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► **To cite this version:**

Adrian Tempescul, Jean-Christophe Ianotto, Frédéric Morel, Veronique Marion, Marc Braekeleer, et al.. Lenalidomide, as a single agent, induces complete remission in a refractory mantle cell lymphoma. *Annals of Hematology*, 2009, 88 (9), pp.921-922. 10.1007/s00277-008-0692-4 . hal-00535025

HAL Id: hal-00535025

<https://hal.science/hal-00535025>

Submitted on 11 Nov 2010

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Lenalidomide, as a single agent, induces complete remission in a refractory mantle cell lymphoma

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Received: 15 September 2008 / Accepted: 23 December 2008 / Published online: 13 January 2009
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Dear Editor,

Mantle cell lymphoma (MCL) is an aggressive non-Hodgkin's lymphoma that is characterized by a typical cytological presentation, the presence of the t(11;14)(q13;q32) chromosomal translocation, and overexpression of cyclin D1. MCL has a low response rate and short progression-free survival (PFS) after conventional therapy. In refractory or relapsed MCL, the prognosis is even worse. Several novel therapeutic approaches have been proposed, including monoclonal antibodies, radioimmunotherapy, proteasome inhibitors, m-TOR inhibitors, and the immunomodulatory drugs thalidomide and lenalidomide. In our patient with refractory MCL, the use of lenalidomide as single agent therapy allowed for complete cytological, phenotypic, and cytogenetic remission in a very short period of time.

A 74-year-old woman was first seen for asthenia and the presence of abnormally circulating B lymphocytes. The clinical examination only identified grade I splenomegaly.

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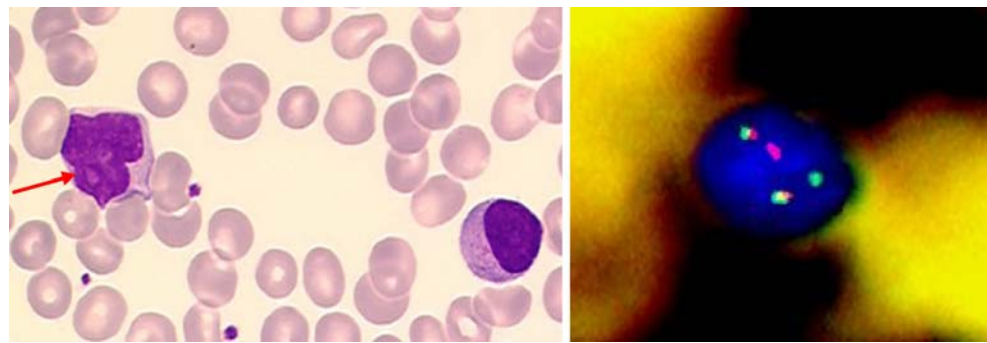
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The blood count revealed lymphocytosis at 8.96 Giga/L with 30% circulating lymphocytes, which presented with the typical MCL phenotype, CD5⁺, CD19⁺, CD23⁻, CD20⁺, and cyclin D1⁺. Genetic studies revealed the presence of the translocation t(11;14)(q11;q32), and molecular biological analyses indicated overexpression of the cyclin D1 protein. Using an 18 FDG PET/CT procedure, we identified an infiltration of the mediastin and the spleen. Bone marrow evaluation showed a 31% infiltration by MCL lymphocytes. Using the Ann Arbor classification, a diagnosis of stage IV mantle cell lymphoma with IPI 3 was made. The patient was treated using rituximab associated with the vincristine, doxorubicin, dexamethasone (VAD)-chlorambucil protocol. After three courses of chemotherapy, the 18 fluorodeoxyglucose position emission tomography/computed tomography (FDG PET/CT) procedure revealed a decreased signal in the initial areas. Blood and marrow evaluations also failed to demonstrate infiltration. The patient was considered to be in very good partial remission, and we decided to continue with three additional cycles of VAD-chlorambucil standard therapy. Before beginning the sixth cycle, the blood count revealed that approximately 40% of the patient's lymphocytes (2.34 Giga/L) had the morphology and phenotype of MCL. Fluorescence in situ hybridization (FISH) analysis confirmed the presence of the typical MCL translocation t(11,14) (Fig. 1).

We initiated continuous treatment with lenalidomide as a single agent, at 25 mg daily. Five weeks after beginning this treatment, cytological, immunophenotypic, cytogenetic (conventional and FISH), and molecular biological analyses of blood and marrow showed complete remission. The tolerance of the treatment was very good without any side effects. Due to moderate cytopenia, the dose of lenalidomide was reduced to 20 mg and then to 15 mg after confirming complete remission.

Fig. 1 Morphological presentation and FISH using LSI 11q13 CCND1 (spectrum orange)/LSI 14q32 IGH (spectrum green), dual fusion translocation probes (Abbott, Rungis, France) showing the t(11;14)(q13;q32) in patient's lymphocytes at the time of the relapse



MCL represents a distinct clinicopathologic entity among the non-Hodgkin lymphomas, characterized by a short PFS [1]. Patients with refractory or relapsed disease have a worse prognosis [2]. It has been recognized that stromal cells provide important stimuli in the survival of malignant B cells [3, 4]. Immunomodulatory drugs interact with the microenvironment, altering cytokine secretion and expression of adhesion molecules, which can result in apoptosis of malignant B cells [5, 6]. In a German study, the use of a combination therapy of rituximab and thalidomide led to an 81% response to treatment, including 31% of patients who underwent complete remission [7]. There are some publications that report the efficacy of thalidomide used as single agent [8, 9]. In 2008, Smith et al. presented the work of Cancer and Leukemia Group B. In 24 patients with relapsed/refractory MCL, the use of thalidomide as single agent allowed for only a 12.5% response, with grades 3–4 adverse events [10]. In a phase I/II study, Wang et al. [11] used lenalidomide as a single agent and obtained five responses from six patients, including one complete remission, one partial remission, and three minor responses.

In our patient, we used 25 mg of lenalidomide daily and continuously. The tolerance of the treatment by the patient was good. Five weeks after beginning the treatment, a blood and marrow analysis indicated complete cytological, immunophenotypical, and cytogenetic remission. Due to the presence of cytopenia, we reduced the dose of lenalidomide to 20 mg and then to 15 mg daily. Six months after initiating the treatment, the patient is still in complete remission.

Despite the short follow-up, our case confirms the results already published. The rapidity of the response allows us to suppose that lenalidomide (alone or in combination) would be an interesting therapeutic addition to the standard treatment of refractory/relapsed MCL.

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