



CITINGS

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Novel Therapies Issue

The International Myeloma Foundation (IMF) presents this edition of *Citings*, our premiere publication featuring the most up-to-date information on myeloma treatment, focused on the novel therapies currently under study and in use. This edition corresponds with articles published between March and May 2010.

It is our hope that *CITINGS* will be a valuable tool in keeping you informed on the latest developments in myeloma treatment. Please feel free to contact us at (800) 452-CURE (2873) or visit us on the web at www.myeloma.org.

– Susie Novis, President, IMF

Novel Therapies Publications MAY 2010

 ***Management of disease- and treatment-related complications in patients with multiple myeloma.***

Gay F, Palumbo A.

Med Oncol. 2010 May 14. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20467920>

The authors provide an overview of frequency and management of main complications related to myeloma itself and to the use of new drugs, including thalidomide, lenalidomide, and bortezomib, in newly diagnosed and relapsed patients.

 ***The PD-1 / PD-L1 axis modulates the natural killer cell versus multiple myeloma effect: a therapeutic target for CT-011, a novel, monoclonal anti-PD-1 antibody.***

Benson DM Jr, Bakan CE, Mishra A, Hofmeister CC, Efebera Y, Becknell B, Baiocchi RA, Zhang J, Yu J, Smith MK, Greenfield CN, Porcu P, Devine SM, Rotem-Yehudar R, Lozanski G, Byrd JC, Caligiuri MA.

Blood. 2010 May 11. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20460501>

The authors demonstrate a role for CT-011 in enhancing the natural killer cell versus myeloma effect and conclude that a phase 2 clinical trial of CT-011 in combination with lenalidomide for patients with myeloma should be considered.

 ***The quality of response to lenalidomide plus dexamethasone is associated with improved clinical outcomes in patients with relapsed or refractory multiple myeloma.***

Harousseau JL, Dimopoulos MA, Wang M, Corso A, Chen C, Attal M, Spencer A, Yu Z, Olesnyckyj M, Zeldis JB, Knight RD, Weber DM.

Haematologica. 2010 May 11. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20460639>

This retrospective pooled analysis of two phase III trials compares clinical outcomes of patients who achieved complete response or very good partial response with lenalidomide plus dexamethasone with those who only achieved partial response. It finds that continuing treatment with lenalidomide plus dexamethasone achieves best response, in the absence of disease progression and toxicity, and provides deeper remissions and greater clinical benefit over time for patients in this study.

 ***Integrating novel agents into multiple myeloma treatment – current status in Switzerland and treatment recommendations.***

Taverna C, Bargetzi M, Betticher D, Gmür J, Gregor M, Heim D, Hess U, Ketterer N, Lerch E, Matthes T, Mey U, Pabst T, Renner C.

Swiss Med Wkly. 2010 May 10. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20458652>

This article summarizes the discussions of an expert meeting which was held to debate current treatment practices for myeloma in Switzerland concerning the role of novel agents (especially thalidomide, bortezomib and lenalidomide) and to provide recommendations for their use in different treatment stages.

 ***Melphalan and prednisone plus thalidomide or placebo in elderly patients with multiple myeloma.***

Waage A, Gimsing P, Fayers P, Abildgaard N, Ahlberg L, Björkstrand B, Carlson K, Dahl IM, Forsberg K, Gulbrandsen N, Haukas E, Hjertner O, Hjorth M, Karlsson T, Knudsen L, Nielsen JL, Linder O, Mellqvist UH, Nesthus I, Rolke J, Strandberg M, Sorbo JH, Wisloff F, Juliusson G, Turesson I.

Blood. 2010 May 6. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20448107>

In this double blind placebo-controlled study, 363 patients with untreated myeloma are randomized to receive either melphalan-prednisone and thalidomide (MPT) or melphalan-prednisone and placebo (MP). The authors find that MPT has significant anti-myeloma effect, but this does not translate into improved survival.

 ***Bortezomib plus melphalan and prednisone compared with melphalan and prednisone in previously untreated multiple myeloma: updated follow-up and impact of subsequent therapy in the phase III VISTA trial.***

Mateos MV, Richardson PG, Schlag R, Khuageva NK, Dimopoulos MA, Shpilberg O, Kropff M, Spicka I, Petrucci MT, Palumbo A, Samoilova OS, Dmoszynska A, Abdulkadyrov KM, Schots R, Jiang B, Esseltine DL, Liu K, Cakana A, van de Velde H, San Miguel JF.

J Clin Oncol. 2010 May 1;28(13):2259-66. [Epub 2010 Apr 5.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20368561>

The authors find that bortezomib-melphalan-prednisone (VMP) significantly prolongs overall survival versus MP after lengthy follow-up and extensive subsequent antimyeloma therapy; first-line bortezomib use does not induce more resistant relapse. They also find that VMP used upfront appears more beneficial than first treating with conventional agents and saving bortezomib- and other novel agent-based treatment until relapse.

 ***Blockade of the MEK/ERK signalling cascade by AS703026, a novel selective MEK1/2 inhibitor, induces pleiotropic anti-myeloma activity in vitro and in vivo.***

Kim K, Kong SY, Fulciniti M, Li X, Song W, Nahar S, Burger P, Rumizen MJ, Podar K, Chauhan D, Hideshima T, Munshi NC, Richardson P, Clark A, Ogden J, Goutopoulos A, Rastelli L, Anderson KC, Tai YT.

Br J Haematol. 2010 May;149(4):537-49. [Epub 2010 Mar 12.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20331454>

This study investigates the cytotoxicity and mechanism of action of AS703026, a novel, selective, orally bioavailable MEK1/2 inhibitor, in myeloma, with results supporting clinical evaluation, alone or in combination with other anti-myeloma agents (including lenalidomide and bortezomib), to improve patient outcome.

 ***Bortezomib, thalidomide, dexamethasone induction therapy followed by melphalan, prednisolone, thalidomide consolidation therapy as a first line of treatment for patients with multiple myeloma who are non-transplant candidates: results of the Korean Multiple Myeloma Working Party (KMMWP).***

Eom HS, Kim YK, Chung JS, Kim K, Kim HJ, Kim HY, Jin JY, Do YR, Oh SJ, Suh C, Seong CM, Kim CS, Lee DS, Lee JH.

Ann Hematol. 2010 May;89(5):489-97. [Epub 2009 Dec 10.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20012045>

The authors find that as first-line therapy, bortezomib-thalidomide-dexamethasone followed by melphalan-prednisolone-thalidomide has the potential to provide high-quality responses with durable remission among elderly and high-risk myeloma patients.

 ***Clinical efficacy of a bortezomib, cyclophosphamide, thalidomide, and dexamethasone (Vel-CTD) regimen in patients with relapsed or refractory multiple myeloma: a phase II study.***

Kim YK, Sohn SK, Lee JH, Yang DH, Moon JH, Ahn JS, Kim HJ, Lee JJ; Korean Multiple Myeloma Working Party (KMMWP).

Ann Hematol. 2010 May;89(5):475-82. [Epub 2009 Nov 18.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19921192>

The authors find that bortezomib combined with cyclophosphamide, thalidomide, and dexamethasone is a highly effective salvage therapy with manageable toxicity for patients with relapsed or refractory myeloma.

 ***A dose-finding and pharmacodynamic study of bortezomib in combination with weekly paclitaxel in patients with advanced solid tumors.***

Ramaswamy B, Bekaii-Saab T, Schaaf LJ, Lesinski GB, Lucas DM, Young DC, Ruppert AS, Byrd JC, Culler K, Wilkins D, Wright JJ, Grever MR, Shapiro CL.

Cancer Chemother Pharmacol. 2010 May;66(1):151-8. [Epub 2009 Sep 23.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19774377>

This phase I study seeks to determine the maximum tolerated dose of bortezomib when combined with weekly paclitaxel in patients with advanced solid tumors. The authors find that sequential paclitaxel and bortezomib in previously treated patients with advanced solid tumors results in acceptable toxicity and no evidence of interaction; a recommended phase II dose of bortezomib in combination with weekly paclitaxel is 1.8 mg/m².

 ***Frail elderly patients with relapsed-refractory multiple myeloma: efficacy and toxicity profile of the combination of bortezomib, high-dose dexamethasone, and low-dose oral cyclophosphamide.***

Mele G, Giannotta A, Pinna S, Loseto G, Coppi MR, Brocca CM, Melpignano A, Quarta G.

Leuk Lymphoma. 2010 May;51(5):937-40.

 <http://www.ncbi.nlm.nih.gov/pubmed/20350279>

No abstract available.

 ***Lenalidomide for multiple myeloma.***

Hutchinson L.

Nat Rev Clin Oncol. 2010 May;7(5):241.

 <http://www.ncbi.nlm.nih.gov/pubmed/20432526>

Comment on: *Blood.* 2010 Feb 18;115(7):1343-50.

 **Renal recovery with lenalidomide in a patient with bortezomib-resistant multiple myeloma.**

Ludwig H, Zojer N.

Nat Rev Clin Oncol. 2010 May;7(5):289-94. [Epub 2010 Mar 30.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20351701>

The authors present the case of a 51 year-old man diagnosed with Durie-Salmon stage IIIB myeloma with IgG lambda gammopathy and renal impairment associated with urinary excretion of free lambda light chains. At 2 years after initiation of lenalidomide-based therapy and subsequent stem-cell transplantation, the patient remains in partial remission with stable renal function and excellent performance status.

 **Salvage treatment with upfront melphalan 100 mg/m(2) and consolidation with novel drugs for fulminant progression of multiple myeloma.**

Krejci M, Adam Z, Buchler T, Krivanova A, Pour L, Zahradova L, Holanek M, Sandecka V, Mayer J, Vorlicek J, Hajek R.

Ann Hematol. 2010 May;89(5):483-7. [Epub 2009 Nov 19.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19924414>

The authors find that treatment with upfront melphalan 100 mg/m(2) followed by a thalidomide- or bortezomib-based regimen can prolong overall survival to more than 12 months in 33% of patients with fulminant progression of myeloma.

APRIL 2010

 **A staged approach with vincristine, adriamycin, and dexamethasone followed by bortezomib, thalidomide, and dexamethasone before autologous hematopoietic stem cell transplantation in the treatment of newly diagnosed multiple myeloma.**

Chim CS, Lie AK, Chan EY, Leung YY, Cheung SC, Chan SY, Liang R, Kwong YL.

Ann Hematol. 2010 Apr 29. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20428873>

The authors test the efficacy of a total therapy with a staged approach where newly diagnosed myeloma patients received vincristine/adriamycin/dexamethasone (VAD). They find that their approach reduces the use of bortezomib without compromising the ultimate complete response rate, which is also of financial significance for less affluent communities.

 **Stem cell collection in patients with de novo multiple myeloma treated with the combination of bortezomib and dexamethasone before autologous stem cell transplantation according to IFM 2005-01 trial.**

Moreau P, Hulin C, Marit G, Caillot D, Facon T, Lenain P, Berthou C, Pégourié B, Stoppa AM, Casassus P, Michallet M, Benboubker L, Maisonneuve H, Doyen C, Leyvraz S, Mathiot C, Avet-Loiseau H, Attal M, Harousseau JL.

Leukemia. 2010 Apr 29. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20428201>

No abstract available.

 **Bortezomib and donor lymphocyte infusion in multiple myeloma relapsed after allo-SCT does not result in durable remissions.**

Hoevenaren IA, van Vulpen LF, Levenga H, Minnema MC, Raymakers R.

Bone Marrow Transplant. 2010 Apr 26. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20421868>

No abstract available.

 ***Stem cell collection in patients with multiple myeloma: impact of induction therapy and mobilization regimen.***

Nazha A, Cook R, Vogl DT, Mangan PA, Gardler M, Hummel K, Cunningham K, Luger SM, Porter DL, Schuster S, O'Doherty U, Siegel D, Stadtmauer EA.

Bone Marrow Transplant. 2010 Apr 26. [Epub ahead of print.]



<http://www.ncbi.nlm.nih.gov/pubmed/20421869>

This retrospective data analysis suggests that lenalidomide does not prevent the harvest of adequate numbers of CD34 cells for autologous stem cell transplant, but mobilization with G-CSF and CY may be required to obtain adequate numbers of stem cells. The authors also find that the number of lenalidomide cycles does not correlate with stem cell yield.

 ***XBP1s levels are implicated in the biology and outcome of myeloma mediating differential clinical outcomes to thalidomide-based treatments.***

Bagrutuni T, Wu P, Gonzalez de Castro D, Davenport EL, Dickens NJ, Walker BA, Boyd K, Johnson DC, Gregory WM, Morgan GJ, Davies FE.

Blood. 2010 Apr 26. [Epub ahead of print.]



<http://www.ncbi.nlm.nih.gov/pubmed/20421453>

This study highlights the importance of XBP1 in myeloma, its significance as an independent prognostic marker and as a predictor of thalidomide response.

 ***Thalidomide maintenance treatment increases progression-free but not overall survival in elderly patients with myeloma.***

Ludwig H, Adam Z, Tothova E, Hajek R, Labar B, Egyed M, Spicka I, Gisslinger H, Drach J, Kuhn I, Hinke A, Zojer N. *Haematologica.* 2010 Apr 23. [Epub ahead of print.]



<http://www.ncbi.nlm.nih.gov/pubmed/20418244>

This study assesses the impact of thalidomide-interferon in comparison to interferon (IFN) maintenance therapy in elderly patients with myeloma. The authors find that thalidomide plus interferon maintenance therapy increases progression-free survival, but not overall survival, and is associated with slightly more toxicity than maintenance with IFN alone.

 ***Once- versus twice-weekly bortezomib induction therapy with CyBorD in newly diagnosed multiple myeloma.***

Reeder CB, Reece DE, Kukreti V, Chen C, Trudel S, Laumann K, Hentz J, Pirooz NA, Piza JG, Tiedemann R, Mikhael JR, Bergsagel PL, Leis JF, Fonseca R, Stewart AK.

Blood. 2010 Apr 22;115(16):3416-7.



<http://www.ncbi.nlm.nih.gov/pubmed/20413666>

No abstract available.

 ***Complete heart block secondary to bortezomib use in multiple myeloma.***

Dasanu CA.

J Oncol Pharm Pract. 2010 Apr 20. [Epub ahead of print.]



<http://www.ncbi.nlm.nih.gov/pubmed/20406745>

The author discusses the rare occurrences of various heart rhythm and other autonomic nervous system abnormalities attributed to bortezomib in the existing literature and advocates for increased attention by physicians and pharmacists at the first indication of an abnormality.

 **Major tumor shrinking and persistent molecular remissions after consolidation with bortezomib, thalidomide, and dexamethasone in patients with autografted myeloma.**

Ladetto M, Pagliano G, Ferrero S, Cavallo F, Drandi D, Santo L, Crippa C, De Rosa L, Pregno P, Grasso M, Liberati AM, Caravita T, Pisani F, Guglielmelli T, Callea V, Musto P, Cangialosi C, Passera R, Boccadoro M, Palumbo A.

J Clin Oncol. 2010 Apr 20;28(12):2077-84. [Epub 2010 Mar 22.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20308672>

This first study documenting the occurrence of persistent molecular remissions in a proportion of myeloma patients treated without allogeneic transplantation finds that the major reduction in tumor load recorded by real-time quantitative polymerase chain reaction after bortezomib-thalidomide-dexamethasone suggests that unprecedented levels of tumor cell reduction can be achieved in myeloma thanks to the new nonchemotherapeutic drugs.

 **Importance of Achieving a Complete Response in Multiple Myeloma, and the Impact of Novel Agents.**

Chanan-Khan AA, Giralt S.

J Clin Oncol. 2010 Apr 12. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20385994>

The authors review the prognostic significance of achieving complete response (CR) in myeloma and highlight the importance of CR as an increasingly realizable goal at all stages of treatment, and how this goal is informed by the advent of novel therapies, including bortezomib, thalidomide, and lenalidomide.

 **Lenalidomide, bortezomib, and dexamethasone combination therapy in patients with newly diagnosed multiple myeloma.**

Richardson PG, Weller E, Lonial S, Jakubowiak AJ, Jagannath S, Raje NS, Avigan DE, Xie W, Ghobrial IM, Schlossman RL, Mazumder A, Munshi NC, Vesole DH, Joyce R, Kaufman JL, Doss D, Warren DL, Lunde LE, Kaster S, Delaney C, Hideshima T, Mitsiades CS, Knight R, Esseltine DL, Anderson KC.

Blood. 2010 Apr 12. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20385792>

This phase I/II study, the first prospective evaluation of lenalidomide-bortezomib-dexamethasone in front-line myeloma, finds that the combination demonstrates favorable tolerability and is highly effective in the treatment of newly diagnosed myeloma.

 **Venous thromboembolism in multiple myeloma: Current perspectives in pathogenesis.**

Uaprasert N, Voorhees PM, Mackman N, Key NS.

Eur J Cancer. 2010 Apr 10. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20385482>

The authors address the relationship of immunomodulatory agents, such as thalidomide and lenalidomide, with the substantial increase of the incidence of venous thromboembolism in myeloma patients.

 **A novel aurora-A kinase inhibitor MLN8237 induces cytotoxicity and cell cycle arrest in multiple myeloma.**

Görgün G, Calabrese E, Hideshima T, Ecsedy J, Perrone G, Mani M, Ikeda H, Bianchi G, Hu Y, Cirstea D, Santo L, Tai YT, Nahar S, Zheng M, Bandi M, Carrasco RD, Raje N, Munshi N, Richardson P, Anderson KC.

Blood. 2010 Apr 9. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20382844>

The authors assess the in vitro and in vivo anti-myeloma activity of MLN8237, a small molecule Aurora-A kinase inhibitor. They find that combining MLN8237 with dexamethasone, doxorubicin or bortezomib induces synergistic/additive anti-myeloma activity in vitro.

 ***Lenalidomide, melphalan, prednisone and thalidomide (RMPT) for relapsed/refractory multiple myeloma.***

Palumbo A, Larocca A, Falco P, Sanpaolo G, Falcone AP, Federico V, Canepa L, Crugnola M, Genuardi M, Magarotto V, Petrucci MT, Boccadoro M.

Leukemia. 2010 Apr 8. [Epub ahead of print.]



<http://www.ncbi.nlm.nih.gov/pubmed/20376079>

This multicenter, open-label, non-comparative phase II trial evaluates the safety and efficacy of salvage therapy with lenalidomide, melphalan, prednisone and thalidomide (RMPT) in patients with relapsed/refractory myeloma. The authors find that RMPT is an active salvage therapy with good efficacy and manageable side effects.

 ***Single agent lenalidomide in newly diagnosed multiple myeloma: a retrospective analysis.***

Baz R, Patel M, Finley-Oliver E, Lebovic D, Hussein MA, Miller KC, Wood M, Sher T, Lee K, Chanan-Khan AA.

Leuk Lymphoma. 2010 Apr 6. [Epub ahead of print.]



<http://www.ncbi.nlm.nih.gov/pubmed/20367570>

This retrospective analysis evaluates the single agent activity of lenalidomide in newly diagnosed myeloma. The authors' findings suggest that lenalidomide alone can induce an anti-myeloma effect in previously untreated patients who are considered poor candidates for concurrent dexamethasone.

 ***Analysis of efficacy and prognostic factors of lenalidomide treatment as part of a Dutch compassionate use program.***

Kneppers E, Lokhorst HM, Eeltink CM, Huls G, Kersten MJ, Koedam J, Minnema MC, van Oers MH, Raymakers RA, Schaafsma MR, Vellenga E, Wijermans PW, Wittebol S, Sonneveld P, Zweegman S.

Clin Lymphoma Myeloma Leuk. 2010 Apr 1;10(2):138-43.



<http://www.ncbi.nlm.nih.gov/pubmed/20371448>

The authors analyze the clinical data of 114 patients with refractory or relapsed myeloma treated with lenalidomide on a compassionate use basis. Their analysis confirms that, outside clinical prospective trials, treatment with lenalidomide is highly effective and feasible in heavily pretreated patients with myeloma.

 ***Decrease in CD4+ T-cell counts in patients with multiple myeloma treated with bortezomib.***

Heider U, Rademacher J, Kaiser M, Kleeberg L, von Metzler I, Sezer O.

Clin Lymphoma Myeloma Leuk. 2010 Apr 1;10(2):134-7.



<http://www.ncbi.nlm.nih.gov/pubmed/20371447>

The authors investigate the influence of bortezomib on T-cell subpopulations in 53 patients with myeloma before initiation of bortezomib and during therapy. Their results show that bortezomib leads to a transient decrease in CD4+ lymphocytes, accompanied by an increased incidence of varicella zoster virus infections. The antiviral prophylaxis with acyclovir is effective in patients with myeloma treated with bortezomib.

 ***Vorinostat plus bortezomib for the treatment of relapsed/refractory multiple myeloma: a case series illustrating utility in clinical practice.***

Mazumder A, Vesole DH, Jagannath S.

Clin Lymphoma Myeloma Leuk. 2010 Apr 1;10(2):149-51.



<http://www.ncbi.nlm.nih.gov/pubmed/20371450>

This case series reports the experience of combined vorinostat and bortezomib in six patients with relapsed/refractory myeloma after previous bortezomib. The authors find that combined vorinostat and bortezomib therapy is effective in patients with relapsed/refractory myeloma after failure of previous bortezomib-based regimens, supporting further evaluation of this combination in randomized trials.

 ***Bortezomib-induced painful neuropathy in rats: a behavioral, neurophysiological and pathological study in rats.***

Meregalli C, Canta A, Carozzi VA, Chiorazzi A, Oggioni N, Gilardini A, Ceresa C, Avezza F, Crippa L, Marmiroli P, Cavaletti G.

Eur J Pain. 2010 Apr;14(4):343-50. [Epub 2009 Aug 19.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19695912>

In order to obtain a pre-clinical model to reproduce the characteristic pain symptoms in bortezomib-treated patients, the authors develop an animal model of bortezomib-induced nociceptive sensory neuropathy.

 ***Bortezomib-induced peripheral neuropathy in multiple myeloma: a comparison between previously treated and untreated patients.***

Corso A, Mangiacavalli S, Varettoni M, Pascutto C, Zappasodi P, Lazzarino M.

Leuk Res. 2010 Apr;34(4):471-4. [Epub 2009 Aug 11.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19674790>

The authors compare the incidence, risk factors, severity and outcome of peripheral neuropathy (PN) and neuropathic pain in patients treated with bortezomib up-front or at relapse. They find that severity and outcome of bortezomib-related PN are similar in untreated and pre-treated myeloma patients, except for neuropathic pain, which has lower incidence and shorter duration in untreated patients with less frequent need for bortezomib discontinuation.

 ***Captivating bortezomib: an active but still mysterious drug.***

Di Raimondo F, Conticello C.

Leuk Res. 2010 Apr;34(4):411-2. [Epub 2009 Oct 12.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19819547>

Comment on: *Leuk Res.* 2010 Apr;34(4):498-506.

 ***Changes of gene expression profile in human myeloma cell line induced by thalidomide.*** [Article in Chinese]

Wang HY, Zhang M, He PC, Yang BJ, Shao LY, Shao WB.

Zhongguo Shi Yan Xue Ye Xue Za Zhi. 2010 Apr;18(2):396-402.

 <http://www.ncbi.nlm.nih.gov/pubmed/20416176>

The authors investigate the anti-myeloma molecular mechanism of thalidomide by detecting gene expression profiles of human myeloma cell line RPMI8226 treated with thalidomide. They conclude that 22 differentially expressed genes are involved in protein synthesis and degradation, cell signal transduction, cytoskeletal movement, immune modulation, cell metabolism, regulation of anti-oncogene and cell apoptosis, which relate directly or indirectly to molecular mechanisms of anti-myeloma effects induced by thalidomide.

 ***Clonal evolution at leukemic relapse of multiple myeloma (secondary plasma cell leukemia) responding to re-treatment with bortezomib-based therapy. A case record.***

Bernardeschi P, Pirrotta MT, Montenora I, Giustarini G, Ferreri MI, Simi P, Fiorentini G.

Leuk Res. 2010 Apr;34(4):e104-5. [Epub 2009 Nov 3.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19889456>

No abstract available.

 ***Home administration of bortezomib: making a difference to myeloma patients' lives.***

Meenaghan T, O'Dwyer M, Hayden P, Hayat A, Murray M, Dowling M.

Eur J Oncol Nurs. 2010 Apr;14(2):134-6. [Epub 2009 Oct 8.]

 <http://www.ncbi.nlm.nih.gov/pubmed/19818684>

No abstract available.

 ***Lenalidomide in multiple myeloma: current role and future directions.***

Zeldis JB, Knight RD, Jacques C, Tozer A, Bizzari JP.

Expert Opin Pharmacother. 2010 Apr;11(5):829-42.

 <http://www.ncbi.nlm.nih.gov/pubmed/20210686>

This review describes current data on lenalidomide in myeloma and how the unique properties of lenalidomide may lend its use in new settings, such as maintenance and preventive therapy.

 ***Rapid control of previously untreated multiple myeloma with bortezomib-lenalidomide-dexamethasone (BLD).***

Wang M, Delasalle K, Giralt S, Alexanian R.

Hematology. 2010 Apr;15(2):70-3.

 <http://www.ncbi.nlm.nih.gov/pubmed/20423566>

The authors find that the combination of bortezomib-lenalidomide-dexamethasone given for one or two courses is an effective primary treatment for newly diagnosed myeloma patients.

 ***Severe bortezomib-induced peripheral neuropathy in a patient with multiple myeloma.***

Sanada Y, Nakazato T, Suzuki K, Mihara A, Aisa Y, Iwabuchi M, Kakimoto T.

Rinsho Ketsueki. 2010 Apr;51(4):264-9.

 <http://www.ncbi.nlm.nih.gov/pubmed/20467223>

The authors find that close monitoring of neurological symptoms and prompt dose-reduction or cessation of bortezomib are important to prevent the progression of irreversible peripheral neuropathy.

 ***Thalidomide inhibited the synthesis of IgM and IgG whereas Thalidomide + Dexamethasone and Dexamethasone alone acted as co-stimulants with pokeweed and enhanced their synthesis.***

Shannon EJ, Sandoval F.

Int Immunopharmacol. 2010 Apr;10(4):487-92. [Epub 2010 Feb 1.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20123041>

The authors find that thalidomide's ability to suppress Ig may explain its activity and effective treatment in diseases such as myeloma.

MARCH 2010

 ***How best to use new therapies in multiple myeloma.***

Dingli D, Rajkumar SV.

Blood Rev. 2010 Mar 31. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20359801>

The authors summarize the key observations from recent completed and ongoing studies that determined the effect of novel therapies, including thalidomide, lenalidomide, and bortezomib, both in the setting of newly diagnosed myeloma and for relapsed disease. They also discuss their approach to the use of these agents in specific myeloma settings.

 ***Histone deacetylases are critical targets of bortezomib-induced cytotoxicity in multiple myeloma.***

Kikuchi J, Wada T, Shimizu R, Izumi T, Akutsu M, Mitsunaga K, Noborio-Hatano K, Nobuyoshi M, Ozawa K, Kano Y, Furukawa Y.

Blood. 2010 Mar 29. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20351311>

The authors show that histone deacetylases (HDACs) are critical targets of bortezomib, which specifically down-regulate the expression of class I HDACs (HDAC1, 2 and 3) in myeloma cell lines and primary myeloma cells at the transcriptional level, accompanied by reciprocal histone hyperacetylation. These results suggest that bortezomib targets HDACs via distinct mechanisms from conventional HDAC inhibitors, providing a novel molecular basis and rationale for the use of bortezomib in myeloma treatment.

 ***Bortezomib, doxorubicin, and dexamethasone combination therapy followed by thalidomide and dexamethasone consolidation as a salvage treatment for relapsed or refractory multiple myeloma: analysis of efficacy and safety.***

Lee SS, Suh C, Kim BS, Chung J, Joo YD, Ryoo HM, Do YR, Jin JY, Kang HJ, Lee GW, Lee MH, Shim H, Kim K, Yoon SS, Bang SM, Kim HY, Lee JJ, Park J, Lee DS, Lee JH; the Korean Multiple Myeloma Working Party (KMMWP). *Ann Hematol.* 2010 Mar 27. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20349060>

The authors conduct a phase 2 study with bortezomib, doxorubicin, and dexamethasone (PAD) followed by thalidomide and dexamethasone (TD) in patients with relapsed myeloma. They find the treatment regimen to be very effective and tolerable.

 ***Multiple myeloma: chemotherapy or transplantation in the era of new drugs.***

Palumbo A, Rajkumar SV.

Eur J Haematol. 2010 Mar 23. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20345446>

The authors review the current results of studies incorporating novel agents, including bortezomib, thalidomide, and lenalidomide in myeloma and discuss the role of autologous stem-cell transplantation in the era of new active drugs for the treatment of this disease.

 ***Ultra low dose thalidomide in myeloma revisited.***

Patrick HE, Bowcock SJ.

Br J Haematol. 2010 Mar 21. [Epub ahead of print.]

 <http://www.ncbi.nlm.nih.gov/pubmed/20346009>

No abstract available.

 ***Factors affecting the response of thalidomide therapy for patients with multiple myeloma. [Article in Japanese]***

Agata M, Sameshima Y, Oda T, Kondo T, Ishiyama M, Yasunami T, Kazama H, Okamura T, Yoshinaga K, Shiseki M, Mori N, Yamada O, Sagawa K, Teramura M, Motoji T.

Rinsho Ketsueki. 2010 Mar;51(3):189-95.

 <http://www.ncbi.nlm.nih.gov/pubmed/20379113>

The authors address factors that affect the response to thalidomide of 40 myeloma who were not eligible for chemotherapy.

 ***Neurological monitoring reduces the incidence of bortezomib-induced peripheral neuropathy in multiple myeloma patients.***

Velasco R, Petit J, Clapés V, Verdú E, Navarro X, Bruna J.

J Peripher Nerv Syst. 2010 Mar;15(1):17-25.

 <http://www.ncbi.nlm.nih.gov/pubmed/20433602>

The authors study 58 relapsed/refractory myeloma patients treated with bortezomib, aiming to compare bortezomib-induced peripheral neuropathy (BIPN) incidence and severity between both groups and to identify risk factors of BIPN.

 ***Treatment of AL-amyloidosis--results from one clinic and review of published experience with new agents (bortezomib, thalidomide and lenalidomide) in AL-amyloidosis. [Article in Czech]***

Adam Z, Pour L, Krejčí M, Zahradová L, Krivanová A, Mardová J, Kovárová L, Stepánková S, Moulis M, Kren L, Veselý K, Svobodová I, Germáková Z, Nedbálková M, Mayer J, Hájek R.

Vnitř Lek. 2010 Mar;56(3):190-209.



<http://www.ncbi.nlm.nih.gov/pubmed/20394205>

Fifteen patients with light chain deposits in the form of AL-amyloidosis and two patients with light chain deposition as amorphous matter (light chain deposition disease) were treated at the authors' clinic as of 1999. Per their limited experience and published information, they conclude that bortezomib may be considered a very effective and well-tolerated agent, suitable, in combination, for patients with the diagnosis of AL-amyloidosis.



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