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 antibody-mediated effector functions such as antibody-dependent cellular cytotoxicity/phagocytosis (ADCC/ADCP). Studies in trastuzumab-resistant xenograft models and syngeneic tumor models indicate that HER2-targeted ISACs elicit potent and durable immune-mediated antitumor efficacy, leading to complete tumor regression in a TLR- and Fc receptor-dependent manner.\(^1\)\(^2\) Importantly, BDC-1001 did not induce interstitial lung disease, cytokine release syndrome, or thrombocytopenia in non-human primate studies. A four-part phase 1/2 study in patients with HER2-expressing or HER2-amplified advanced/metastatic solid tumors.

Methods: This dose-escalation and dose-expansion study is enrolling up to 390 patients with HER2-expressing (ICH2+ 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 monotherapy (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; 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 inhibition. This global study is currently recruiting patients.

Results: N/A

Conclusions: N/A

Abstracts

PHASE 1/2 STUDY OF NOVEL HER2-TARGETING, TLR7/8 IMMUNE-STIMULATING ANTIBODY CONJUGATE (ISAC) BDC-1001 WITH OR WITHOUT IMMUNE CHECKPOINT INHIBITOR IN PATIENTS WITH ADVANCED HER2-EXPRESSING SOLID TUMORS


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REFERENCE


ETHICS

Approval: The study and the protocol were or will be approved by the Institutional Review Board or ethics committee at each site.

Consent: N/A

TRIAL REGISTRATION

ClinicalTrials.gov (NCT04278144).

REFERENCES


DRAGON: PHASE 1 TRIAL OF SRK-181, A LATENT TGFβ1 INHIBITOR IN COMBINATION WITH ANTI-PD-(L)1 INHIBITORS FOR PATIENTS WITH SOLID TUMORS UNRESPONSIVE TO ANTI-PD-(L)1 THERAPY ALONE

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Background: TGFβ1 is a key mediator of primary resistance to PD1 (programmed cell death protein 1) pathway blockade. SRK-181 is a high-affinity, fully humanized antibody that selectively binds to latent TGFβ1 and inhibits its activation on suppressive immune cells as well as within tumor stroma. Preclinical data demonstrated that selective inhibition of latent TGFβ1 with SRK-181 overcomes primary anti-PD-1 resistance and has an improved safety profile compared to broad inhibition of the TGFβ pathway.

Methods: The DRAGON trial is a multi-center, open-label, Phase 1, first-in-human (FIH), dose-escalation, and dose expansion study to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and efficacy of SRK-181 administered by IV infusion every 3 weeks (q3w) alone and in combination with an anti-PD-(L)-1 in adult patients with locally advanced or metastatic solid tumors. The study is divided into 3 parts: Part A1, a single agent dose escalation, will determine the maximum tolerated dose (MTD) or maximum administered dose (MAD) of SRK-181 as a single agent. Part A2, a combination dose escalation, will determine the MTD or MAD of SRK-181 in combination with anti-PD-(L)1 therapy and the RP2D of the combination treatment for use in Part B. Part B, the dose expansion, will enroll parallel cohorts of patients with non-small cell lung cancer, urothelial cancer, etc.
carcinoma, melanoma, or other advanced solid tumors, to confirm the tolerability of the RP2D and to evaluate the anti-tumor activity of SRK-181 in combination with an anti-PD-(L)1 therapy. Patients in Part A2 and Part B will have previously received anti-PD-(L)1 therapy and considered non-responders to anti-PD-(L)1 therapy alone. Patients will receive SRK-181 alone or in combination with anti-PD-(L)1 until disease progression, unacceptable toxicity, or other reasons for study discontinuation. Safety, PK, PD and efficacy data will be collected and monitored throughout the study. PD effects will be assessed by measuring modulation of tumor immune cells and TGFβ pathway within the tumor microenvironment.

**Results**

An enrollment update will be provided

**Conclusions**

Trial Registration NCT04291079

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0402

### 403 EARLY RESULTS FROM A PHASE 1 STUDY TO EVALUATE SAFETY, PHARMACOKINETICS, AND EFFICACY OF AMG 404, A PROGRAMMED DEATH-1 (PD-1) ANTIBODY, IN PATIENTS WITH ADVANCED SOLID TUMORS

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**Background**

Enhancement of antitumor immunity through inhibition of the checkpoint PD-1 receptor has been effective in the treatment of many malignancies. AMG 404 is a monoclonal antibody (mAb) targeting PD-1. This phase 1, open-label, multicenter first-in-human study (NCT03853109) will evaluate the safety, tolerability, pharmacokinetics, and efficacy of AMG 404 monotherapy in adult patients with advanced solid tumors.

**Methods**

The primary study endpoint is dose-limiting toxicity (DLT) and safety; key secondary endpoints include pharmacokinetic parameters, objective response rate (assessed Q8W), duration of response, and progression-free survival. Key inclusion criteria include histologically or cytologically proven metastatic or locally advanced solid tumors not amenable to curative treatment with surgery or radiation for which standard therapies have been exhausted or not available. Prior anti-PD-(L)1 or other checkpoint inhibitors were not allowed. Five dose-finding cohorts, including 2 expansion cohorts, ranged from 3–20 patients each. AMG 404 was given until disease progression, intolerance, or consent withdrawal.

**Results**

As of the data cutoff date of May 4, 2020, 62 patients received at least 1 dose of AMG 404 and were included in the safety and efficacy analysis sets. Fifty percent were men, 72% had ECOG 1 performance status, median age was 62 years (range: 28–83), and 42% had ≥3 lines of prior anticancer therapy. Median AMG 404 exposure was −3 months (maximum: −12 months). No DLTs were observed. Treatment-related adverse events (TRAEs) were reported for 29 patients (47%); those reported for ≥2 patients were fatigue (n=7); hypothyroidism (n=6); increased blood thyroid stimulating hormone and nausea (n=4 each); increased aspartate aminotransferase, decreased appetite, and pyrexia (n=3 each); and increased alanine aminotransferase, arthralgia, diarrhea, and increased weight (n=2 each). AEIs leading to withdrawal of AMG 404 were reported for 3 patients (5%); all were serious and considered to be not related to AMG 404. Sixteen (26%) patients died on study; no deaths were considered related to AMG 404. Preliminary pharmacokinetic results were consistent with those of other therapeutic anti-PD-1 mAbs. Three patients had a confirmed partial response (pancreatic cancer, clear cell cancer, and pleomorphic sarcoma); an additional 4 patients had one scan with a partial response and are pending a confirmatory scan (clear cell renal carcinoma, undifferentiated nasopharyngeal carcinoma, sarcomatoid carcinoma of unknown primary, and colon cancer).

**Conclusions**

AMG 404 is tolerable at the tested doses with no DLTs reported. All observed TRAEs are consistent with other anti-PD-1 therapies. Encouraging anti-tumor activity has been observed in heavily pretreated patients. The study is continuing enrollment into additional cohorts.

Trial Registration NCT03853109

**Ethics Approval**

The study was approved by the Ethics Board of each institution involved in this study and can be produced upon request.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0403

### 404 ALX148, A CD47 BLOCKER, IN COMBINATION WITH STANDARD CHEMOTHERAPY AND ANTIBODY REGIMENS IN PATIENTS WITH GASTRIC/ GASTROESOPHAGEAL JUNCTION (GC) CANCER AND HEAD AND NECK SQUAMOUS CELL CARCINOMA (HNSCC)

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**Background**

CD47 is a myeloid checkpoint up-regulated by tumors to evade the anticancer immune response. ALX148 is a high affinity CD47-blocking fusion protein with an inactivating Fn region designed to safely enhance anticancer therapeutics.1 2 ALX148 in combination with standard chemotherapy and antibody regimens was evaluated in patients (pts) with advanced HER2-positive GC or HNSCC.

**Methods**

Pts with previously treated advanced HER2-positive GC or untreated advanced HNSCC received ALX148 (A) 10 mg/kg QW or 15 mg/kg QW in combination with trastuzumab (T) + ramucirumab (ram) + paclitaxel (pac) as 2nd or later-line treatment or pembrolizumab (P) + SFU + platinum (cisplatin or carboplatin) as 1st line therapy, respectively. The primary endpoint was dose limiting toxicity (DLT). Tumor response, pharmacokinetic (PK), and pharmacodynamic (PD) markers were assessed in all pts. Preliminary data from enrolling cohorts, and follow-up data from pts with GC