Poster 242

A phase 1 multicenter, dose escalation study of CBT-501, a novel anti-PD-1 inhibitor in subjects with select advanced or relapsed/recurrent solid tumors

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BACKGROUND

- Checkpoint blockades, such as the Programmed Death-1 (PD-1) / Programmed Death Ligand 1 (PD-L1) pathway regulate the progression of productive immune responses.
- Blocking the PD-1 / PD-L1 pathway can increase the function of effector CD8+ T cells and enhance the anti-tumor response.
- Monoclonal antibodies (mAbs) to block the PD pathway is a clinically validated approach for cancer immunotherapy.

CBT-501

- CBT-501, genolimzumab (GB226), is a novel humanized IgG4 mAb targeting the PD-1 membrane receptor on T cells with a highly specific binding to PD-1 of human (Kd=505 pM) and cynomolgus monkeys (Kd=7.2 nM)[1].
- CBT-501 occupancy in activated CD4+ and CD8+ T-cells increases rapidly after a single dose **(Figure 1)** and upon multi-dosing, receptor occupancy rises to nearly 100% **(Figure 2)**.[1] Six weeks after the last dose, occupancy on CD4+ and CD8+ cells does not significantly decline.
- CBT-501 has demonstrated anti-tumor activity in the in vivo animal model and no abnormal drug-related toxicity has been observed in the GLP toxicology studies.[1] **(Figure 3)**
- CBT-501 demonstrated dose dependency with a half-life of 5 to 10 days and exhibited linear pharmacokinetic features in the in-vivo monkeys[1]. **(Figure 4)**
- Data from all pre-clinical pharmacodynamics and toxicology studies of CBT-501 indicate pharmacological activity at effective doses with a wide margin of safety.
- Based on these findings, CBT has initiated a Phase 1 study in Australia with CBT-501 for subjects with select advanced or relapsed/recurrent solid tumors. Genor, CBT's China partner, has also initiated a Phase 1 trial in China.

PRE-CLINICAL RATIONALE

Figure 1: Single Dose Receptor Occupancy on Activated CD4+ and CD8+ T Cells in Cynomolgus Monkeys

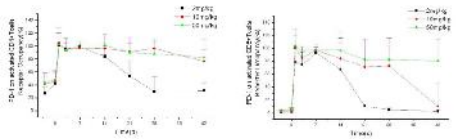


Figure 2: Multi-Dose Receptor Occupancy on Activated CD4+ and CD8+ T Cells in Cynomolgus Monkeys

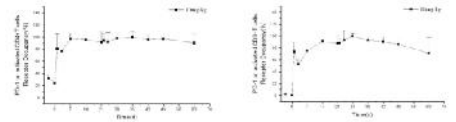


Figure 3: Humanized Genetically Engineered (huGEMM) MC38 Mouse Colon Adenocarcinoma Demonstrates Anti-tumor Activity Comparable to Nivolumab

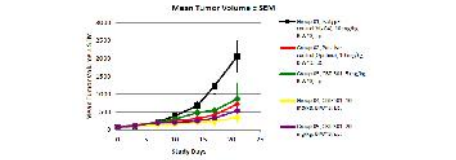
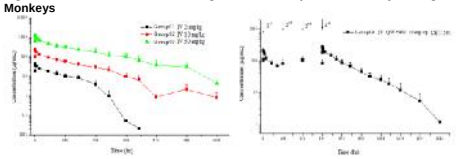


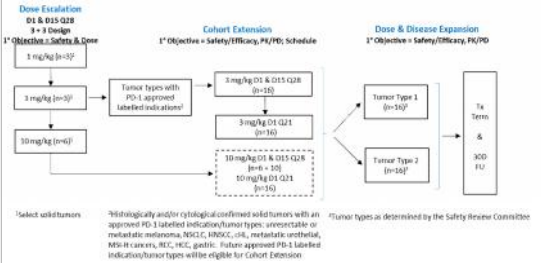
Figure 4: Pharmacokinetics after Single Dose and Repeat Doses in Cynomolgus Monkeys



PHASE 1 STUDY METHODS

- CBT-501-01 is a Phase 1, multicenter, dose escalation study of CBT-501 in subjects in select advanced or relapsed/recurrent solid tumors, including cHL, currently in progress in Australia (NCT03053466).
- The primary study objective is to identify the overall safety and tolerability, including any dose limiting toxicities (DLT), and determine the recommended Phase 2 dose (RP2D).
- Secondary study objectives include assessing efficacy by overall response rate (ORR), best overall response rate (BOR) per RECIST v1.1 and irRECIST, time to response, duration of response (DOR), disease control rate (DCR) by RECIST v1.1 and irRECIST, progression free survival (PFS), and determining the pharmacokinetic (PK) parameters.
- Exploratory objectives involve the assessment of PD-1 and PD-L1 expression, receptor occupancy and the host immune response in peripheral blood or formalin-fixed paraffin-embedded (FFPE) samples.
- This is a 3-part study with a dose-escalation segment, cohort extension, and dose and disease expansion cohorts. Up to 82 subjects will be enrolled.

CLINICAL STUDY DESIGN



ELIGIBILITY CRITERIA

MAJOR INCLUSION	MAJOR EXCLUSION
≥ 18 years of age	Hypersensitivity to mAbs
Confirmation of select solid tumor	Active malignancy within 2 years
ECOG 0 - 1	Prior therapy with antibody targeting T cell co-stimulation
Life expectancy > 3 months	Known autoimmune disease
Measurable disease per RECIST v1.1	Known significant mental illness

PARTICIPATING STUDY CENTERS

- **Australia, New South Wales**
  Chris O'Brien Lifehouse
  Principal Investigator: Catriona McNeil, MBBS
- **Australia, Victoria**
  Cabrini Education and Research Precinct
  Principal Investigator: Gary Richardson, MBBS
  Nucleus Network
  Principal Investigator: Mark Voskoboynik, MBBS
- **Australia, Western Australia**
  Linear Clinical Research
  Principal Investigator: Michael Millward, MBBS

REFERENCE

1. Qing Z, Nian W, Sun Z et al. CBT-501, a novel humanized anti-PD-1 antibody shows differentiated activity in a humanized genetically engineered mouse model of colon carcinoma. ASCO-SITC, 2017, Abstract 108.

FURTHER INFORMATION

Please visit CBT Pharmaceutical's website at www.cbtpharma.com for a PDF version of the poster presentation.

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