correlation was seen between response to COTI-2 or APR-246, suggesting that the compounds act differently in inhibiting cell growth.
Conclusion We conclude that targeting mutant p53 with COTI-2 is a potential new approach for treating p53-mutated TNBC.

PO-038 PDGFRβ AS A NEW BIOMARKER FOR METASTATIC TRIPLE-NEGATIVE BREAST CANCER: DEVELOPMENT OF A THERANOSTIC ANTI-PDGFRβ APTAMER FOR IMAGING AND SUPPRESSION OF METASTASES

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Introduction Triple-negative breast cancers (TNBCs) are a heterogeneous group of aggressive tumours lacking oestrogen and progesterone receptors and HER2 receptor, thus excluding the possibility of using targeted therapy against these proteins. Mesenchymal-like (ML) subtype, characterised by a stem-like, undifferentiated phenotype, is more invasive and metastatic than other TNBC subtypes and has a strong tendency to form vasculogenic mimicry (VM). Recently, platelet derived growth factor receptor β (PDGFRβ) has been shown to play a role in VM of TNBC. Regrettably, therapies targeting PDGFRβ with tyrosine kinase inhibitors are not effective in treating TNBCs, thus developing new strategies to target PDGFRβ in TNBC patients is crucial to improve their chances of survival. Here, we describe the characterisation of the Gint4.T anti-PDGFRβ nuclease-resistant RNA aptamer as high efficacious theranostic tool for imaging and suppression of ML TNBC metastases.
Material and methods Immunohistochemical analyses on a human TNBC tissue microarray was performed to correlate PDGFRβ expression with clinical and molecular features of different subtypes. Functional assays were conducted on PDGFRβ-positive ML BT-549 and MDA-MB-231 cells to investigate the effect of Gint4.T in interfering with cell growth in 3D conditions, migration, invasion and VM formation. Gint4.T was conjugated with near-infrared (NIR) fluorescent VivoTag-S680 and its binding specificity to receptor was confirmed both *in vitro* (confocal microscopy and flow cytometry analyses of TNBC cells) and *in vivo* (fluorescence molecular tomography in mice bearing TNBC xenografts). MDA-MB-231 cells were i.v. injected in nude mice and Gint4.T-NIR was used to detect lung metastases in mice untreated or i.v. injected with Gint4.T or a scrambled aptamer.
Results and discussions The expression of PDGFRβ was observed in human TNBC samples characterised by higher metastatic behaviour. Treatment of TNBC cell lines with Gint4.T aptamer blocked their invasive growth and vasculogenic properties in 3D culture conditions, and strongly reduced cell migration/invasion *in vitro* and metastases formation *in vivo*. The Gint4.T-NIR was able to specifically bind to TNBC xenografts and detect lung metastases *in vivo*. Therefore, the aptamer revealed a high efficacious theranostic tool for imaging and suppression of TNBC metastases.
Conclusion These studies indicate PDGFRβ as a new biomarker for ML and metastatic TNBC subtype and propose a novel targeting agent for the diagnosis and treatment of metastatic TNBCs.

PO-039 EXAMINATION OF THE ANTI-TUMOUR AND NEUROPATHIC SIDE EFFECT RESPONSES OF FIRST GENERATION AND SECOND GENERATION PROTEASOME INHIBITORS

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Introduction The overall goal in cancer treatment is to damage cancer cell macromolecules that causes the cancer cells to die. But in the treatment process, the defense mechanisms developed by the cancer cells affect the response to the treatment. As we have shown in our studies, cancer cells after anti-cancer stress have about 10–20 times more proteasome activation than healthy cells. Therefore, proteasome inhibition plays an important role in the prevention of resistance and recurrence in cancer treatment.

Bortezomib, the first generation proteasome inhibitor, is used intensively, in hematologic cancer types, and significantly increases patient survival. However, it causes significant side effects such as neuropathy. New proteasome inhibitors are being produced to reduce side effects in the market. These inhibitors include clinical studies as well as preclinical studies. However, the lack of side-effect studies causes the early termination of clinical trials.
Material and methods In this study, we compared the antitumour effects and neural toxicities of first generation and second-generation proteasome inhibitors in co-culture model. In this direction, human neural progenitor cells and K562 leukaemia cells were used. Co-cultures were incubated with 100 nM proteasome inhibitors for 24 hour and effects on the cancer cells and neural cells were analysed separately. Apoptotic cell death was evaluated with Annexin V/PI double staining by flow cytometry in K562 cells, and also PARP, Caspase 9 protein levels have been analysed in both cells. Protein oxidation related parameters such as protein carbonyls, ubiquitinated proteins, and HSP levels were investigated for understanding the stress response in both cells. Additionally, cytoskeleton proteins β-actin and β- tubulin changes were assessed in neural cells with confocal microscopy.
Results and discussions Our data showed that new proteasome inhibitors are less toxic in neural cells when compared to bortezomib. Protein carbonyls and ubiquitinated proteins were highest in bortezomib treated cells. On the other hand, especially carfilzomib has a lower anti-tumour activity in K562 cells when compared to bortezomib.
Conclusion This study may bring a highlight for the clinical usage and side effects of new proteasome inhibitors.

PO-040 DEVELOPMENT OF A TUNABLE FORM OF INTERFERON ALPHA FOR *IN VIVO* CANCER GENE THERAPY

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Introduction The immune system is a double-edge sword in cancer. On the one hand, it exerts immunosurveillance to eradicate