Methods Eligible pts were aged ≥18 years with an Eastern Cooperative Oncology Group performance status of 0–1. The cSCC cohorts enrolled pts with histologically confirmed meta-
static or locally advanced cSCC not amenable to local therapy. The NSCLC cohort enrolled previously untreated NSCLC pts with advanced disease and a PD-L1 tumor proportion score of at least 50%. Pts received a fixed dose of 800 mg costibeli-
ma administered intravenously every two weeks. Anti-tumor activity was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and were conducted every 8
weeks for the initial 32 weeks on study, and every 12 weeks thereafter.

Results As of August 2020, 114 pts (73M/41F, median age 66
years) with diverse tumor types have been enrolled and
treated with costibelimab. Among these pts, 103 (90%) experi-
enced ≥1 treatment-emergent adverse event (AE), 42 (37%)
experienced a grade ≥3 AE, and 6 (5%) experienced a grade
≥3 drug-related AE. The most common AEs were fatigue
(25%), anemia (21%), rash (18%) and nausea (16%) and the
most common drug-related AEs were fatigue (15%) and rash
(14%). In 42 cSCC pts evaluable for response, ORR based on
investigator assessment of tumor response was 55% (95% con-
fidence interval [CI]: 39, 70), including 5 (12%) complete
responses, with 20/33 (62%) responses ongoing and 10
responses ≥6 months in duration as of data cutoff. In 23
NSCLC pts evaluable for response, ORR based on investigator
assessment was 44% (95% CI: 24, 65), with 5/11 (45%)
responses ongoing and 10 responses ≥6 months in duration.

Conclusions Costibelimab has a predictable and manageable
safety profile and demonstrated robust clinical activity in
cSCC and NSCLC pts, including durable complete and partial
responses. Updated results will be presented.

Trial Registration NCT03212404

Ethics Approval The study was approved by an appropriate
ethics committee for each participating institution. Informed
consent was obtained for all subjects.

Consent Written informed consent was obtained from the
patient for publication of this abstract and any accompanying
images. A copy of the written consent is available for review
by the Editor of this journal.

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400 COUPLEDCAR T TREATMENT FOR TREATING THYROID CANCER

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Background Chimeric antigen receptor modified T cells (CAR
T) have demonstrated remarkable clinical efficacy in the treat-
ment of B cell malignancies and multiple myeloma. Significant
challenges restrict their application across solid tumors due to
multiple obstacles, including the lack of robust in vivo CAR-T
cell expansion and persistence, the immunosuppressive tumor
microenvironment, and tumor escape due to heterogeneous
tumor cell composition with a potential loss of the targeted
tumor antigen. To address these difficulties, we generated CAR
T cells using a novel CoupledCAR® technology. Specifically,
we engineered CoupledCAR T cells with lentiviral vectors
encoding an anti-thyroid stimulating hormone receptor
(TSHR) CAR molecule. Immunohistochemistry (IHC) results
showed that TSHR was highly expressed in thyroid cancer
cells making it an ideal tumor-specific target antigen. In vitro
culture experiments showed that TSHR CAR T cells specific-
ically recognized and subsequently killed TSHR-positive tumor
cells. Animal model experiments showed that TSHR CAR T
cells inhibited the proliferation of TSHR-positive tumor cells.

Methods We designed a ‘CoupledCAR’ lentivirus vector con-
taining a single-chain variable fragment (scFv) targeting human
TSHR. The lentivirus was produced by transfecting HEK-293T cells with ‘CoupledCAR’ lentiviral vectors and viral
packaging plasmids. Patient’s CD3 T cells were cultured in X-
VIVO medium containing 125U/mL interleukin-2 (IL-2), and
transduced with ‘CoupledCAR’ lentivirus at certain MOI.
Transduction efficiency and was evaluated at 7 to 9 days after
‘CoupledCAR’ lentivirus transduction, and quality controls for
fungi, bacteria, mycoplasma, chlamydia, and endotoxin were
performed. After infusion, serial peripheral blood samples
were collected, and the expansion and the cytokine release of
CAR T cells were detected by FACS and QPCR. The evalua-
tion of response level for patients were performed at month
1, month 3, and month 6 by PET/CT.

Results To evaluate the clinical safety and efficacy of anti-
TSHR CoupledCAR T cells on refractory or relapsed thyroid
cancer, we treated refractory/relapsed post-thyroidectomy thy-
roid cancer patients according to an IRB approved protocol.
We treated two patients using anti-TSHR CoupledCAR T cells
and observed the rapid expansion of CAR T cells and enhanced
the killing of tumor cells. One patient’s best response was complete remission, and the other was near complete remission. Patient Profile: Patient 1 Male, 64Y, Papil-
lary Thyroid Carcinoma. In May 2017, Thyroid cancer was
diagnosed, bilateral total thyroidectomy, and right cervical
tumor node functional dissection were performed in Jun
2018, followed by iodine 131 isotope therapy. In December
2018, bilateral multiple cervical lymph nodes were enlarged,
especially on the right side. In February 2019, right neck lym-
phadenectomy was performed. Patient 2 Female, 60Y, Thyroid
Carcinoma. In Aug 2013, a ‘double lobectomy of the thyroid
gland’ was performed. From Oct 2013 to Jan 2014, she
received iodine 131 isotope therapy. In Sep 2014, she
was diagnosed with iodine resistant thyroid cancer. From Sep
2016, 5 cycles of chemotherapy were performed. In Jun
2016, she enrolled in the Anlotinib experimental group. In
Mar 2019, multiple metastases in both lungs and multiple
enlarged lymph nodes in the mediastinum were observed.
Observations and Results: Patient 1: One month after infusion
(M1), the patient was evaluated as PR: lymph node metastasis
became undetectable and the size of the thoracic paratracheal
nodule decreased significantly. Three months after
infusion (M3), the patient was evaluated as CR, and the
tumor tissue was substantially smaller than M1. Patient 2: M1,
the patient was evaluated as PR (Partial Response): the tumor
volume in the right lower lobe of the lung was reduced by
approximately 67.51% (decreased from 65*55 mm to 42*39
mm). Three months after infusion (M3), compared with that
before, the tumor volume was reduced by approximately
73.54% and SUV max value decreased from 4.9 to 2.8,
therefore, the patient was evaluated as nCR (near complete
remission).

Conclusions We show that TSHR is a good target for treating
thyroid cancer, and our anti-TSHR CoupledCAR T cells are
safe and effective for treating thyroid cancer. Recruitment is
ongoing to evaluate the safety and efficacy of our Coupled-
CAR T cells. Further, since our CoupledCAR® technology is a
Background In spite of advances made in the management of patients with HER2-expressing or -driven solid tumors, there remains a significant unmet need for novel approaches to improve patient outcomes. Intratumoral delivery of antitumor antibodies and immunostimulatory adjuvants such as toll-like receptor (TLR)/7/8 agonists has been shown to activate tumor resident antigen-presenting cells (APCs), driving uptake, processing, and presentation of tumor neoantigens to T cells that mediate antitumor immunity. BDC-1001 is delivered systemically and has demonstrated superior preclinical biology. This novel ISAC consists of an investigational biosimilar of the humanized monoclonal antibody trastuzumab chemically conjugated to a TLR7/8 agonist with a non-cleavable linker. BDC-1001 activates human myeloid APCs in addition to retaining antibodies and immunostimulatory adjuvants such as toll-like receptor (TLR) agonists with a non-cleavable linker. BDC-1001 elicits robust myeloid activation and anti-tumor immune responses in a TLR- and Fc receptor-dependent manner.

Methods This dose-escalation and dose-expansion study is enrolling up to 390 patients with HER2-expressing (IHC2+ or 3+) protein, irrespective of gene amplification) or HER2-amplified (by in situ hybridization or next-generation sequencing) advanced solid tumors. Primary objectives of the dose-escalation phase are to define safety and tolerability and determine the recommended phase 2 dose of BDC-1001 as mono-therapy (Part 1) and in combination with an immune checkpoint inhibitor (Part 2). Part 2 is planned to start once BDC-1001 safety data are available. Primary endpoints include incidence of 1) adverse events and serious adverse events; and 2) dose-limiting toxicities within a 3+3 design; and 3) potential immune-related toxicities. The dose-expansion portion of the trial will evaluate preliminary antitumor activity of BDC-1001 alone (Part 3) and in combination with an immune checkpoint inhibitor (Part 4). Secondary objectives will evaluate pharmacokinetic parameters and pharmacodynamic biomarkers in tumor tissue and in peripheral blood associated with drug exposure. These exploratory studies will help elucidate the mechanism of action and seek to identify biomarkers associated with BDC-1001 biological activity with or without immune checkpoint inhibitors. This global study is currently recruiting patients.

Results N/A

Conclusions N/A

REFERENCES