

P07.03 'MYTCELL': A SMARTPHONE APPLICATION GUIDES LOGISTICS AND MANAGEMENT OF CAR T-CELL & BiTE RELATED TOXICITIES

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Background Bispecific T-cell engagers (BiTE) and CD19-specific Chimeric Antigen Receptor (CAR) T-cell products are approved for relapsed and refractory B-cell neoplasms. However, rapid disease progression and the pre-treatment workflow during manufacturing challenges several specialities of health care professionals and involves a well educated team in the in-patient and out-patient setting. In addition, CARs and BiTEs are accompanied by a new spectrum of immune related toxicities. Currently, clinical trials investigate the safety of out-patient CAR T-cell administration, requiring high-level care during the early post-infusion period. To support the optimal management of these patients, we developed the interactive smartphone application 'myTcell', which guides and educates physicians in the pre-treatment logistics of CARs and BiTEs and management of related toxicities.

Materials and Methods We initiated a multi step content development process with an extensive literature research of toxicity guidelines consented by the ASTCT, SITC, NCCN and EBMT as well as of officially released drug information. Findings were translated into an information platform with diagnostic and therapeutic recommendations as well as algorithms for interactive toxicity grading tools. A prototype has been validated at five German treatment centers through a questionnaire, which measures the advantage over common guideline practice. 'myTcell' will become available as medicinal product class I for iOS, Android and desktop in Europe on 15th of July. App development has been funded through educational grants by Celgene, Gilead Sciences, Janssen and Novartis.

Results 'myTcell' guides disease and product specific in a step by step process through the clinical workflow of cell therapy. This includes recommendations for patient screening, safety assessment and stopping rules prior to leukapheresis and CAR T-cell transfusion. Upon entering relevant clinical data for grading of CRS, ICANS and HLH interactive tools display toxicity grade or likelihood of toxicity as well as grade-specific management. Further, 'myTcell' assists with the diagnosis and treatment of pancytopenia and infections. A map visualizes the availability of CAR T-cell therapy in Germany and links in-patient and out-patient care. Besides, 'myTcell' includes an overview of important publications and refers directly to respective PubMed abstracts.

Conclusions 'myTcell' has the potential to become a highly usable smartphone app supporting the application of T-cell recruiting immunotherapies as well as the assessment and treatment of novel immunotoxicities. In addition, it facilitates outreach and connects treatment centers and referring physicians. Thus, 'myTcell' can translate into increased guideline adherence, accelerated broader and safer application of CARs and BiTEs and improved patient outcomes.

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P08 Combination Therapy

P08.01 RATIONALE OF USING THE COMBINATION OF ANTI-PD-1 ANTIBODY AND ANTI-IL-8 ANTIBODY FOR THE PANCREATIC CANCER TREATMENT

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Background Pancreatic ductal adenocarcinoma (PDAC) does not respond to immune checkpoint inhibitors (ICI) therapy as single agent treatments including anti-PD-1 antibody. One of the mechanisms for the resistance of PDAC to ICI is now attributed to the immunosuppressive microenvironment (TME) in PDAC. Myeloid cells are thought to be the predominant immunosuppressive cells in the TME. Human interleukin-8 (IL-8) is a pro-inflammatory chemokine in the CXC family and has the capability of recruiting myeloid cells into the TME to promote tumor progression and immune escape. Therefore, several anti-IL-8 blockade antibodies were developed including HuMax-IL8 and B108-IL8, which both are fully human IgG1 kappa monoclonal antibodies. We therefore tested whether anti-IL-8 antibodies can potentiate anti-tumor activity of anti-PD-1 antibody in a humanized model of PDAC.

Materials and Methods We reconstituted the immune system of the NGS mice with ex vivo activated human T cells and a combination of CD14+ and CD16+ myeloid cells after the mice were orthotopically implanted with human PDAC cells. 10x single nuclei RNA-Seq data processing was further performed to analyze differentially expressed genes among certain cell clusters.

Results Our results showed that anti-PD-1 antibody alone had a minimal anti-tumor activity when mice was reconstituted with ex vivo activated T cells. Interestingly, the infusion of the combination of CD14+ and CD16+ myeloid cells together with anti-PD-1 antibody resulted in a modest anti-tumor activity. Adding either HuMAX-IL8 or B108-IL8 led to a significantly enhanced anti-tumor activity. Both CD14+ and CD16+ myeloid cells appeared to be needed for the full anti-tumor activity of IL-8 blockade because mice infused with only CD14+ myeloid cells did not respond to IL-8 blockade and mice infused with only CD16+ myeloid cells responded partially to IL-8 blockade. This result suggested that the target of IL-8 is mainly present in CD16+ myeloid cells and is likely to be granulocytes. Tumor infiltrating immune cells were isolated and demonstrated that IL-8 blockade increases CD45+CD11b+CD15+CD14- myeloid cells, which is known to comprise neutrophils and granulocytic myeloid derived suppressive cells (G-MDSC), in the tumors. Reconstitution of the mice with myeloid cells led to a decrease of CD8+ T cells in the tumors; however, IL-8 blockade brought the CD8+ T cell