# Safety and early efficacy results of phase 1 study of affinity tuned and trackable AIC100 CAR T cells in ICAM-1 positive relapsed and/or refractory advanced poorly differentiated and anaplastic thyroid cancers

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## BACKGROUND

- ICAM-1 is a cell surface glycoprotein that is overexpressed in anaplastic (ATC) and poorly differentiated thyroid cancer (PDTC)
- AIC100 is a 3rd-generation CAR T cell with micromolar affinity to ICAM-1, tuned lower than most CARs used to date in preclinical** and clinical studies (**Figure 1**)
- Affinity tuned AIC100 are expected to selectively bind and kill tumor cells while safely sparing healthy cells
- AIC100 also co-expresses somatostatin receptor 2 (SSTR2), which enables *in vivo* monitoring of AIC100 distribution and expansion by $^{68}$Gallium DOTATATE PET/CT scan

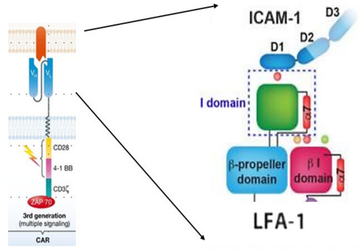






**Figure 1** Lymphocyte function-associated antigen 1

## METHODS

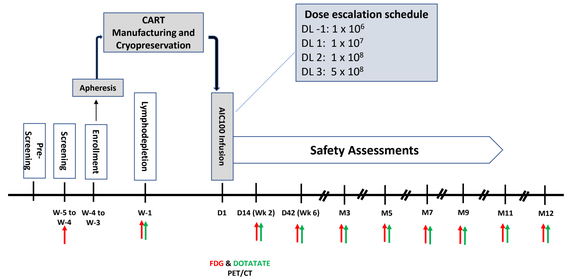
- This is a Phase 1 multicenter, dose escalation with modified toxicity probability interval (mTPI) design, clinical trial in patients with ICAM-1 expressing relapsed and/or refractory PDTC or ATC
- AIC100 is manufactured using AffyImmune's Tune and Track CAR T cell platform, and 3 dose levels (DL) are being explored as outlined in **Figure 2**
- AIC100 is given as a single infusion at Day 1. Lymphodepletion consists of Fludarabine and Cyclophosphamide x 3 days
- F-fluorodeoxyglucose (FDG) and $^{68}$Gallium DOTATATE PET/CT scans are used to assess response and to track AIC100 *in vivo*, respectively.
- Response is assessed by RECIST1.1, starting at day 42 post AIC100 infusion
  - Assessments are based on investigators/site reports
  - Blinded independent Central Review is planned

### Study Population

- Adult patients ≥18 years of age with thyroid cancer that expresses ICAM-1 and that meets one of the following diagnoses:
  - ATC BRAF wild-type at any stage, including newly diagnosed
  - ATC BRAF mutant after failure of or inability to tolerate BRAF-specific therapy
  - PDTC that has failed any of the following treatments: surgery RAI, chemotherapy, radiation therapy, and/or targeted therapies

## PHASE I CLINICAL TRIAL DESIGN

**Figure 2** Clinical Trial Design




Abbreviations:
D, day; DOTATATE, dodecanetetraacetic acid-tyrosine-3-octreotide; DL, Dose level; Wk/W, week; M, month

## METHODS Cont'd

### Primary Objectives

- To assess the safety and tolerability of AIC100 CAR T Cells in patients with relapsed/refractory PDTC or ATC including newly diagnosed
- Determine RP2D

### Secondary Objectives

- To assess the presence and frequency of AIC100 CAR T Cells in peripheral blood and tumor samples, and to assess their relationship to cytokine levels and to tumor response

### Exploratory Objectives - Efficacy

- To assess the preliminary efficacy of AIC100 CAR T Cells in patients with relapsed/refractory ICAM-1-expressing PDTC and in patients with ATC, including those who are newly diagnosed

## RESULTS

- **As of May 01, 2023,** 7 patients (4 ATC; 3 PDTC) with a median age of 59 (range, 47-69) years were infused with AIC100
  - 3 patients (2 ATC, 1 PDTC) in DL1
  - 4 patients (2 ATC, 2PDTC) in DL2
- AIC100 was successfully manufactured for all patients and all infusion products met target transduction efficiency

## RESULTS Cont'd

### Safety

- No DLTs were reported
- Two patients had transient grade 1 CRS
- No ICANs was reported

### Efficacy

- In three evaluable patients in DL1 (N=3):
  - One patient with PDTC had stable disease (SD)
- For the four patients infused in the DL2 (N=4):
  - Two patients were evaluable for efficacy assessment at day 42. Both had tumor reductions, one achieved PR with 42% reduction in target tumor lesion (a patient with ATC, **Figure 3**) and a second patient (PDTC) had SD.
  - One patient in DL2 (ATC) could not be assessed due to early withdrawal for disease-related toxicity.
  - The fourth patient in DL2 is a patient with relapsed PDTC who completed the DLT evaluation period, and efficacy is pending

## Transient DOTATATE PET-CT activity associated with AIC100 expansion and resolution with subsequent tumor regression

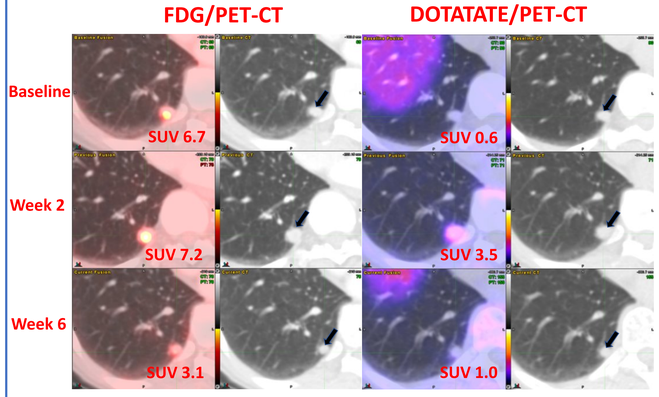



**Figure 3** FDG and DOTATATE PET/CT imaging of Pt. 4. Scans are done 24 hours apart, FDG first followed by DOTATATE. One of the representative lesions is shown for illustration. At baseline, the lesion is FDG active but no DOTATATE activity. At 2 weeks, the lesion shows DOTATATE uptake consistent with CAR T-cell infiltration. At 6 weeks, DOTATATE activity subsided upon response with significant improvement in FDG activity

## CAR T cell Expansion in Blood by ddPCR

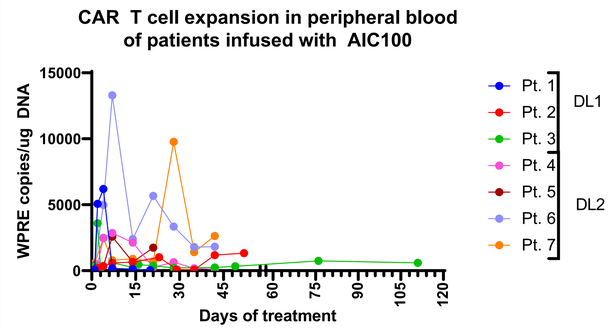



**Figure 4** Cell kinetics of AIC100 at DLs 1 and 2: CAR T cell expansion determined by ddPCR analysis of DNA purified from peripheral blood mononuclear cells.

## CONCLUSIONS

- AIC100 demonstrated an excellent safety profile in DL1/DL2 treated patients with ATC and PDTC and with no DLTs observed
- The objective partial response in DL2 for a patient with metastatic ATC who failed multiple lines of therapy is unprecedented and very encouraging
- The DOTATATE PET/CT shows promise as a tool for *in vivo* tracking of CAR T cells in AIC100 treated patients, and also demonstrates potential correlation to response
- Study is ongoing (NCT04420754) for exploring AIC100 at higher dose levels and optimizing RP2D

## Acknowledgement

We thank our patients, investigators and all study centers' faculty and staff
AffyImmune sponsored and funded the study

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****Reference:** Vedvyas Y, et al. Sci Rep 2019;9:10634. **PMID 31337787**