CD3 8 is a 45 kDa type II transmembrane glycoprotein widely expressed in many hematologic malignancies including multiple myeloma (rMM).

MOR202 is a HuCAL-derived human immunoglobulin G 1 anti-CD3 8 antibody that has demonstrated high affinity and in vivo anti-tumor activity in preclinical models.

The main mode of action for MOR202 involves targeting and killing of anti-CD3 8+ cells.

Introduction

This phase I/IIa study of the human anti-CD38 antibody MOR202 (MOR03087) in relapsed or refractory multiple myeloma (rMM) was designed to evaluate safety, PK/PD profiles, immunomodulatory effects, and preliminary efficacy.

Study objectives

- To evaluate MOR202 in adult patients with relapsed or refractory MM.

- Primary outcome measures:
  - Maximum tolerated dose (MTD) and/or recommended dose/schedule of MOR202.
  - Safety: Incidence and severity of adverse events (AEs).
  - Preliminary efficacy: Overall response rate, duration of response, time-to-progression, and best change in M-protein.

- Secondary outcome measures:
  - Pharmacokinetics and immunogenicity.
  - Conclusions

Patients and methods

- Inclusion criteria:
  - Adult patients with rMM who had failed 2–3 previous regimens including immunomodulatory drug and a proteasome inhibitor.

- Exclusion criteria:
  - Patients with a history of any malignancy (except basal cell carcinoma or carcinoma in situ of the cervix).

- Overall design:
  - Dose-escalation study (1–24 mg/kg).

- Overall design details:
  - Cohorts 1–8: MOR202 with LEN/DEX, q1w.
  - Cohorts 7d–8d: MOR202 monotherapy without/with DEX, q1w or q2w.

- Pharmacology:
  - MOR202 is a human anti-CD38 monoclonal antibody.

- PK/PD parameters:
  - PK: Concentration-time profile and accumulation.
  - PD: Immunomodulatory effects.

- Safety:
  - Immediate and delayed toxicities.

- Efficacy:
  - Imaging and clinical response criteria.

- Immunogenicity:
  - Presence and characterization of anti-MOR202 antibodies.

Study design

- Each cohort included 4 patients. Patients received a 2-hour IV infusion of MOR202 every 2–4 weeks.

- Cohorts 1–4 and 5–8, respectively.

- Cohort 8a (16 mg/kg w/o DEX) did not initiate according to Data Monitoring Committee recommendation.

- Safety and efficacy data were collected throughout the study.

- Overall study design

- Safety: Incidence and severity of AEs.

- Efficacy: Overall response rate, duration of response, time-to-progression, and best change in M-protein.


Results

- Preclinical studies indicated high specificity and in vivo efficacy in preclinical models.

- Study cohort 1: Safety, pharmacokinetics, and immune activation study (1–3 doses; Figure 2).

- Study cohort 2: Study design (1–3 doses).

- Study cohort 3: Study design (1–3 doses).

- Study cohort 4: Study design (1–3 doses).

- Study cohort 5: Study design (1–3 doses).

- Study cohort 6: Study design (1–3 doses).

- Study cohort 7: Study design (1–3 doses).

- Study cohort 8: Study design (1–3 doses).

- Overall study design

- Safety: Incidence and severity of AEs.

- Efficacy: Overall response rate, duration of response, time-to-progression, and best change in M-protein.


Pharmacokinetics and immunogenicity

- Immunomodulatory effects: IgG and/or IgM antibodies.

- Antibody-dependent cellular cytotoxicity (ADCC) and phagocytosis (ADCP).

- Maximum tolerated dose (MTD) and/or recommended dose/schedule of MOR202.

- Patients from subsequent cohorts were/will be treated until disease progression or withdrawal.

- Conclusions

- MOR202 is well tolerated and demonstrated anti-MM activity in preclinical models.

- Further clinical evaluation is warranted.

References

- The study was supported by Matthew Young, Cancer Communications and Consultancy Ltd.

Acknowledgements

- The study was supported by the National Cancer Institute and the U.S. Department of Defense.