The THINK clinical trial: Preliminary evidence of clinical activity of NKG2D Chimeric Antigen Receptor T cell therapy (CYAD-01) in acute myeloid leukemia

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CYAD-01 CAR T-CELL THERAPY

- CYAD-01 (previously named NKR-2) is an adoptive cell therapy consisting of engineered T cells expressing a chimeric antigen receptor (CAR) based on the natural killer group 2, type, in case of signs of clinical activity in previous segment.
- CYAD-01 may be an effective therapeutic approach for solid and hematological tumor types.
- Preclinical results indicate that CYAD-01 may have anti-tumor effects beyond direct cancer cell killing.
- Dose escalation segment: the study will evaluate the RecD in each tumor.
- Patients receive 3 doses of CYAD-01 at 2-week intervals. The surface adaptor molecule DNAX-activating protein of 10kDa (DAP-10), which is endogenously expressed on T-cells, associates with and stabilizes CYAD-01 CAR expression.
- CYAD-01 showed promising results in multiple preclinical models and in the clinic.
- CYAD-01 CAR is composed of the full-length human NKG2D fused to the CD3 zeta domain, signaling domain (see Foster 2018).
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THINK PROTOCOL AMENDMENT

- THINK amendment to explore further the potential of CYAD-01 with standard of care chemotherapy, prior preconditioning regimen and local administration of CYAD-01 (LINK) clinical studies.
- FIGURES AND TABLES

THINK ENDPOINTS & STATUS

- Early observations by April 2018:
  - No significant toxicities highlighting the potential of targeting NKG2D ligands
  - First objective response to CAR-T in a refractory AML patient using CYAD-01 without prior lymphodepleting chemotherapy
  - Case study: a 48-year-old patient who relapsed from salvage CLAG-M chemotherapy reached a remission without prior lymphodepleting conditioning therapy for allogeneic hematopoietic stem cell transplantation (allo-HCT). At 5 months post allo-HCT, the patient is in complete remission (MRD neg) with 100% donor chimerism.
  - There is variation in the phenotype of the CYAD-01 cells (e.g. CD4/CD8 ratio).

THINK TREATMENT DESIGN

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