



CITINGS

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Thalidomide and Revlimid® Issue

The International Myeloma Foundation (IMF) is pleased to present our third edition of CITINGS for 2008. This quarterly publication features citations to the most up-to-date studies on myeloma treatment. In this issue, we focus on thalidomide and Revlimid for the treatment of multiple myeloma. Inside you will find references to the latest published journal articles on both thalidomide and Revlimid from the third quarter of this year.

It is our hope that CITINGS will help keep you abreast of the latest developments in myeloma treatment. As always, we welcome your feedback; you may contact the IMF at (800) 452-CURE (2873) or at our website www.myeloma.org.

— Susie Novis, President, IMF

Thalidomide/Revlimid Publications – 3rd Quarter, 2008

- 🕒 **New therapeutic strategies for multiple myeloma. Efficacy and cost-effectiveness analyses.** [Article in Spanish] García Quetglas E, Azanza Perea JR, Lecumberri Villamediana R. *Med Clin (Barc).* 2008 May 3;130(16):626-35.
💻 http://www.ncbi.nlm.nih.gov/pubmed/18482531?ordinalpos=115&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
The article reviews the most important therapeutic innovations in the treatment of myeloma in terms of efficacy and cost-effectiveness, including a discussion of lenalidomide.
- 🕒 **Nonthromboembolic 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 May 13. [Epub ahead of print.]
💻 http://www.ncbi.nlm.nih.gov/pubmed/18480066?ordinalpos=110&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
The authors study clinical and subclinical nonthromboembolic pulmonary hypertension (PH) in MM patients after thalidomide treatment. They conclude that preexisting endothelial dysfunction due to structural cardiac disease enhances the vasoactive substances release causing increased pulmonary vascular resistance and that thalidomide possibly causes a vasodilator and vasoconstriction imbalance, which may cause abnormal pulmonary vascular response interfering to a vicious circle perpetuating PH.

 **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 Jr JD, Tricot G, Zangari M, Zeldis J, Barer S, Crowley J.

Blood. 2008 May 20. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18492953?ordinalpos=105&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

Further follow-up of Total Therapy 2, which examined the clinical benefit of adding thalidomide up-front to a tandem transplant regimen for newly diagnosed patients with multiple myeloma, shows a presently emerging separation in favor of thalidomide that may eventually reach statistical significance as well.

 **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 May 27. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18505783?ordinalpos=104&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This study in newly diagnosed myeloma patients confirms activity of melphalan, prednisone for progression-free survival, but fails to show any survival advantage.

 **The addition of liposomal doxorubicin to bortezomib, thalidomide and dexamethasone significantly improves clinical outcome of advanced multiple myeloma.**

Ciolli S, Leoni F, Casini C, Breschi C, Santini V, Bosi A.

Br J Haematol. 2008 Jun;141(6):814-9. [Epub 2008 Apr 10.]

 http://www.ncbi.nlm.nih.gov/pubmed/18410447?ordinalpos=68&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

In this study, liposomal doxorubicin is added to a bortezomib/thalidomide/ dexamethasone (VTD) treatment in relapsed/refractory myeloma patients. The authors find increased overall response rate and progression-free survival with this combination, compared to VTD alone and that toxicity is manageable although more pronounced.

 **Compromised stem cell mobilization following induction therapy with lenalidomide in myeloma.**

Paripati H, Stewart AK, Cabou S, Dueck A, Zepeda VJ, Pirooz N, Ehlenbeck C, Reeder C, Slack J, Leis JF, Boesiger J, Torloni AS, Fonseca R, Bergsagel PL.

Leukemia. 2008 Jun;22(6):1282-4. Epub 2008 Jan 24.

 http://www.ncbi.nlm.nih.gov/pubmed/18216870?ordinalpos=90&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
Comment on: *Leukemia.* 2008 Jun;22(6):1280-1; author reply 1281-2.

 **Effect of lenalidomide therapy on mobilization of peripheral blood stem cells in previously untreated multiple myeloma patients.**

Mazumder A, Kaufman J, Niesvizky R, Lonial S, Vesole D, Jagannath S.

Leukemia. 2008 Jun;22(6):1280-1; author reply 1281-2. Epub 2007 Nov 22.

 http://www.ncbi.nlm.nih.gov/pubmed/18033320?ordinalpos=91&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
Comment on: *Leukemia.* 2007 Sep;21(9):2035-42.

 **Effects of Thalidomide on CD4(+)CD25(+) T Regulatory Cells in Patients with Multiple Myeloma. [Article in Chinese]**

Yang Y, Zhang WG, He AL, Yang HY, Wang JL, Tian W.

Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2008 Jun;16(3):538-42.

 http://www.ncbi.nlm.nih.gov/pubmed/18549624?ordinalpos=100&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors conclude that the significant increase of CD4(+)CD25(+) regulatory T cells in peripheral blood of patients with myeloma is concerned with myeloma's pathogenesis; thalidomide may exert its anti-myeloma effects by down-regulating CD4(+)CD25(+) Treg.

The effects of thalidomide on chemotactic migration of multiple myeloma cell lines.

Fuchida SI, Shimazaki C, Hirai H, Akamatsu S, Yamada N, Uchida R, Okano A, Okamoto M, Inaba T, Taniwaki M.

Int J Lab Hematol. 2008 Jun;30(3):220-9.



http://www.ncbi.nlm.nih.gov/pubmed/18479301?ordinalpos=86&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors examine the effect of thalidomide and dexamethasone on the migration of multiple myeloma cell lines and find that the inhibition of chemotactic migration might be one of the mechanisms of the success of thalidomide in controlling myeloma.

Features and risk factors of peripheral neuropathy during treatment with bortezomib for advanced multiple myeloma.

El-Cheikh J, Stoppa AM, Bouabdallah R, de Lavallade H, Coso D, de Collela JM, Auran-Schleinitz T, Gastaut JA, Blaise D, Mohy M.

Clin Lymphoma Myeloma. 2008 Jun;8(3):146-52.



http://www.ncbi.nlm.nih.gov/pubmed/18650177?ordinalpos=91&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This retrospective, single-center study aims to determine the characteristics of bortezomib-associated peripheral neuropathy (PN). It concludes that bortezomib-associated PN seems to be dependent on previous therapy with thalidomide, suggesting that bortezomib followed by thalidomide could be an optimal sequence of administration of these drugs in the salvage setting.

Gastrointestinal side effects associated with novel therapies in patients with multiple myeloma: consensus statement of the IMF Nurse Leadership Board.

Smith LC, Bertolotti P, Curran K, Jenkins B; IMF Nurse Leadership Board.

Clin J Oncol Nurs. 2008 Jun;12(3 Suppl):37-52.



http://www.ncbi.nlm.nih.gov/pubmed/18490256?ordinalpos=74&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The International Myeloma Foundation's Nurse Leadership Board develops a consensus statement for the management of gastrointestinal side effects associated with novel therapies, including thalidomide and lenalidomide, to be used by healthcare providers in any medical setting.

Impact of pretransplant therapy in patients with newly diagnosed myeloma undergoing autologous SCT.

Kumar SK, Dingli D, Dispenzieri A, Lacy MQ, Hayman SR, Buadi FK, Rajkumar SV, Litzow MR, Gertz MA.

Bone Marrow Transplant. 2008 Jun;41(12):1013-9. [Epub 2008 Mar 10.]



http://www.ncbi.nlm.nih.gov/pubmed/18332915?ordinalpos=67&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors study 472 patients undergoing autologous stem cell transplant (ASCT) within 12 months of diagnosis to assess the effect of initial therapy, including with thalidomide and lenalidomide, on the outcome after ASCT. They find that the nature of initial treatment utilized has no long-term impact on the outcome of ASCT.

Lenalidomide and its role in the management of multiple myeloma.

Falco P, Cavallo F, Larocca A, Liberati AM, Musto P, Boccadoro M, Palumbo A.

Expert Rev Anticancer Ther. 2008 Jun;8(6):865-74.



http://www.ncbi.nlm.nih.gov/pubmed/18533796?ordinalpos=83&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This review summarizes the profile of lenalidomide and its current role in the treatment of multiple myeloma.

Maintenance treatment in multiple myeloma.

Harousseau JL.

Ann Oncol. 2008 Jun;19 Suppl 4:iv54-5.



http://www.ncbi.nlm.nih.gov/pubmed/18519405?ordinalpos=65&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

No abstract available.

Myelosuppression associated with novel therapies in patients with multiple myeloma: consensus statement of the IMF Nurse Leadership Board.

Miceli T, Colson K, Gavino M, Lilleby K; IMF Nurse Leadership Board.

Clin J Oncol Nurs. 2008 Jun;12(3 Suppl):13-20.



http://www.ncbi.nlm.nih.gov/pubmed/18490253?ordinalpos=76&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The International Myeloma Foundation's Nurse Leadership Board developed a consensus statement that includes toxicity grading, strategies for monitoring and managing myelosuppression associated with novel therapies, including thalidomide and lenalidomide, and offers educational recommendations for patients and their caregivers.

 ***Pathophysiological considerations to thrombophilia in the treatment of multiple myeloma with thalidomide and derivates.***

Gieseler F.

Thromb Haemost. 2008 Jun;99(6):1001-7.



http://www.ncbi.nlm.nih.gov/pubmed/18521500?ordinalpos=98&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This review discusses the complex interactions between an activated coagulation-system in myeloma patients and the molecular effects of lenalidomide and thalidomide.

 ***Peripheral neuropathy associated with novel therapies in patients with multiple myeloma: consensus statement of the IMF Nurse Leadership Board.***

Tariman JD, Love G, McCullagh E, Sandifer S; IMF Nurse Leadership Board.

Clin J Oncol Nurs. 2008 Jun;12(3 Suppl):29-36.



http://www.ncbi.nlm.nih.gov/pubmed/18490255?ordinalpos=75&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The International Myeloma Foundation Nurse Leadership Board provides specific management strategies for peripheral neuropathy caused by novel therapies, including thalidomide, based on the grade of severity and on signs and symptoms; strategies include dose and schedule modifications, pharmacologic interventions, nonpharmacologic approaches, and patient education.

 ***Pulmonary embolism in a patient with multiple myeloma receiving thalidomide-dexamethasone therapy.***

Jeng WJ, Kuo MC, Shih LY, Chu PH.

Int J Hematol. 2008 Jun;87(5):542-4. [Epub 2008 Apr 15.]



http://www.ncbi.nlm.nih.gov/pubmed/18414984?ordinalpos=85&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors present the first report of a patient with a rare complication of pulmonary embolism from thalidomide-treated multiple myeloma.

 ***Rapid complete remission in multiple myeloma with bortezomib/thalidomide/ dexamethasone combination therapy following development of tumor lysis syndrome.***

Chim CS.

Cancer Chemother Pharmacol. 2008 Jun;62(1):181-2. [Epub 2007 Aug 31.]



http://www.ncbi.nlm.nih.gov/pubmed/17846773?ordinalpos=71&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

No abstract available.

 ***Single-institute phase 2 study of thalidomide treatment for refractory or relapsed multiple myeloma: prognostic factors and unique toxicity profile.***

Hattori Y, Okamoto S, Shimada N, Kakimoto T, Morita K, Tanigawara Y, Ikeda Y.

Cancer Sci. 2008 Jun;99(6):1243-50. [Epub 2008 Mar 31.]



http://www.ncbi.nlm.nih.gov/pubmed/18384432?ordinalpos=73&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors extend their clinical trial of thalidomide monotherapy for Japanese patients with refractory or relapsed multiple myeloma into a phase 2 study. The efficacy and prognostic factors of this treatment were confirmed in long-term observation, while special attention should be paid to toxicities such as hematological and pulmonary complications as well as peripheral neuropathy in long-term users.

 ***Thalidomide maintenance following high-dose melphalan with autologous stem cell support in myeloma.***

Chang JE, Juckett MB, Callander NS, Kahl BS, Gangnon RE, Mitchell TL, Longo WL.

Clin Lymphoma Myeloma. 2008 Jun;8(3):153-8.



http://www.ncbi.nlm.nih.gov/pubmed/18650178?ordinalpos=78&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors further explore the tolerability and efficacy of lower doses of maintenance after high-dose chemotherapy with autologous stem cell transplantation and conclude that thalidomide at 100 mg per is a reasonable maintenance dose.

Individualizing treatment of patients with myeloma in the era of novel agents.

San-Miguel J, Harousseau JL, Joshua D, Anderson KC.

J Clin Oncol. 2008 Jun 1;26(16):2761-6. [Epub 2008 Apr 21.]



http://www.ncbi.nlm.nih.gov/pubmed/18427148?ordinalpos=88&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This review focuses on current available agents already approved for myeloma, and discusses individualized treatment approaches for both transplantation candidates (subdivided into standard and high-risk patients) and elderly patients.

Frontline treatment of multiple myeloma in elderly patients.

Moreau P, Hulin C, Facon T.

Blood Rev. 2008 Jun 10. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18550234?ordinalpos=59&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article discusses highly active new treatment options now available to treat elderly patients with myeloma, including melphalan-prednisone-thalidomide and melphalan-prednisone-lenalidomide.

Bortezomib in the front-line treatment of multiple myeloma.

Richardson PG, Mitsiades C, Schlossman R, Ghobrial I, Hideshima T, Munshi N, Anderson KC.

Expert Rev Anticancer Ther. 2008 Jul;8(7):1053-72.



http://www.ncbi.nlm.nih.gov/pubmed/18588451?ordinalpos=49&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors discuss the rapid evolution of front-line therapy for multiple myeloma with the development of new, highly active regimens based on novel agents such as combinations including thalidomide and lenalidomide.

Chemotherapy-induced peripheral neuropathy: Prevention and treatment strategies.

Wolf S, Barton D, Kottschade L, Grothey A, Loprinzi C.

Eur J Cancer. 2008 Jul;44(11):1507-15. [Epub 2008 Jun 18.]



http://www.ncbi.nlm.nih.gov/pubmed/18571399?ordinalpos=48&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article provides a review of studies conducted to look at ways of preventing or alleviating established chemotherapy-induced peripheral neuropathy (CIPN), including CIPN as a side effect of lenalidomide treatment.

Does lenalidomide plus dexamethasone improve outcome in patients with relapsed multiple myeloma?

Dhodapkar MV, Cooper DL.

Nat Clin Pract Oncol. 2008 Jul;5(7):372-3. [Epub 2008 May 13.]



http://www.ncbi.nlm.nih.gov/pubmed/18477992?ordinalpos=25&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

No abstract available.

Lenalidomide plus dexamethasone is efficacious in patients with relapsed or refractory multiple myeloma.

Munshi NC, Mitsiades C, Richardson PG, Anderson KC.

Nat Clin Pract Oncol. 2008 Jul;5(7):374-5. [Epub 2008 Jun 10.]



http://www.ncbi.nlm.nih.gov/pubmed/18542118?ordinalpos=24&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

No abstract available.

NF-kappaB in the pathogenesis and treatment of multiple myeloma.

Li ZW, Chen H, Campbell RA, Bonavida B, Berenson JR.

Curr Opin Hematol. 2008 Jul;15(4):391-9.



http://www.ncbi.nlm.nih.gov/pubmed/18536579?ordinalpos=40&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This review summarizes recent advances in the mechanisms through which the activation of the transcription factor NF-kappaB contributes to the pathogenesis of myeloma, including the finding that several drugs that are effective against myeloma, including thalidomide and lenalidomide, also block activation of NF-kappaB.

 **Osteoprogenitor differentiation is not affected by immunomodulatory thalidomide analogs but is promoted by low bortezomib concentration, while both agents suppress osteoclast differentiation.**

Munemasa S, Sakai A, Kuroda Y, Okikawa Y, Katayama Y, Asaoku H, Kubo T, Shimose S, Kimura A.

Int J Oncol. 2008 Jul;33(1):129-36.

 http://www.ncbi.nlm.nih.gov/pubmed/18575758?ordinalpos=45&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors investigate the effects of bortezomib and immunomodulatory thalidomide analogs (including lenalidomide) on osteoblast and osteoclast differentiation in vitro. They conclude that by combining bortezomib with immunomodulatory compounds, it is possible to improve treatment strategy for myeloma patients without damaging BM stromal cells.

 **Prospective evaluation of coagulopathy in multiple myeloma patients before, during and after various chemotherapeutic regimens.**

van Marion AM, Auwerda JJ, Lisman T, Sonneveld P, de Maat MP, Lokhorst HM, Leebeek FW.

Leuk Res. 2008 Jul;32(7):1078-84. [Epub 2008 Feb 1.]

 http://www.ncbi.nlm.nih.gov/pubmed/18241919?ordinalpos=52&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors perform a prospective study in myeloma patients in whom coagulation factor levels are evaluated longitudinally before, during induction and after intensification. Patients are randomized to induction treatment consisting of adriamycin and dexamethasone, in combination with either vincristin, thalidomide, or bortezomib followed by high-dose melphalan and autologous stem cell transplant. The authors find that during induction treatment several changes in coagulation factor levels are observed, which may result in a prothrombotic state. They conclude that larger studies are required to establish whether the changes in these coagulation factors during induction treatment contribute to the increased risk of venous thromboembolism in myeloma patients.

 **Stem cell mobilization with cyclophosphamide overcomes the suppressive effect of lenalidomide therapy on stem cell collection in multiple myeloma.**

Mark T, Stern J, Furst JR, Jayabalan D, Zafar F, LaRow A, Pearse RN, Harpel J, Shore T, Schuster MW, Leonard JP, Christos PJ, Coleman M, Niesvizky R.

Biol Blood Marrow Transplant. 2008 Jul;14(7):795-8.

 http://www.ncbi.nlm.nih.gov/pubmed/18541199?ordinalpos=36&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors find that cyclophosphamide can be added to granulocyte-colony stimulating factor for stem cell mobilization to successfully overcome the suppressive effect of prior treatment with lenalidomide.

 **Thalidomide and lenalidomide: Mechanism-based potential drug combinations.**

Vallet S, Palumbo A, Rajé N, Boccadoro M, Anderson KC.

Leuk Lymphoma. 2008 Jul;49(7):1238-45.

 http://www.ncbi.nlm.nih.gov/pubmed/18452080?ordinalpos=46&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article reviews the mechanism of action of thalidomide and lenalidomide, providing a rationale for combination studies in order to improve patient outcome and reduce side effects.

 **Thalidomide in multiple myeloma – clinical trials and aspects of drug metabolism and toxicity.**

Breitkreutz I, Anderson KC.

Expert Opin Drug Metab Toxicol. 2008 Jul;4(7):973-985.

 http://www.ncbi.nlm.nih.gov/pubmed/18624684?ordinalpos=41&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article reviews thalidomide as first-line and relapsed/refractory treatment in myeloma, and focuses on the importance and toxicity of thalidomide in today's clinical use.

 **VTD combination therapy with bortezomib-thalidomide-dexamethasone is highly effective in advanced and refractory multiple myeloma.**

Pineda-Roman M, Zangari M, van Rhee F, Anaissie E, Szymonifka J, Hoering A, Petty N, Crowley J, Shaughnessy J, Epstein J, Barlogie B. *Leukemia. 2008 Jul;22(7):1419-27. [Epub 2008 Apr 24.]*

 http://www.ncbi.nlm.nih.gov/pubmed/18432260?ordinalpos=52&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

In this study, bortezomib was combined with thalidomide and dexamethasone in a phase I/II trial to determine dose-limiting toxicities and clinical activity of this regimen in 85 patients with advanced and refractory myeloma.

 **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 Jul 3. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18596740?ordinalpos=14&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.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.

 **Duration of survival in patients with myeloma treated with thalidomide.**

Barlogie B, Shaughnessy JD Jr, Crowley J.

N Engl J Med. 2008 Jul 10;359(2):210-2.



http://www.ncbi.nlm.nih.gov/pubmed/18614793?ordinalpos=31&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

Comment on: *N Engl J Med*. 2006 Mar 9;354(10):1021-30.

 **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 Jul 10. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18637031?ordinalpos=30&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

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

 **Inhibition of the mevalonate pathway potentiates the effects of lenalidomide in myeloma.**

van der Spek E, Bloem AC, Lokhorst HM, van Kessel B, Bogers-Boer L, van de Donk NW.

Leuk Res. 2008 Jul 11. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18621417?ordinalpos=12&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors analyze the effects of the combination of simvastatin and lenalidomide in myeloma and find data that provide a rationale for the clinical evaluation of this combination in myeloma 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 Jul 11. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18637123?ordinalpos=28&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article updates the new approaches in the diagnosis and treatment of myeloma, including new agents such as thalidomide and lenalidomide.

 **Effective prophylaxis of thromboembolic complications with low molecular weight heparin in relapsed multiple myeloma patients treated with lenalidomide and dexamethasone.**

Klein U, Kosely F, Hillengäß J, Hundemer M, Schmitt S, Neben K, Moehler T, Hegenbart U, Ho AD, Goldschmidt H.

Ann Hematol. 2008 Jul 31. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18668241?ordinalpos=17&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors analyze 45 patients with relapsed myeloma who were treated with lenalidomide and dexamethasone and conclude that low molecular weight heparin should be used in patients being treated with lenalidomide and dexamethasone at least for the first three months of treatment until randomized trials have proven the equality of other pharmacological prophylaxis.

 **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 Jul 31. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18669874?ordinalpos=18&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors conduct a phase II trial in 76 eligible patients with smoldering multiple myeloma (SMM), combining thalidomide (200mg/d) with monthly pamidronate. They find that a four-year survival and event-free survival estimates of 91% and 60% together with a median post-salvage therapy survival of more than five years justify the conduct of a prospective randomized clinical trial to determine the clinical value of pre-emptive therapy in SMM.

 **Extramedullary progression of multiple myeloma under thalidomide therapy despite concomitant response of medullary disease.**

Candoni A, Simeone E, Fanin R.

Am J Hematol. 2008 Aug;83(8):680-1.

 http://www.ncbi.nlm.nih.gov/pubmed/18459108?ordinalpos=32&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
No abstract available.

 **Gene therapy for Multiple Myeloma.**

Adachi Y, Yoshio-Hoshino N, Nishimoto N.

Curr Gene Ther. 2008 Aug;8(4):247-55.

 http://www.ncbi.nlm.nih.gov/pubmed/18691020?ordinalpos=36&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This review presents the current progress of gene therapy related to myeloma treatments as well as the overview of myeloma treatment history, including the advent of molecular target drugs such as thalidomide and lenalidomide.

 **Lenalidomide plus dexamethasone is efficacious in patients with relapsed or refractory multiple myeloma.**

Munshi NC, Mitsiades C, Richardson PG, Anderson KC.

Nat Clin Pract Oncol. 2008 Aug;5(8):493.

 http://www.ncbi.nlm.nih.gov/pubmed/18668029?ordinalpos=14&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum
No abstract available.

A meta-analysis and systematic review of thalidomide for patients with previously untreated multiple myeloma.

Hicks LK, Haynes AE, Reece DE, Walker IR, Herst JA, Meyer RM, Imrie K; Hematology Disease Site Group of the Cancer Care Ontario Program in Evidence-based Care.

Cancer Treat Rev. 2008 Aug;34(5):442-52. [Epub 2008 Apr 1.]

 http://www.ncbi.nlm.nih.gov/pubmed/18381234?ordinalpos=34&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors conduct a systematic review and meta-analysis to determine the efficacy and toxicity of thalidomide in previously untreated patients with myeloma. They find that thalidomide appears to improve the overall survival of patients with newly diagnosed myeloma both when it is added to standard, non-transplantation therapy, and when it is given as maintenance therapy following ASCT, but that thalidomide is also associated with toxicity, particularly a significantly increased risk of VTE.

 **The role of high-dose chemotherapy followed by peripheral blood stem cell transplantation for the treatment of multiple myeloma.**

Siddiqui M, Gertz M.

Leuk Lymphoma. 2008 Aug;49(8):1436-51.

 http://www.ncbi.nlm.nih.gov/pubmed/18608872?ordinalpos=42&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This review summarizes the role of stem cell transplantation in myeloma and how the advent of novel therapies, such as thalidomide and lenalidomide, have started to redefine the role of peripheral stem cell transplantation.

Treatment of relapsed and refractory myeloma.

Reece DE, Leitch HA, Atkins H, Voralia M, Canning LA, Leblanc R, Belch AR, White D, Kovacs MJ.

Leuk Lymphoma. 2008 Aug;49(8):1470-85.



http://www.ncbi.nlm.nih.gov/pubmed/18608859?ordinalpos=43&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article reviews the literature for the treatment of relapsed/refractory myeloma and considers the influence of prior therapy, optimal sequencing of regimens, sequential versus combination use of agents, and the role of cytogenetic and other prognostic factors, both for established regimens and newer regimens incorporating thalidomide, bortezomib and lenalidomide.

Tumor cell gene expression changes following short-term *in vivo* exposure to single agent chemotherapeutics are related to survival in multiple myeloma.

Burinton B, Barlogie B, Zhan F, Crowley J, Shaughnessy JD Jr.

Clin Cancer Res. 2008 Aug 1;14(15):4821-9.



http://www.ncbi.nlm.nih.gov/pubmed/18676754?ordinalpos=35&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors find that, combined with baseline molecular features, changes in gene expression profiles following short-term single-agent exposure may help guide treatment decisions for patients with myeloma. Genes whose drug-altered expressions were found to be related to survival may point to molecular switches related to response and/or resistance to different classes of drugs.

Survival and Outcome of Blastoid Variant Myeloma Following Treatment with the novel Thalidomide Containing Regime DT-PACE.

Srikanth M, Davies FE, Wu P, Jenner MW, Ethell ME, Potter MN, Shaw BE, Saso RM, Dines S, Morgan GJ.

Eur J Haematol. 2008 Aug 6. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18691254?ordinalpos=30&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors use DT-PACE to treat 26 relapsed and or refractory patients with extramedullary/blastoid myeloma, and find that the clinical outcome of the group of cases is poor even when treated with this regimen; however, a subgroup can do well if DT-PACE is consolidated by ASCT.

First thalidomide clinical trial in multiple myeloma: a decade.

van Rhee F, Dhodapkar M, Shaughnessy JD Jr, Anaissie E, Siegel D, Hoering A, Zeldis J, Jenkins B, Singhal S, Mehta J, Crowley J, Jagannath S, Barlogie B.

Blood. 2008 Aug 15;112(4):1035-8. [Epub 2008 May 23.]



http://www.ncbi.nlm.nih.gov/pubmed/18502827?ordinalpos=24&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This article updates the clinical outcomes of 169 patients enrolled in the first clinical trial of thalidomide for advanced or refractory myeloma. Seventeen patients remain alive and 10 are event-free, with a median follow-up of 9.2 years. Patients who had received cumulative thalidomide doses in excess of 42 g in the first 3 months enjoyed superior overall and event-free survival.

Validation of PDGFRbeta and c-Src tyrosine kinases as tumor/vessel targets in patients with multiple myeloma: preclinical efficacy of the novel, orally available inhibitor dasatinib.

Coluccia AM, Cirulli T, Neri P, Mangieri D, Colanardi MC, Gnoni A, Di Renzo N, Dammacco F, Tassone P, Ribatti D, Gambacorti-Passerini C, Vacca A.

Blood. 2008 Aug 15;112(4):1346-56. [Epub 2008 Jun 4.]



http://www.ncbi.nlm.nih.gov/pubmed/18524994?ordinalpos=23&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors in part assess the anti-tumor/vessel activity of dasatinib, a novel orally bioactive PDGFRbeta/Src TK-inhibitor that significantly delayed MM tumor growth and angiogenesis *in vivo*, which shows a synergistic cytotoxicity with conventional and novel anti-myeloma drugs, including thalidomide.

 **Combined bendamustine, prednisolone and thalidomide for refractory or relapsed multiple myeloma after autologous stem-cell transplantation or conventional chemotherapy: results of a Phase I clinical trial.**

Pönisch W, Rozanski M, Goldschmidt H, Hoffmann FA, Boldt T, Schwarzer A, Ritter U, Rohrberg R, Schwalbe E, Uhlig J, Zehrfeld T, Schirmer V, Haas A, Kreibich U, Niederwieser D; for the East German Study Group of Haematology and Oncology (OSHO).

Br J Haematol. 2008 Aug 24. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18752593?ordinalpos=17&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

This phase I study found that a combination of low-dose thalidomide with bendamustine and prednisolone maintained or increased efficacy while avoiding dose-limiting toxicity in 28 patients with refractory myeloma or myeloma that had relapsed after conventional chemotherapy or high-dose therapy with stem-cell support.

 **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 Aug 26. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18637031?ordinalpos=16&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors conduct a systematic review of studies evaluating thalidomide/ dexamethasone (Thal/Dex) 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.

 **Clarithromycin with low dose dexamethasone and thalidomide is effective therapy in relapsed/refractory myeloma.**

Morris TC, Kettle PJ, Drake M, Jones FC, Hull DR, Boyd K, Morrison A, Clarke P, O'Reilly P, Quinn J.

Br J Haematol. 2008 Aug 28. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18759764?ordinalpos=14&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

The authors find that although clarithromycin has only minimal anti-myeloma properties when used as a single agent, its combination with thalidomide and dexamethasone appears very effective, allowing these to be used in lower and more tolerable doses with good clinical effects.

 **New drugs in multiple myeloma.**

Berenson JR, Yellin O.

Curr Opin Support Palliat Care. 2008 Sep;2(3):204-10.



http://www.ncbi.nlm.nih.gov/pubmed/18685422?ordinalpos=29&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

This review discusses new antimyeloma arsenal, including combinations involving both thalidomide and lenalidomide, that has shown its worth in both the relapsed/refractory and frontline setting.

 **The combination of bortezomib, melphalan, dexamethasone and intermittent thalidomide is an effective regimen for relapsed/refractory myeloma and is associated with improvement of abnormal bone metabolism and angiogenesis.**

Terpos E, Kastritis E, Roussou M, Heath D, Christoulas D, Anagnostopoulos N, Eleftherakis-Papaiakovou E, Tsionos K, Croucher P, Dimopoulos MA.

Leukemia. 2008 Sep 4. [Epub ahead of print.]



http://www.ncbi.nlm.nih.gov/pubmed/18769451?ordinalpos=25&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors find that the combination of bortezomib, melphalan, dexamethasone and intermittent thalidomide is an active and well-tolerated regimen for relapsed/refractory myeloma, affecting abnormal bone remodeling and angiogenesis.

 **Lenalidomide in combination with dexamethasone for the treatment of relapsed or refractory multiple myeloma.**

Palumbo A, Dimopoulos M, Miguel JS, Harousseau JL, Attal M, Hussein M, Knop S, Ludwig H, von Lilienfeld-Toal M, Sonneveld P. *Blood Rev.* 2008 Sep 5. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18774632?ordinalpos=8&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors present recommendations for the use of lenalidomide in the treatment of myeloma in order to aid the safe administration and avoid unnecessary dose reduction and discontinuation, thus assuring the best efficacy of treatment.

 **Thalidomide plus dexamethasone as primary therapy for newly diagnosed patients with multiple myeloma.**

Dimopoulos MA, Kastritis E.

Nat Clin Pract Oncol. 2008 Sep 9. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18779849?ordinalpos=22&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors explore previous findings on the use of thalidomide-dexamethasone in previously untreated myeloma patients. They find the combination to be a convenient oral and relatively inexpensive non-myelosuppressive regimen.

 **Lenalidomide alone or in combination with dexamethasone is highly effective in patients with relapsed multiple myeloma following allogeneic stem cell transplantation and increases the frequency of CD4(+) Foxp3(+) T cells.**

Minnema MC, van der Veer MS, Aarts T, Emmelot M, Mutis T, Lokhorst HM.

Leukemia. 2008 Sep 11. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18784738?ordinalpos=6&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

No abstract available.

 **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 Sep 13. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18637123?ordinalpos=16&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

This myeloma treatment update addresses the optimization of different treatment options and schedules, including the use of thalidomide and lenalidomide.

 **Lenalidomide plus dexamethasone is more effective than dexamethasone alone in patients with relapsed or refractory multiple myeloma regardless of prior thalidomide exposure.**

Wang M, Dimopoulos MA, Chen C, Cibeira MT, Attal M, Spencer A, Rajkumar SV, Yu Z, Olesnyckyj M, Zeldis JB, Knight RD, Weber DM.

Blood. 2008 Sep 17. [Epub ahead of print.]

 http://www.ncbi.nlm.nih.gov/pubmed/18799726?ordinalpos=12&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The authors assess the efficacy and safety of lenalidomide plus dexamethasone in patients with relapsed or refractory myeloma previously treated with thalidomide. They find that lenalidomide plus dexamethasone is superior to placebo plus dexamethasone in relapsed or refractory myeloma, independent of prior thalidomide exposure.



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