Plitidepsin (PharmaMar) shows activity against the cells responsible for the destruction of bone in myeloma multiple

- Plitidepsin showed the capability to cancel out the activity of the osteoclasts –cells responsible for the destruction of bone- at a concentration of up to 100 times less than we believe necessary to kill myeloma cells

- In combination with proteasome inhibitors, we believe that plitidepsin has the potential to provide a therapeutic alternative for the treatment of multiple myeloma

Madrid, 11th December, 2017. PharmaMar (MSE: PHM) presented new preclinical data on plitidepsin showing how it regulates the viability and function of bone cells in combination with other anti-multiple myeloma drugs. This presentation took place during the 59th American Society of Hematology' annual meeting that is being held in Atlanta from the 9th to the 12th of December.

In multiple myeloma, the growth of tumor cells inside the patient´s bone marrow increases the destruction of the bone, causing severe injuries. Despite the latest therapeutic progress in this pathology, the damage to the bone caused by the disease often persists even after the patient is in complete remission. Therefore, the challenge for investigators is to identify new treatments that eliminate the growth of tumor cells at the same time as protecting the bone.

The objective of this study, titled *"Plitidepsin regulates viability and function of myeloma cells and bone cells in combination with other anti-MM drugs"* (#3065), was to determine the effect of plitidepsin, as a single agent or in combination with other compounds, on bone cells (osteocytes, in charge of maintaining the bone once formed; osteoblasts, responsible for bone growth; and osteoclasts, that destroy old bone, so that the osteoblasts can generate new bone).

Firstly, we observed that plitidepsin had activity against myeloma cells, even when these were resistant to conventional chemotherapy, and also it had a synergistic effect when used in combination with glucocorticoids or proteasome inhibitors (bortezomib).

Plitidepsin showed the capability to cancel out the activity of the osteoclasts –cells responsible for the destruction of the bone- at a concentration of up to 100 times lower than we believe necessary to kill myeloma cells. Accordingly, we believe that plitidepsin has the potential to help to maintain the delicate balance within the bone during the treatment in combination with bortezomib.

The principle conclusion of the study was that plitidepsin, in combination with proteasome inhibitors, has the potential to provide a therapeutic alternative for multiple myeloma in light of the observed high antitumoral response and lack of impact on bone.

About plitidepsin

Plitidepsin is an investigational anticancer agent of marine origin, originally obtained from the ascidian *Aplidium albicans*. It specifically binds to the eEF1A2 and targets the non-canonical role of this protein, resulting in tumor cell death via apoptosis (programed death). Plitidepsin is currently in clinical development for hematological cancers, including a Phase Ib trial in relapsed or refractory multiple myeloma as a triple combination of plitidepsin and bortezomib, and a Phase II in patients with multiple myeloma refractory to lenalidomida and bortezomib. Furthermore, a Phase II study in relapsed or refractory angioimmunoblastic T-cell lymphoma. A Phase III trial in multiple myeloma relapsed or refractory has been completed. Plitidepsin has received orphan drug designation in the European Union and the United States of America.

About multiple myeloma

Multiple myeloma is a relatively uncommon type of blood cancer, which accounts for 10% of all hematological malignancies, this being caused by malignant plasma cells that very rapidly multiply[i]. Normal plasma cells are white blood cells, which form part of the immune system, found in the bone marrow that produce the antibodies necessary for fighting infections[ii]. Abnormal cells produce a type of antibody that does not benefit the body and accumulate, thus preventing normal cells from functioning properly. In 2015, 26,850 new cases were diagnosed in the US, and about 11,200 people died from this disease[iii].In Europe, the incidence is 4.5–6.0 out of 100 000 diagnosed per year[iv].

About PharmaMar

Headquartered in Madrid, PharmaMar is a world-leading biopharmaceutical company in the discovery and development of innovative marine-derived anticancer drugs. The company has a pipeline of drug candidates and a robust R&D oncology program. PharmaMar develops and commercializes YONDELIS® in Europe and has other clinical-stage programs under development for several types of solid and hematological cancers, Zepsyre™ (PM1183), plitidepsin, PM184 and PM14. PharmaMar is a global biopharmaceutical company with subsidiaries in Germany, Italy, France, Switzerland, United Kingdom, Belgium, Austria and the United States. PharmaMar fully owns other companies: GENOMICA, leading molecular diagnostics company; Sylentis, dedicated to researching therapeutic applications of gene silencing (RNAi); and two other chemical enterprises, Zelnova Zeltia and Xylazel. To learn more about PharmaMar, please visit us at www.pharmamar.com.

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[i] http://www.cancer.org/cancer/multiplemyeloma/detailedguide/multiple-myeloma-what-is-it
[ii] http://www.myeloma.org.uk/information/what-is-myeloma/
[iii] http://seer.cancer.gov/statfacts/html/mulmy.html
[iv] http://www.esmo.org/Guidelines/Haematological-Malignancies/Multiple-Myeloma