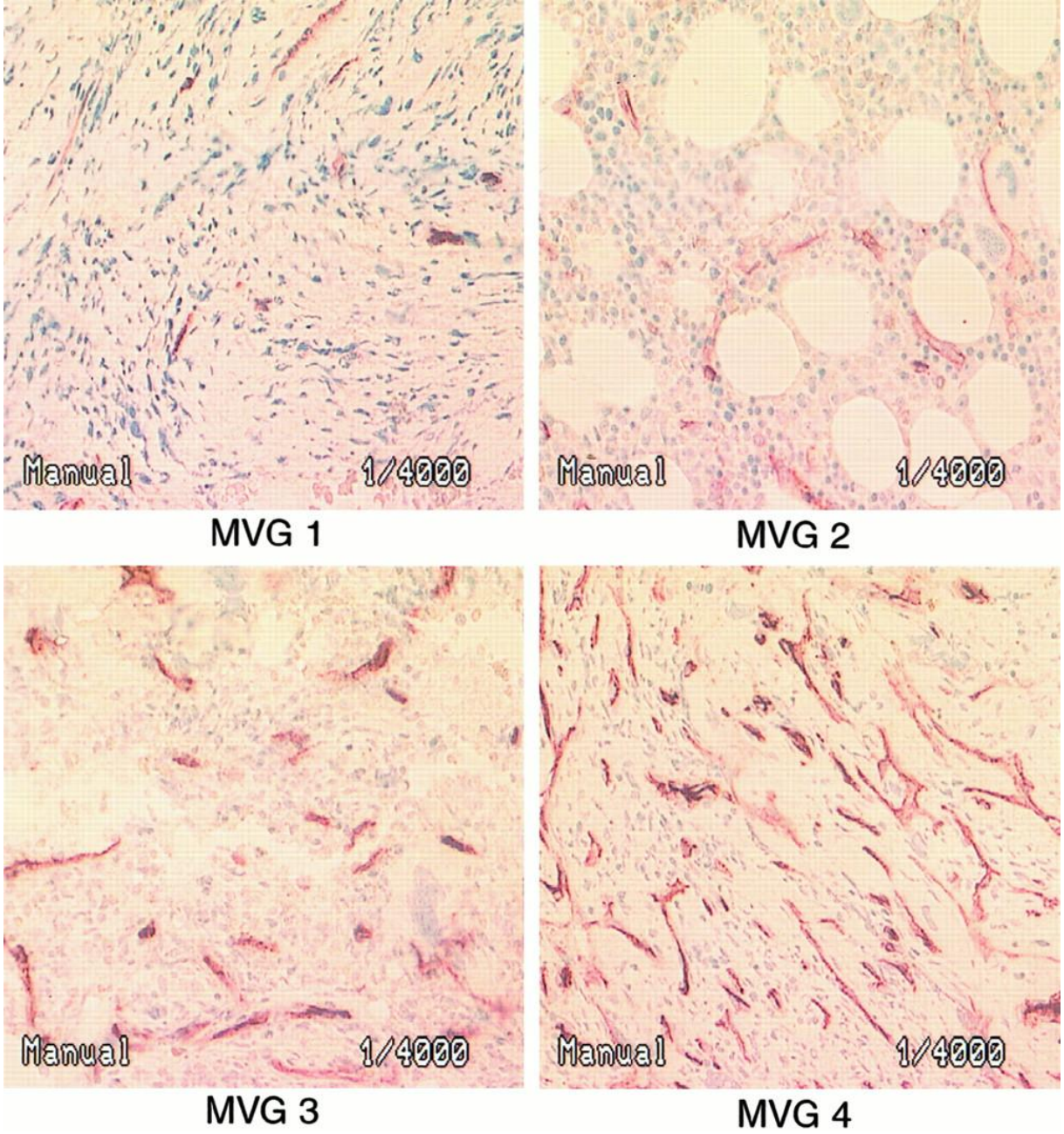


Figure 1: Marked Increases in Angiogenesis in Myelofibrosis

Silver et. al. EHA 2010

•Patients received bevacizumab at a dose of 15 mg/kg intravenously on day 1 of a 21-day cycle for 4 cycles.

• Patients were evaluated for response after cycle 4 and 8.

• Non-responders would go off study after cycle 8, responders could receive up to 17 cycles.

Silver et. al. EHA 2010

Demographics					*Baseline Features at Trial Entry*					
Pt ID	**Gender**	**Age**	**MF Type**	**Date Diagnosis**	**Spleen Size (cm BLCM)**	**Hb g/dL**	**Platelets X 10^9/L**	**WBC X 10^9/L**	**DIPSS MF Risk at Enrollment**	**Jak2 V617F Mutation Status**
1	M	85	Post ET MF	Apr-10-2008	0	8.4	411	9.9	High	Wild type
2	M	71	PMF	May-01-2006	5	7.6	93	4.3	High	Wild type
3	M	72	PMF	Jun-28-2004	22	9.5	257	16.7	High	Mutated
4	M	76	PMF	Oct-02-2007	4	8.9	313	7.6	High	*Unknown*
5	M	56	PMF	Oct-01-2005	24	10.7	289	17.3	Intermediate 1	Wild type
6	M	61	Post ET MF	Jan-02-2008	8	9.9	131	2.1	Intermediate 2	Mutated
7	F	49	PMF	Jul-15-1996	0	8.8	115	3.5	Intermediate 2	Wild type
8	M	77	Post PV MF	May-20-2008	0	9.0	30	30.2	High	Mutated
9	M	73	PMF	Feb-12-2008	19	8.0	125	77.5	High	Mutated
10	F	59	PMF	Feb-27-2008	0	10.2	283	2.0	Intermediate 1	Wild type
11	M	81	Post ET MF	Jul-13-2007	9	10.4	287	59.7	High	Mutated
12	F	64	PMF	Sep-17-2008	5	10.3	78	36.5	Intermediate 2	Wild type
13	M	81	Post PV MF	Jun-15-2000[i]	22	2.6	378	24.6	High	Mutated

Silver et. al. EHA 2010

PT ID	Enrollment	Reason for Cessation	Date Off Study	Cycle 1 Given?	Cycle 2 Given?	Cycle 3 Given?	Cycle 4 Given?	Cycle 5 Given?	Cycle 6 Given?	Cycle 7 Given?	Cycle 8 Given?
1	May-07-2008	Patient's refusal	Sep-30-2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	-
2	Jun-17-2008	Death	Jul-12-2008	Yes	-	-	-	-	-	-	-
3	Jun-17-2008	Physician's decision	Jul-24-2008	Yes	-	-	-	-	-	-	-
4	Jun-18-2008	Patient's refusal	Sep-10-2008	Yes	Yes	Yes	Yes	-	-	-	-
5	Jul-07-2008	Patient's refusal	Sep-29-2008	Yes	Yes	-	-	-	-	-	-
6	Jul-10-2008	Patient's refusal	Jul-31-2008	No	-	-	-	-	-	-	-
7	Aug-04-2008	Physician's decision	Jan-28-2009	Yes	Yes	Yes	Yes	Yes	Yes	-	-
8	Sep-12-2008	Patient's refusal	Sep-12-2008	No	-	-	-	-	-	-	-
9	Dec-04-2008	End of study	Jan-13-2009	Yes	Yes	-	-	-	-	-	-
10	Dec-11-2008	Physician's decision	Jun-04-2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
11	Dec-16-2008	Physician's decision	Apr-07-2009	Yes	Yes	Yes	Yes	No	-	-	-
12	Jan-23-2009	Physician's decision	Apr-07-2009	Yes	Yes	Yes	-	-	-	-	-
13	Mar-25-2009[i]	Physician's decision	Apr-28-2009	Yes	Yes	-	-	-	-	-	-

10 of 11 treated stopped early
- 5 for toxicity
- 1 Disease progression
- 4 patient choice

61% Grade 3 or 4 toxicity
No vascular events

Silver et. al. EHA 2010

Conclusions

- At this dose bevacizumab was not well tolerated largely from constitutional symptoms
- It is difficult to make an assessment of the impact of bevacizumab on the biology due to inadequate exposure
- Combination therapy with lower doses may still be worth considering given solid tumor experience

Silver et. al. EHA 2010

MPD Research Consortium

Clinical Trials

Protocol 101 -Study of Fludarabine Based Conditioning for Allogeneic Stem Cell Transplantation for Myelofibrosis

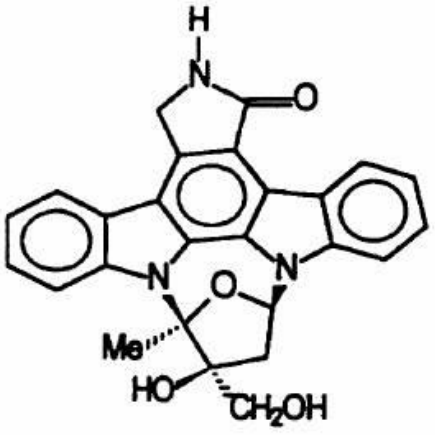
Protocol 102 (Europe Only) -Open-Label, Phase 1/2 Study of VELCADE (Bortezomib) for Injection in Subjects with Myelofibrosis with Myeloid Metaplasia (MMM)

Protocol 103 -Phase II Study of Bevacizumab (Avastin®) in Myelofibrosis

Protocol 104 -CEP-701 (Lestaurtinib) in Myelofibrosis

CEP-701 (lestaurtinib)

- Multikinase inhibitor targeting FLT3, JAK2 and Trk tyrosine kinases
- In vitro IC_{50} wild-type JAK2: 1 nM
- Selectively inhibits proliferation and JAK2/STAT signaling in primary cells from patients with MPN



Hexner et. al. ASH 2009

Dose Rationale

- Nausea/diarrhea previously most significant toxicity
- A true maximum tolerated dose for CEP-701 has not been identified
  - Highly protein bound in vivo
- AML studies (40 -100 mg BID):
  - Incomplete target inhibition
- Formulation change
  - May improve tolerability

DOSE LEVEL	DOSE
1	80 mg BID (liquid)
2	100 mg BID (liquid)
2a	100 mg BID (capsules)
3	120 mg BID (capsules)
4	140 mg BID (capsules)
5	**160 mg BID (capsules)**

Hexner et. al. ASH 2009

Baseline Characteristics

Ph- MPN	**PMF**	**PV MF**	**ET MF**
MPN subtype	16 (62%)	7 (26%)	3 (12%)
History of hemorrhagic events	4 (25%)	5 (71%)	0
History of thrombotic events	5 (31%)	2 (29%)	1(33%)
Transfusion dependent (13/50%)	10	2	1
Prognostic Group*			
High (Lille Score 2)	2 (13%)		
Intermediate (Lille Score 1)	16 (62%)		

*For 8 subjects (30%) symptomatic splenomegaly was reason for inclusion

Hexner et. al. ASH 2009

Early (28 Day) Gastrointestinal Toxicity
capsule formulation, 100-160 mg (n=19)

Gastrointestinal	Grade 1	Grade 2	Grade 1/2 (%)	Grade 3
Diarrhea	5	2	37%	1 (DLT)
Nausea	6	1	37%	0
Vomiting	0	0	0%	0
Dyspepsia	1	1	11%	0
Anorexia	2	0	11%	0
Constipation	1	0	5%	0
Dry mouth	1	0	5%	0
Flatulence	0	1	5%	0
GI- other	0	1	5%	0

Hexner et. al. ASH 2009

Early (28 Day) Toxicity
liquid and capsule formulation
80-160 mg; n=26

Adverse Event	Grade 1	Grade 2
Fatigue	3	1
AST/ALT elevation	3	0
Alk. Phos. Elevation	2	0
Hypoalbuminemia	1	0
Increased serum Cr	1	0
Bone pain	1	0
Myalgias	1	0
Weight loss	1	0
Agitation	1	0
Ataxia	1	0

Hexner et. al. ASH 2009

Effect on Clinical Parameters
Patients on Treatment for 12+ Weeks

- No significant change in white blood and platelet counts
  - 2 patients with marked increase in wbc
- No significant change in hemoglobin or transfusion requirements
- Spleen size reduced from baseline by median of 5.8 cm
  - range: decrease of 14 cm to and increase 7 cm
  - 6 decreases, 2 no change, 3 increases

Hexner et. al. ASH 2009

MPD Research Consortium

Clinical Trials – Laboratory Studies

Protocol 105 - Familial Myeloproliferative Disorders

Protocol 106 - Research Tissue Bank

Protocol 107- Correlative Biomarker Study

Myeloproliferative Disorders (MPD) Research Consortium

Tissue Bank Core C

PI: Rona Singer Weinberg, PhD

Co-PI: Alessandro Rambaldi, MD

Specific Aim 1: Receive, process, and store tissues from MPN patients diagnosed at MPD-RC clinical sites in an efficient and organized way.

Table 1. Patient/Sample Accrual										
	Biobank				Correlative Biomarkers					Familial
	106				101	102	103	104	107	105
Trial					BMT	Bortezo-mib	Bevacizu-mab	Cep-701	Total	
First Patient	9/07				5/07	1/07	5/08	5/08		7/08
Diagnosis	PV	ET	MF	Total	MF	MF	MF	MF		MPN
NY	176	109	92	377	39	0	12	27	83	4
Italy	52	61	20	133	11	11	0	0	22	15
Total	228	170	112	510	50	11	12	27	106	20

NewYork BloodCenter

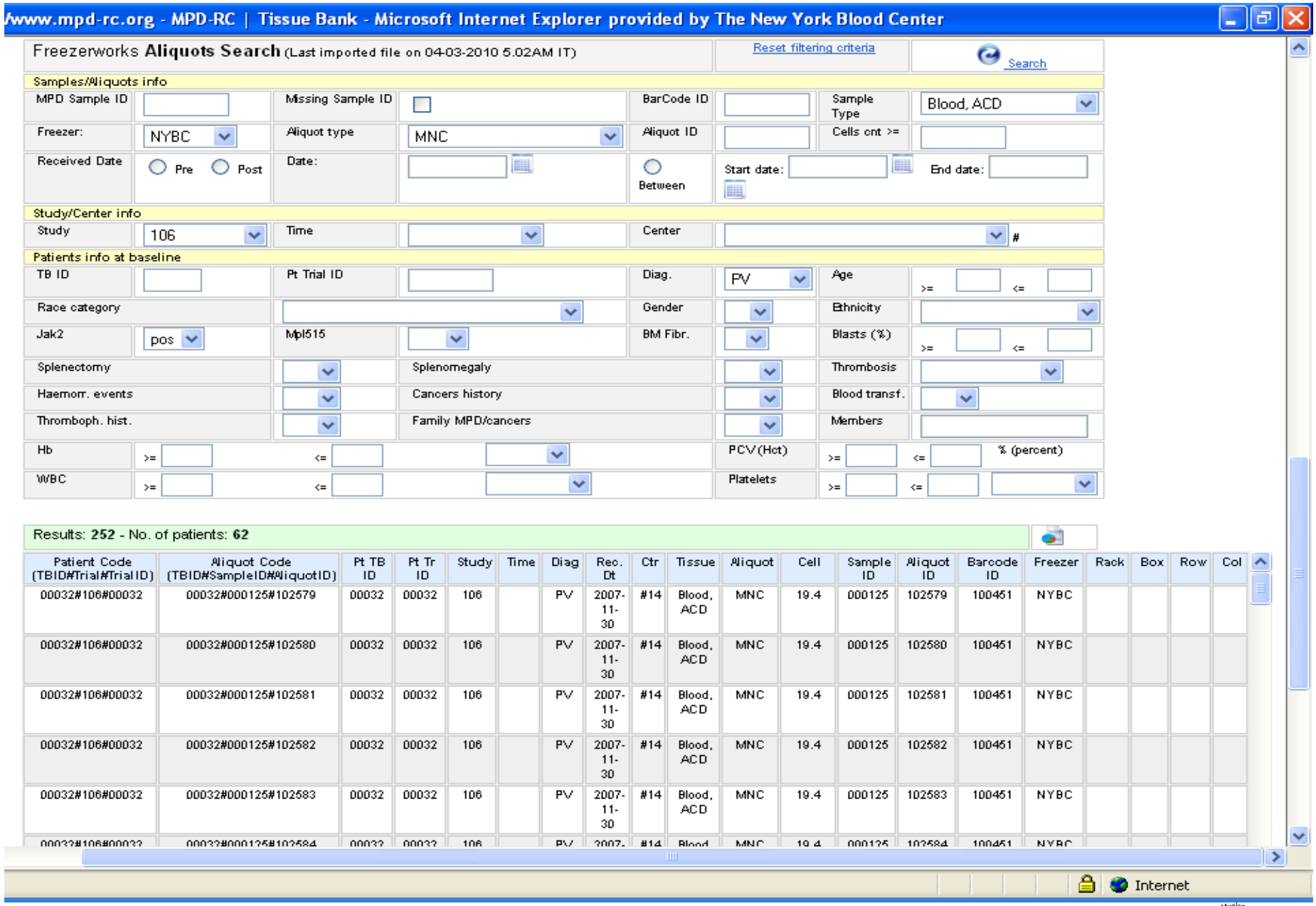
MPD-RC Myeloproliferative Disorders Research Consortium

Specific Aim 1: Receive, process, and store tissues from MPN patients diagnosed at MPD-RC clinical sites in an efficient and organized way.

Table 2. Individual Patients with Tissue Available for Distribution										
	Biobank				Correlative Biomarkers					Familial
	106				101	102	103	104	107	105
Trial					BMT	Bortezo-mib	Bevacizu-mab	Cep-701	Total	
First Patient	9/07				5/07	1/07	5/08	5/08		7/08
Diagnosis	PV	ET	MF	Total	MF	MF	MF	MF	MF	MPN
Blood										
MNC	106	145	98	349	47	10	12	25	94	17
Granulo-cytes	154	128	92	374	47	10	12	25	94	17
Plasma	166	148	97	411	48	10	12	25	95	14
Platelets	184	145	101	426	48	10	12	25	95	13
Bone Marrow										
MNC	36	46	17	99	36	3	5	9	53	0
Spleen	0	0	0	0	0	0	0	0	0	0
Toe nails	103	98	52	253	29	8	11	15	63	0
Slides	40	58	18	116	45	4	11	24	84	0

NewYork BloodCenter

MPD-RC Myeloproliferative Disorders Research Consortium



NewYork BloodCenter

MPD-RC Myeloproliferative Disorders Research Consortium

MPD-RC

1. Who is the MPD-RC?
2. What has been learned from prior trials?
3. Which trials are ongoing?

MPD Research Consortium

Clinical Trials – Open

Protocol 108 - Phase II, Randomized, Double-Blind Control International Study Using Clopidogrel and Aspirin for the Treatment of Polycythemia Vera

Protocol 109- A Phase I/II Study of Vorinostat (Suberoylanilide Hydroxamic Acid [SAHA]) in Combination with Azacitidine in Patients with Primary Myelofibrosis (PMF) or Myelofibrosis Following Polycythemia Vera or Essential Thrombocythemia

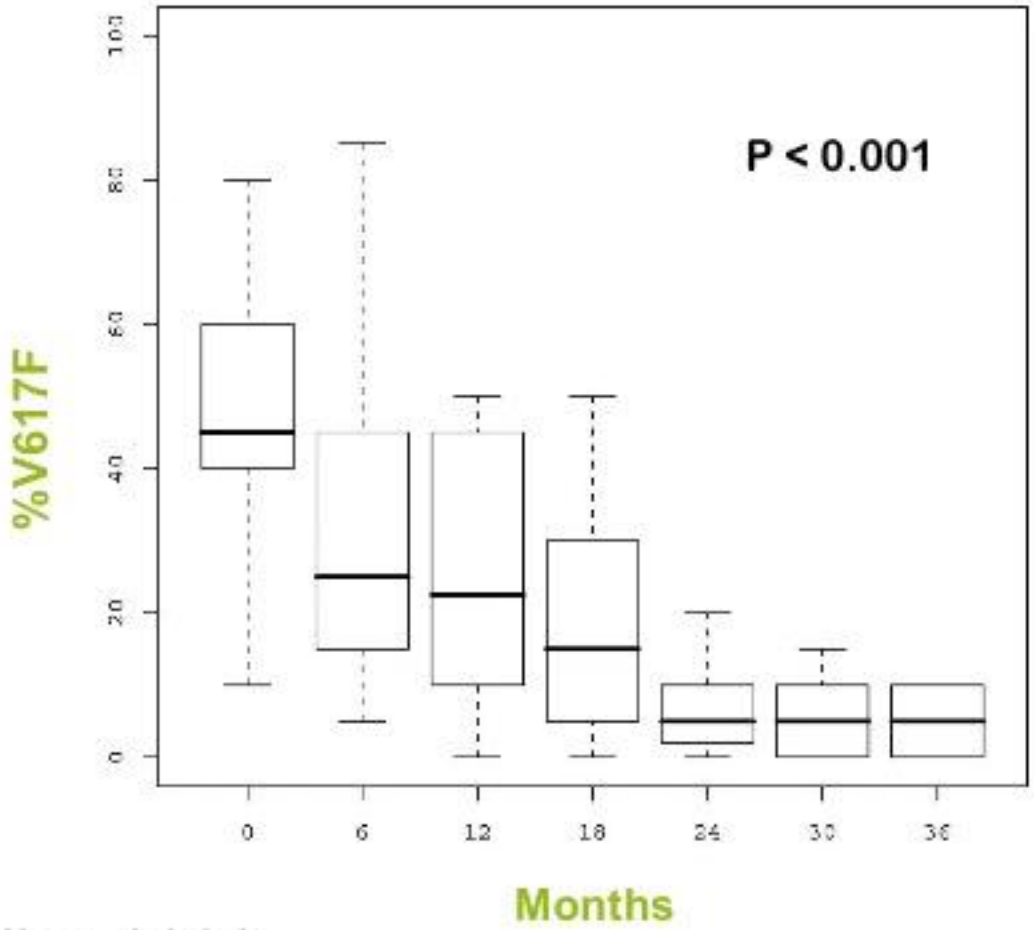
MPD Research Consortium

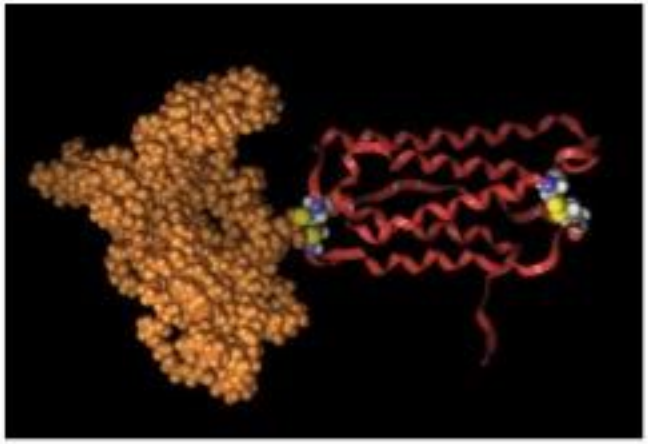
Clinical Trials – Opening

Protocol 111 – Single arm phase II trial Pegylated Interferon Alpha-2a in High Risk ET and PV patients whom are resistant or intolerant to hydroxyurea

Protocol 112- A randomized phase III trial of pegylated interferon alpha -2a vs. hydroxyurea in newly diagnosed patients with high risk ET and PV

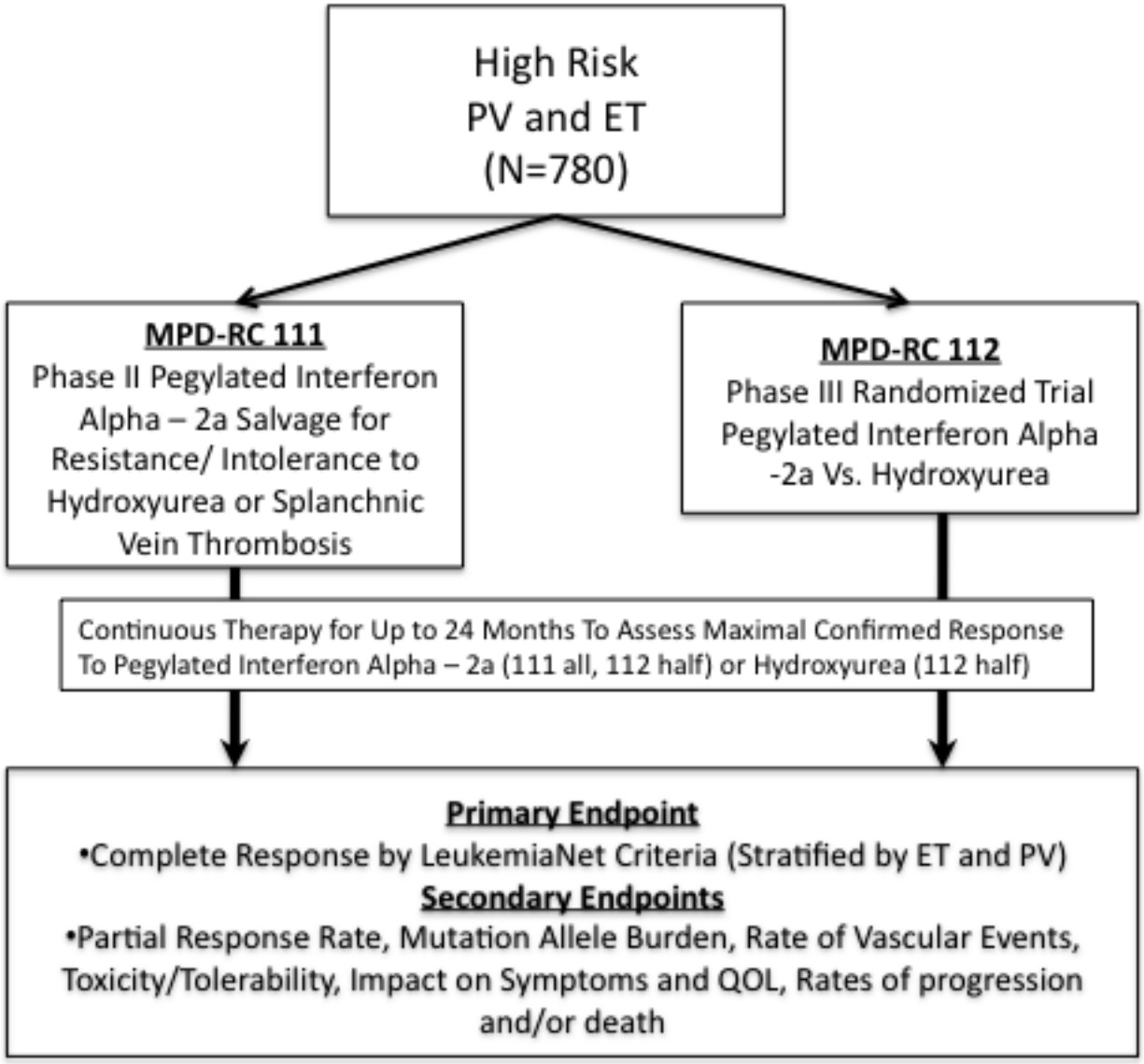
PEG-IFN is able to induce molecular remission in patients with PV





Kiladjian 2008

Pegylated Interferon Alpha–2a in Polycythemia Vera (PV) and Essential Thrombocythemia (ET)
Myeloproliferative Disorders Research Consortium (MPD-RC)



Conclusions

1. The MPD-RC represents the only international cooperative group currently organizing therapeutic clinical trials

2. The infrastructure of the MPD-RC allows valuable correlative studies to be done in conjunction with clinical trials

3. Completed trials have provided valuable negative results with bortezomib and bevacizumab, and helpful steps for allo SCT and CEP701

4. Future trials in all forms of MPNs are ongoing or planned

Ackowledgements

Centers-USA

Mayo Clinic Arizona
Emory University, Winship Cancer Institute

Duke University
Geisinger Cancer Center
Georgetown University Medical Center

John H. Stroger Hospital of Cook County

Johns Hopkins University School of Medicine

Mount Sinai Medical Center
Ohio State University
Roswell Park Cancer Institute
The Palo Alto Clinic
University of California at San Francisco

University of Illinois at Chicago
University of Maryland
University of Pennsylvania School of Medicine

University of Utah
Weill Cornell Medical College
Princess Margaret Medical Center

Centers-Europe

Cliniques Universitaires Saint-Luc

Hopitaux de Paris
Hopital Claude Huriez, Lille
Hopital de la Cavale Blanche, Brest
Institute Paoli-Calmettes, Marseille
Ospedali Riuniti de Bergamo
Ospedale San Martino Genova
San Matteo Hospital
Universita Cattolica del Sacro Cuore
University of Florence
VU University Medical Centre, Amsterdam

Erasmus Medical Center Rotterdam
Stockholm South Hospital, Sweden
Sahlgrenska University Hospital Hematology Section, Medical Dept.
Guy's and St Thomas' NHS Foundation Trust

Belfast City Hospital, Belfast
Royal Hallamshire Hospital, Sheffield
University of Cambridge