KDDF
Korea Drug Development Fund

Asset #30
Weill Cornell Medicine

Anti-ART1 Monoclonal Antibody for Improved Anticancer Immunotherapy

Therapeutic Area	Oncology	**Indications**	NSCLC, Melanoma
Modality	Monoclonal Antibody	**Development Stage**	Pre-clinical

Overview

Background

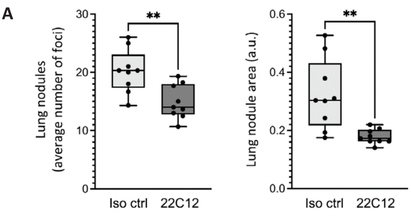
- In the KEYNOTE-189 trial, treatment-naïve NSCLC patients who received pembrolizumab (anti-PD-1) in addition to standard chemotherapy achieved a 48% objective response, compared to 19% in patients receiving chemotherapy alone
- However, only 0.5% of patients in the KEYNOTE-189 trial achieved a complete response, with only 34% of pembrolizumab-treated patients alive and progression-free at 12 months
- Unmet Need: While ICIs have improved outcomes for NSCLC, there remains a persistent unmet need for additional therapies that synergize with ICIs to prolong survival and deliver a durable response

Technology Advantages

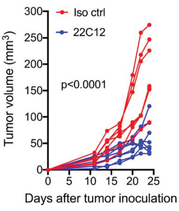
- ART1 modifies P2X7R through ADP-ribosylation, causing continuous channel opening and cell death
- The lead mAb candidate 22C12 binds ART1 with high affinity (EC50 = ~1 nM) and strong inhibition of enzymatic activity (IC50 = 4.5 nM)
- Can be used alone or in combination with other immune checkpoint inhibitor therapies or chemotherapies
- Targeting ART1 may overcome the lack of consistent response to immune checkpoint inhibition
- Inhibition of ART1 may overcome failures of CD38 blockade trials through the opposite mechanism, as inhibition of CD38 may upregulate ADP-ribosylation

Key Data

Blockade of ART1 with 22C12 reduces tumor burden in in vivo lung tumor models

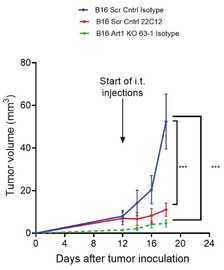


The number and area of tumor nodules were decreased in orthotopic ART1-overexpressing KP1 lung tumor model.
(A) Average lung tumor nodule counts and (B) average lung nodule area were measured on day 19 after tumor inoculation. Data in (A and B) were analyzed using Welch's t-test.



Growth of subcutaneous ART1-overexpressing KP1 flank tumors is suppressed by intratumoral injections of 22C12 mAb or isotype control mAb.

22C12 demonstrated further anti-tumor effects in a mouse model of melanoma



- In addition to NSCLC, human melanomas are shown to strongly express ART1 in the Human Protein Atlas
- Administration of mAb 22C12 significantly reduced the growth of subcutaneous B16 flank tumors (****P ≤ 0.0001) compared to isotype controls, similar to that seen with ART1 knock-out
- Additional cancers with high ART1 expression include colorectal cancer and glioblastoma, suggesting the possibility of a multiple indication anti-ART1 drug franchise

IP Status & Publication(s)

Intellectual Property

Patent Number
PCT-US2023-062151 (2023.02.07)

Patent Family
PCT

Publication(s)

- Wennerberg at al. (2022). The ART of tumor immune escape. OncoImmunology
- Wennerberg at al. (2022). Expression of the mono-ADP-ribosyltransferase ART1 by tumor cells mediates immune resistance in non–small cell lung cancer. Science Translational Medicine
- Chen at al. (2016). ART1, an extracellular ADP-ribosyltransferase, is over-expressed in non-small cell lung cancer and facilitates cancer cell survival by immune-mediated mechanisms. Journal of Thoracic Oncology