Material and methods The effect of NHI-Glc-2 on cell growth is tested in our primary PDAC cancer cell cultures, characterised for their hypoxic signature and LDH-A/GLUT-1 expression levels by next-generation sequencing. Inhibition of cell and tumour growth was evaluated by the SRB assay, 3D spheroid-cultures and with an orthotopic bioluminescent *in vivo* model. Additionally, LDH-A enzyme activity inhibition and the effect on the glycolytic rate by NHI-Glc-2 were assessed by spectrophotometry and with the Seahorse XF analyzer, respectively.

Results and discussions NHI-Glc-2 is capable of inhibiting PDAC cell growth in, especially in hypoxia, in nanomolar range and shows a synergistic effect with gemcitabine. In 3D cultures NHI-Glc-2 disrupts spheroid integrity, and preliminary *in vivo* studies show promising results.

Conclusion Lactate dehydrogenase A is a viable target in PDAC, and the novel LDH-A inhibitor showed improved pharmacological effect in normoxic and hypoxic PDAC cells compared to NHI-1 and NHI-2. Moreover, this compound displays a synergistic cytotoxic activity with gemcitabine, offering an innovative tool in hypoxic tumours.

PO-043 DEVELOPMENT OF TWO NOVEL MONOCLONAL ANTIBODIES AGAINST OVEREXPRESSED ANTIGENS ON PANCREATIC CANCER CELLS FOR USE IN DIAGNOSIS AND THERAPY

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Introduction Pancreatic cancer is one of the deadliest cancer types with very poor survival rates and limited treatment options. Therefore, novel treatments are urgently needed. Monoclonal antibody (mAb) technology is an excellent tool for the discovery of overexpressed cell surface tumour antigens and development of mAb-based products for use in diagnosis and treatment of cancer. While several mAbs have been approved for the treatment of a wide range of cancers, none have been approved for pancreatic cancer yet. The aim of our study was to develop novel mAbs against overexpressed cell surface antigens on pancreatic cancer cells for use in cancer diagnosis and therapy.

Material and methods Novel mAbs were generated against CFPAC-1 cells using hybridoma technology and those directed against overexpressed cell surface antigens were selected and purified by affinity chromatography. Further characterisation was performed by ELISA, flow cytometry, cell proliferation and migration assays, internalisation studies, immunoprecipitation and mass spectrometry, immunohistochemistry and Western blotting.

Results and discussions We developed two novel mouse mAbs named KU44.13A and KU44.22B that were found to target CD26 and integrin alpha-3 respectively. Integrin alpha-3 was found to be widely overexpressed in human pancreatic cancer cell lines by ELISA and flow cytometry. Treatment with mAb KU44.22B induced receptor downregulation and internalisation and inhibited the growth *in vitro* of the human pancreatic cancer cell line Capan-2 with an IC50 of 4.5 nM. Paradoxically, treatment with this antibody increased the migration of BxPC-3 and CFPAC-1 cancer cell lines. CD26 expression, in turn, was limited to pancreatic cancer cell lines derived from ascites (HPAF-II and AsPC-1). Treatment with targeting mAb KU44.13A did not have any effect on cell proliferation, migration or receptor downregulation and internalisation. While neither of the two mAbs immunodetected the target antigen by Western blot, they were useful for immunohistochemical detection of the target antigens in formalin-fixed paraffin-embedded tumour sections.

Conclusion We believe these two novel mAbs are useful tools for investigating the relative expression, prognostic significance and predictive value of CD26 and integrin alpha-3 in patients with pancreatic cancer. Further studies are warranted to elucidate the therapeutic potential of these novel mAbs including their humanised or conjugated versions, in patients pancreatic and other types of cancer.

PO-044 DEVELOPMENT OF FLOW CYTOMETRIC ASSAYS FOR CAR T CELL MANUFACTURING AND PATIENT IMMUNOMONITORING

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Introduction Adoptive cell therapy using genetically engineered chimeric antigen receptor (CAR) T cells has demonstrated unprecedented potency in B cell malignancies, and offers new hope for curative responses in patients suffering from cancer. However, the manufacturing process for CAR T cells is very complex and has extensive demands on personnel and infrastructure, which is a major obstacle for their routine clinical use. To overcome these hurdles, the CliniMACS Prodigy allows generation of CAR T cells in a single automated and closed system.

Material and methods CliniMACS Prodigy
MACSQuant Analyzer
MACS Antibodies

Results and discussions For assessment of CAR T cells during cell manufacturing and patient immunomonitoring we developed a set of different flow cytometric assays. These assays will be used for 1) in-process control, QC release testing, and concomitant research during the manufacturing process, and 2) for determination of CAR T cell persistance and phenotyping during patient immunomonitoring. Among others these assays allow to determine the general immune cell composition, CAR transduction efficiency, and further functional CAR T cell phenotypes like differentiation, activation, or exhaustion status.

For identification of CAR T cells we developed CAR detection reagents that specifically bind to the antigen-recognition domain of the receptor. Thus, these detection reagents discriminate between various CAR constructs, and can be used for enumeration of CAR T cells during manufacturing and immunomonitoring.

For all flow assays mentioned above so-called Express Modes have been programmed, that allow an automated acquisition and analysis of stained samples on MACSQuant Analyzers. These Express Modes feature predefined experiment settings and analysis templates, and apply a fully automated gating strategy that adapts for each individual data file. This