Epigenetic resensitisation
- for relapsed/refractory patients with multiple myeloma

All myeloma patients receiving IMiDs will eventually develop resistance, which can be overcome with epigen resensitisation.

**Key points:**
- Multiple myeloma (MM) is the second most common hematological malignancy.
- IMiDs (lenalidomide, pomalidomide) are an essential therapy for MM; however, all patients will experience relapse.
- Azacytidine (a DNMT inhibitor) and EPZ-6438 (an EZH2 inhibitor) are able to restore sensitivity to IMiDs.
- Both drugs are known epigenetic drugs, already in the market.

The combination of Az and EPZ effectively resensitized pomalidomide-resistant cells (OPMD-PR) to pomalidomide.

The epigenetic combination is currently being tested in animal models.
Background

Multiple myeloma (MM) is a malignant hematological disease, with devastating symptoms, such as bone destruction and fractured and kidney failure. It is the second most common hematological malignancy and accounts for 1% of all malignancies. There are approximately 300 new cases of MM annually in Denmark, according to data from the Danish Myeloma Study.

The development of new drugs, especially thalidomide and its derivatives, lenalidomide and pomalidomide (also called IMiDs) has improved the survival and quality of life of myeloma patients and IMiDs are the backbone of standard myeloma therapy. However, the disease is still considered incurable and all patients receiving an IMiD will eventually develop resistance and experience a disease relapse, requiring a different treatment regimen.

The invention

Our group has previously shown that development of IMiD resistance is associated with significant epigenetic changes in the myeloma cells. Thus, treatment with epigenetic drugs could potentially restore sensitivity to IMiDs.

By combining a DNA-methylation inhibitor, 5-Azacytidine (AZA) and an EZH2 inhibitor, EPZ-6438 (EPZ), we were able to not only reverse the epigenetic changes of IMiD-resistant cells, but also resensitize them to IMiDs. This could have huge implications in the treatment of myeloma patients with IMiD resistance, since it offers the potential of reusing an effective treatment, without the need of changing to a potentially more expensive and toxic therapy.

Key selling points

Both AZA and EPZ are known epigenetic drugs, already tested individually in clinical trials. We provide a novel indication for the combination of AZA and EPZ, which does not involve a direct cytotoxic or anticancer effect, but the resensitization of myeloma patients, who are refractory to IMiDs.

Development status

- The in vitro efficacy of AZA and EPZ in resensitizing myeloma cells to IMiDs has been extensively investigated and validated.
- Clinical studies have already been conducted for both drugs (under different indications) showing a favorable safety profile.
- We are currently performing in vivo studies, further aiming for clinical phase I/II studies that will verify our preclinical observations.

Intellectual property rights

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