CITINGS

Published by the International Myeloma Foundation VOLUME III, ISSUE I Q1/2006

# Thalidomide and Revlimid™ Issue

**The International Myeloma Foundation** *(IMF) is pleased to present our first edition of CITINGS for 2006. 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 first 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 or www.myeloma.org.*

*– Susie Novis, President, IMF*

## Thalidomide/Revlimid™ Publications January–March, 2006

***Doxorubicin and dexamethasone followed by thalidomide and dexamethasone is an effective well tolerated initial therapy for multiple myeloma.***

Hassoun H, Reich L, Klimek VM, Dhodapkar M, Cohen A, Kewalramani T, Zimman R, Drake L, Riedel ER, Hedvat CV, Teruya-Feldstein J, Filippa DA, Fleisher M, Nimer SD, Comenzo RL.

*Br J Haematol. 2006 Jan;132(2):155-61.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16398649&query_hl=1&itool=pubmed_DocSum**

This study found that doxorubicin and dexamethasone for 2 or 3 months followed by thalidomide and dexamethasone for 2 months (AD-TD regimen) administered with low-dose aspirin for deep vein thrombosis prophylaxis was well tolerated and yielded a high response rate with minimal treatment-related morbidity for patients with multiple myeloma (MM).



Funded by an educational grant from Celgene Corporation.

***Immunomodulatory analogues of thalidomide in the treatment of multiple myeloma.***

Suppiah R, Srkalovic JG, Hussein MA.

*Clin Lymphoma Myeloma. 2006 Jan;6(4):301-5.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16507207&query_hl=1&itool=pubmed_docsum**

The clinical trial development of second-generation immunomodulatory drugs lenalidomide (Revlimid) and CC-4047 (Actimid) are reviewed in this article. The authors state that both agents demonstrate potent activity with manageable toxicities and provide another treatment opportunity for patients with MM.

***Intravenous melphalan, thalidomide and prednisone in refractory and relapsed multiple myeloma.***

Palumbo A, Avonto I, Bruno B, Ambrosini MT, Bringhen S, Cavallo F, Falco P, Boccadoro M.

*Eur J Haematol. 2006 Jan 23; [Epub ahead of print].*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16438704&query_hl=1&itool=pubmed_docsum**

The authors discuss the significant anti-myeloma activity of thalidomide combined with conventional chemotherapies, including oral melphalan. Feasibility and efficacy of a three-drug combination consisting of intravenous (i.v.) melphalan, prednisone, and thalidomide [M(i.v.)PT] was evaluated in advanced myeloma patients.

***Low-dose thalidomide with pegylated liposomal doxorubicin and high-dose dexamethasone for relapsed/refractory multiple myeloma: a prospective, multicenter, phase II study.***

Offidani M, Corvatta L, Marconi M, Visani G, Alesiani F, Brunori M, Galieni P, Catarini M, Burattini M, Centurioni R, Rupoli S, Scortechini AR, Giuliodori L, Candela M, Capelli D, Montanari M, Olivieri A, Piersantelli MN, Leoni P.

*Haematologica. 2006 Jan;91(1):133-6.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16434383&query_hl=1&itool=pubmed_docsum**

The aim of this prospective, multicenter, phase II study was to investigate the combination of pegylated liposomal doxorubicin (Caelyx) 40 mg/m$^2$ on day 1 every 28 days, dexamethasone 40 mg p.o. on days 1-4 and 9-12, and thalidomide 100 mg daily in 50 patients with advanced multiple myeloma.

***Low-dose Velcade, thalidomide and dexamethasone (LD-VTD): an effective regimen for relapsed and refractory multiple myeloma patients.***

Ciolli S, Leoni F, Gigli F, Rigacci L, Bosi A.

*Leuk Lymphoma. 2006 Jan;47(1):171-3.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16321846&query_hl=1&itool=pubmed_DocSum**

The study found that the LD-VTD regimen applied appears feasible and effective in elderly and heavily pre-treated relapsed and refractory MM patients.

***Novel treatment approaches for patients with multiple myeloma.***

Sinha R, Kaufman JL, Lonial S.

*Clin Lymphoma Myeloma. 2006 Jan;6(4):281-8.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16507205&query_hl=1&itool=pubmed_docsum**

The authors discuss the discovery of key signaling pathways needed for myeloma cell growth and proliferation and the resultant plethora of new and different treatment options. Chief among these new agents are the proteasome inhibitor bortezomib and the immunomodulatory agents thalidomide and lenalidomide.

***Thalidomide and dexamethasone: a new standard of care for initial therapy in multiple myeloma.***

Richardson P, Anderson K.

*J Clin Oncol. 2006 Jan 20;24(3):334-6. Epub 2005 Dec 19.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16365174&query_hl=1&itool=pubmed_DocSum**

Editorial.

***Treatment of multiple myeloma. [Article in French].***

Terriou L, Leleu X, Yakoub-Agha I.

*Bulletin du Cancer. 2006 Jan 1;93(1):101-6.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16455512&query_hl=1&itool=pubmed_docsum**

This article examines the impact of thalidomide and its derivatives and Velcade on the history of multiple myeloma.

***Phase III clinical trial of thalidomide plus dexamethasone compared with dexamethasone alone in newly diagnosed multiple myeloma: a clinical trial coordinated by the Eastern Cooperative Oncology Group.***

Rajkumar SV, Blood E, Vesole D, Fonseca R, Greipp PR; Eastern Cooperative Oncology Group.

*J Clin Oncol. 2006 Jan 20;24(3):431-6. Epub 2005 Dec 19.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16365178&query_hl=1&itool=pubmed_DocSum**

This study found that thalidomide plus dexamethasone demonstrates significantly superior response rates in newly diagnosed myeloma compared with dexamethasone alone. However, this must be balanced against the greater toxicity seen with the combination.

***Current therapeutic uses of lenalidomide in multiple myeloma.***

Hideshima T, Richardson PG, Anderson KC.

*Expert Opin Investig Drugs. 2006 Feb;15(2):171-9.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16433596&query_hl=1&itool=pubmed_docsum**

The researchers discuss the varying avenues of research into the molecular mechanisms of antitumour activity of lenalidomide. They conclude that lenalidomide represents a new class of antitumour agents that is useful in the treatment of MM.

***Primary treatment with pulsed melphalan, dexamethasone and thalidomide for elderly symptomatic patients with multiple myeloma.***

Dimopoulos MA, Anagnostopoulos A, Terpos E, Repoussis P, Zomas A, Katodritou E, Kyrtsonis MC, Delibasi S, Vassou A, Pouli A, Zervas K, Anagnostopoulos N, Maniatis A; Greek Myeloma Study Group.

*Haematologica. 2006 Feb;91(2):252-4.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16461313&query_hl=1&itool=pubmed_docsum**

The researchers report on fifty patients with MM who received primary treatment with melphalan, dexamethasone and thalidomide. Sixty-two percent of patients achieved a partial response and 10% a complete response. The median time to response was 2 months.

***Role of lenalidomide in the treatment of multiple myeloma and myelodysplastic syndrome.***

Maier SK, Hammond JM.

*Ann Pharmacother. 2006 Feb;40(2):286-9. Epub 2006 Jan 10.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16403850&query_hl=1&itool=pubmed_DocSum**

The authors conclude that lenalidomide is a potent immunomodulating drug that offers different mechanisms of action and therapeutic potential for the treatment of MM, MDS, and other malignancies.

***Should we screen patients for inherited thrombophilia before starting thalidomide?***

Otrock ZK, Mahfouz RA, El-Hajj II, Harb MI, Sawaya RA.

*Am J Clin Oncol. 2006 Feb;29(1):100-1.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16462512&query_hl=1&itool=pubmed_docsum**

The authors suggest that patients required to be on thalidomide should be screened for inherited thrombophilia and should be considered for prophylactic anticoagulation therapy.

***Thalidomide in multiple myeloma.***

Garcia-Sanz R.

*Expert Opin Pharmacother. 2006 Feb;7(2):195-213.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16433584&query_hl=1&itool=pubmed_DocSum**

This article reviews the current knowledge of thalidomide in myeloma treatment, focusing especially on the possible mechanisms of action, clinical results, and adverse events related to this drug.

***First-line therapy with thalidomide, dexamethasone and zoledronic acid decreases bone resorption markers in patients with multiple myeloma.***

Tosi P, Zamagni E, Cellini C, Parente R, Cangini D, Tacchetti P, Perrone G, Ceccolini M, Boni P, Tura S, Baccarani M, Cavo M.

*Eur J Haematol. 2006 Feb 15; [Epub ahead of print].*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16480429&query_hl=1&itool=pubmed_docsum**

The study found that among all bone resorption markers, urinary N-terminal telopeptide of collagen I (NTX) and C-terminal telopeptide (serum crosslaps) seem to be strictly related to the extent of bone involvement in MM. Combined thalidomide + dexamethasone and zoledronic acid seem to be highly effective in reducing bone resorption in sensitive patients, although the relative contribution of each drug cannot yet be determined.

***Do new therapeutic approaches (autotransplants, thalidomide, dexamethasone) improve the survival of patients with multiple myeloma followed in a rheumatology department?***

El Mahou S, Attal M, Jamard B, Constantin A, Cantagrel A, Mazieres B, Arnaud C, Laroche M.

*Clin Rheumatol. 2006 Mar;25(2):175-82. Epub 2005 Nov 23.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16328086&query_hl=1&itool=pubmed_DocSum**

The aim of this study was to determine if survival increased with the usage of new treatments for MM. Independent analysis showed increased median survival in MM patients treated using autotransplantation compared with untreated patients. Survival was also longer in MM patients treated with thalidomide than in untreated patients.

***Stimulation of erythropoiesis by thalidomide in multiple myeloma patients: its influence on FasL, TRAIL and their receptors on erythroblasts.***

Grzasko N, Dmoszynska A, Hus M, Soroka-Wojtaszko M.

*Haematologica. 2006 Mar;91(3):386-9.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16531263&query_hl=1&itool=pubmed_docsum**

The results of this study suggest that thalidomide may stimulate erythropoiesis in MM patients by decreasing the expression of tumor necrosis factor (TNF) -like ligands/receptors on erythroblasts.

***A systematic review of phase-II trials of thalidomide monotherapy in patients with relapsed or refractory multiple myeloma.***

Glasmacher A, Hahn C, Hoffmann F, Naumann R, Goldschmidt H, von Lilienfeld-Toal M, Orlopp K, Schmidt-Wolf I, Gorschluter M.

*Br J Haematol. 2006 Mar;132(5):584-93.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16445831&query_hl=1&itool=pubmed_docsum**

This study found that thalidomide monotherapy achieved complete and partial responses in 29.4% of patients with relapsed or refractory MM.

***Lovastatin and thalidomide have a combined effect on the rate of multiple myeloma cell apoptosis in short term cell cultures.***

Dmoszynska A, Podhorecka M, Klimek P, Grzasko N.

*Eur J Clin Pharmacol. 2006 Mar 8; [Epub ahead of print].*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16523333&query_hl=1&itool=pubmed_docsum**

The authors conclude that the mixture of lovastatin and thalidomide may increase the rate of MM cell apoptosis in comparison to the single drug. The precise mechanism of this effect should be determined by further research.

***Thalidomide and hematopoietic-cell transplantation for multiple myeloma.***

Barlogie B, Tricot G, Anaissie E, Shaughnessy J, Rasmussen E, van Rhee F, Fassas A, Zangari M, Hollmig K, Pineda-Roman M, Lee C, Talamo G, Thertulien R, Kiwan E, Krishna S, Fox M, Crowley J.

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

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16525139&query_hl=1&itool=pubmed_docsum**

The authors concluded that thalidomide, when incorporated into high-dose therapy for myeloma, increased the frequency of complete responses and extended event-free survival at the expense of added adverse effects without improving overall survival.

***Oral melphalan and prednisone chemotherapy plus thalidomide compared with melphalan and prednisone alone in elderly patients with multiple myeloma: randomised controlled trial.***

Palumbo A, Bringhen S, Caravita T, Merla E, Capparella V, Callea V, Cangialosi C, Grasso M, Rossini F, Galli M, Catalano L, Zamagni E, Petrucci MT, De Stefano V, Ceccarelli M, Ambrosini MT, Avonto I, Falco P, Ciccone G, Liberati AM, Musto P, Boccadoro M; Italian Multiple Myeloma Network, GIMEMA.

*Lancet. 2006 Mar 11;367(9513):825-31.*

**http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=16530576&query_hl=1&itool=pubmed_docsum**

The authors found that oral melphalan and prednisone plus thalidomide (MPT) is an effective first-line treatment for elderly patients with MM. Anticoagulant prophylaxis reduces frequency of thrombosis. Longer follow-up is needed to assess effect on overall survival.

**(800) 452-CURE (2873)**

**www.myeloma.org**