



Lighthouse Cellular Immunotherapy

... develops novel immunotherapies for clinical application in cancer patients

... major focus on Chimeric Antigen Receptor (CAR) and T Cell Receptor (TCR) genetically-modified T cells

Speaker: Prof. Dr. Wolfgang Herr, Regensburg

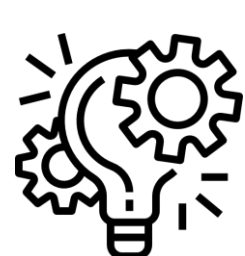
Background and concept

- ❖ **CURRENT SITUATION:** CAR T cell immunotherapy has shown ground-breaking success in B-cell neoplasia but needs to be applied to other hematological and solid cancers.
- ❖ **FIELDS OF ACTION:** Selection of potential target antigens & effective CAR/TCR constructs; regulatory aspects in the development and clinical implementation of such advanced therapy medicinal products (ATMPs); GMP production of ATMPs; characterization of the ATMPs mode of action in patients; overcoming primary and secondary therapy resistance; novel side effects prevention and immunomonitoring.
- ❖ **ADDED VALUE:** Combining the extensive previous experience and expertise of the Bavarian University Hospitals; allocation of tasks based on existing strengths, cross-site development and utilization concept.

Tasks per Module

Achievements (Milestones 1st FP)

PRECLINICAL DEVELOPMENT (University Hospital Würzburg)



- ❖ Strategic planning for translation and development.
- ❖ Performance of the required assays.
- ❖ Data preparation and presentation for authorities.

Identification of lead candidates (CAR/TCR) for joint clinical trial(s)

- ✓ Candidate characterization in hard-to-treat cancers: uveal melanoma (CSPG4), colorectal carcinoma (CEA) and AML (FLT3, Siglec-6, CLEC12A).
- ✓ Investigation of epigenetic modulation and combinatorial antigen targeting on increased tumour specificity and selectivity.
- ✓ Translational pipeline: Collection of preclinical safety and efficacy data for clinical trial applications



REGULATORY AFFAIRS (Hospital TU Munich)



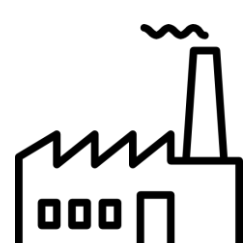
- ❖ Establishment of a regulatory work group
- ❖ Networking and exchange with regulatory authorities and biotech companies.

Establishment of a counselling center

- ✓ Networking with regulatory authorities, governmental institutions, the Paul-Ehrlich Institute, the Bavarian patent alliance, patient advocacy groups and pharmaceutical industries.
- ✓ Counselling center has been established, external visibility is under development



GMP-MANUFACTURING ATMPs (University Hospital Erlangen)



- ❖ Consultation, establishment and validation of ATMPs' manufacturing and quality control methods.
- ❖ Application for and obtaining of manufacturing authorization.

Establishment of a communication platform and coordination of GMP production activities

- ✓ Confluence as the joint BZKF communication platform.
- ✓ Survey on the manufacturing activities and specific competences of all sites.
- ✓ Information exchange on GMP-manufacturing experiences, technical and regulatory aspects and potential future strategies.



TOXICITY MANAGEMENT (Hospital LMU Munich)



- ❖ Interdisciplinary BZKF research network for cell therapy toxicities.
- ❖ Central data collection of cell therapy toxicities.
- ❖ App-based publication of current therapy recommendations for toxicity management.

Availability of "myTcell" App in the iOS & Android-AppStores

- ✓ "myTcell" App with current toxicity management standards in iOS & Android-AppStores and via browser (major update: expected release Sep 23).
- ✓ Interdisciplinary cooperation network on CAR-T cell associated hematotoxicity and infectious complications is being established (currently with UKER)



IMMUNOMONITORING (University Hospital Regensburg)



- ❖ Receipt, coding, pseudonymization and storage of bio-samples.
- ❖ Consulting, sample analysis, sample evaluation.
- ❖ Data storage & transfer.

Centralized access Immunomonitoring laboratory for external senders

- ✓ Access lab for the collection, storage and analysis of external patient samples from all BZKF sites in a centralized manner.
- ✓ GLP-compliant coding, pseudonymization and storing of bio-probes.
- ✓ Establishment of advanced immunomonitoring for patients treated with commercial CD19-CART products



Work plan (Milestones 2nd FP)

PRECLINICAL DEVELOPMENT:

- ✓ Select and refine 1-2 lead CAR/TCR constructs for joint clinical trial
- ✓ Validation of at least one new technology to improve specificity/selectivity for tumor cells and increasing efficacy
- ❖ IND package and clinical trial development

REGULATORY AFFAIRS:

- ✓ Establish pocket guide with PEI & regulatory hub
- ✓ Catalyze joint ATMP development (PEI Advice)
- ✓ Development of an academic Network structure (Academic QP Network for ATMPs)

GMP MANUFACTURING:

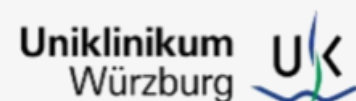
- ✓ Joint audits, develop joint SOPs
- ✓ Pilot study for obtaining a production license (GD-2-IL-18 CAR-T study, funding via BMBF, UK Münster, UKER, UKR (LIT))
- ❖ Production of a novel ATMP for clinical trial

TOXICITY MANAGEMENT:

- ✓ Shared data collection / SOPs for different CAR/TCRs
- ✓ Patient advocacy program to implement patients view in future CAR/TCR trials
- ❖ Implementation of eCRF platform, based on SERIO registry for immune-checkpoint inhibition-related toxicities

IMMUNOMONITORING:

- ✓ Extend methods portfolio for fluid (hematologic) tumors
- ✓ Establish advanced immunomonitoring methods to analyze fresh solid tumors
- ❖ Establish advanced immunomonitoring methods to analyze frozen solid tumors



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