CITINGS

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Thalidomide and Revlimid® Issue

The International Myeloma Foundation *(IMF) presents this special edition of CITINGS, our premiere publication featuring the most up-to-date information on myeloma treatment, focused on thalidomide and Revlimid. This special edition corresponds with the 50th American Society of Hematology (ASH) annual meeting. In this CITINGS, we have highlighted selected thalidomide and Revlimid data presentations from the ASH meeting. We also provide references to the latest published journal articles on both thalidomide and Revlimid from the fourth quarter of this year.*

It is our hope that CITINGS will be a valuable tool in keeping you up to date on the latest developments in myeloma treatment. Please feel free to contact us at (800) 452-CURE or www.myeloma.org.

– Susie Novis, President, IMF

American Society of Hematology Presentations 2008

Saturday, December 6, 2008

The Administration of Bortezomib, Dexamethasone and Thalidomide (VTD) after ASCT in Myeloma Patients Who Do Not Receive Bisphosphonates Normalizes sRANKL, Dickkopf-1 and Improves Abnormal Osteoclast Function and Impaired Angiogenesis

Evangelos Terpos, Efstathios Kastritis, Dimitrios Christoulas, Magdalini Migkou, Maria Gavriatopoulou and Meletios A. Dimopoulos

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**

Abstract No.: 1728 **Poster Board: I-833**

Myeloma – Therapy, Excluding Transplantation Poster I

Effect of Venous Thrombotic Events on Overall Survival in Multiple Myeloma: Analysis of Thrombotic Events Occurring in E4A03A Randomized Trial of Lenalidomide Plus High-Dose Dexamethasone (RD) Versus Lenalidomide Plus Low-Dose Dexamethasone (Rd) in Newly Diagnosed Multiple Myeloma, a Trial Coordinated by the Eastern Cooperative Oncology Group (ECOG)

Susanna Jacobus, Shaji Kumar, Natalie Scott Callander, Rafat Abonour, Rafael Fonseca, David Siegel, Philip Greipp and S. Vincent Rajkumar

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**

Abstract No.: 1740 **Poster Board: I-845**

Myeloma – Therapy, Excluding Transplantation Poster I

Funded by an unrestricted educational grant from Celgene Corporation

Genetic Variation in ADME Genes Is Associated with Thalidomide-Related Peripheral Neuropathy in Multiple Myeloma Patients

David C Johnson, Christine Ramos, Alex J. Szubert, Walter M Gregory, J. Anthony Child, Faith E Davies, Brian GM Durie, Brian G. Van Ness, and Gareth J Morgan

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1675 **Poster Board: I-780**

Myeloma – Biology and Pathophysiology, Excluding Therapy Poster I

Immunomodulatory Effects of Lenalidomide and Bortezomib on Bone Marrow Stroma Cell and CD4 T Cell Interaction in Multiple Myeloma

Gullu Gorgun, Elisabetta Calabrese, Teru Hideshima, Hiroshi Ikeda, Giulia Perrone, Loredana Santo, Diana Cirstea, Paul G Richardson and Kenneth C Anderson

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1690 **Poster Board: I-795**

Myeloma – Biology and Pathophysiology, Excluding Therapy Poster I

The Impact of Cytogenetics on the Outcomes of Treatment with Lenalidomide Plus Dexamethasone in Relapsed or Refractory Multiple Myeloma

Nizar J Bahlis, Kevin W. Song, Tommy Fu, Birgitte J Roland, Hong Chang, Doug Horsman, Adnan Mansoor, Christine Chen, Esther Masih-Khan, Young Trieu, Helene Bruyere, Douglas A. Stewart, and Donna E. Reece

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1731 **Poster Board: I-836**

Myeloma – Therapy, Excluding Transplantation Poster I

Immunomodulatory Drugs (Thalidomide and Lenalidomide) Up-Regulate Endothelial Tissue Factor in Vitro Resulting in An Acquired Hypercoagulable State

Serena Valsami, Maria Sybille Leikauf, Jerzy Madon, Wolfram Ruf, and Lars M Asmis

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1893 **Poster Board: I-998**

Vascular Wall Biology, Endothelial Progenitor Cells, and Platelet Adhesion Poster I

Lenalidomide, Bortezomib, and Dexamethasone in Patients with Relapsed or Relapsed/Refractory Multiple Myeloma (MM): Encouraging Response Rates and Tolerability with Correlation of Outcome and Adverse Cytogenetics in a Phase II Study

Paul Richardson, Sundar Jagannath, Andrzej Jakubowiak, Sagar Lonial, Noopur Raje, Melissa Alsina, Irene Ghobrial, Amitabha Mazumder, Nikhil C Munshi, David H Vesole, Kathleen Colson, Mary L McKenney, Laura Lunde, Sarah Kennedy, Kara Kosakowski, Constantine Mitsiades, Teru Hideshima, Robert D Knight, Dixie-Lee Esseltine, and Kenneth C Anderson

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1742 **Poster Board: I-847**

Myeloma – Therapy, Excluding Transplantation Poster I

Long Term Follow-up of Patients with Immunoglobulin Light Chain Amyloidosis Treated with Lenalidomide and Dexamethasone

Angela Dispenzieri, Martha Lacy, Stephen R. Zeldenrust, Suzanne R. Hayman, Shaji K. Kumar, John A. Lust, Jake Allred, S. Vincent Rajkumar, Philip R. Greipp, Kristina Laumann, Stephen Russell, Francis Buadi, Thomas E Witzig and Morie A Gertz

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1737 **Poster Board: I-842**

Myeloma – Therapy, Excluding Transplantation Poster I

A Multicenter Phase I/II Dose Escalation Study of Lenalidomide in Combination with Melphalan and Dexamethasone in Subjects with Newly-Diagnosed Light-Chain (AL)-Amyloidosis

Philippe Moreau, Arnaud Jaccard, Lotfi Benboubker, Bruno Royer, Valerie Coiteux, Franck Bridoux, Jean-Luc Harousseau, Catherine Traulle, Bernard Grosbois, Veronique Leblond, May Alakl, Olivier Hermine and Jean-Paul Fermand

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1732 **Poster Board: I-837**

Myeloma – Therapy, Excluding Transplantation Poster I

Phase I/II Study of Lenalidomide, Intermediate Dose Dexamethasone and Low Dose Cyclophosphamide (RDC) for the Treatment of Patients with Primary Systemic Amyloidosis (AL)

Efstathios Kastritis, Flora Zagouri, Maria Roussou, Magdalini Migkou, John Boletis, Theofanis Apostolou and Meletios A. Dimopoulos

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1734 **Poster Board: I-839**

Myeloma – Therapy, Excluding Transplantation Poster I

Phase I-II Trial of Oral Cyclophosphamide, Prednisone and Lenalidomide (Revlimid®) [CPR] for the Treatment of Patients with Relapsed and Refractory Multiple Myeloma

Donna E. Reece, Esther Masih-Khan, Arooj Khan, Peter Anglin, Christine Chen, Vishal Kukreti, Joseph R. Mikhael, and Suzanne Trudel

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1723 **Poster Board: I-828**

Myeloma – Therapy, Excluding Transplantation Poster I

Prognostic Impact of the Plasma Cell Labeling Index (LI) in Newly Diagnosed Myeloma Patients Treated with Thalidomide-Dexamethasone (Thal/Dex) or Lenalidomide-Dexamethasone (Len/Dex)

Prashant Kapoor, Shaji Kumar, Philip R Greipp, Kristina M. Laumann, Sumithra Mandrekar, S. Vincent Rajkumar, and Thomas E. Witzig

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1729 **Poster Board: I-834**

Myeloma – Therapy, Excluding Transplantation Poster I

Regulatory T Cells (Treg) Are Depressed in Patients with Relapsed/ Refractory Multiple Myeloma (MM) and Increases towards Normal Range in Responding Patients Treated with Lenalidomide (LEN)

Hang Quach, David Ritchie, Paul Neeson, Simon Harrison, Tsin Tai, Kellie Tainton, Kevin Lynch, and Miles Prince

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1696 **Poster Board: I-801**

Myeloma – Biology and Pathophysiology, Excluding Therapy Poster I

Risk-Adapted Cyclophosphamide, Thalidomide and Dexamethasone (CTD) for the Treatment of Systemic AL Amyloidosis: Long Term Outcomes among 202 Patients

Simon DJ Gibbs, Prayman T Sattianayagam, Helen J Lachmann, Mark Offer, Julian D Gillmore, Philip N Hawkins and Ashutosh Wechalekar

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1733 **Poster Board: I-838**

Myeloma – Therapy, Excluding Transplantation Poster I

Single Center Experience of Lenalidomide / Dexamethasone Treatment in 40 Patients with Light Chain Amyloidosis: High Toxicity in Patients with Severe Impaired Renal and Cardiac Function

Stefan O Schoenland, Tilmann Bochtler, Sascha Dietrich, Ulrike Klein, Hartmut Goldschmidt, Anthony Ho and Ute Hegenbart

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1736 **Poster Board: I-841**

Myeloma – Therapy, Excluding Transplantation Poster I

Superior Rate of Complete Response with up-Front VELCADE-Thalidomide-Dexamethasone Versus Thalidomide-Dexamethasone in Newly Diagnosed Multiple Myeloma Is Not Affected by Adverse Prognostic Factors, Including High-Risk Cytogenetic Abnormalities

Michele Cavo, Nicoletta Testoni, Carolina Terragna, Giulia Marzocchi, Sandra Durante, Renato Zambello, Chiara Nozzoli, Lucia Pantani, Paola Tacchetti, Luciano Masini, Michela Ceccolini, Paola Agostini, Elena Zamagni, Valerio De Stefano, Patrizia Tosi, Daniele Derudas, Laura Dessanti, Stelvio Ballanti, Salvatore Palmieri, Andrea Nozza, Gioacchino Catania, Jacopo Peccatori, Alfonso D'Arco, Pellegrino Musto, Mariella Grasso, Maria Caterina Pallotti, Silvana Pasini, Pier Paolo Fattori, Anna Baraldi, Delia Cangini, Filippo Ballerini, Alessandro Petrucci, and Michele Baccarani.

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1662 **Poster Board: I-767**

Myeloma – Biology and Pathophysiology, Excluding Therapy Poster I

Treatment of Relapsed and Refractory Multiple Myeloma in Patients with p53 Deletion

Donna E. Reece, Young Trieu, Hong Chang, Wei Xu, Peter Anglin, Christine Chen, Vishal Kukreti, Suzanne Trudel, and Joseph Mikhael

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1724 **Poster Board: I-829**

Myeloma – Therapy, Excluding Transplantation Poster I

Treatment of Patients with Relapsed/Refractory Multiple Myeloma (MM) with Lenalidomide and Dexamethasone with or without Bortezomib Depending on Prior Neurotoxicity: Prospective Evaluation of the Impact of Cytogenetic Abnormalities and Assessment

Meletios A. Dimopoulos, Efstathios Kastritis, Dimitrios Christoulas, Magdalini Migkou, Maria Gavriatopoulou, Flora Zagouri and Evangelos Terpos

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 1726 **Poster Board: I-831**

Myeloma – Therapy, Excluding Transplantation Poster I

Sunday, December 7, 2008

Phase II Trial of Lenalidomide (Revlimid™) with Cyclophosphamide and Dexamethasone (RCd) for Newly Diagnosed Myeloma

Shaji Kumar, Suzanne Hayman, Francis Buadi, Martha Lacy, Keith Stewart, Jacob Allred, Kristina Lauman, Tammy McCarty, Leif Bergsagel, David Dingli, Rafael Fonseca, Morie Gertz, Philip Greipp, John Lust, Stephen Russell, Craig Reeder, Thomas Witzig, Steven Zeldenrust, Robert Kyle, S. Vincent Rajkumar and Angela Dispenzieri

Time: **4:30 PM** **Location: Halls B and C (Moscone Center)**

Abstract No.: 91

Myeloma Therapy: Newly Diagnosed Myeloma

Lenalidomide, Bortezomib, and Dexamethasone in Patients with Newly Diagnosed Multiple Myeloma: Encouraging Efficacy in High Risk Groups with Updated Results of a Phase I/II Study

Paul Richardson, Sagar Lonial, Andrzej Jakubowiak, Sundar Jagannath, Noopur S Raje, David Avigan, Irene M Ghobrial, Robert L Schlossman, Amitabha Mazumder, Nikhil C Munshi, David H Vesole, Robin Joyce, Deborah Doss, Diane L Warren, Stephen W Hayes, Sarah Kaster, Carol Delaney, Marisa Lauria, Constantine Mitsiades, Teru Hideshima, Robert D. Knight, Dixie-Lee Esseltine, and Kenneth C Anderson

Time: **4:45 PM** **Location: Halls B and C (Moscone Center)**

Abstract No.: 92

Myeloma Therapy: Newly Diagnosed Myeloma

Safety and Efficacy of Novel Combination Therapy with Bortezomib, Dexamethasone, Cyclophosphamide, and Lenalidomide in Newly Diagnosed Multiple Myeloma: Initial Results from the Phase I/II Multi-Center EVOLUTION Study

Shaji Kumar, Ian W Flinn, Stephen J. Noga, Parameswaran Hari, Robert M. Rifkin, Natalie Scott Callander, Manish Bhandari, Jeffrey Lee Wolf, Cristina Gasparetto, Amrita Krishnan, Daren D Grosman, Jonathan Glass, Entezam Asim Sahovic, Hongliang Shi, Iain J. Webb, Paul Richardson, and S. Vincent Rajkumar

Time: **5:00 PM** **Location: Halls B and C (Moscone Center)**

Abstract No.: 93

Myeloma Therapy: Newly Diagnosed Myeloma

A Phase II Study of Bortezomib (VELCADE ®), Cyclophosphamide (Cytoxan®), Thalidomide (Thalomid®) and Dexamethasone as First-Line Therapy for Multiple Myeloma

William Bensinger, Sundar Jagannath, Robert Vescio, Elber S. Camacho, Jeffrey Lee Wolf, David H Irwin, Gerardo Capo III, Marti McKinley, Phyllis Potts, David H. Vesole, Amitabha Mazumder, Dixie-Lee Esseltine, Pamela Becker, John Crowley, and Brian GM Durie.

Time: **5:15 PM** **Location: Halls B and C (Moscone Center)**

Abstract No.: 94

Myeloma Therapy: Newly Diagnosed Myeloma

Survival in Patients with Newly Diagnosed Myeloma Undergoing Therapy with Lenalidomide and Dexamethasone: Impact of High-Risk Cytogenetic Risk Status on Outcome

Prashant Kapoor, Shaji Kumar, Rafael Fonseca, Martha Q. Lacy, Thomas E Witzig, Suzanne R. Hayman, Angela Dispenzieri, Francis Buadi, P. Leif Bergsagel, Morie Gertz, Robert Dalton, Joseph Mikhael, David Dingli, Craig B. Reeder, John A. Lust, Stephen Russell, Vivek Roy, Steven R. Zeldenrust, Keith Stewart, Robert A Kyle, Philip R. Greipp, and S. Vincent Rajkumar

Time: **5:30 PM** **Location: Halls B and C (Moscone Center)**

Abstract No.: 95

Myeloma Therapy: Newly Diagnosed Myeloma

Biochemical Basis for Interactions Between Thalidomide and Inhibitors of the Isoprenoid Biosynthetic Pathway in Multiple Myeloma Cells

Sarah A. Holstein, Huaxiang Tong, and Raymond J. Hohl

Time: **6:00 PM - 8:00 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 2635 **Poster Board: II-729**

Molecular Pharmacology, Drug Resistance Poster II

Clinical Epidemiological Study on Multiple Myeloma in China: A 18-Year Retrospective Study in a Representative Center

Lugui Qiu, Yafei Wang, Peijing Qi, Dehui Zou, Yaozhong Zhao, and Junyuan Qi

Time: **6:00 PM - 8:00 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 2723 **Poster Board: II-817**

Myeloma – Biology and Pathophysiology, Excluding Therapy Poster II

Economic Evaluation of Lenalidomide Combined with Dexamethasone for the Treatment of Multiple Myeloma in the UK

Baris Deniz, Gareth Morgan, Steve Schey, Jack Ishak, Peter Dale, Arran Shearer and J. Jaime Caro

Time: **6:00 PM - 8:00 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 2400 **Poster Board: II-494**

Health Services and Outcomes Research Poster II

Economic Evaluation of Thalidomide Combined with Melphalan and Prednisone in Previously Untreated Multiple Myeloma in Scotland

Baris Deniz1, Thierry Facon, Ian Singer, Paul Micallef-Eynaud, Ian Joseph, Arran Shearer and J. Jaime Caro

Time: **6:00 PM - 8:00 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 2395 **Poster Board: II-489**

Health Services and Outcomes Research Poster II

Evaluation of the Relationship Between Venous Thromboembolism Risk Factors and the Use of Antithrombotic Prophylaxis in Multiple Myeloma Patients Treated with Thalidomide and Dexamethasone Combination Regimens

Nancy A Brandenburg, Thomas F Goss, Tyler Knight, Xiao Xu, and Robert D. Knight

Time: **6:00 PM - 8:00 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 2369 **Poster Board: II-463**

Health Services and Outcomes Research Poster II

The Immunomodulatory Role of Lenalidomide on Prevnar® Responses in Patients with Relapsed Multiple Myeloma: A Comprehensive Analysis of the Immune Response

Kimberly Ann Noonan, Anna Ferguson, Carol A. Huff, Amy Emerling, Stephanie Mgebroff, Rose Wilson, Robert D. Knight, and Ivan M. Borrello

Time: **6:00 PM - 8:00 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 2772 **Poster Board: II-866**

Myeloma – Therapy, Excluding Transplantation Poster II

Indirect Comparison of the Efficacy of Melphalan-Prednisone-Bortezomib Relative to Melphalan-Prednisone-Thalidomide and Melphalan-Prednisone for the First Line Treatment of Multiple Myeloma

Yating Yeh, James Chambers, Sabine Gaugris, and Jeroen Jansen

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2367 **Poster Board: II-461**

Health Services and Outcomes Research Poster II

Lenalidomide, Adriamycin and Dexamethason (RAD) in Relapsed and Refractory Multiple Myeloma: Final Results from a Phase I/II Trial of "Deutsche Studiengruppe Multiples Myelom"

Christian Gerecke, Stefan Knop, Max S. Topp, Peter Liebisch, Christina Vollmuth, Uwe Platzbecker, Uwe Mäder, Hermann Einsele and Ralf C. Bargou

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2782 **Poster Board: II-876**

Myeloma – Therapy, Excluding Transplantation Poster II

Novel Agents Overcome the Adverse Prognosis Imparted by Compromised Renal Function in Patients with Multiple Myeloma

Mehul Patel, Taimur Sher, Sikander Ailawadhi, Terry Mashtare Jr., Wei Tan, Pranay Soni, Gregory Wilding, Kena C Miller, Alice Mohr, Kelvin P. Lee and Asher Alban Chanan-Khan

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2726 **Poster Board: II-820**

Myeloma – Biology and Pathophysiology, Excluding Therapy Poster II

Opposing Effects of Dexamethasone on Lenalidomide Activity in Multiple Myeloma: Additive/Synergistic Effects on Anti-Proliferative Activity on Myeloma Cells and Antagonistic Effects on Immune Function

Peter H Schafer, Anita K Gandhi, Ling-Hua Zhang, Jian Kang, Lori Capone, Stacey Parton, Lei Wu and Blake Bartlett

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2761 **Poster Board: II-855**

Myeloma – Pathophysiology and Preclinical Studies Excluding Therapy Poster II

Oral Melphalan, Prednisone, and Lenalidomide for Newly Diagnosed Multiple Myeloma Patients: Kinetics of Neutropenia/Thrombocytopenia and Time to Event Results

Antonio Palumbo, Patrizia Falco, Francesca Gay, Paolo Corradini, Claudia Crippa, Francesco Di Raimondo, Antonietta Falcone, Nicola Giuliani, Pellegrino Musto, Fortunato Morabito, Letizia Canepa, Alessandro Gozzetti, Simona Caltagirone, Jerome B. Zeldis, Robert D. Knight, Mario Boccadoro, and Maria Teresa Petrucci

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2768 **Poster Board: II-862**

Myeloma – Therapy, Excluding Transplantation Poster II

Phase II Study of Melphalan, Prednisone and Lenalidomide Combination for Newly Diagnosed Multiple Myeloma Patients Who Are Not Candidates for Stem Cell Transplantation

Vivek Roy, A. Keith Stewart, P. Leif Bergsagel, Angela Dispenzieri, Kristina Laumann, Jake Allred, Martha Q. Lacy, Rafael Fonseca, Craig B. Reeder, Shaji Kumar, Candido E. Rivera, Morie A. Gertz, Philip R. Greipp, Francis K. Buadi, Suzanne R. Hayman, and S. Vincent Rajkumar

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2769 **Poster Board: II-863**

Myeloma – Therapy, Excluding Transplantation Poster II

Phase II Testing of Lenalidomide Plus Melphalan for Previously Untreated Older Patients with Multiple Myeloma: The NCIC CTG MY.11 Trial

Darrell J White, Nizar J Bahlis, Deborah C Marcellus, Andrew Belch, A. Keith Stewart, Christine Chen, Michael J Kovacs, David A Macdonald, Donna E Reece, Erica Harnett, Judy-Anne W Chapman, and Ralph M Meyer

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2767 **Poster Board: II-861**

Myeloma – Therapy, Excluding Transplantation Poster II

Stimulation of T Cells by Lenalidomide Involves Putative Lenalidomide Binding Proteins CD3-Epsilon-Associated Protein and GDP-Mannose Pyrophosphorylase a

Anita K Gandhi, Audrey Rogovitz, Antonia Lopez-Girona, Derek Mendy, Lisa Morrison, Weilin Xie and Peter H Schafer

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2606 **Poster Board: II-700**

Lymphoma: Pre-Clinical – Chemotherapy and Biologic Agents Poster II

Synergistic Activity of Adenosine A2A and Beta-2 Adrenergic Receptor Agonists in Myeloma Cells in the Context of Tumor-Stromal Interactions

Douglas W. McMillin, Richard Rickles, Joseph Negri, Jake Delmore, Melissa G. Ooi, Melissa Farwell, David Crowe, Mei Chen, William Avery, Vikram Kansra, Kenneth C. Anderson, Margaret S. Lee, and Constantine S. Mitsiades

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2663 **Poster Board: II-757**

Molecular Pharmacology, Drug Resistance Poster II

Thalidomide (thal), Lenalidomide (len), and Dexamethasone (dex)-Associated Venous Thromboembolism (VTE) and Reported VTE Rates Pre- and Post-FDA Approval: Optimal Prophylaxis Strategies Are Still Unclear

Monica Boen, June McKoy, Dennis West, Beatrice Edwards, Jayesh Mehta, Seema Singhal and Charles L. Bennett

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2403 **Poster Board: II-497**

Health Services and Outcomes Research Poster II

Thalidomide Versus Bortezomib-Based Regimens for Relapsed Myeloma: Meta-Analysis and Indirect Meta-Analysis

Ambuj Kumar, Iztok Hozo, and Benjamin Djulbegovic

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2362 **Poster Board: II-456**

Health Services and Outcomes Research Poster II

Treatment Patterns among Patients with Recently-Diagnosed Multiple Myeloma in a National Registry

Carla M. Van Bennekom, Noopur Raje, Kenneth C. Anderson, Theresa E. Anderson, and David W. Kaufman

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2374 **Poster Board: II-468**

Health Services and Outcomes Research Poster II

VELCADE®, Thalidomide, Dexamethasone (VTD) Followed by Melphalan, Prednisone, Thalidomide (MPT) Maintenance as a First Line Treatment Demonstrates High Response Rates for High-Risk Patients with Multiple Myeloma (MM) Who Are Non-Transplant Candidates: Updated Results of Phase II Trial

HyeonSeok Eom, Yeo-Kyeoung Kim, Joo-Seop Chung, Kihyun Kim, Hyo-Jung Kim, HoYoung Kim, Jong-Youl Jin, Young-Rok Do, Suk-Joong Oh, Cheolwon Suh, Chu-Myong Seong, Chul Soo Kim, Dong Soon Lee and Jae Hoon Lee

Time: 6:00 PM - 8:00 PM **Location: Hall A (Moscone Center)**

Abstract No.: 2785 **Poster Board: II-879**

Myeloma – Therapy, Excluding Transplantation Poster II

Final Analysis of HOVON-50 Randomized Phase III Study on the Effect of Thalidomide Combined with Adriamycine, Dexamethasone (AD) and High Dose Melphalan (HDM) in Patients with Multiple Myeloma (MM)

Henk Lokhorst, Bronno van der Holt, Sonja Zweegman, Peter A. Von Dem Borne, Gerard M.J. Bos, Sandra Croockewit, Jan J. Cornelissen, Marinus van Oers, Martyn Ronald Schaafsma, Harm Sinnige, Michel Delforge, Okke de Weerdt, Pierre W Wijermans, Shulamiet Wittebol, Edo Vellenga, Asiong Jie, Henriette Berenschot, Marinus Marwijk-kooy, and Pieter Sonneveld.

Time: 7:00 AM **Location: 120-121-122-123-124-125 - North (Moscone Center)**

Abstract No.: 157

Autologous Transplantation: Myeloma, Amyloidosis and Autoimmune Diseases

Superior Complete Response Rate and Progression-Free Survival after Autologous Transplantation with up-Front VELCADE-Thalidomide-Dexamethasone Compared with Thalidomide-Dexamethasone in Newly Diagnosed Multiple Myeloma

Michele Cavo, Paola Tacchetti, Francesca Patriarca, Maria Teresa Petrucci, Lucia Pantani, Michela Ceccolini, Monica Galli, Francesco Di Raimondo, Claudia Crippa, Elena Zamagni, Patrizia Tosi, Franco Narni, Sara Bringhen, Vittorio Montefusco, Massimo Offidani, Silvia Buttignol, Anna Levi, Ausilia Gorgone, Annamaria Brioli, Maria Caterina Pallotti, Tonino Spadano, Norbert Pescosta, Luca Baldini, Antonio Ledda, Tommaso Caravita, Antonietta Falcone, Alfonso Zaccaria, Giulia Perrone, Alessandro Petrucci, Antonio Palumbo, Mario Boccadoro, and Michele Baccarani.

Time: 7:15 AM **Location: 120-121-122-123-124-125 - North (Moscone Center)**

Abstract No.: 158

Autologous Transplantation: Myeloma, Amyloidosis and Autoimmune Diseases

Bortezomib-Doxorubicin-Dexamethasone as Induction Prior to Reduced Intensity Autologous Transplantation Followed by Lenalidomide as Consolidation/Maintenance in Elderly Untreated Myeloma Patients

Antonio Palumbo, Patrizia Falco, Francesca Gay, Vittorio Montefusco, Claudia Crippa, Francesca Patriarca, Milena Gilestro, Anna M. Liberati, Fausto Rossini, Tommaso Caravita, Antonietta Falcone, Federica Cavallo, Paolo Corradini, Giuseppe Rossi, and Mario Boccadoro

Time: 7:30 AM **Location: 120-121-122-123-124-125 - North (Moscone Center)**

Abstract No.: 159

Autologous Transplantation: Myeloma, Amyloidosis and Autoimmune Diseases

Ninety Percent Sustained Complete Response (CR) Rate Projected 4 Years after Onset of CR in Gene Expression Profiling (GEP)-Defined Low-Risk Multiple Myeloma (MM) Treated with Total Therapy 3 (TT3): Basis for GEP-Risk-Adapted TT4 and TT5

Bart Barlogie, Elias J. Anaissie, John D. Shaughnessy Jr., Frits van Rhee, Mauricio Pineda-Roman, Jeff Haessler, Klaus A. Hollmig, Yazan Alsayed, Sarah Waheed, Monica Graziutti, Elias Kiwan, and John Crowley

Time: 8:15 AM **Location: 120-121-122-123-124-125 - North (Moscone Center)**

Abstract No.: 162

Autologous Transplantation: Myeloma, Amyloidosis and Autoimmune Diseases

Preclinical Evaluation of CRx-501, a Potent Selective A2A Agonist as a Novel Drug Candidate for the Treatment of Multiple Myeloma

Richard J Rickles, Laura Pierce, Thomas Giordano, William Avery, Melissa Farwell, David Crowe, Winnie F. Tam, Mei Chen, Vikram Kansra, Douglas W. McMillin, Kenneth C Anderson, Constantine Mitsiades, and Margaret S. Lee

Abstract No.: 252 **Location: 2009-2011-2022-2024 - West (Moscone Center)**

Time: 8:45 AM

Pathophysiology and Translational Models

Melphalan + Prednisone Versus Melphalan + Prednisone + Thalidomide in Induction Therapy for Multiple Myeloma in Elderly Patients: Final Analysis of the Dutch Cooperative Group HOVON 49 Study

P. Wijermans, M. Schaafsma, Y. van Norden, R. Ammerlaan, S. Wittebol, H. Sinnige, Sonja Zweegman, M. van Marwijk Kooi, R. Van der Griend, H. Lokhorst and P. Sonneveld

Time: 3:30 PM **Location: Halls B and C (Moscone Center)**

Abstract No.: 649

Myeloma Therapy: Phase III Trials

Bortezomib (VELCADE)-Melphalan-Prednisone (VMP) Versus VELCADE-Thalidomide-Prednisone (VTP) in Elderly Untreated Multiple Myeloma Patients: Which Is the Best Partner for VELCADE: An Alkylating or An Immunomodulator Agent?

Maria-Victoria Mateos, Albert Oriol, Joaquín Martínez, Mª Teresa Cibeira, Raquel de Paz, Mª José Terol, José García-Laraña, Enrique Bengoechea, Rafael Martínez, Alejandro Martin, Felipe de Arriba, Luis Palomera, José Hernández, Jose-Luis Bello, María-Luisa Martín, Yolanda González, Joan Blade, Juan José Lahuerta and J.F San Miguel

Time: 4:00 PM **Location: Halls B and C (Moscone Center)**

Abstract No.: 651

Myeloma Therapy: Phase III Trials

A Prospective, Randomized, Phase III Study of Bortezomib, Melphalan, Prednisone and Thalidomide (VMPT) Versus Bortezomib, Melphalan and Prednisone (VMP) in Elderly Newly Diagnosed Myeloma Patients

Antonio Palumbo, Sara Bringhen, Davide Rossi, Valeria Magarotto, Francesco Di Raimondo, Roberto Ria, Massimo Offidani, Chiara Nozzoli, Francesca Patriarca, Vincenzo Callea, Giulia Benevolo, Roberto Marasca, Tommasina Guglielmelli, Manuela Rizzo, Mariella Grasso, Maria Teresa Petrucci, Paola Omedè, Gianluca Gaidano, and Mario Boccadoro

Time: 4:15 PM **Location: Halls B and C (Moscone Center)**

Abstract No.: 652

Myeloma Therapy: Phase III Trials

Thalidomide/Dexamethasone (TD) Vs. Bortezomib (VELCADE®)/Thalidomide / Dexamethasone (VTD) Vs. VBMCP/VBAD/ VELCADE® As Induction Regimens Prior Autologous Stem Cell Transplantation (ASCT) in Younger Patients with Multiple Myeloma (MM): First Results of a Prospective Phase III PETHEMA/Gem Trial

Laura Rosinol, Mª Teresa Cibeira, Joaquin Martinez, Maria Victoria Mateos, Mª José Terol, Javier de la Rubia, Luis Palomera, Felipe de Arriba, Albert Oriol, Adrian Alegre, Juan Besalduch, Raquel de Paz, José Garcia-Laraña, Joaquín Díaz-Mediavilla, Anna Sureda, Juan José Lahuerta, J.F. San Miguel and Joan Blade

Time: 4:45 PM **Location: Halls B and C (Moscone Center)**

Abstract No.: 654

Myeloma Therapy: Phase III Trials

Improved Survival of Patients with Multiple Myeloma after the Introduction of Novel Agents and the Applicability of the International Staging System (ISS) An Analysis of the Greek Myeloma Study Group (GMSG)

Efstathios Kastritis, Konstantinos Zervas, Argiris Symeonidis, Evangelos Terpos, Sossana Delimpassi, Nicolaos Anagnostopoulos, Evridiki Michali, Athanasios Zomas, Irini Katodritou, Dimitra Gika, Anastasia Pouli, Dimitrios Christoulas, Maria Roussou, Theofanis Economopoulos and Meletios A Dimopoulos

Time: 5:00 PM **Location: Halls B and C (Moscone Center)**

Abstract No.: 655

Myeloma Therapy: Phase III Trials

Maintenance Thalidomide May Improve Progression Free but Not Overall Survival; Results from the Myeloma IX Maintenance Randomisation

Gareth J Morgan, Graham H Jackson, Faith E Davies, Mark T Drayson, Roger G Owen, Walter M Gregory, Dena C Cohen, Alex J. Szubert, Susan E Bell, Fiona Ross and James A Child.

Time: 5:15 PM **Location: Halls B and C (Moscone Center)**

Abstract No.: 656

Myeloma Therapy: Phase III Trials

Clinical Efficacy of VEL-CTD (Bortezomib, Cyclophosphamide, Thalidomide, and Dexamethasone) Regimen in Patients with Relapsed or Refractory Multiple Myeloma: A Phase II Study

Yeo-Kyeoung Kim, Je-Jung Lee, Sang-Kyun Sohn, Ho-Jin Shin, Joo-Seop Chung, Young-Jin Choi, Joon-Ho Moon, Yee-Soo Chae, Jong-Gwang Kim, Jae-Sook Ahn, Deok-Hwan Yang, Hyeoung-Joon Kim and the Korean Multiple Myeloma Working Party (KMMWP).

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3693 **Poster Board: III-775**
Myeloma – Therapy, Excluding Transplantation Poster III

Combination of a Novel Proteasome Inhibitor NPI-0052 and Lenalidomide Trigger in Vivo Synergistic Cytotoxicity in Multiple Myeloma

Dharminder Chauhan, Ajita V. Singh, Mohan Brahmandam, Giada Bianchi, Klaus Podar, Teru Hideshima, Nikhil Munshi, Paul Richardson, Michael A. Palladino, and Kenneth C. Anderson

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3662 **Poster Board: III-744**
Myeloma – Pathophysiology and Preclinical Studies Excluding Therapy Poster III

CRD: A Phase 1 Dose Escalation Study to Determine the Maximum Tolerated Dose of Cyclophosphamide in Combination with Lenalidomide and Dexamethasone in Relapsed/Refractory Myeloma

Stephen Schey, Gareth J Morgan, Karthik Ramasamy, Beth Hazel, Karen Phekoo, Sophie Corderoy, Matthew Jenner and Faith Davies

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3707 **Poster Board: III-789**
Myeloma – Therapy, Excluding Transplantation Poster III

Declining Rates of Adverse Events and Dose Modifications with Lenalidomide in Combination with Dexamethasone

Jack Ishak, Meletios A Dimopoulos, Donna Weber, Robert D. Knight, Arran Shearer, and J. Jaime Caro

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3708 **Poster Board: III-790**
Myeloma – Therapy, Excluding Transplantation Poster III

Dimethylaminoparthenolide (DMAPT) in Multiple Myeloma

Colin D. Crean, Genglin Zhang, Karen E. Pollok, Anthony L. Sinn, Peter A Crooks, Sherif Farag, Rafat Abonour and Attaya Suvannasankha

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3672 **Poster Board: III-754**
Myeloma – Pathophysiology and Preclinical Studies Excluding Therapy Poster III

Impact of Chromosomal Abnormalities Del(13), T(4;14), and Del(17p) and Prior Treatment on Outcomes in Patients with Relapsed or Refractory Multiple Myeloma Treated with Lenalidomide

Herve Avet Loiseau, Jean Soulier, Jean-Paul Fermand, Thierry Facon, Michel Attal, Jean-Luc Harousseau, Karim Belhadj, Cyril Hulin, Laurent Garderet, Veronique Dorvaux, and Philippe Moreau

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3685 **Poster Board: III-767**
Myeloma – Therapy, Excluding Transplantation Poster III

Initial Treatment with Bortezomib (VELCADE®), Doxil®, and Dexamethasone (VDD) Is Superior to Thalidomide and Dexamethasone (TD) as Initial Therapy Prior to Autologous Stem Cell Transplantation (ASCT) for Multiple Myeloma (MM)

Andrzej Jakubowiak, Tara Kendall, Ammar Al-Zoubi, Yasser Khaled, Shin Mineishi, Christine Brozo, Erica Campagnaro, Moshe Talpaz and Mark S. Kaminski

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**
Abstract No.: 3713 **Poster Board: III-795**
Myeloma – Therapy, Excluding Transplantation Poster III

Lenalidomide as Salvage Therapy after Allogeneic Stem Cell Transplantation in Multiple Myeloma

Friederike Lehmann, Jean El-Cheikh Jr., Tatjana Zabelina, Francis Ayuk, Christine Wolschke, Djordje Atanackovic, Ulrike Bacher, Axel R. Zander, Didier Blaise, Mohamad Mohty and Nicolaus Kroeger

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3704 **Poster Board: III-786**

Myeloma – Therapy, Excluding Transplantation Poster III

Long-Term Outcomes of Autologous Transplantation in Multiple Myeloma: Benefit from the Newer Drugs Used in the Relapsed Setting

Roman Hajek, Marta Krejci, Vlastimil Scudla, Elena Tothova, Martin Mistrik, Jaroslav Bacovsky, Miroslava Schutzova, Vladimir Koza, Tomas Papajik, Libuse Novosadova, Hana Frankova, Yvetta Stavarova, Frantisek Lehanka, Milena Vranova, Petr Kessler, Marketa Zemanova, Ivana Meluzinova, Nadezda Seifertova, Elen Sumna, Ludek Pour, Vladimir Maisnar and Zdenek Adam

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3331 **Poster Board: III-413**

Clinical Results - Autologous Transplantation Poster III

Longer Duration of Treatment and Maintenance of Best Response with Lenalidomide and Dexamethasone Prolongs Overall Survival in Patients with Relapsed or Refractory Multiple Myeloma

Jesús F San Miguel, Meletios A Dimopoulos, Edward A. Stadtmauer, S. Vincent Rajkumar, David Siegel, Marie-Laure Bravo, Marta Olesnyckyj, Robert D. Knight, Jerome B. Zeldis, Jean-Luc Harousseau and Donna M. Weber

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3702 **Poster Board: III-784**

Myeloma – Therapy, Excluding Transplantation Poster III

Major Shrinking of Residual Tumor Cell Burden and Achievement of Molecular Remissions in Myeloma Patients Undergoing Post-Trasplant Consolidation with Bortezomib, Thalidomide and Dexamethasone: A Qualitative and Quantitative PCR Study

Marco Ladetto, Gloria Pagliano, Simone Ferrero, Federica Cavallo, Daniela Drandi, Michela Boi, Loredana Santo, Patrizia Pregno, Mariella Grasso, Anna Marina Liberati, Tommaso Caravita, Francesco Pisani, Claudia Crippa, Vincenzo Callea, Antonietta Falcone, Sergio Morandi, Mario Boccadoro, and Antonio Palumbo.

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3683 **Poster Board: III-765**

Myeloma – Therapy, Excluding Transplantation Poster III

The Novel Aurora Kinase Inhibitor ENMD-2076 Has Potent Single Agent Activity against Multiple Myeloma (MM) in Vitro and in Vivo, and Shows Synergistic Activity in Combination with Lenalidomide

Xiaojing Wang, Anthony L. Sinn, Attaya Suvannasankha, Colin D. Crean, Li Chen, Shuhong Zhang , Jing Liang, Genglin Zhang, Karen E. Pollok, Rafat Abonour, Carolyn Sidor, Mark R. Bray, and Sherif S. Farag

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3660 **Poster Board: III-742**

Myeloma – Pathophysiology and Preclinical Studies Excluding Therapy Poster III

Phase I Results of Perifosine (KRX-0401) in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma (MM)

Andrzej Jakubowiak, Paul Richardson, Todd M. Zimmerman, Melissa Alsina, Jonathan L. Kaufman, Colleen Harvey, Christine Brozo, Tara Kendall, Amanda McAllister, Teru Hideshima, Peter Sportelli, Lesa Gardner, Kenneth C. Anderson, and Kathy Giusti

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3691

Myeloma – Therapy, Excluding Transplantation Poster III

A Phase I Study of Vorinostat in Combination with Lenalidomide and Dexamethasone in Patients with Relapsed or Refractory Multiple Myeloma

David Siegel, Donna Weber, Constantine S. Mitsiades, Syed Rizvi, Jose Garcia-Vargas, Jason Howe, David Reiser, Kenneth C. Anderson, and Paul Richardson

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3705 **Poster Board: III-787**

Myeloma – Therapy, Excluding Transplantation Poster III

A Phase III Study of Enoxaparin Versus Low-Dose Warfarin Versus Aspirin as Thromboprophylaxis for Patients with Newly Diagnosed Multiple Myeloma Treated up-Front with Thalidomide-Containing Regimens

Michele Cavo, Antonio Palumbo, Sara Bringhen, Antonietta Falcone, Pellegrino Musto, Fabio Ciceri, Mariella Grasso, Renato Zambello, Maria Concetta Petti, Fabrizio Ciambelli, Giovanni De Sabbata, Stefano Rocco, Luigi Gugliotta, Filippo Gherlinzoni, Alfonso D'Arco, Massimo Martelli, Tommasina Guglielmelli, Paola Tacchetti, Michele Baccarani, and Mario Boccadoro

Time: **5:30 PM - 7:30 PM** **Locaiton: Hall A (Moscone Center)**

Abstract No.: 3017 **Poster Board: III-99**

Antithrombotic Therapy Poster III

Risk of Venous Thromboembolism with Thalidomide in Cancer Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Keriann N Gray, David Chu, Shenhong Wu, and Richard Z. Lin

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3820 **Poster Board: III-902**

Pathophysiology of Thrombosis Poster II

Safety and Efficacy Outcomes with Lenalidomide Plus Dexamethasone in Relapsed or Refractory Multiple Myeloma Were Not Significantly Different for the Treatment of Patients with or without High-Risk Disease or Elderly Status

Asher Chanan-Khan, Meletios A Dimopoulos, Donna M. Weber, Andrew Spencer, Michel Attal, Andrew Belch, Alessandro Corso, Tommy Fu, Jerome B. Zeldis, Marta Olesnyckyj, Robert D. Knight, and Sagar Lonial

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3701 **Poster Board: III-783**

Myeloma – Therapy, Excluding Transplantation Poster III

Sequential Administration of Bortezomib, Liposomal Doxorubicin and Dexamethasone (BDD) Followed by Thalidomide and Dexamethasone (TD) Results in Rapid Control of Untreated High-Risk Multiple Myeloma (MM) and Improves Depth of Response

Heather Landau, Hani Hassoun, Adam Cohen, Elizabeth Hoover, Tarun Kewalramani, Adam Boruchov, Virginia Klimek, Lillian Reich, Elyn Riedel, Neeta Pandit-Taskar, Stephen D. Nimer, and Raymond L. Comenzo

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3712 **Poster Board: III-794**

Myeloma – Therapy, Excluding Transplantation Poster III

Sequential VAD (Vincristine, Adriamycin, Dexamethasone) and VTD (Bortezomib, Thalidomide, Dexamethasone) Induction Followed by High-Dose Therapy with Autologous Stem Cell Transplantation and Maintenance Treatment with Bortezomib for Newly Diagnosed Multiple Myeloma: Final Analysis of Phase II Trial

Sung-Soo Yoon, Hye Jin Kim, Joo Seop Chung, HyeonSeok Eom, Jun-Ho Jang, Hye Jin Kang, Cheol Soo Kim, Kihyun Kim, Dongsoon Lee, Jae Hoon Lee, Junglim Lee, Sang Jae Lee, Yoo Hong Min, Chu-Myong Seong, Sang-Kyun Sohn, Cheolwon Suh and Jong-Ho Won

Time: **5:30 PM - 7:30 PM** **Location: Hall A (Moscone Center)**

Abstract No.: 3330 **Poster Board: III-412**

Clinical Results - Autologous Transplantation Poster III

Stem Cell Mobilization Following Initial Therapy with Lenalidomide and Dexamethasone in Patients with Newly Diagnosed Multiple Myeloma

Shaji Kumar, Martha Lacy, Angela Dispenzieri, Suzzanne Hayman, Francis Buadi, David Dingli, Teresa Miceli, Mark Litzow, S.Vincent Rajkumar and Morie Gertz

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**

Abstract No.: 3467 **Poster Board: III-549**

Ex Vivo Expansion, Mobilization and Engraftment Poster II

Superior Incidence of Progression-Free Survival (PFS) Following High-Dose Melphalan (HDM) and Autologous Stem Cell Transplant (ASCT) for Multiple Myeloma (MM) Patients Receiving Pre-Transplant Induction with IMiDs Versus Conventional VAD Induction Chemotherapy

H. Kent Holland, Scott R. Solomon, Asad Bashey, and Lawrence E. Morris

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**

Abstract No.: 3335 **Poster Board: III-417**

Clinical Results - Autologous Transplantation Poster III

Thalidomide + Dexamethasone as Maintenance after Single Autologous Stem Cell Transplantation Improves Progression-Free Survival (PFS) in Advanced Multiple Myeloma. A Prospective Brazilian Randomized Trial

Angelo Maiolino, Vania T. Hungria, G. Oliveira-Duarte, LC Oliveira, DR Mercante, Ecm Miranda, A. Quero, AL Miguel Peres, Jc Barros, P. Tanaka, RP Magalhães, Eduardo M. Rego, M. Nucci, Irene Lorand-Metze, CSP Lima, I. Zalcberg, E. Braggio, and Carmino De Souza.

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**

Abstract No.: 3703 **Poster Board: III-785**

Myeloma – Therapy, Excluding Transplantation Poster III

VAMP/ThaCyDex: VELCADE® (Bortezomib), Adriamycin, Melphalan and Prednisone Alternating with Thalidomide, Cyclophosphamide and Dexametasone as a Salvage Regimen in Relapsed Multiple Myeloma Patients

Enrique Colado, Maria-Victoria Mateos, Maria-Jose Moreno, Felipe de Arriba, Javier de la Rubia, Juan José Lahuerta, Pastora Iniesta, Maria Cruz Viguria, Ana Pilar Gonzalez, Ramón García-Sanz, Juan Olazabal, and Jesús F San Miguel.

Time: 5:30 PM - 7:30 PM **Location: Hall A (Moscone Center)**

Abstract No.: 3694 **Poster Board: III-776**

Myeloma – Therapy, Excluding Transplantation Poster III

Tuesday, December 9, 2008

Combination of Lenalidomide, Melphalan, Prednisone and Thalidomide (RMPT) in Relapsed/Refractory Multiple Myeloma: Results of a Multicenter Phase II Clinical Trial

Antonio Palumbo, Patrizia Falco, Grazia Sanpaolo, Antonietta Falcone, Vincenzo Ferderico, Letizia Canepa, Monica Crugnola, Luca Baldini, Alessandra Larocca, Valeria Magarotto, Maria Teresa Petrucci, and Mario Boccadoro

Time: 8:00 AM **Location: Gateway Ballroom 103 - South (Moscone Center)**

Abstract No.: 868

Novel Therapies for Myeloma and Related Disorders

Immunomodulatory Derivatives of Thalidomide (IMiD)-Induced Neutropenia Is Associated with PU.1 Downregulation and Myeloid Maturation Arrest

Rekha Pal, G. David Roodman, Markus Mapara, Lynn Mocsinski, Alan F List, and Suzanne Lentzsch

Time: 8:15 AM **Location: 2005-2007-2018-2020 - West (Moscone Center)**

Abstract No.: 845

Molecular Pathology of Myeloma

Thalidomide/Revlimid Publications – 4th Quarter, 2008

The role of novel drugs in multiple myeloma.

Dimopoulos MA, Kastritis E.

Ann Oncol. 2008 Sep;19 Suppl 7:vii121-7.

http://www.ncbi.nlm.nih.gov/pubmed/18790953?ordinalpos=46&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

No abstract available.

Update on recent developments for patients with newly diagnosed multiple myeloma.

Palumbo A, Magarotto V, Gay F, Falco P, Bringhen S, Boccadoro M.

Ann N Y Acad Sci. 2008 Sep;1138:19-21.

http://www.ncbi.nlm.nih.gov/pubmed/18837878?ordinalpos=45&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors discuss the use of thalidomide as a new standard of care in elderly patients with myeloma.

Recent studies have demonstrated that novel therapeutic combinations are challenging melphalan and prednisone (MP) as the standard of care in elderly patients with multiple myeloma. Combination regimens containing bortezomib or thalidomide can achieve response rates, especially complete response rates, which are superior to those seen with standard MP alone, and offer new possibilities for this patient population.

Treatment of patients with advanced cardiac AL amyloidosis with oral melphalan, dexamethasone, and thalidomide.

Palladini G, Russo P, Lavatelli F, Nuvolone M, Albertini R, Bosoni T, Perfetti V, Obici L, Perlini S, Moratti R, Merlini G.

Ann Hematol. 2008 Sep 9. [Epub ahead of print.]

http://www.ncbi.nlm.nih.gov/pubmed/18779964?ordinalpos=40&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors find that treatment with oral melphalan, thalidomide, and reduced intensity dexamethasone is feasible in patients with advanced cardiac AL amyloidosis.

Patients with primary (AL) amyloidosis and heart failure have a very poor prognosis and cannot tolerate aggressive therapy, such as autologous stem cell transplantation and high-dose dexamethasone-based regimens. We prospectively treated 22 patients with advanced cardiac amyloidosis combining oral melphalan, thalidomide, and reduced intensity dexamethasone (MTD). Six patients died due to cardiac amyloidosis before completing cycle 3. Early death was associated with reduced ejection fraction. Eight patients achieved a hematological response and four achieved a durable improvement of cardiac dysfunction. Treatment with MTD is feasible in patients with advanced cardiac AL amyloidosis and effective in subjects with preserved systolic function.

Genetic associations with thalidomide mediated venous thrombotic events in myeloma identified using targeted genotyping.

Johnson DC, Corthals S, Ramos C, Hoering A, Cocks K, Dickens NJ, Haessler J, Goldschmidt H, Child JA, Bell SE, Jackson G, Baris D, Rajkumar SV, Davies FE, Durie BG, Crowley J, Sonneveld P, Van Ness B, Morgan GJ.

Blood. 2008 Sep 19. [Epub ahead of print.]

http://www.ncbi.nlm.nih.gov/pubmed/18805967?ordinalpos=29&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

This analysis shows that the set of SNPs associated with thalidomide-related venous thromboembolism (VTE) are enriched in genes and pathways important in drug transport/metabolism, DNA repair, and cytokine balance.

A venous thromboembolism (VTE) with the subsequent risk of pulmonary embolism is a major concern in the treatment of multiple myeloma patients with thalidomide. The susceptibility to developing a VTE in response to thalidomide therapy is likely to be influenced by both genetic and environmental factors. To test genetic variation associated with treatment related VTE in patient peripheral blood DNA, we used a custom-built molecular inversion probe (MIP) based single nucleotide polymorphism (SNP) chip containing 3404 SNPs. SNPs on the chip were selected in "functional regions" within 964 genes spanning 67 molecular pathways thought to be involved in the pathogenesis, treatment response and side effects associated with myeloma therapy. Cases and controls were taken from three large clinical trials: MRC Myeloma IX, Hovon-50 and ECOG EA100, which compared conventional treatments with thalidomide in myeloma patients. Our analysis showed that the set of SNPs associated with thalidomide-related VTE were enriched in genes and pathways important in drug transport/metabolism, DNA repair and cytokine balance. The effects of the SNPs associated with thalidomide related VTE may be functional at the level of the tumor cell, the tumor-related microenvironment, and the endothelium.

Retraction: Barlogie et al. Duration of survival in patients with myeloma treated with thalidomide. N Engl J Med 2008;359:210-2.

Barlogie B, Shaughnessy JD Jr, Crowley J.

N Engl J Med. 2008 Sep 25;359(13):1410.

http://www.ncbi.nlm.nih.gov/pubmed/18815407?ordinalpos=28&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Retraction of: Barlogie B, Shaughnessy JD Jr, Crowley J. *N Engl J Med.* 2008 Jul 10;359(2):210-2.

Comparison of dissolution profile and plasma concentration-time profile of the thalidomide formulations made by Japanese, Mexican and British companies. [Article in Japanese]

Fujita Y, Yamamoto K, Aomori T, Murakami H, Horiuchi R.

Yakugaku Zasshi. 2008 Oct;128(10):1449-57.

http://www.ncbi.nlm.nih.gov/pubmed/18827465?ordinalpos=52&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

In order to determine appropriate amounts of Japanese thalidomide capsules in the treatment of Japan-based multiple myeloma patients, the authors compare the dissolution profile and plasma thalidomide concentrations of Japanese and British capsules and Mexican tablets.

Thalidomide is an important advance in the treatment of multiple myeloma. In Japan thalidomide is now on the approval step for the treatment of multiple myeloma. The drug has some bothersome side effects such as defect of organogenesis, neuropathy, constipation and fatigue, but is likely more effective than standard chemotherapy and is changing multiple myeloma treatment. At this moment, Japanese patients must import the thalidomide preparations from Mexico, Britain and elsewhere, but after approval, the patients will be able to get the new Japanese thalidomide capsules. In order to determine appropriate amounts of Japanese thalidomide capsules in the treatment of multiple myeloma, we compared the dissolution profile and plasma thalidomide concentrations of Japanese and British capsules and Mexican tablets. The dissolution test was performed according to the Japanese and the United States Pharmacopoeia. The pharmacokinetic data for Japanese capsules were obtained from the clinical trial in Japanese subjects and compared with those data published for other formulations. The dissolution rate of the Japanese capsule was the fastest, followed by British and Mexican formulations. The pharmacokinetic profiles of Japanese and British capsules were similar, while the 100 mg Japanese thalidomide capsule demonstrated a 1.6-fold higher maximum plasma concentration than the 200 mg Mexican thalidomide tablet (1.7 vs. 1.1 microg/ml), greatly shortened t(max) (4.5 vs. 6.2 h), and the apparent half life was only one-third of the Mexican tablet (4.8 vs. 13.5 h). A comparison of the dissolution and the pharmacokinetic absorption profiles demonstrated a rank-order correlation. Physicians and pharmacists should be aware of the probable alteration in plasma thalidomide concentration when switching to the Japanese capsule, especially from the Mexican tablet, and should monitor clinical response carefully.

Consolidation Therapy with Bortezomib/Lenalidomide/ Dexamethasone Versus Bortezomib/Dexamethasone After a Dexamethasone-Based Induction Regimen in Patients with Multiple Myeloma: A Randomized Phase III Trial.

Fonseca R, Rajkumar SV.

Clin Lymphoma Myeloma. 2008 Oct;8(5):315-7.

http://www.ncbi.nlm.nih.gov/pubmed/18854289?ordinalpos=37&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors introduce an upcoming clinical trial that will study the potential role of bortezomib and dexamethasone (VD) or VD plus lenalidomide as primary first-line therapy in the treatment of myeloma.

In recent years, we have seen tremendous progress in our ability to achieve durable responses in patients with multiple myeloma. At the center of this progress, we have the development of 2 unrelated classes of drugs: proteasome inhibitors such as bortezomib and immunomodulatory drugs such as thalidomide and lenalidomide. The depth and durability of responses attained with these agents in the first-line setting has raised the possibility that they may be considered primary therapy. The Eastern Cooperative Oncology Group E1A05 clinical trial addresses the potential role of bortezomib and dexamethasone (VD) or VD plus lenalidomide (VRD) as primary first-line therapy. This clinical trial enrolls patients who have completed a dexamethasone-based induction (excluding patients using bortezomib). Assuming that most patients entering this clinical trial have been previously treated with thalidomide or lenalidomide, the trial will test whether switching to a proteasome inhibitor (VD arm) versus adding a proteasome inhibitor (VRD) results in superior longterm disease control. Patients entering this clinical trial will have deferred stem cell transplantation until the time of relapse. The primary endpoint of the trial is progression-free survival. By using an alkylator-free consolidation and reserving stem cell transplantation until the time of relapse, we hope that these treatment strategies will further prolong the survival of patients with myeloma.

Lenalidomide in combination with dexamethasone for the treatment of multiple myeloma after one prior therapy.

Hazarika M, Rock E, Williams G, Dagher R, Sridhara R, Booth B, Farrell A, Justice R, Pazdur R.

Oncologist. 2008 Oct;13(10):1120-7. [Epub 2008 Oct 15.]

http://www.ncbi.nlm.nih.gov/pubmed/18922829?ordinalpos=48&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

In two randomized, double-blind, multicenter studies, the combination of lenalidomide and dexamethasone (LD) is compared with placebo and dexamethasone (PD) in patients with myeloma who have received at least one prior therapy. The major toxicity observed during these trials is myelosuppression. The serious toxicities include thromboembolic events.

PURPOSE: Lenalidomide (CC-5013, Revlimid; Celgene Corporation, Summit, NJ), a thalidomide analogue, was granted approval by the U.S. Food and Drug Administration (FDA) on June 29, 2006, for use in combination with dexamethasone in patients with multiple myeloma (MM) who have received at least one prior therapy. The FDA approved lenalidomide with a restricted distribution program, RevAssist. EXPERIMENTAL DESIGN: In two randomized, double-blind, multicenter studies, the combination of lenalidomide and dexamethasone (LD) was compared with placebo and dexamethasone (PD) in patients with MM who had received at least one prior therapy. The primary endpoint was time to progression (TTP). RESULTS: Following a prespecified interim analysis of TTP, an independent data-monitoring committee advised the sponsor to halt the two studies. For both studies, the interim analysis for efficacy revealed a statistically significant longer TTP with LD than with PD. The most clinically relevant grade 3 and 4 adverse events that occurred more frequently in the LD arm were neutropenia, thrombocytopenia, deep vein thrombosis, pulmonary embolism, and atrial fibrillation. Thrombotic or thromboembolic events, including deep vein thrombosis, pulmonary embolism, thrombosis, and intracranial venous sinus thrombosis were reported more frequently in patients treated with LD than with PD. CONCLUSIONS: The FDA approved lenalidomide based on interim results from two multicenter, placebo-controlled, randomized trials comparing the combination of LD with PD that revealed a longer TTP with LD than with PD. The major toxicity observed during these trials was myelosuppression. The serious toxicities included thromboembolic events.

Lenalidomide inhibits osteoclastogenesis, survival factors and bone-remodeling markers in multiple myeloma.

Breitkreutz I, Raab MS, Vallet S, Hideshima T, Raje N, Mitsiades C, Chauhan D, Okawa Y, Munshi NC, Richardson PG, Anderson KC.

Leukemia. 2008 Oct;22(10):1925-32. [Epub 2008 Jul 3.]

http://www.ncbi.nlm.nih.gov/pubmed/18596740?ordinalpos=21&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors investigate the effect of lenalidomide on osteoclast (OCL) formation and osteoclastogenesis in comparison with bortezomib and conclude that both agents specifically target key factors in osteoclastogenesis, and could directly affect the myeloma-OCL- bone marrow stromal cells activation loop in osteolytic bone disease.

Osteolytic bone disease in multiple myeloma (MM) is caused by enhanced osteoclast (OCL) activation and inhibition of osteoblast function. Lenalidomide and bortezomib have shown promising response rates in relapsed and newly diagnosed MM, and bortezomib has recently been reported to inhibit OCLs. We here investigated the effect of lenalidomide on OCL formation and osteoclastogenesis in comparison with bortezomib. Both drugs decreased alpha V beta 3-integrin, tartrate-resistant acid phosphatase-positive cells and bone resorption on dentin disks. In addition, both agents decreased receptor activator of nuclear factor-kappaB ligand (RANKL) secretion of bone marrow stromal cells (BMSCs) derived from MM patients. We identified PU.1 and pERK as major targets of lenalidomide, and nuclear factor of activated T cells of bortezomib, resulting in inhibition of osteoclastogenesis. Furthermore, downregulation of cathepsin K, essential for resorption of the bone collagen matrix, was observed. We demonstrated a significant decrease of growth and survival factors including macrophage inflammatory protein-alpha, B-cell activating factor and a proliferation-inducing ligand. Importantly, in serum from MM patients treated with lenalidomide, the essential bone-remodeling factor RANKL, as well as the RANKL/OPG ratio, were significantly reduced, whereas osteoprotegerin (OPG) was increased. We conclude that both agents specifically target key factors in osteoclastogenesis, and could directly affect the MM-OCL-BMSCs activation loop in osteolytic bone disease.

Non-thromboembolic pulmonary hypertension in multiple myeloma, after thalidomide treatment: a pilot study.

Lafaras C, Mandala E, Verrou E, Platogiannis D, Barbetakis N, Bischiniotis T, Zervas K.

Ann Oncol. 2008 Oct;19(10):1765-9. [Epub 2008 May 13.]

http://www.ncbi.nlm.nih.gov/pubmed/18480066?ordinalpos=34&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors aim to detect clinical and subclinical nonthromboembolic pulmonary hypertension (PH) in myeloma patients after thalidomide treatment and conclude that thalidomide possibly causes a vasodilator and vasoconstriction imbalance, which may cause abnormal pulmonary vascular response interfering to a vicious circle perpetuating PH.

BACKGROUND: Multiple myeloma (MM) is thrombogenic as a consequence of multiple hemostatic effects and endothelial damage. Thalidomide has been associated with an increased risk of thromboembolic pulmonary hypertension (PH). PH in the absence of venous thromboembolism has also been described in MM patients during thalidomide treatment. Aim: Detection of clinical and subclinical nonthromboembolic PH in MM patients after thalidomide treatment. PATIENTS AND METHODS: Eighty-two patients, 46-82 years (median age 61 years), 42 males, were studied. They underwent echocardiographic study at baseline, 1 month thereafter, 6 months later and whenever symptoms indicating deterioration of cardiac function appeared. Echocardiographic signs of PH were especially identified. RESULTS: Clinical and echocardiographic evaluation revealed four patients (out of 82 patients, 4.87%) with PH. Nonimaging and imaging diagnostic methods excluded thromboembolic PH. Statistical analysis demonstrated significant correlation between structural heart disease and PH (r = 14.078; P = 0.008). No significant correlation between age (r = 0.770; P = 0.724), gender (r = 1.157; P = 0.285), International Staging System (ISS) (r = 0.316; P = 0.716) and PH was found. CONCLUSIONS: Preexisted endothelial dysfunction due to structural cardiac disease enhances the vasoactive substances release causing increased pulmonary vascular resistance. Thalidomide possibly causes a vasodilator and vasoconstriction imbalance, which may cause abnormal pulmonary vascular response interfering to a vicious circle perpetuating PH.

Role of thalidomide in previously untreated patients with multiple myeloma.

Musto P, D'Auria F, Pietrantuono G, Bringhen S, Morabito F, Di Raimondo F, Pozzi S, Sacchi S, Boccadoro M, Palumbo A; Gruppo Italiano Malatte Ematologiche dell'Adulto Multiple Myeloma Working Party; Italian Myeloma Network and Gruppo Italiano Studio Linfomi.

Expert Rev Anticancer Ther. 2008 Oct;8(10):1569-80.

http://www.ncbi.nlm.nih.gov/pubmed/18925849?ordinalpos=43&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors report and discuss the clinical results achieved with thalidomide alone or in combination with other drugs in previously untreated myeloma patients.

Thalidomide represents one of the most relevant therapeutic advances for patients with multiple myeloma over the last 10 years. Despite some toxicities, it has demonstrated significant efficacy in elderly patients, as well as in the setting of younger subjects receiving autologous stem cell transplantation. Here, we report and discuss the clinical results achieved with thalidomide alone or in combination with dexamethasone or other drugs, such as melphalan, cyclophosphamide, doxorubicin and bortezomib, in previously untreated myeloma patients.

Serum C-reactive protein at diagnosis and response to therapy is the most powerful factor predicting outcome of multiple myeloma treated with thalidomide/ anthracycline-based therapy.

Offidani M, Corvatta L, Polloni C, Piersantelli MN, Galieni P, Visani G, Alesiani F, Catarini M, Brunori M, Burattini M, Centurioni R, Ferranti M, Giuliodori L, Candela M, Mele A, Marconi M, Leoni P.

Clin Lymphoma Myeloma. 2008 Oct;8(5):294-9.

http://www.ncbi.nlm.nih.gov/pubmed/18854284?ordinalpos=38&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors investigate factors affecting response, progression-free survival, and overall survival in patients with myeloma treated with the thalidomide, dexamethasone, and pegylated liposomal doxorubicin regimen with the aim to select patients benefiting more from this therapy. They conclude that Serum C-reactive protein before therapy and response after therapy are the only factors useful in identifying patients benefiting from anthracycline/thalidomide-based therapy.

Background: Few studies have focused on factors affecting outcome in patients with multiple myeloma (MM) treated with thalidomide-based therapy. We investigated factors affecting response, progression-free survival (PFS), and overall survival (OS) in patients with MM treated with the thalidomide, dexamethasone, and pegylated liposomal doxorubicin (ThaDD) regimen with the aim to select patients benefiting more from this therapy. Patients and Methods: Sixty-six patients with MM were treated first line with the ThaDD regimen. We analyzed demographics and disease-related characteristics to search for factors affecting response (>/= very good partial remission [VGPR] vs. < VGPR], PFS, and OS. Results: Overall, 45 patients (68%) showed response >/= VGPR; median TTP and OS were 23.5 months and 35.5 months, respectively. Multivariate analysis selected only serum C-reactive protein (sCRP) as a predictive factor for response (P < .0001). By multivariate analysis, normal sCRP level (P = .001) and response to treatment >/= VGPR (P = .007) were found to be associated with longer PFS. The factors that remained significantly associated with a longer OS when assessed by multivariate analysis were normal sCRP level (P = .005) and response to therapy >/= VGPR (P = .019). Conclusion: Serum C-reactive protein before therapy and response after therapy are the only factors useful in identifying patients benefiting from anthracycline/thalidomide-based therapy.

A systematic review of phase II trials of thalidomide/dexamethasone combination therapy in patients with relapsed or refractory multiple myeloma.

von Lilienfeld-Toal M, Hahn-Ast C, Furkert K, Hoffmann F, Naumann R, Bargou R, Cook G, Glasmacher A.

Eur J Haematol. 2008 Oct;81(4):247-52. [Epub 2008 Jul 10.]

http://www.ncbi.nlm.nih.gov/pubmed/18637031?ordinalpos=41&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors conduct a systematic review of studies evaluating thalidomide/dexamethasone in relapsed/refractory myeloma and find that using thal/dex results in an improved response rate in relapsed/refractory myeloma, with a toxicity rate comparable to thalidomide monotherapy.

Thalidomide monotherapy in relapsed/refractory multiple myeloma (MM) has a response rate of 30%. The combination of thalidomide with dexamethasone (Thal/Dex) is expected to improve responses, but it is unknown if the combination increases the rate of adverse events. Here, we conducted a systematic review of studies evaluating Thal/Dex in relapsed/refractory MM. Twelve studies were included, comprising 451 patients. The response rate (CR and PR) was 46% (95% CI 42-51%). Therapy-related toxicity was comparable to thalidomide monotherapy and included somnolence (26%, 95% CI 22-31%), constipation (37%, 95% CI 32-42%) and peripheral neuropathy (27%, 95% CI 23-32%). Only venous thromboembolism appeared to occur more often with Thal/Dex (5%, 95% CI 3-8%). Thus, using Thal/Dex results in an improved response rate in relapsed/refractory MM, with a toxicity rate comparable to thalidomide monotherapy.

Treatment for multiple myeloma: current status and future strategy in Japan. [Article in Japanese]

Iida S.

Rinsho Ketsueki. 2008 Oct;49(10):1368-73.

http://www.ncbi.nlm.nih.gov/pubmed/18833921?ordinalpos=50&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

No abstract available.

Multiple myeloma: diagnosis and treatment.

Nau KC, Lewis WD.

Am Fam Physician. 2008 Oct 1;78(7):853-9.

http://www.ncbi.nlm.nih.gov/pubmed/18841734?ordinalpos=32&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors provide an overview of myeloma and its treatment, including discussion of thalidomide and lenalidomide.

Multiple myeloma, the most common bone malignancy, is occurring with increasing frequency in older persons. Typical symptoms are bone pain, malaise, anemia, renal insufficiency, and hypercalcemia. Incidental discovery on comprehensive laboratory panels is common. The disease is diagnosed with serum or urine protein electrophoresis or immunofixation and bone marrow aspirate analysis. Skeletal radiographs are important in staging multiple myeloma and revealing lytic lesions, vertebral compression fractures, and osteoporosis. Magnetic resonance imaging and positron emission tomography or computed tomography are emerging as useful tools in the evaluation of patients with myeloma; magnetic resonance imaging is preferred for evaluating acute spinal compression. Nuclear bone scans and dual energy x-ray absorptiometry have no role in the diagnosis and staging of myeloma. The differential diagnosis of monoclonal gammopathies includes monoclonal gammopathy of uncertain significance, smoldering (asymptomatic) and symptomatic multiple myeloma, amyloidosis, B-cell non-Hodgkin lymphoma, Waldenström macroglobulinemia, and rare plasma cell leukemia and heavy chain diseases. Patients with monoclonal gammopathy of uncertain significance or smoldering multiple myeloma should be followed closely, but not treated. Symptomatic multiple myeloma is treated with chemotherapy followed by autologous stem cell transplantation, if possible. Melphalan, prednisolone, dexamethasone, vincristine, doxorubicin, bortezomib, and thalidomide and its analogue lenalidomide have been used successfully. It is important that family physicians recognize and appropriately treat multiple myeloma complications. Bone pain is treated with opiates, bisphosphonates, radiotherapy, vertebroplasty, or kyphoplasty; nephrotoxic nonsteroidal anti-inflammatory drugs should be avoided. Hypercalcemia is treated with isotonic saline infusions, steroids, furosemide, or bisphosphonates. Because of susceptibility to infections, patients require broad-spectrum antibiotics for febrile illness and immunization against influenza, pneumococcus, and Haemophilus influenzae B. Five-year survival rates approach 33 percent, and the median survival rate is 33 months.

Bone marrow microenvironment and the identification of new targets for myeloma therapy.

Podar K, Chauhan D, Anderson KC.

Leukemia. 2008 Oct 9. [Epub ahead of print.]

http://www.ncbi.nlm.nih.gov/pubmed/18843284?ordinalpos=24&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors discuss new agents, including thalidomide and lenalidomide, which mediate myeloma tumor cytotoxicity in the bone marrow milieu.

The development of multiple myeloma (MM) is a complex multi-step process involving both early and late genetic changes in the tumor cell as well as selective supportive conditions by the bone marrow (BM) microenvironment. Indeed, it is now well established that MM cell-induced disruption of the BM homeostasis between the highly organized cellular and extracellular compartments supports MM cell proliferation, survival, migration and drug resistance through activation of various signaling (for example, PI3K/Akt, JAK/Stat-, Raf/MEK/MAPK-, NFkappaB- and Wnt-) pathways. Based on our enhanced understanding of the functional importance of the MM BM microenvironment and its inter-relation with the MM cell resulting in homing, seeding, proliferation and survival, new molecular targets have been identified and derived treatment regimens in MM have already changed fundamentally during recent years. These agents include thalidomide, its immunomodulatory derivative lenalidomide and the proteasome inhibitor bortezomib, which mediate tumor cytotoxicity in the BM milieu. Ongoing studies are further delineating MM pathogenesis in the BM to enhance cytotoxicity, avoid drug resistance and improve patient outcome.

Oral melphalan, prednisone, and thalidomide in elderly patients with multiple myeloma: updated results of a randomized controlled trial.

Palumbo A, Bringhen S, Liberati AM, Caravita T, Falcone A, Callea V, Montanaro M, Ria R, Capaldi A, Zambello R, Benevolo G, Derudas D, Dore F, Cavallo F, Gay F, Falco P, Ciccone G, Musto P, Cavo M, Boccadoro M.

Blood. 2008 Oct 15;112(8):3107-14. [Epub 2008 May 27.]

http://www.ncbi.nlm.nih.gov/pubmed/18505783?ordinalpos=20&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors update analysis of the oral combination melphalan, prednisone, and thalidomide (MPT) in newly diagnosed patients with myeloma. The updated data confirm activity of MPT for progression free survival but fail to show any survival advantage, as opposed to benefit found in their initial analysis. They conclude that new agents in the management of relapsed disease could explain this finding.

The initial analysis of the oral combination melphalan, prednisone, and thalidomide (MPT) in newly diagnosed patients with myeloma showed significantly higher response rate and longer progression-free survival (PFS) than did the standard melphalan and prednisone (MP) combination and suggested a survival advantage. In this updated analysis, efficacy and safety end points were updated. Patients were randomly assigned to receive oral MPT or MP alone. Updated analysis was by intention to treat and included PFS, overall survival (OS), and survival after progression. After a median follow-up of 38.1 months, the median PFS was 21.8 months for MPT and 14.5 months for MP (P = .004). The median OS was 45.0 months for MPT and 47.6 months for MP (P = .79). In different patient subgroups, MPT improved PFS irrespective of age, serum concentrations of beta(2)-microglobulin, or high International Staging System. Thalidomide or bortezomib administration as salvage regimens significantly improved survival after progression in the MP group (P = .002) but not in the MPT group (P = .34). These data confirm activity of MPT for PFS but failed to show any survival advantage. New agents in the management of relapsed disease could explain this finding.

Seven-year median time to progression with thalidomide for smoldering myeloma: partial response identifies subset requiring earlier salvage therapy for symptomatic disease.

Barlogie B, van Rhee F, Shaughnessy JD Jr, Epstein J, Yaccoby S, Pineda-Roman M, Hollmig K, Alsayed Y, Hoering A, Szymonifka J, Anaissie E, Petty N, Kumar NS, Srivastava G, Jenkins B, Crowley J, Zeldis JB.

Blood. 2008 Oct 15;112(8):3122-5. [Epub 2008 Jul 31.]

http://www.ncbi.nlm.nih.gov/pubmed/18669874?ordinalpos=19&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors conduct a phase 2 trial in 76 eligible patients with smoldering multiple myeloma, combining thalidomide with monthly pamidronate. They conclude that excellent four-year survival and event-free survival estimates together with a median post-salvage therapy survival of more than 5 years justify the conduct of a prospective randomized clinical trial to determine the clinical value of preemptive therapy in smoldering myeloma.

Smoldering multiple myeloma (SMM) is usually followed expectantly without therapy. We conducted a phase 2 trial in 76 eligible patients with SMM, combining thalidomide (THAL, 200 mg/d) with monthly pamidronate. In the first 2 years, THAL dose reduction was required in 86% and drug was discontinued in 50%. Within 4 years, 63% improved, including 25% qualifying for partial response (PR); by then, 34 patients had progressed and 17 required salvage therapy. Unexpectedly, attaining PR status was associated with a shorter time to salvage therapy for disease progression (P < .001), perhaps reflecting greater drug sensitivity of more aggressive disease. Low beta-2-microglobulin levels less than 2 mg/L were independently associated with superior overall and event-free survival. Four-year survival and event-free survival estimates of 91% and 60%, respectively, together with a median postsalvage therapy survival of more than 5 years justify the conduct of a prospective randomized clinical trial to determine the clinical value of preemptive therapy in SMM.

Thalidomide arm of Total Therapy 2 improves complete remission duration and survival in myeloma patients with metaphase cytogenetic abnormalities.

Barlogie B, Pineda-Roman M, van Rhee F, Haessler J, Anaissie E, Hollmig K, Alsayed Y, Waheed S, Petty N, Epstein J, Shaughnessy JD Jr, Tricot G, Zangari M, Zeldis J, Barer S, Crowley J.

Blood. 2008 Oct 15;112(8):3115-21. [Epub 2008 May 20.]

http://www.ncbi.nlm.nih.gov/pubmed/18492953?ordinalpos=21&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

This thalidomide arm of Total Therapy 2 examines the clinical benefit of adding thalidomide up-front to a tandem transplant regimen for newly diagnosed patients with multiple myeloma.

Total Therapy 2 examined the clinical benefit of adding thalidomide up-front to a tandem transplant regimen for newly diagnosed patients with multiple myeloma. When initially reported with a median follow-up of 42 months, complete response rate and event-free survival were superior among the 323 patients randomized to thalidomide, whereas overall survival was indistinguishable from that of the 345 patients treated on the control arm. With further follow-up currently at a median of 72 months, survival plots segregated 5 years after initiation of therapy in favor of thalidomide (P = .09), reaching statistical significance for the one third of patients exhibiting cytogenetic abnormalities (CAs; P = .02), a well-recognized adverse prognostic feature. The duration of complete remission was also superior in the cohort presenting with CAs such that, at 7 years from onset of complete remission, 45% remained relapse-free as opposed to 20% on the control arm (P = .05). These observations were confirmed when examined by multivariate analysis demonstrating that thalidomide reduced the hazard of death by 41% among patients with CA-positive disease (P = .008). Because two thirds of patients without CAs have remained alive at 7 years, the presently emerging separation in favor of thalidomide may eventually reach statistical significance as well.

Atypical serum immunofixation patterns frequently emerge in immunomodulatory therapy and are associated with a high degree of response in multiple myeloma.

Mark T, Jayabalan D, Coleman M, Pearse RN, Wang YL, Lent R, Christos PJ, Lee JW, Agrawal YP, Matthew S, Ely S, Mazumdar M, Cesarman E, Leonard JP, Furman RR, Chen-Kiang S, Niesvizky R.

Br J Haematol. 2008 Oct 16. [Epub ahead of print.]

http://www.ncbi.nlm.nih.gov/pubmed/18950461?ordinalpos=9&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors discuss the emergence of oligoclonal banding as a recognized but benign finding in the postautologous stem cell transplantation setting (ASCT) for myeloma with its significance during non-myeloablative therapy unknown. They study the immunomodulatory combination BiRD, (lenalidomide and dexamethasone with clarithromycin), and frequently detect the emergence of mono- and oligoclonal immunoglobulins unrelated to the baseline diagnostic M-protein.

The M-protein is the major reference measure for response in multiple myeloma (MM) and its correct interpretation is key to clinical management. The emergence of oligoclonal banding is recognized as a benign finding in the postautologous stem cell transplantation setting (ASCT) for MM but its significance during non-myeloablative therapy is unknown. In a study of the immunomodulatory combination BiRD, (lenalidomide and dexamethasone with clarithromycin), we frequently detected the emergence of mono- and oligo-clonal immunoglobulins unrelated to the baseline diagnostic M-protein. The new M-proteins seen on serum immunofixation electrophoresis were clearly different in either heavy or light chain component(s) from the original M-spike protein and were termed atypical serum immunofixation patterns (ASIPs). Overall, 24/72 (33%) patients treated with BiRD developed ASIPs. Patients who developed ASIPs compared with patients treated with BiRD without ASIPs, had a significantly greater overall response (100% vs. 85%) and complete response rates (71% vs. 23%). ASIPs were not associated with new clonal plasma cells or other lymphoproliferative processes, and molecular remissions were documented. This is the first time this phenomenon has been seen with regularity in non-myeloablative therapy for MM. Analogous to the ASCT experience, ASIPs do not signal incipient disease progression, but rather herald robust response.

Thalidomide-dexamethasone compared to melphalan-prednisolone in elderly patients with multiple myeloma.

Ludwig H, Hajek R, Tothova E, Drach J, Adam Z, Labar B, Egyed M, Spicka I, Gisslinger H, Greil R, Kuhn I, Zojer N, Hinke A.

Blood. 2008 Oct 27. [Epub ahead of print.]

http://www.ncbi.nlm.nih.gov/pubmed/18955563?ordinalpos=10&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors compare thalidomide-dexamethasone (TD) with melphalan-prednisolone (MP) as first line treatment in 289 elderly patients with myeloma. They find that TD yields higher response rates, but is more toxic in older patients and is associated with shorter overall survival.

Thalidomide-dexamethasone (TD) has successfully been used for treatment of young patients with multiple myeloma (MM). We compared TD with melphalan-prednisolone (MP) as first line treatment in 289 elderly patients with MM. Patients were randomized to either thalidomide 200mg plus dexamethasone 40mg, days 1-4, and 15-18 on even cycles and on days 1-4 on odd cycles, during a 28-day cycle or to melphalan 0.25mg/kg and prednisolone 2mg/kg orally on days 1-4 during a 28 to 42 day cycle. For maintenance, patients achieving stable disease or better were randomized to either thalidomide 100mg daily and 3 MU interferon alpha-2b TIW or to 3 MU interferon alpha-2b TIW only, but results on this phase will only be presented after longer follow up. TD resulted in a higher proportion of complete and very good remissions (26% vs. 13%, P=0.0066) and overall responses (68% vs. 50%, P=0.0023) compared to MP. Time to progression (21.2 vs. 29.1 months, P=0.2), and progression-free survival was similar (16.7 vs. 20.7 months, P=0.1), but overall survival was significantly shorter in the TD group (41.5 vs. 49.4 months, P=0.024). Toxicity was higher with TD, particularly in patients above 75 years with poor performance status. TD yielded higher response rates, but was more toxic in older patients and was associated with shorter overall survival.

Thalidomide treatment down-regulates SDF-1alpha and CXCR4 expression in multiple myeloma patients.

Oliveira AM, Maria DA, Metzger M, Linardi C, Giorgi RR, Moura F, Martinez GA, Bydlowski SP, Novak EM.

Leuk Res. 2008 Oct 29. [Epub ahead of print.]

http://www.ncbi.nlm.nih.gov/pubmed/18976811?ordinalpos=9&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors' findings indicate that thalidomide therapy induces down-regulation of CXCR4 and its ligand SDF-1alpha in multiple myeloma.

The chemokine stromal-derived factor-1alpha (SDF-1alpha) and its receptor CXCR4 are critically involved in directional migration and homing of plasma cells in multiple myeloma. Here, we show that the expression of SDF-1alpha and CXCR4 was significantly down-regulated in patients treated with thalidomide (n=10) as compared to newly diagnosed MM patients (n=31) and MM patients treated with other drugs (n=38). SDF-1 alpha and CXCR4 expression was also significantly decreased in a RPMI 8226 cell line treated with 10 and 20mumol/L of thalidomide. Our findings indicate that thalidomide therapy induces down-regulation of CXCR4 and its ligand SDF-1alpha in multiple myeloma.

Advances in therapy of multiple myeloma.

Bladé J, Rosiñol L.

Curr Opin Oncol. 2008 Nov;20(6):697-704.

http://www.ncbi.nlm.nih.gov/pubmed/18841053?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

This article summarizes the results of treatment of multiple myeloma in the era of novel agents, including the combination of thalidomide or lenalidomide with melphalan-prednisone or with dexamethasone as highly effective regimens for patients not eligible for high-dose therapy/stem cell transplantation.

PURPOSE OF REVIEW: To summarize the results of treatment of multiple myeloma in the era of novel agents. RECENT FINDINGS: Recent publications comparing autologous stem cell transplantation (ASCT) with conventional chemotherapy in the era of 'old' drugs have shown that the contribution of ASCT in the treatment of multiple myeloma has been modest. Five trials comparing single vs. double ASCT showed an increased progression-free survival in three of them, whereas the overall survival was significantly prolonged in one. The benefit would be only for patients failing to achieve very good partial response with the first transplant. The results of allogeneic transplantation with reduced-intensity conditioning, particularly after debulking with an ASCT, are encouraging. On the contrary, the impact of pretransplant induction regimens with novel agents (thalidomide, bortezomib and lenalidomide) on the posttransplant outcome is being investigated in several large phase III trials. For elderly patients, the combination of 'old' therapies with thalidomide, bortezomib or lenalidomide has resulted in the melphalan-prednisone-thalidomide, melphalan-prednisone-Velcade, melphalan-prednisone-Revlimid and lenalidomide/dexamethasone regimens, which are highly effective. SUMMARY: ASCT has resulted in a modest contribution in the treatment of multiple myeloma. Hopefully, its impact will be increased with the incorporation of novel agents in the pretransplant induction regimens. The combination of thalidomide, bortezomib or lenalidomide with melphalan-prednisone or with dexamethasone has resulted in highly effective regimens for patients not eligible for high-dose therapy/stem cell transplantation.

Frontline treatment of multiple myeloma in elderly patients.

Moreau P, Hulin C, Facon T.

Blood Rev. 2008 Nov;22(6):303-9. [Epub 2008 Jun 11.]

http://www.ncbi.nlm.nih.gov/pubmed/18550234?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors discuss highly active new treatment options available to treat elderly patients with myeloma, including melphalan and prednisone in combination with both thalidomide and lenalidomide.

Until 2007, frontline chemotherapy with melphalan and prednisone (MP) was considered as the standard of care in the treatment of elderly patients with multiple myeloma (MM). Recently, several prospective randomized studies comparing MP with the same combination plus new agents such as thalidomide (MPT) or bortezomib (MPV) clearly showed that MPT and MPV were superior to MP in terms of progression-free and overall survival. Melphalan-prednisone-lenalidomide (MPR) is currently compared to MP in one prospective trial and will also probably be superior to MP. Lenalidomide plus low-dose dexamethasone is a promising combination. Thus, at least four highly active new treatment options are now available to treat elderly patients with MM. The goal of future trials will be to determine the best treatment strategy in this group of patients.

Multiple myeloma – an update on diagnosis and treatment.

Caers J, Vande broek I, De Raeve H, Michaux L, Trullemans F, Schots R, Van Camp B, Vanderkerken K.

Eur J Haematol. 2008 Nov;81(5):329-43. [Epub 2008 Sep 13.]

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This article discusses new approaches in myeloma diagnosis and treatment aiming to identify high-risk patients, including the use of thalidomide and lenalidomide.

Multiple myeloma is a plasma cell (PC) malignancy characterized by the accumulation of monoclonal PCs in the bone marrow and the production of large amounts of a monoclonal immunoglobulin or paraprotein. In the past years, new approaches in the diagnosis and treatment were introduced aiming to identify high-risk patients who need proper anti-myeloma treatment. Intensive therapy including autologous hematopoietic stem cell transplantation and the new agents bortezomib, thalidomide, and lenalidomide have improved patients' responses. Further optimalization of the different treatment schedules in well-defined patient groups may prolong their survival. Patient stratification is currently based on patient characteristics, extent of myeloma disease, and associated cytogenetic and laboratory anomalies. More and more gene expression studies are introduced to stratify patients and to individualize therapy.

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