Abstract

In the clinic, I am following (114) patients suffering from Multiple Myeloma (MM), treated with a single dose capsule daily containing (50- 100 mg) of the drug. Thalidomide [1,2] has shown its efficacy in multiple myeloma [3,4], particularly in combination with cortisone. Currently it is used in combination with Melphalan and Prednisone (MPT) [5,6,7] as first-line therapy or in combination with Dexamethasone [8,9] (Dex-Tal) in relapsing patients. Bortezomib (Velcade®) is a very active drug in patients with multiple myeloma. It has been used in experimental protocols in various stages of the disease (first-line therapy or relapse). Many studies have shown a clear superiority of Bortezomib in combination with high-dose Dexamethasone or other drugs (Thalidomide, Doxorubicin, Cyclophosphamide), compared to conventional therapy. Recently Bortezomib (Velcade®) in association with Melphalan and Prednisone (VMP) has been approved as an alternative to the previous reference (MPT) scheme in patients not candidates for autologous transplantation [10,11,12]. Since it is not eliminated by the kidney it is the drug of first choice in patients with renal insufficiency. In pharmacokinetics profile in patients with multiple myeloma after oral administration of a single dose capsule containing (100mg) of the drug, HPLC – Technique is used for the determination of molecules [13].

Keywords: Multiple Myeloma (MM), Thalidomide, Lenalidomide Velcade®, Melphalan and Prednisone (MPT), HPLC-Technique.

1. Introduction

Multiple myeloma (MM) - KAHLER – BOZZOLO disease

It is a neoplasm supported by the proliferation of a neoplastic clone of plasma cell nature, cells belonging to the immune system present mainly in the bone marrow that have the function of producing antibodies.

Molecular Pathogenesis Etiology 1- 2- 3- 4-Symptoms Therapy ... New therapies

1.1 Etiology

The MM has basic oncogenic but its actual cause is not yet known. Surely ionizing radiation has a causal role, given its high incidence among the survivors of the atomic explosions and between radiologists exposed for a long time for professional reasons. A higher than average incidence was also reported among the farmers who have handled certain classes of pesticides or insecticides, industrial workers who handled based solvents benzene.

1.2 Molecular Pathogenesis

Conventional cytogenetic analysis showed that in 30-59% of myeloma patients can be detected karyotypic abnormalities. The extent and frequency of these can be correlated with disease stage, prognosis and primary response to therapy. For example, it falls into average to find about 20% of abnormalities at I stage of the disease, which become 60% at the stage III and more than 80% when there are extra medullary disseminated metastases.

1.3 Symptoms

Usually the symptoms are:

• Bone pain; normally located along the spine, but can occur in any other way throughout the skeleton area.
• Kidney failure
• Hypercalcemia
• Fatigue and general weakness
• Neuropathy
• Anaemia

1.4 Therapy

New therapies include:

• The use of Thalidomide and its derivatives,
Lenalidomide, a derivative of thalidomide, is an immunomodulating agent, which interferes with the activity of the immune system. It blocks the development of tumour cells, inhibits angiogenesis (increase vessels of blood) and also stimulates
particular cells of the immune system to attack cancer cells. [14] Lenalidomide, compared to its progenitor molecule (thalidomide), is 50,000 times more effective in inhibiting TNF-α and has a lower incidence of side effects. [15]

- The proteasome inhibitor Bortezomib, approved and given in combination with Melphalan
- The ABT-737, an antagonist of Bcl-2 protein.

It is also being studied in several types of cancers including brain tumours, kidney cancer, prostate cancer, colon carcinoma, pancreatic and breast and hepatocarcinoma.

2. Method

In the clinic, I am following (114) patients suffering from MM, a relatively rare disease. They are of different sex (M, F), age, working classes. They are treated with a single dose capsule containing (50-100 mg) of the drug. The incidence of myeloma increases with age. Most people with myeloma are more than 50 years old, only 10% of patients are under 40 years of age. The incidence has a percentage (1-1.5 / 100,000).

The male-female ratio is about 3-1 which means a greater incidence among males.

3. Strumentation

The analysis was performed using a HPLC [16] Thermo Finingam SCM 1000 with Pump, detector VIS / UV and injector with loop of 20μl.

The best conditions are as follows:
- Analytical Column Hypersil BDS C18 (250 x 4.6 mm), preceded [17] from a pre-column, at a temperature of 20 ° C.
- FM composed of 25% ACN and 75% 10mM ammonium acetate buffer pH 5.5.
- Flow 1.5 ml / min.
- UV detector, wavelength of 220 nm.

4. Materials and reagents

- Thalidomide, Sigma aldrich®
- phthalimide, Sigma aldrich®
- Acetonitrile HPLC grade, Sigma aldrich®
- Ammonium acetate, Carlo Erba.

5. Preparation mobile Phase

A- For each half liter of solution weigh exactly 0.39 g of ammonium acetate (PM 77.08 g /mol) which are dissolved in 450 ml of bidistilled water. The pH is then 5.5 by the addition of acetic acid drop-drop.

B- Acetonitrile.

6. Calibration line of Thalidomide

The intermediate standard was then injected in order to determine the area. As the solution 0.05μg/ml was not quantifiable, the curve was built on 6 points.

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Table 1.

Preparations of the dilutions and the calibration curves of the Phthalimide

The intermediate standards were prepared and injected into as for Thalidomide.

The results obtained are reported in Table 2.

<table>
<thead>
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Table 2.
7. Results and discussions:
A patient [18] is diagnosed with multiple myeloma in 2011. She initially received 6 cycles of Velcade and Dexamethasone, the last in February 2012, followed by radiation to the spine. The revaluation with bone marrow biopsy showed the persistence of 7% plasma thus she received an additional 6 months of the same treatment. In September 2012, the bone marrow taken showed 10% of plasma cells thus she began with Revlimid with cyclophosphamide and Decadron until December 2012; then it went to Velcade with Decadron and Lenalidomide with Acyclovir for 8 cycles until 18 August 2013 with studies on bone marrow in April 2013 showing remission. The patient presented all'AUBMC in August 21, 2013. The evaluation of the disease showed VGPR (BM negative, positive immunofixation). She received G-CSF followed by the collection and cryopreservation of stem cells. She received Melphalan (200 mg / m2) in strong dose followed by autologous peripheral stem cell transplantation in the September 11, 2013. The women in (2014) returns to take the continuous Velcade. The women in (2015) returns again to take the continuous Thalidomide. The women in (2016) returns to take the continuous Lenalidomide in combination with Dexamethasone. For MM patients the chance of real recovery, understood as full eradication of the disease remains poor.

8. Conclusions
It is recommended the giving of Thalidomide a (100 - 200mg) dose daily for three weeks in the month, In the end Lenalidomide has been shown to be superior to a lenalidomide-dexamethasone association with dexamethasone used alone.
Lenalidomide combination with Melphalan and Prednisone(MPL) is more effective than thalidomide combination with Melphalan and Prednisone (MPT), which is why it is used after the thalidomide fever, also because of its effectiveness it is used after interfering with the bone marrow. Since lenalidomide is a derivative of thalidomide, whose teratogenic action is known, its use is strictly prohibited in pregnancy and cannot be taken by women of childbearing age during and shortly after termination. Recommended with a dietary supplement, food rich in complex vitamin and other necessary elements (Na, K, Fe, Ca, Mg, P, Zn, …) and a period of resting, as evidenced by many European Oncology centres.

References


[18] Merjan Teaching Hospital – Babylon Oncology Center. Hilla (Babylon) – IRAQ.

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