

Myeloma
Update on Research and Treatment from the
American Society of Hematology (ASH®) Annual Meeting

someday
is today

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LYMPHOMA
SOCIETY
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Welcome & Introductions

Myeloma

Update on Research and Treatment from the American Society of Hematology (ASH®) Annual Meeting

This program is not sponsored, sanctioned by, or part of the 55th Annual Meeting
of the American Society of Hematology (ASH®)

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Principal Investigator, MD Anderson SPORE in Multiple Myeloma
Chair, Southwest Oncology Group Myeloma Committee



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Cancer Center**
Making Cancer History®



Outline

- **Disease biology**
- Asymptomatic myeloma
- Non-transplant therapies
- Induction before transplant
- Options for therapy after transplant
- Relapsed and/or refractory myeloma
- Aspects of supportive care in myeloma



2013 ASH Abstract 529

Co-existent Hyperdiploidy does not Abrogate the Poor Prognosis Associated with Adverse Cytogenetics in Myeloma

Charlotte Pawlyn, Lorenzo Melchor, Eileen M Boyle, Annamaria Brioli, Martin F Kaiser, Walter Gregory, Mark T Drayson, Graham Jackson, Fiona M Ross, J. Anthony Child, Gareth J Morgan, and Faith E Davies

Hyperdiploidy +/- Other Lesions

- Hyperdiploidy usually means good prognosis

Cytogenetics	Patient #s	PFS (Months)	OS (months)
HD w/o Adverse lesions	304	23	60.9
HD + Del 17p	20	19.1 (p=0.019)	35.2 (p=0.003)
HD + 1q+	142	15.4 (p<0.001)	38.1 (p<0.001)
HD + Adverse Translocation	9	15.4 (p=0.272)	40.1 (p=0.180)
HD + >1 lesion	24	12.1 (p<0.001)	19.9 (p<0.001)

- Hyperdiploidy overcome by poor risk lesions

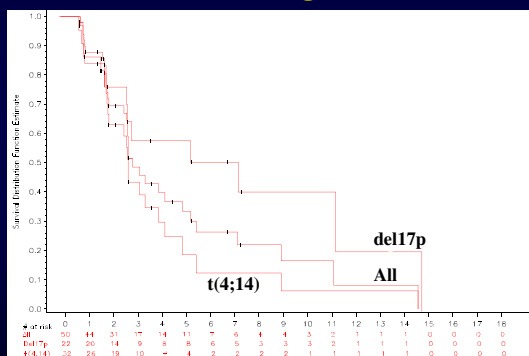
2013 ASH Abstract 689

Pomalidomide + Low-dose Dexamethasone in Relapsed or Refractory Multiple Myeloma with Deletion 17p and/or Translocation t(4;14)

Xavier Leleu, Lionel Karlin, Margaret Macro, Cyrille Hulin, Laurent Garderet, Murielle Roussel, Bertrand Arnulf, Brigitte Pegourie, Brigitte Kolb, Anne-Marie Stoppa, Sabine Brechiniac, Mauricette Michallet, Gerald Marit, Claire Mathiot, Anne Banos, Laurence Lacotte, Mourad Tiab, Mamoun Dib, Jean-Gabriel Fuzibet, Marie-Odile Petillon, Philippe Rodon, Marc Wetterwald, Bruno Royer, Laurence Legros, Lotfi Benboubker, Olivier Decaux, Denis Caillot, Martine Escoffre-Barbe, Jean Paul Fermand, Philippe Moreau, Michel Attal, Hervé Avet-Loiseau, and Thierry Facon

Pomalidomide and Deletion 17p

Time to Progression



- Response rate with pom/dex comparable in patients \pm del 17p
- Pom may overcome this poor risk lesion

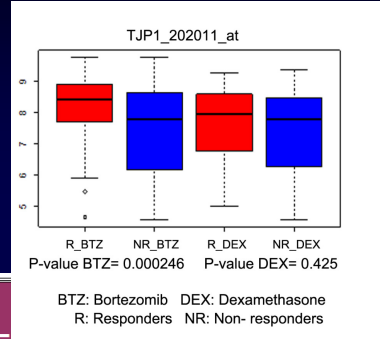
2013 ASH Abstract 123

Identification of Tight Junction Protein (TJP)-1 as a Modulator and Biomarker of Proteasome Inhibitor Sensitivity in Multiple Myeloma

Xing-Ding Zhang, Verrabhadran Baladandayuthapani, Heather Lin, George Mulligan, Bin Li, Dixie-Lee Esseltine, Lin Qi, Jian-Liang Xu, Walter Hunziker, Bart Barlogie, Saad Usmani, Qing Zhang, John Crowley, Bing-Zong Li, Hui-Han Wang, Jie-Xin Zhang, Isere Kuitatse, Jin-Le, Tang, Hua Wang, Richard Eric Davis, Wen-Cai Ma, Zhi-Qiang Wang, Lin Yang, and Robert Z. Orlowski

TJP1 Sensitizes to Bortezomib

- High TJP1 = Good response to bortezomib



	Median TTP (days)	L
TJP1_202011_at (P-value = 0.026)		
1 st tertile	92	78
2 nd tertile	147	87
3 rd tertile	179	127
TJP1_214168_at (P-value = 0.018)		
1 st tertile	109	84
2 nd tertile	139	94
3 rd tertile	158	93

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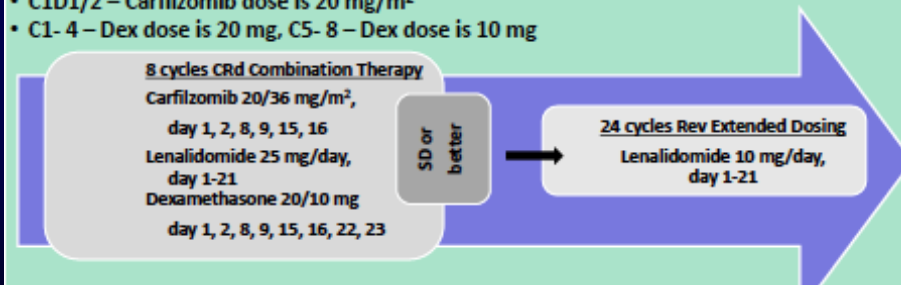
2013 ASH Abstract 1939

Clinical and Correlative Pilot Study of Carfilzomib, Lenalidomide, and Dexamethasone Followed by Lenalidomide Extended Dosing (CRd – R) in High Risk Smoldering Multiple Myeloma Patients

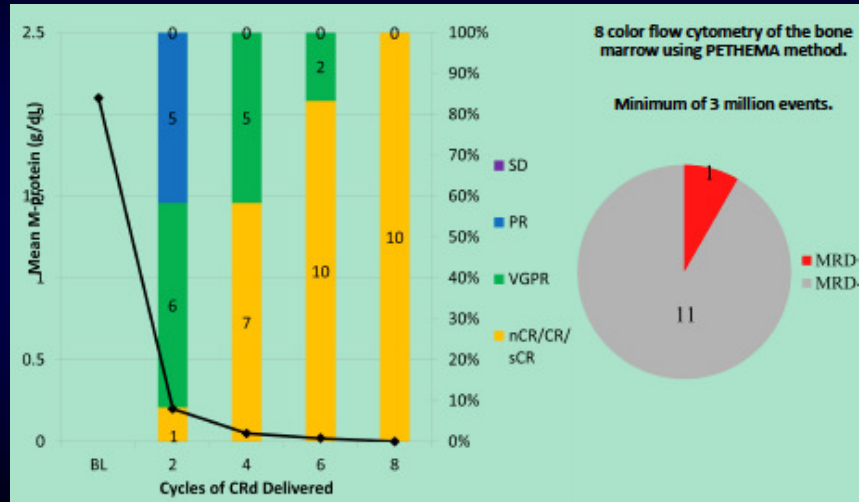
Ola Landgren, Sham Mailankody, Mary Kwok, Elisabet E. Manasanch, Manisha Bhutani, Nishant Tajeja, Dickran Kazandjian, Adriana Zingone, Rene Costello, Debra Burton, Yong Zhang, Peter Wu, George Carter, Marcia Mulquin, Diamond Zuchlinski, Irina Maric, Katherine R Calvo, Raul C. Braylan, Constance Yuan, Maryalice Stetler-Stevenson, Diane C Arthur, Liza Lindenberg, Karen Kurdziel, Peter Choyke, Seth M. Steinberg, Mark Roschewski, and Neha Korde

Study Design

- Each cycle is 28 days.
- Patients younger than 75 years underwent stem cell harvest after 4 cycles of CRd and continued therapy.
- C1D1/2 – Carfilzomib dose is 20 mg/m²
- C1- 4 – Dex dose is 20 mg, C5- 8 – Dex dose is 10 mg



Response Rate and Quality



Toxicities

Non-Hematologic	Grade 3/4, n(%)
Electrolyte disturbances	3(25)
LFT elevation	2(17)
Rash/Pruritus	3(25)
Acute kidney injury	2(17)
Heart Failure	1(8)
Dyspnea	1(8)
Infections	1(8)
VTE	1(8)
Diarrhea	1(8)
Hyperglycemia	1(8)
Hematologic	Grade 3/4, n(%)
Lymphopenia	5(42)
Anemia	2(17)
Neutropenia	1(8)
Thrombocytopenia	3(25)

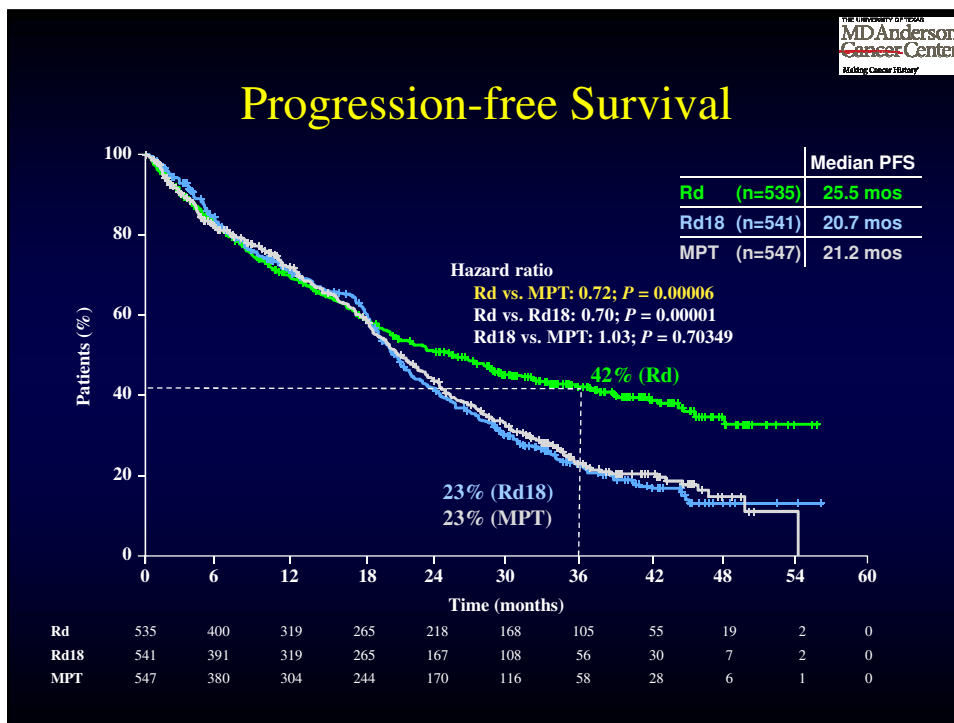
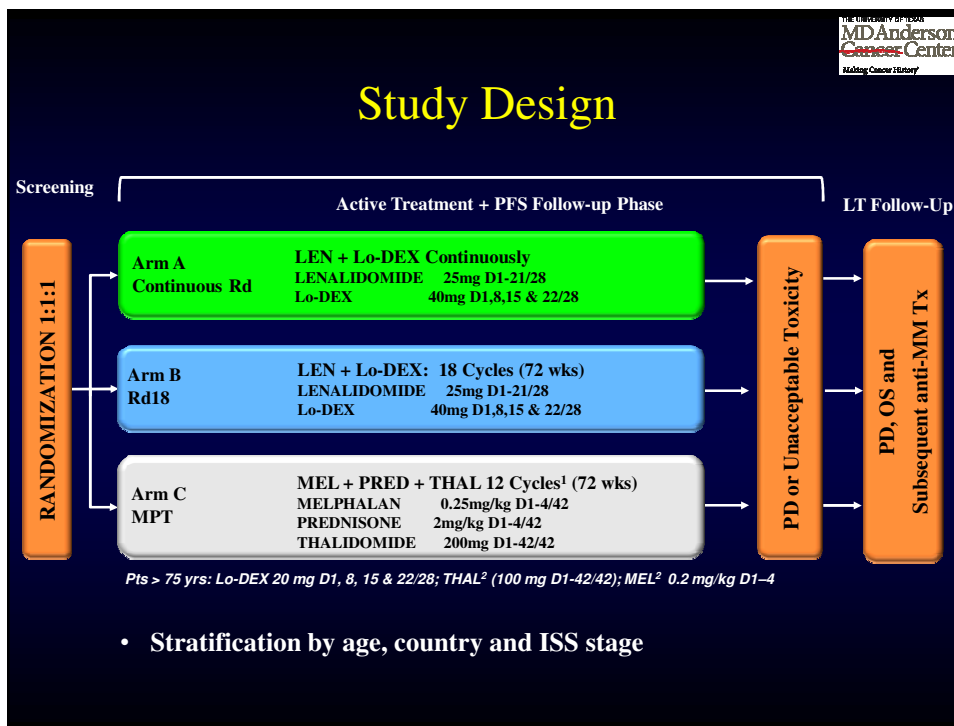
Outline

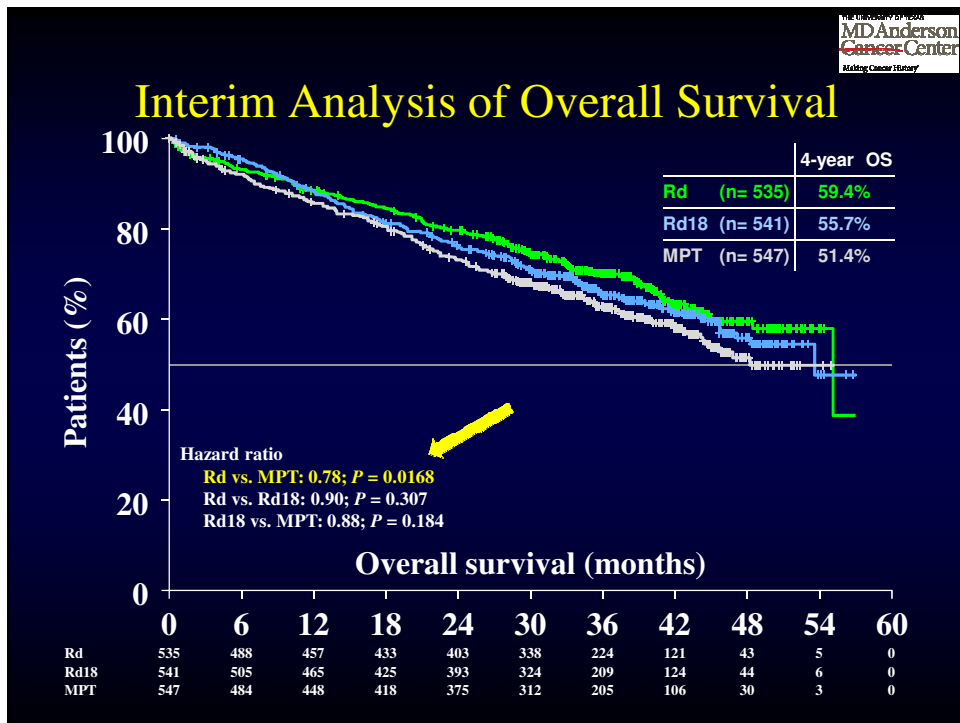
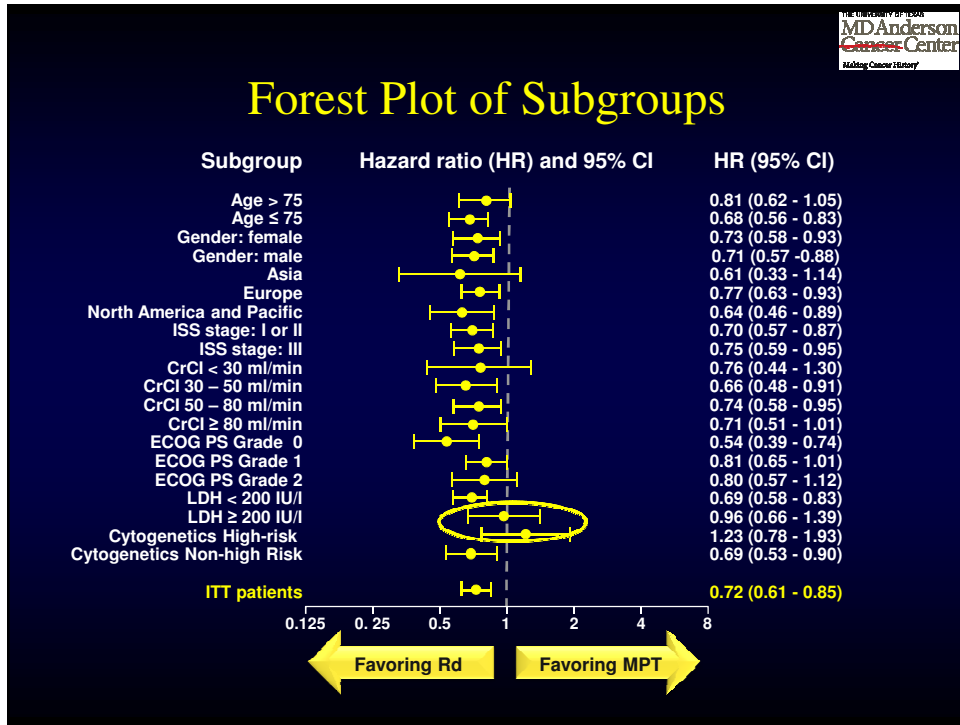
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2013 ASH Abstract 2

Initial Phase 3 Results of the FIRST (Frontline Investigation of Lenalidomide + Dexamethasone vs. Standard Thalidomide) Trial (MM-020/IFM 07 01) in Newly Diagnosed Multiple Myeloma Patients Ineligible for Stem Cell Transplantation

Thierry Facon, Meletios A. Dimopoulos, Angela Dispenzieri, John V. Catalano, Andrew R Belch, Cyrille Hulin, Michele Cavo, Antonello Pinto, Katja Weisel, Heinz Ludwig, Nizar J. Bahlis, Anne Banos, Mourad Tiab, Michel Delforge, James D Cavenagh, Catarina Geraldles, Je-Jung Lee, Christine I. Chen, Albert Oriol, Javier De La Rubia, Lugui Qiu, Darrell J. White, Daniel Binder, Kenneth C. Anderson, Philippe Moreau, Michel Attal, Robert Knight, Guang Chen, Jason Van Oostendorp, Christian J. Jacques, Annette Ervin-Haynes, and Lofti Benboubker





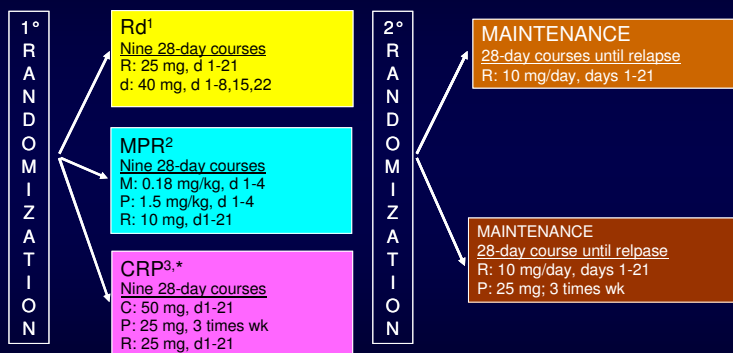
2013 ASH Abstract 536

A Randomized Phase 3 Trial of Melphalan-Lenalidomide-Prednisone (MPR) or Cyclophosphamide-Prednisone-Lenalidomide (CPR) vs. Lenalidomide + Dexamethasone (Rd) in Elderly Newly Diagnosed Multiple Myeloma Patients

Antonio Palumbo, Valeria Magarotto, Sara Bringhen, Massimo Offidani, Giuseppe Pietrantuono, Anna Marina Liberati, Giulia Benevolo, Antonio Ledda, Milena Gilestro, Monica Galli, Francesca Patriarca, Mariella Genuardi, Nicola Giuliani, Renato Zambello, Adam Zdenek, Alessia La Fauci, Paolo Corradini, Antonietta Pia Falcone, Caterina Musolino, Davide Rossi, Patrizia Caraffa, Pellegrino Musto, Federica Cavallo, Roman Hajek, and Mario Boccadoro

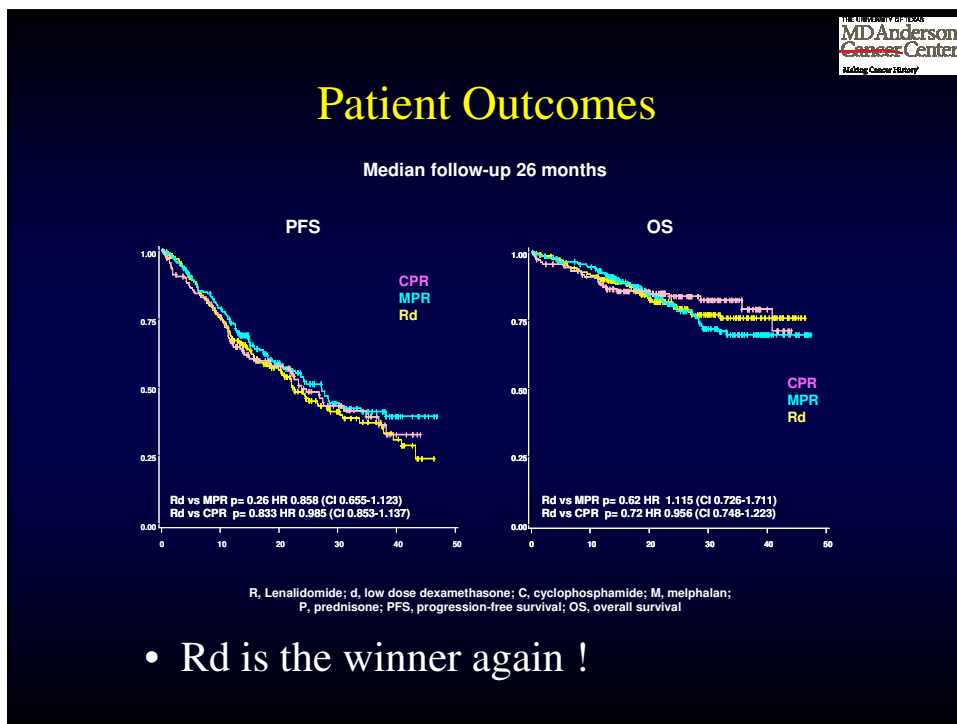
Study Design

- 660 patients have been randomized
- Symptomatic multiple myeloma patients not transplant-eligible



Reduction by age (>75 years): ¹Dexamethasone 20 mg/week; ²Melphalan 0.13 mg/Kg; ³Cyclophosphamide: 50 mg eod on days 1-21

* 59 CPR patients were treated with lower dose of Lenalidomide (10 mg) and Cyclophosphamide (50 mg eod) [Amendment 2, 2010, Aug]



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2013 ASH Abstract 405

PFS2 in Elderly Patients with Newly Diagnosed Multiple Myeloma (NDMM): Results from the MM-015 Study

Meletios A. Dimopoulos, Maria Teresa Petrucci, Robin Foà, John V. Catalano,
 Martin Kropff, Zhinuan Yu, Lara Grote, Christian J. Jacques, and Antonio Palumbo

Emerging Concept : PFS2

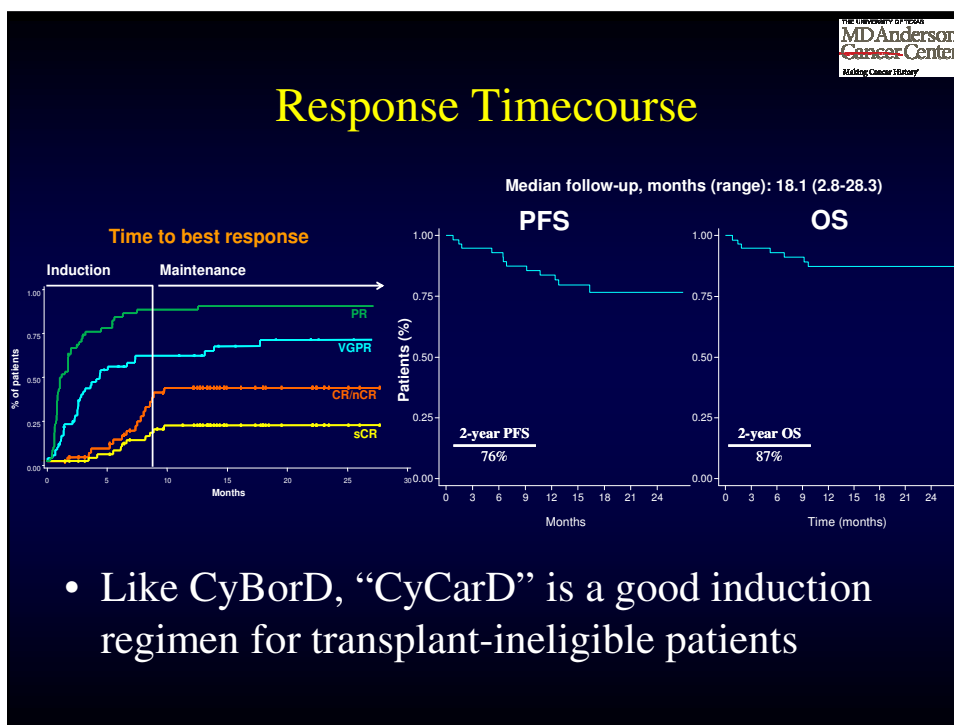
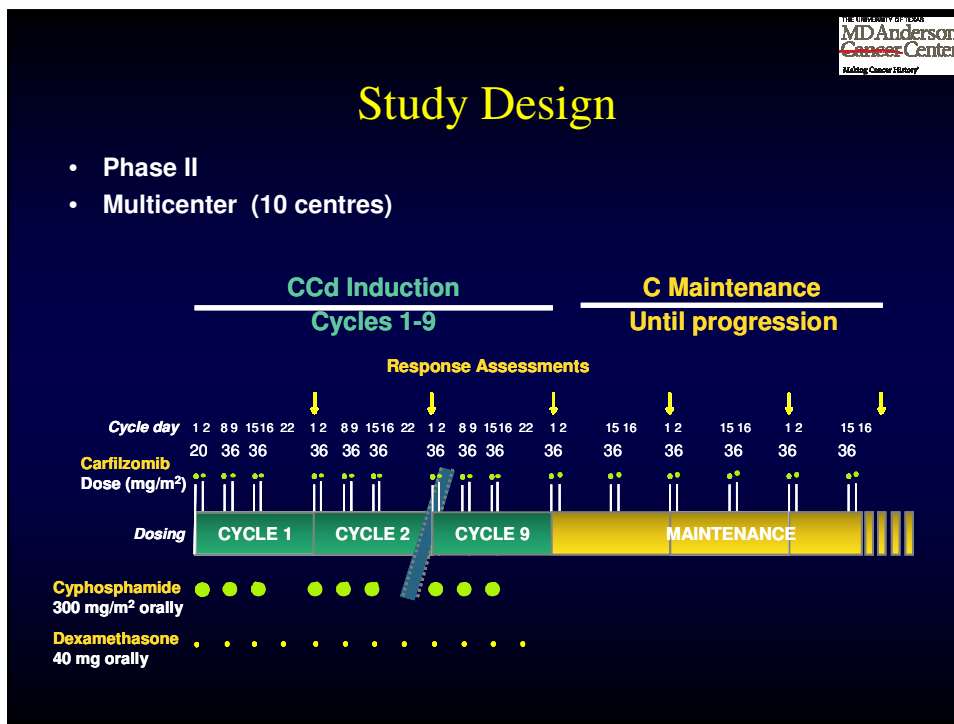
	MPR-R (n = 152)	MPR (n = 153)	MP (n = 154)
Any 2 nd Line	81 (53)	18 (77)	126 (82)
LEN	24 (30)	70 (59)	91 (72)
BORT	40 (49)	32 (27)	27 (21)
THAL	11 (14)	9 (8)	6 (5)
Other	31 (38)	23 (20)	22 (18)
PFS2	39.7 mos.		28.5 mos.

- Len maintenance does not induce growth of more drug-resistant myeloma clones

2013 ASH Abstract 685

A Phase II Study With Carfilzomib, Cyclophosphamide and Dexamethasone (CCd) For Newly Diagnosed Multiple Myeloma

Sara Brinthen, Chiara Cerrato, Maria Teresa Petrucci, Mariella Genuardi, Fabiana Gentilini, Concetta Conticello, Stefania Oliva, Lucia Pantani, Massimo Offidani, Carmela Palladino, Giulia Benevolo, Vittorio Montefusco, Monica Astolfi, Oreste Villani, Agostina Siniscalchi, Alberto Rocci, Lorenzo De Paoli, Mario Boccadoro, Pieter Sonneveld, and Antonio Palumbo



- Like CyBorD, “CyCarD” is a good induction regimen for transplant-ineligible patients

Outline

- Disease biology
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2013 ASH Abstract 688

Dose Escalation Phase 2 Trial of Carfilzomib Combined with Thalidomide and Low-Dose Dexamethasone in Newly Diagnosed, Transplant Eligible Patients with Multiple Myeloma: A Trial of the European Myeloma Network

Pieter Sonneveld, Emilie Asselberg-Hacker, Sonja Zweegman, Bronno van der Holt,
Marie Jose Kersten, Edo Vellenga, Marinus van Marwijk Kooy, Okke de Weerd,
Sarah Lonergan, Antonio Palumbo, and Henk Lokhorst

Study Design

Induction

4 cycles

Carfilzomib
20/27mg/m² days 1, 2,
8, 9, 15, 16 of a 28 day
cycle.

Thalidomide 200 mg
days 1-28 of a 28 day
cycle

Dexamethasone 40
mg days 1, 8, 15, 21 of
a 28 day cycle

Intensification

1 cycle

HDM
200 mg/m²
ASCT

Consolidation

4 cycles

Carfilzomib 27 mg/m²
days 1, 2, 8, 9, 15, 16
of a 28 day cycle.

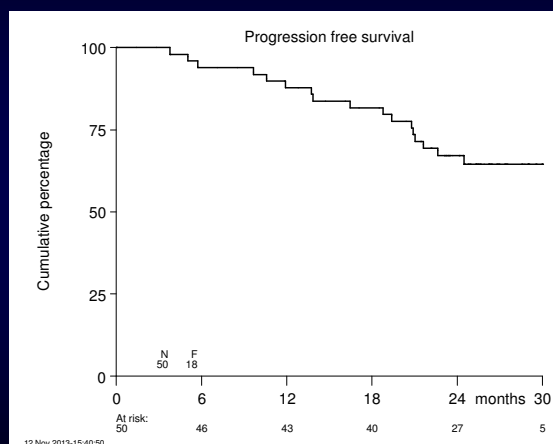
Thalidomide 50 mg
days 1-28 of a 28 day
cycle

Dexamethasone 40
mg days 1, 8, 15, 21 of
a 28 day cycle

Response Data

		Carfilzomib dose				Total	
		27 mg/m ²		36 mg/m ²			
		#	%	#	%	#	%
	Total	50		20		70	
After Induction	sCR/CR	9	18	3	15	12	17
	≥VGPR	29	58	16	80	45	64
	≥PR	46	92	19	95	65	93
After HDM	sCR/CR	15	30	7	35	22	31
	≥VGPR	34	68	16	80	50	71
	≥PR	47	94	20	100	67	96
After Consol	sCR/CR	28	56	8	40	36	51
	≥VGPR	43	86	16	80	59	84
	≥PR	47	94	20	100	67	96

Long-term Outcomes

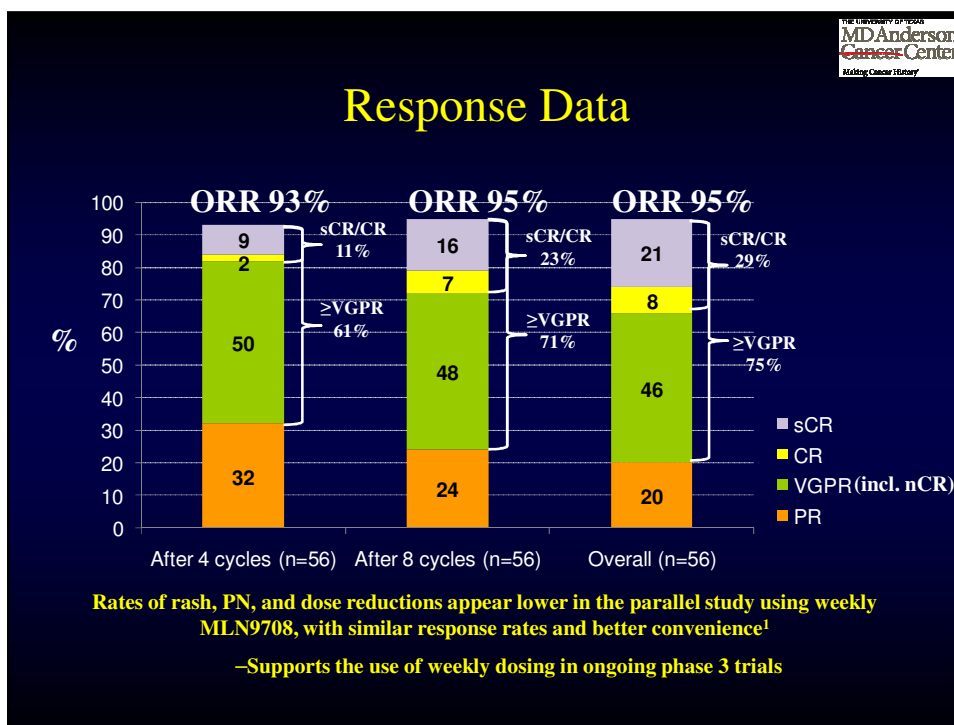
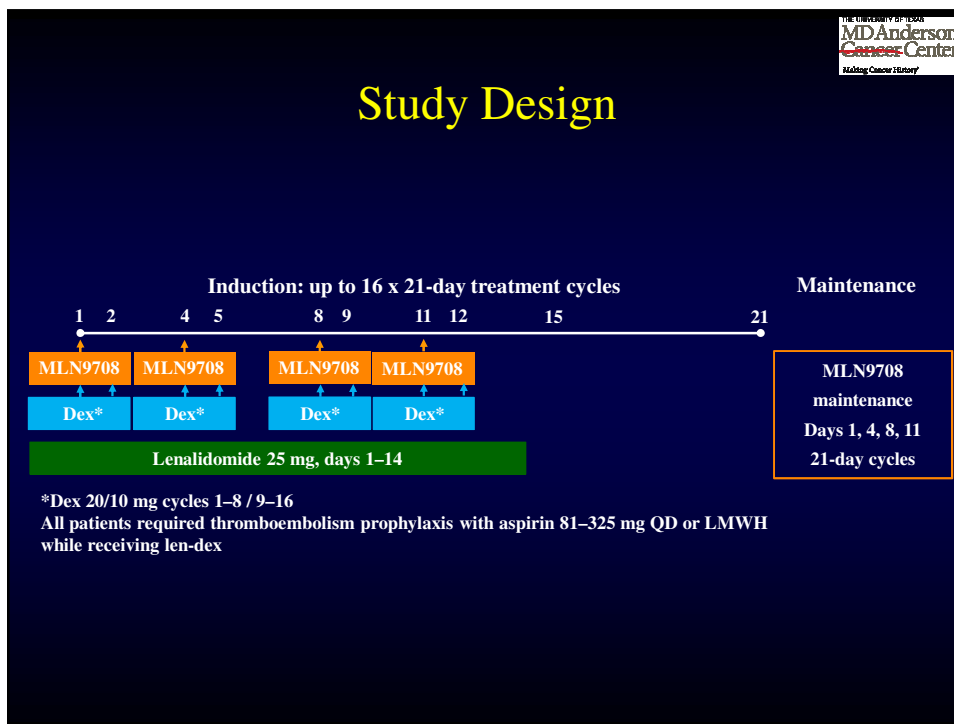


- Carfilzomib-based regimen with that is an excellent option prior to transplant
- Consolidation therapy deepens response further

2013 ASH Abstract 535

Twice-weekly Oral MLN9708 (Ixazomib Citrate), an Investigational Proteasome Inhibitor, in Combination with Lenalidomide and Dexamethasone in Patients with Newly Diagnosed Multiple Myeloma: Final Phase 1 Results and Phase 2 Data

Paul G. Richardson, Craig C Hofmeister, Cara A Rosenbaum, Myo Htut, David H. Vesole, Jesus Berdeja, Michaela Liedtke, Ajai Chari, Stephen D Smith, Daniel Lebovic, Deborah Berg, Eileen Liao, Neeraj Gupta, Alessandra Di Bacco, Jose Estevam, Ai-Min Hui and Rachid Baz



2013 ASH Abstract 538

Phase II Clinical and Correlative Study of Carfilzomib, Lenalidomide, and Dexamethasone Followed by Lenalidomide Extended Dosing (CRD-R) Induces High Rates of MRD Negativity in Newly Diagnosed Multiple Myeloma Patients

Neha Korde, Adriana Zingone, Mary L Kwok, Elisabet E. Manasanch, Manisha Bhutani, Nishant Tajeja, Dickran Kazandjian, Sham Mailankody, Rene Costello, Yong Zhang, Debra Burton, George Carter, Peter Wu, Marcia Mulquin, Diamond Zuchlinski, Irina Maric, Katherine R Calvo, Raul C. Braylan, Mark Roschewski, Constance Yuan, Maryalice Stetler-Stevenson, Diane C Arthur, Liza Lindenberg, Karen Kurdziel, Pete Choyke, Seth M. Steinberg, and Ola Landgren

Study Design

8 cycles CRd Combination Therapy

Carfilzomib 20/36 mg/m²,

day 1, 2, 8, 9, 15, 16

Lenalidomide 25 mg/day,

day 1-21

Dexamethasone 20/10 mg

day 1, 2, 8, 9, 15, 16, 22, 23

SD or
 better?

24 cycles Rev Extended Dosing

Lenalidomide 10 mg/day,
 day 1-21

Response Data

Response	2 cycles n/N (%)	8 cycles n/N (%)	Best response n/N (%)
ORR (\geq PR)	42/43 (98)	32/33 (97)	42/43 (98)
\geq VGPR	22/43 (51)	30/33 (91)	38/43 (88)
nCR/CR/sCR	7/43 (16)	24/33 (73)	29/43 (67)
CR/sCR	3/43 (7)	14/33 (42)	22/43 (51)
VGPR	15/43 (35)	6/33 (18)	9/43 (21)
PR	20/43 (47)	2/33 (6)	4/43 (9)
SD	1/43 (2)	1/33 (3)	1/43 (2)

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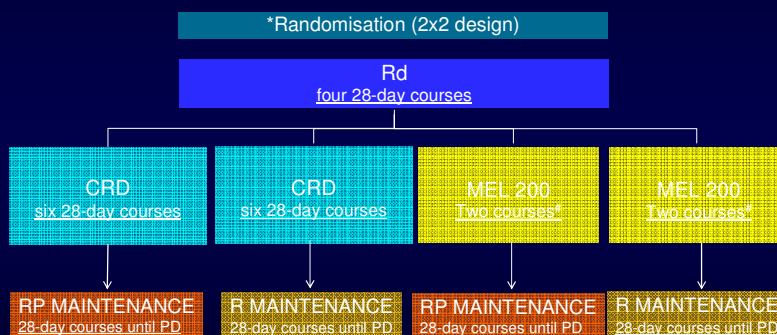
2013 ASH Abstract 763

A Phase III Study of ASCT vs. Cyclophosphamide-Lenalidomide-Dexamethasone and Lenalidomide-Prednisone Maintenance vs. Lenalidomide Alone in Newly Diagnosed Myeloma Patients

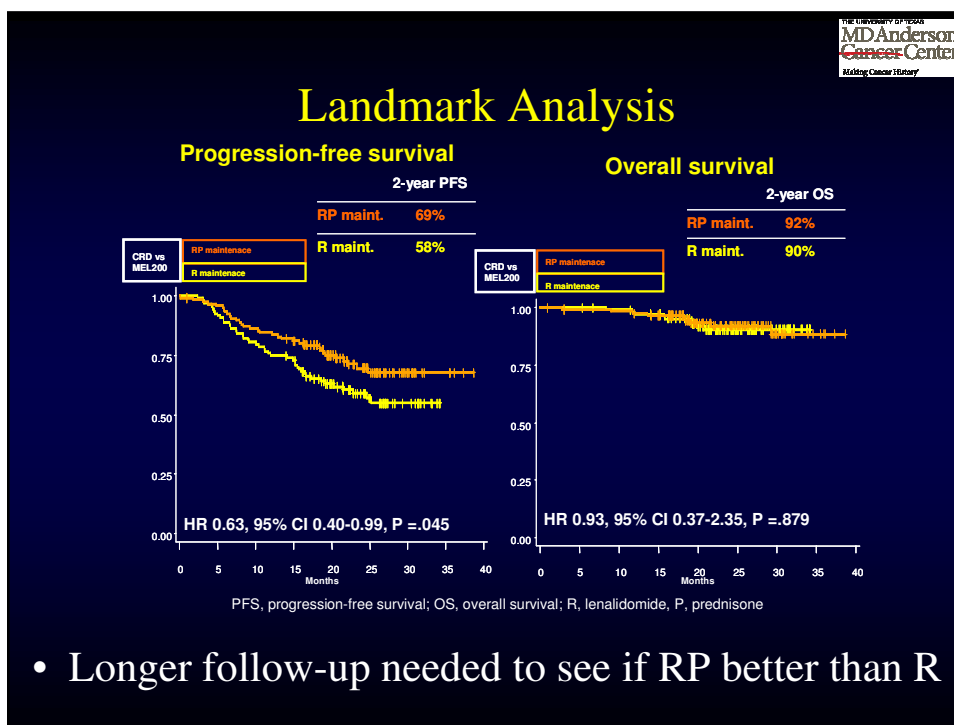
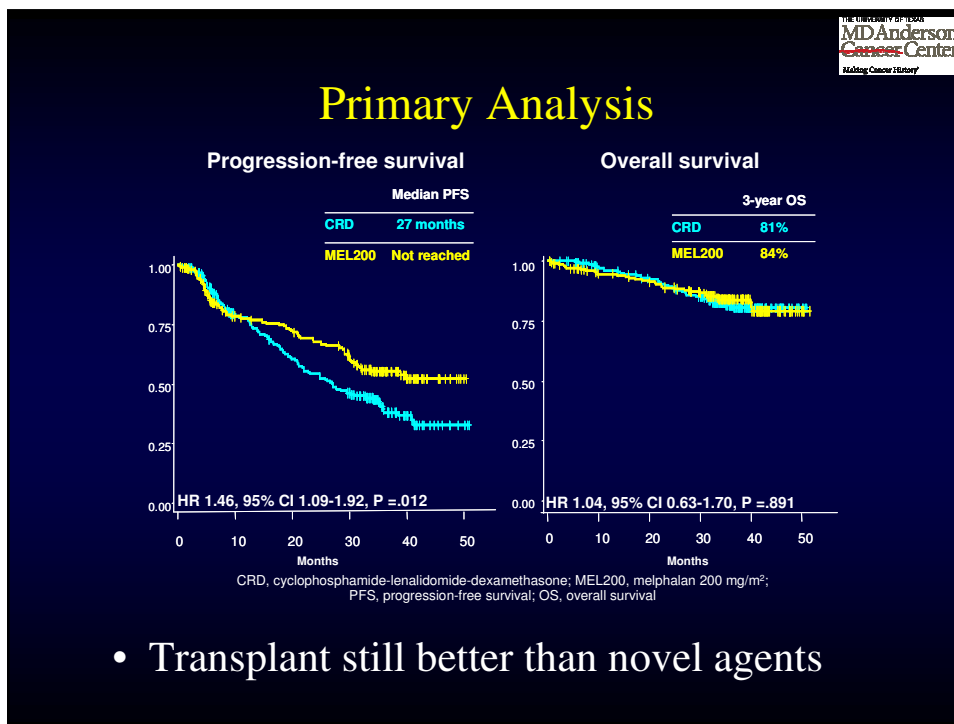
Antonio Palumbo, Francesca Gay, Andrew Spencer, Francesco Di Raimondo, Adam Zdenek, Alessandra Larocca, Antonietta Pia Falcone, Lucio Catalano, Paola Finsinger, Scudla Vlastimil, Simona Aschero, Massimo Offidani, Anna Marina Liberati, Angelo Michele Carella, Maisnar Vladimir, Francesca Donato, Tommaso Caravita, Paolo Corradini, Roberto Ria, Stefano Pulini, Raffaella Stocchi, Concetta Conticello, Maria Teresa Petrucci, Roman Hajek, and Mario Boccadoro

Study Design

- 389 patients (younger than 65 years) randomized from 59 centers
- Patients: Symptomatic disease, organ damage, measurable disease



* CRD vs MEL 200; RP maintenance vs R maintenance; Rd (R: 25 mg/d, days 1-21; d: 40 mg/d, days 1, 8, 15, 22); CRD (C: 300 mg/m²/d, days 1, 8, 15; d: 40 mg/d, days 1, 8, 15, 22; R: 25 mg, d 1-21); MEL 200 (M: 200 mg/m², day -2); RP maint (R: 10 mg/day, days 1-21; P: 50 mg every other day); R maint (R: 10 mg/day, days 1-21); # One course MEL 200 if patients achieves VGPR after cycle 1
R: lenalidomide; MEL 200: melphalan 200 mg/m² and autologous stem cell transplant; CRD: cyclophosphamide-lenalidomide-dexamethasone; RP: lenalidomide - prednisone; NDMM: newly diagnosed multiple myeloma.

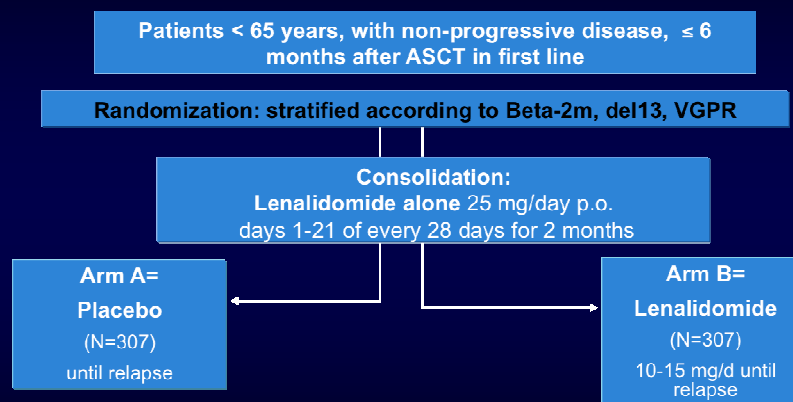


2013 ASH Abstract 406

Lenalidomide Maintenance after Stem-Cell Transplantation for Multiple Myeloma: Follow-up Analysis of the IFM 2005-02 Trial

Michel Attal, Valérie Lauwers-Cances, Gérald Marit, Denis Caillot, Thierry Facon, Cyrille Hulin, Philippe Moreau, Claire Mathiot, Murielle Roussel, Catherine Payen, Pascale Olivier, and Hervé Avet-Loiseau

Study Design



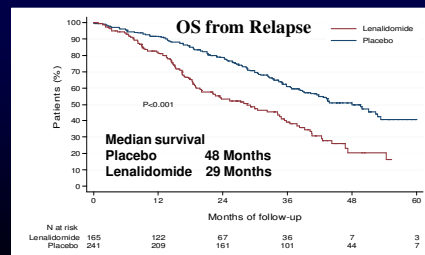
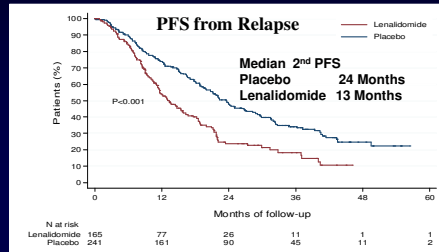
Primary end-point: PFS.

Secondary end-points: CR rate, TTP, OS, feasibility of long-term lenalidomide...

ASCT = autologous stem cell transplant. IFM = Intergroupe Francophone du Myelome.

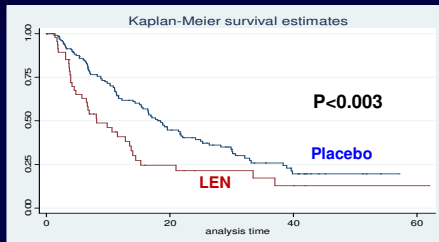
Analysis After Relapse

- Primary analysis: len had better PFS, same OS
- At face value, current data suggest len may cause myeloma chemoresistance

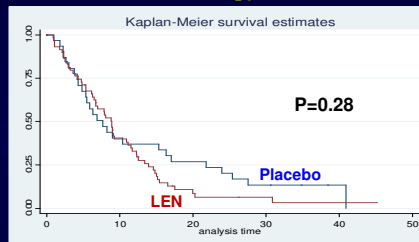


Treatment After Relapse

2nd line immunomodulatory drug-based therapy



2nd line bortezomib-based therapy



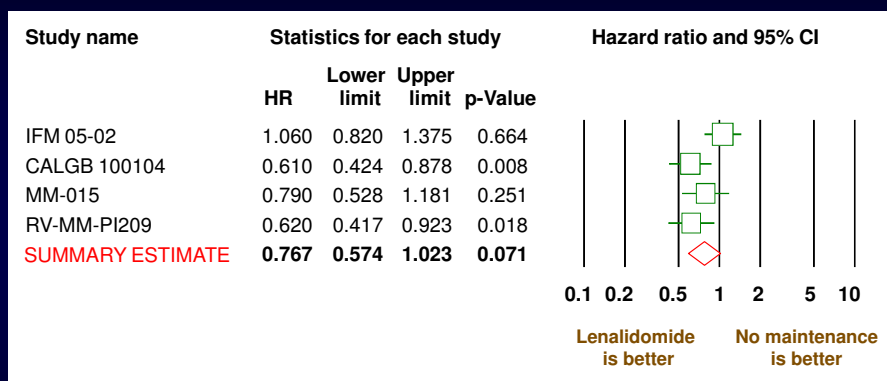
- LESSON: Choice of 2nd line regimens make a big difference in outcomes

2013 ASH Abstract 407

Lenalidomide Maintenance Therapy in Multiple Myeloma: A Meta-Analysis of Randomized Trials

Preet Paul Singh, Shaji K Kumar, Betsy R. LaPlant, Morie A Gertz, Angela Dispenzieri, P. Leif Bergsagel, Martha Q Lacy, Siddharth Singh, Vivek Roy, Francis K Buadi, David Dingli, Robert Kyle, S. Vincent Rajkumar, and Prashant Kapoor

Analysis After Relapse



Outcome: HR for death; Len vs. no maintenance
 (<1 implies better outcome with Len)
 Cochran Q=8.11 (p=0.044), I²=63%



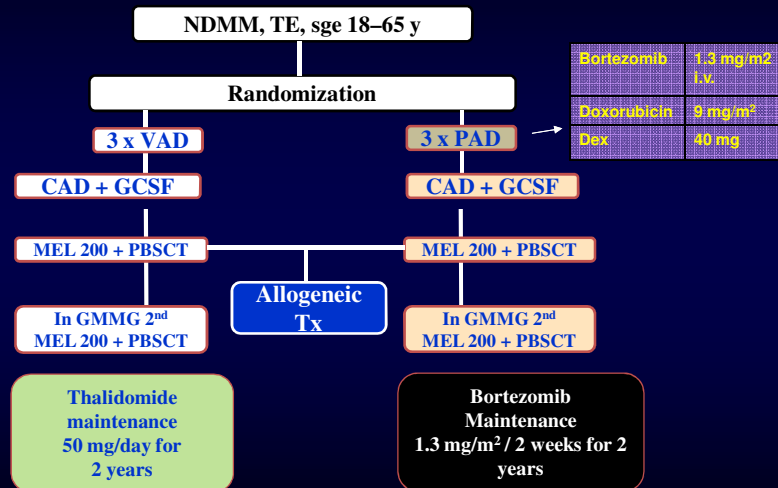
2013 ASH Abstract 404

Bortezomib Induction and Maintenance Treatment Improves Survival in Patients with Newly Diagnosed Multiple Myeloma: Extended Follow-up of the HOVON-65/GMMG-HD4 Trial

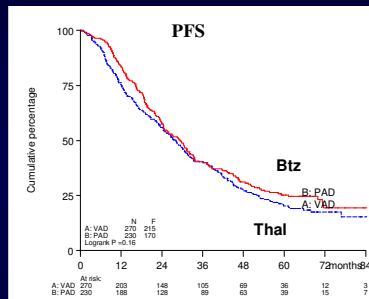
Pieter Sonneveld, Christof Scheid, Bronno van der Holt, Laila el Jarari, Uta Bertsch, Hans Salwender, Sonja Zweegman, Edo Vellenga, Annemiek Broyl, Igor Wolfgang Blau, Katja Weisel, Shulamit Wittebol, Gerard M.J. Bos, Marjan Stevens, Ingo GH Schmidt-Wolf, Michael Pfreundschuh, Dirk Hose, Anna Jauch, Helgi van de Velde, Reinier Raymakers, Martyn Ronald Schaafsma, Marie Jose Kersten, Marinus van Marwijk Kooy, Ulrich Dührsen, Hans Walter Lindemann, Pierre W. Wijermans, Henk Lokhorst and H. Goldschmidt



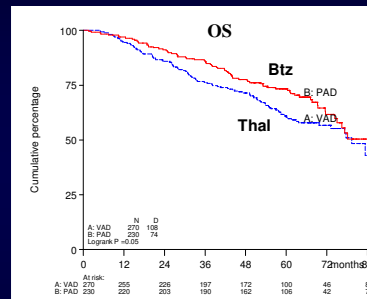
Study Design



Starting with Maintenance



PS = NS



HR=0.71, CI 0.52-0.98, p=0.035

- Bortezomib maintenance may be superior to thalidomide maintenance

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2013 ASH Abstract 283

Novel AKT Inhibitor Afuresertib in Combination with Bortezomib and Dexamethasone Demonstrates Favorable Safety Profile and Significant Clinical Activity in Patients with Relapsed/Refractory Multiple Myeloma

Peter M Voorhees, Andrew Spencer, Heather J. Sutherland, Michael E O'Dwyer, Shang-Yi Huang, Keith Stewart, Ajai Chari, Michael Rosenzweig, Ajay K. Nooka, Cara A Rosenbaum, Craig C Hofmeister, Deborah A Smith, Joyce M Antal, Ademi Santiago-Walker, Jennifer Gauvin, Joanna B Opalinska and Suzanne Trudel

Analysis After Relapse

Dose Cohort	N	Best Unconfirmed Response									
		NE	PD	SD	MR	PR	VGPR	CR	sCR	ORR (>PR)	CBR (>MR)
Part 1	34	2	3	10	2	13	3	1		50%	56%
Part 2	37	7	1	2	3	14	8		2	65%	73%
PK/PD	10		1	5		3	1			40%	40%

Activity by Prior Bortezomib Exposure

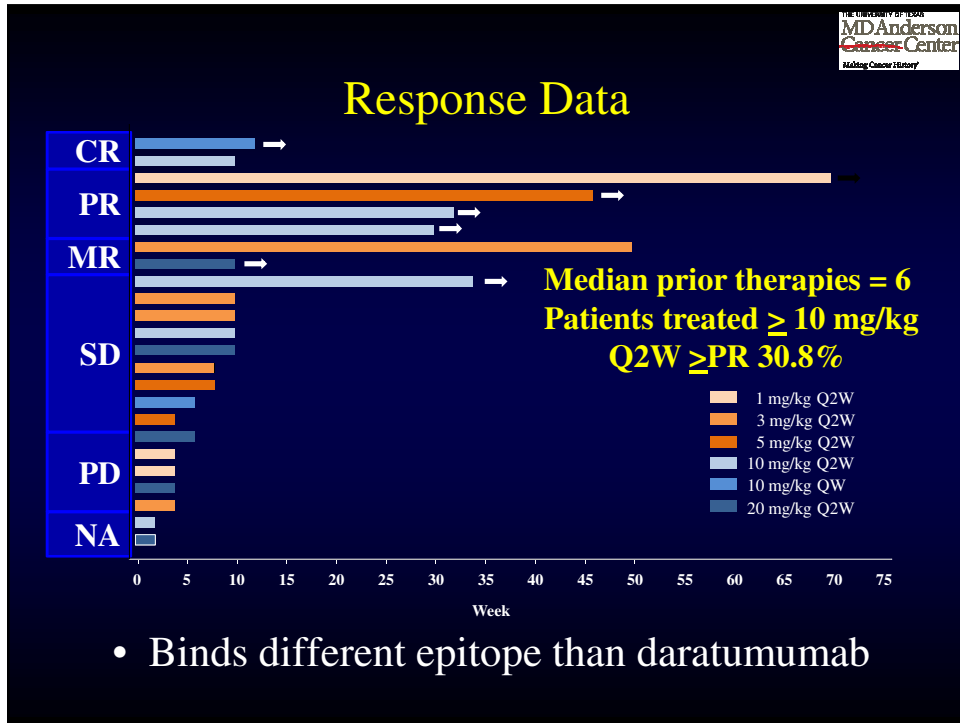
	Bortezomib Exposure			
	Naïve (n=13)	Relapsed (n=44)	Refractory (n=23)	Unk
Part 1	2/3 (67%)	10/18 (56%)	5/13 (38%)	-
Part 2	6/10 (60%)	17/26 (65%)	1/1 (100%)	-
PK/PD	NA	NA	4/9 (44%)	1/10 (10%)
Total	62%	61%	43%	1/10 (10%)

- Akt inhibition may be attractive in myeloma!

2013 ASH Abstract 284

SAR650984, a CD38 Monoclonal Antibody in Patients with Selected CD38⁺ Hematological Malignancies- Data from a Dose-Escalation Phase I Study

Thomas G Martin III, Stephen A. Strickland, Martha Glenn, Wei Zheng, Nikki Daskalakis, and Joseph R. Mikhael

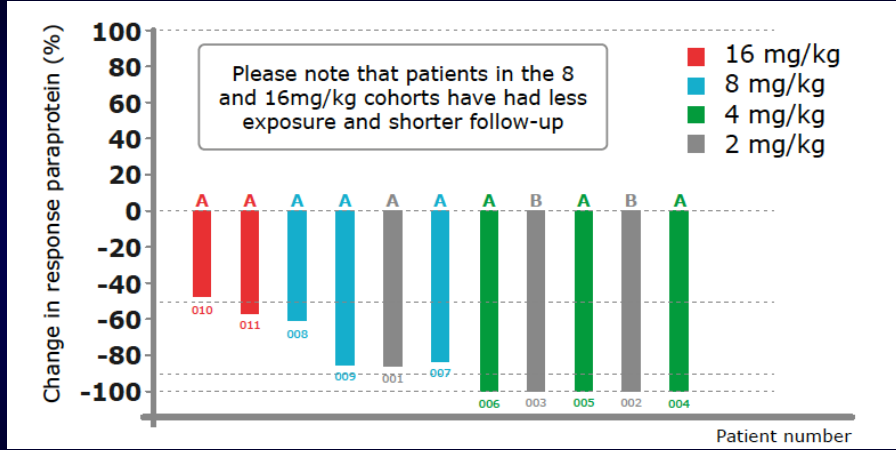


2013 ASH Abstract 1986

Preliminary Safety and Efficacy Data of Daratumumab in Combination with Lenalidomide and Dexamethasone in Relapsed or Refractory Multiple Myeloma

Torben Plesner, Tobias Arkenau, Henk Lokhorst, Peter Gimsing, Jakub Krejciak, Charlotte Lemech, Monique C. Minnema, Ulrik Lassen, Andrew Cakana, Nikolai Constantin Brun, Linda Basse, Antonio Palumbo, and Paul G. Richardson

Response Data



	2 mg/kg Pt no 1/2/3	4 mg/kg Pt no 4/5/6	8 mg/kg Pt no 7/8/9	16 mg/kg Pt no 10/11	Total*(n=8) Median (range)
Time to response ≥ PR, weeks	4.1/2.1/4.1	4.3/2.0/2.1	4.0/ N/A /4.3	N/A	4.1 (2.0-4.3)

Adverse Events

% of patients	2 mg/kg (N=3)	4 mg/kg (N=3)	8 mg/kg (N=4)	16 mg/kg (N=2)	Total (N=12)
Neutropenia	100	33	25	0	42
Diarrhoea	33	100	25	0	42
Constipation	100	33	0	0	33
Nausea	33	67	25	0	33
Fatigue	100	0	25	0	33
Bone pain	33	33	25	0	25
Muscle spasms	33	67	0	0	25
Anaemia	33	67	0	0	25
Insomnia	0	67	25	0	25
Pyrexia	33	33	25	0	25



2013 ASH Abstract 690

Phase I/II Dose Expansion of a Multi-Center Trial of Carfilzomib and Pomalidomide with Dexamethasone (Car-Pom-d) in Patients with Relapsed/Refractory Multiple Myeloma

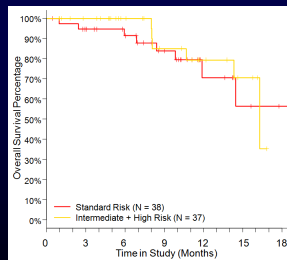
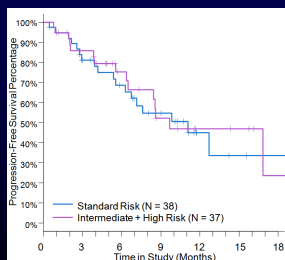
Jatin J. Shah, Edward A. Stadtmauer, Rafat Abonour, Adam D. Cohen, William Bensinger, Cristina Gasparetto, Jonathan L. Kaufman, Suzanne Lentzsch, Dan T. Vogl, Robert Z. Orlowski, Erica L. Kim, Natalia Bialas, David D. Smith, and Brian GM Durie

Response Data/Long-term Outcomes



Best overall response	N=79
VGPR	21 (27%)
PR	34 (43%)
MR	10 (13%)
SD	13 (16%)
PD	1 (1%)

ORR = 70%
CBR = 83%

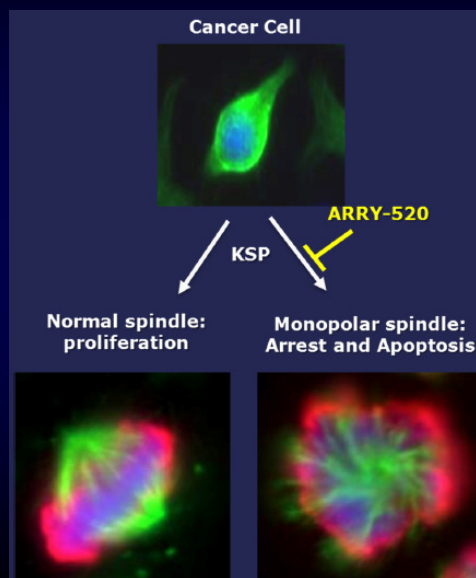


2013 ASH Abstract 285

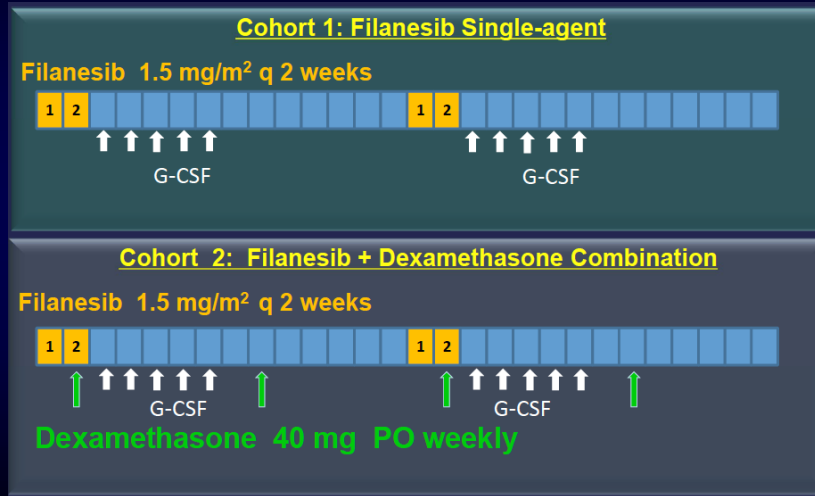
Prolonged Survival and Improved Response Rates with ARRY-520 in Relapsed/Refractory Multiple Myeloma (RRMM) Patients with Low α -1 Acid Glycoprotein (AAG) Levels: Results From a Phase 2 Study

Sagar Lonial, Jatin J. Shah, Jeffrey Zonder, William I. Bensinger, Adam D. Cohen, Jonathan L. Kaufman, Ajay K. Nooka, Donna M. Weber, Brandi Hilder, Selena A. Rush, Ann Ptaszynski, Duncan Walker, and Robert Z. Orlowski

Mechanism of Action



Study Design



Response Data

	Filanesib Single-agent	Filanesib + Dex
	All Pts	All Pts
n	32	55
ORR (≥ PR)	5 (16%)	8 (15%)
CBR (≥ MR)	7 (22%)	11 (20%)
Duration of Response (months)	8.6	5.1
Time to Next Treatment (Months)	3.7	3.4
OS (months)	19.0	10.5

AAG and Outcomes

	Filanesib Single-agent			Filanesib + Dex		
	All Pts ¹	AAG-High	AAG-Low	All Pts ²	AAG-High	AAG-Low
n	32	6	21	55	15	36
ORR (≥ PR)	5 (16%)	0 (0%)	5 (24%)	8 (15%)	0 (0%)	7 (19%)
CBR (≥ MR)	7 (22%)	0 (0%)	7 (33%)	11 (20%)	0 (0%)	10 (28%)
Duration of Response (months)	8.6	-	8.6	5.1	-	5.1
Time to Next Treatment (months)	3.7	2.6	5.3	3.4	2.0	5.1
OS (months)	19.0	4.5	23.3	10.5	2.9	10.8

Outline

- Disease biology
- Asymptomatic myeloma
- Non-transplant therapies
- Induction before transplant
- Options for therapy after transplant
- Relapsed and/or refractory myeloma
- **Aspects of supportive care in myeloma**

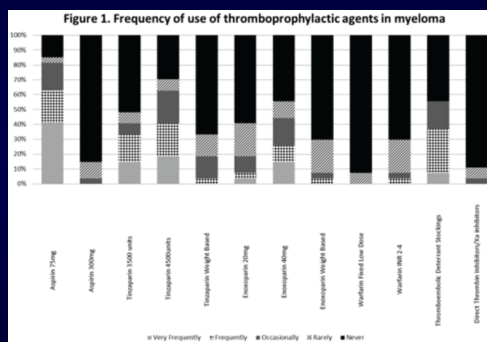
2013 ASH Abstract 1694

Thromboprophylaxis In Myeloma : A National Survey

Maeve P Crowley, Barry M Kevane, Joesph A Eustace, Susan O'Shea, and Oonagh M Gilligan

Study Findings

- Survey of hematologists treating myeloma patients in Ireland
- Only 48% used published guidelines to direct choice of prophylactic therapy





2013 ASH Abstract 1686

Malnutrition is Perceived Differently by Patients, Relatives and Physicians in Routine Hematology Practice. Subgroup Analysis of the French Cross-sectional Nutricancer 2012 Survey

Emmanuel Gyan, Bruno Raynard, Jean Lacau Saint Guily, François Goldwasser and Xavier Hebuterne



Study Findings

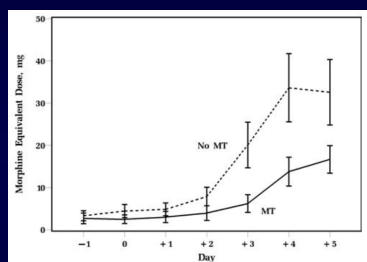
- Cross-sectional survey in 30 French hospitals of 213 pts with heme malignancies (15% myeloma)
- Prevalence of malnutrition according to the standard definition was 46%
 - Physicians identified malnutrition in 35%
 - Sensitivity 55, specificity 81%
 - Patients identified malnutrition in 18%
 - Relatives identified malnutrition in 14%

2013 ASH Abstract 1693

A Randomized Study of Music Therapy in Patients Undergoing Autologous Stem Cell Transplant: Decrease in Narcotic Medication use for Pain Control

Hien K. Duong, Debbie Bates, Lisa A. Rybicki, Matt Kalaycio, Steven Andresen, Ronald Sobecks, Lisa Gallagher, Robert M Dean, Brian T. Hill, Donna M Abounader, Melissa Yurch, Christina Ferraro, Shawnda Tench, Kelly Cherni, Gina Green, Joseph Kohuth, Vanessa Farrow, Heather Koniarczyk, Shannon Jarancik, Linda McLellan, Jane Dabney, Brad Pohlman, and Brian J. Bolwell

Study Findings



- 82 patients undergoing auto (40 with myeloma)
- Interactive music therapy with board-certified therapist
- Day +7: more nausea with music
- No difference in pain, but less narcotic use (24 vs. 73 mg morphine)

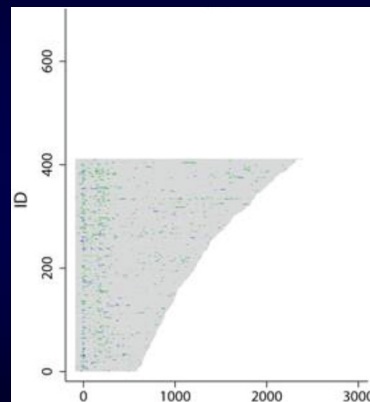
2013 ASH Abstract 2968

Frequency, Health Care Resource Use, and Costs Associated With Skeletal Related Events In US Patients With Multiple Myeloma

Emily Nash Smyth, Ilaria Conti, James Wooldridge, Lee Bowman, David Nelson, Jin Xie, and Daniel E Ball

Study Findings

- Population-based study of 1,112 pts with newly diagnosed myeloma
- 32% had inpatient episode related to an SRE
- Can occur at any time
 - At least as likely after diagnosis as before



Updates on Multiple Myeloma Therapy from ASH: Summary

Robert Z. Orlowski, Ph.D., M.D.

Director, Myeloma Section

Florence Maude Thomas Cancer Research Professor

Departments of Lymphoma/Myeloma & Experimental Therapeutics

Principal Investigator, MD Anderson SPORE in Multiple Myeloma

Chair, Southwest Oncology Group Myeloma Committee



Smoldering Myeloma



- New definitions coming for patients with ultra high risk disease; will be treated like myeloma
 - Presence of bony disease by PET, MRI
- Low risk smoldering myeloma will be treated be followed more like MGUS
- Remaining high risk and intermediate risk patients should enroll on well-designed clinical trials
 - ECOG E3A06 trial

Transplant-ineligible Myeloma

- Newer drugs being incorporated into up-front therapy, such as carfilzomib, ixazomib
- Greater acceptance of need for therapy continuation (maintenance) after induction to deepen response, prolong remission (Rd)
- High risk patients still don't do as well, and should be treated differently vs. standard risk
 - High risk: SWOG S1211 (RVd ± Elotuzumab)
 - Standard risk: ECOG E1A11 (RVd vs. CRd)

Transplant Eligible Myeloma

- Newer drugs being incorporated into up-front therapy, such as carfilzomib, ixazomib
- Emerging role of consolidation post-transplant, and maintenance with multi-drug regimens, especially for high risk patients
- Importance of achieving and maintaining CR with immunofixation- MRD status, again especially for high risk patients

Relapsed and/or Refractory Myeloma

- Monoclonal antibodies with single-agent activity (daratumumab, SAR650984) or in combinations (these and elotuzumab) are attractive approaches
- Novel agents with new mechanisms of action (filanesib, afuresertib) will be entering registration studies
- Better molecular understanding of myeloma will allow us to personalize therapy

Importance of Clinical Trial Participation

- Access emerging novel agents not yet available outside of trials
- Advance knowledge about myeloma biology and myeloma therapy
- Speed the approval of new drugs and improve outcomes for all patients
- Bring us closer to a cure



MDACC Myeloma Center

- Referral Line : 1-855-MYELOMA (toll-free)
- Drs. Elisabet Manasanch, Robert Orlowski (rorlow@mdanderson.org), Jatin Shah, Sheeba Thomas, Michael Wang, Donna Weber
 - E-mail: myelomatrial@mdanderson.org
 - Twitter: @Myeloma_Doc



Myeloma

Update on Research and Treatment from the American Society of Hematology (ASH®) Annual Meeting

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Question and Answer Session

Dr. Orlowski's slides are available for download at
www.LLS.org/programs

Myeloma

Update on Research and Treatment from the
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SOCIETY
fighting blood cancers

MYELOMA AND CAREGIVER ONLINE CHATS

- Every Tuesday evening from 8:00 PM – 10:00 PM ET
- Visit www.LLS.org/chat to register or for more information

The Leukemia & Lymphoma Society's (LLS) Co-Pay Assistance Program offers financial assistance to qualified myeloma patients to help with treatment-related expenses and insurance premiums. Patients may apply online or over the phone with a Co-Pay Specialist.

- WEBSITE: www.LLS.org/copay
- TOLL-FREE PHONE: (877) LLS-COPAY

For more information about myeloma and other LLS programs, please contact an LLS Information Specialist.

- TOLL-FREE PHONE: (800) 955-4572
- EMAIL: infocenter@LLS.org