**APO010 sensitivity in relapsed Multiple Myeloma patients**

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**Introduction**  
Multiple Myeloma is the second most common hematological malignancy and represents a continuous medical challenge since all patients eventually progress despite of many, recently approved drugs. The incidence of Multiple Myeloma is about 6 to 8 out of 100,000 in Western Countries (1). Given the current lack of lasting therapeutic benefit for Multiple Myeloma patients, there is a need for new and personalized treatment strategies.

We aim to address this issue by introducing a new immuno-oncology drug (APO010) in the treatment of Multiple Myeloma combined with an advanced Drug Response Predictor analysis in order to select the patients with the highest likelihood of benefit from APO010 treatment.

**Drug Response Predictor (DRP)**  
A validated response predictor method is used in the evaluation of prediction of sensitivity to APO010. As shown in Fig. 1, the method is based on in vitro sensitivity data and cell line microarray results in a model that also incorporates clinical variables. The DRP method has previously been developed for a number of other drugs (2).

**Results**  
APO010 is a completely new immuno-oncology drug. It is the first in-class of a novel indolyl-form of FAS-ligand which mimics cytotoxic T-lymphocyte (CTL) signaling to induce cancer cell apoptosis. The FASL binds to the cancer cell via the Fas ligand receptor (CD95) on the tumor cell. APO010 is synthesized as a mega Fas, consisting of six FasL, mimicking a CTL that binds to the cancer cells hence inducing apoptosis. This unique and differentiated cytotoxic mechanism of action has the potential of being a breakthrough immunotherapy product in Multiple Myeloma as these cells express CD95 (FAS-receptor).

**Methods**  
APO010 response predictor (APO010-DRP®) is based on gene expression clusters obtained by comparing associations between gene expression profiles and growth-inhibition by APO010 in panel of cell lines. A second step has included filtering the identified gene expression profile against mRNA expression from a collection of 1000 human tumors, thereby making a predictive profile for APO010 responses (Fig. 2). We have initiated screening relapsed/refractory Multiple Myeloma patients by isolating CD138 positive myeloma cells from the bone marrow and applying APO010-DRP® in order to select the patients with the highest likelihood of benefit from APO010 treatment.

**Conclusion**  
Combining APO010 with DRP analysis will add a precision medicine element to immuno-oncology treatment of Multiple Myeloma. This will enable us to identify patients with high likelihood of response and therefore facilitate focused future trial design and patient recruitment to achieve clinical success.

**Expected achievements**  
- Introducing immunotherapy in the treatment of Multiple Myeloma  
- The use of DRP will ensure higher response rate  
- Saving time and reduce cost

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**References**  

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