A phase 1/2 study of BDC-3042, a novel Dectin-2 agonistic antibody, in patients with advanced cancers

ABSTRACT # 720

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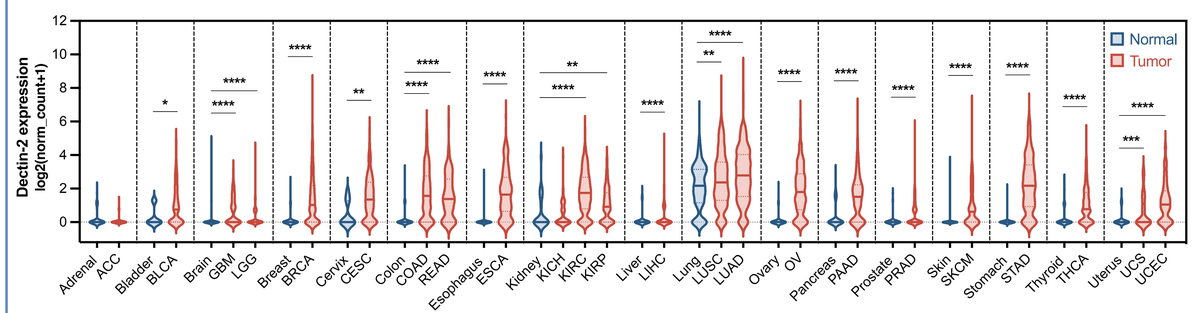
BACKGROUND

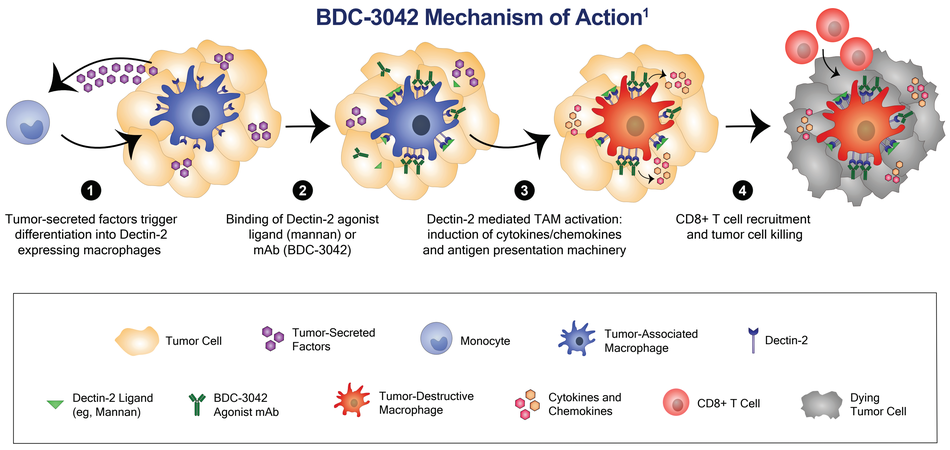
- Tumor-associated macrophages (TAMs) are a major component of the immune infiltrate in most cancers and play a key role in establishing the immunosuppressive tumor microenvironment (TME) that enables tumor progression
- TAMs are phenotypically plastic and have the potential to be reprogrammed into immunostimulatory cells that enhance innate and adaptive anti-tumor immunity
- BDC-3042 is a novel agonistic antibody targeting an immune-activating receptor expressed on TAMs known as Dectin-2 (CLEC6A)[1]
- Dectin-2 is a C-type lectin receptor best known for its role in pathogen recognition and induction of protective immune responses against fungi and other microbes
- Nonclinical studies with BDC-3042 have demonstrated its potential to reprogram TAMs and elicit anti-tumor activity as a novel immunotherapeutic approach for diverse human cancers[2]
- BBI-20233042 is a phase 1/2, first-in-human, four-part trial evaluating BDC-3042 ± anti-PD-1 in patients with metastatic or unresectable triple negative breast cancer (TNBC), clear cell renal cell carcinoma, colorectal cancer, head and neck cancer, non-small lung cancer (NSCLC), or ovarian cancer (NCT06052852)

Dectin-2 gene expression is elevated across tumor types[1]

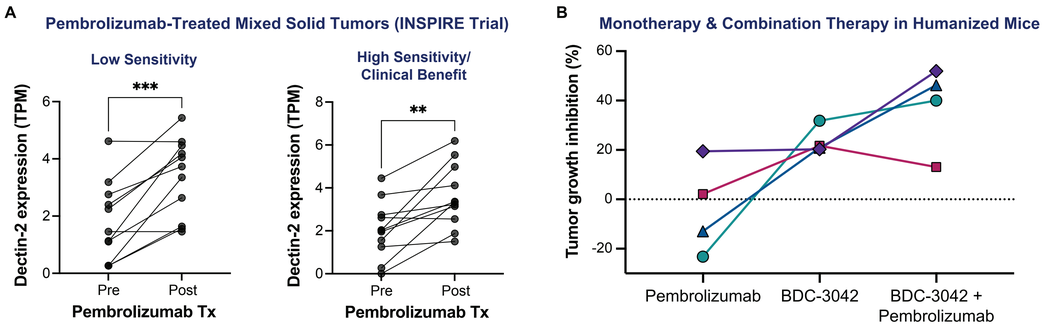


Dectin-2/CLEC6A mRNA expression in human tissue samples from the TCGA (tumor) and GTEX (normal) datasets (accessed Oct. 2019). TCGA study abbreviations are shown for the tumor subtypes. TCGA and GTEX data were processed using a uniform bioinformatic pipeline and obtained from UCSC Xena (xena.ucsc.edu). Median and interquartile range are shown on the violin plots. Statistics were calculated by Mann-Whitney U test; *p≤0.05, **p≤0.01, ***p≤0.001, ****p≤0.0001.

BDC-3042 Mechanism of Action[1]



Anti-PD-1 therapy increases Dectin-2 expression in human tumors and improves anti-tumor activity of BDC-3042 in humanized mice[1]



(A) Dectin-2 gene expression in tumor samples obtained from patients with mixed solid tumors before and after 2-3 cycles of pembrolizumab treatment (data obtained from Cindy Yang et al., Nat Commun 2021). Patients were stratified into subgroups showing "Low Sensitivity" (LS) or "High Sensitivity/Clinical Benefit" (HS/CB) in response to pembrolizumab according to changes in circulating tumor DNA (ΔctDNA) and target lesion measurement (ΔTM) as well as clinical response (described in Cindy Yang et al.) (n=11 per subgroup). LS: ΔctDNA and ΔTM positive; 10/11 PD, 1/11 SD. HS/CB: ΔctDNA negative and/or ΔTM negative; 3/11 SD, 6/11 PR, 2/11 CR. Statistics were calculated by paired t-tests. **p<0.01; ***p<0.001. **(B)** MDA-MB-231 tumor-bearing huNOG-EXL mice from 4 HSC donor cohorts were treated Q7D x 5 with the indicated test article via intraperitoneal administration (BDC-3042: 0.5 mg/kg; pembrolizumab: 5 mg/kg). Tumor growth inhibition relative to the isotype control was calculated on day 35. The connected lines represent data for each HSC donor cohort.

REFERENCES

1. Kenkel JA, et al. *Cancer Research.* 2023;83(suppl 7):2964.
2. Kenkel JA, et al. *Journal for ImmunoTherapy of Cancer.* 2021;9(suppl 2):A903.

STUDY OBJECTIVES AND ENDPOINTS

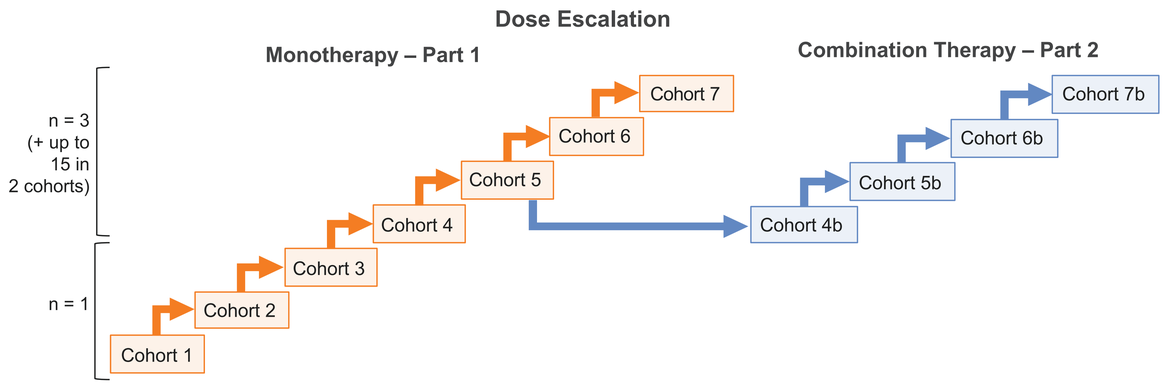
Primary Objectives	Endpoints
• Define safety and tolerability and determine the recommended phase 2 dose of BDC-3042 ± anti-PD-1	• Incidence of AEs and SAEs, DLTs, and changes from baseline in vital signs, laboratory values, and ECGs

Secondary Objectives	Endpoints
• Evaluate preliminary anti-tumor activity of BDC-3042 ± anti-PD-1 • Evaluate pharmacokinetic (PK) parameters and immunogenicity of BDC-3042 ± anti-PD-1	• Objective response rate (ORR) according to RECIST v.1.1 • PK variables, including C_{max}, C_{min}, $AUC_{0-t,}$ AUC_{0-inf}, CL, V_c, V_{ss}, or $T_{1/2}$ • Incidence of anti-drug antibodies

Exploratory Objectives	Endpoints
• Explore potential biomarkers associated with efficacy or safety of BDC-3042 ± anti-PD-1 • Evaluate pharmacodynamic biomarkers and their association with biological activity, efficacy or safety of BDC-3042 ± anti-PD-1	• Evaluation of potential association between baseline biomarkers and BDC-3042 ± anti-PD-1 anti-tumor activity • Evaluation of changes in additional exploratory biomarkers in tumor tissue and blood related to tumor and immune biology by such methods as gene expression profiling, mutational, protein and tissue image analysis

STUDY DESIGN

- Dose escalation will enroll up to 69 patients with metastatic or unresectable TNBC, clear cell renal cell carcinoma, colorectal cancer, head and neck cancer, NSCLC, or ovarian cancer
- Dose expansion is planned to evaluate the preliminary anti-tumor activity of BDC-3042 ± anti-PD-1



ELIGIBILITY

Key Inclusion Criteria

- Histologically- or cytologically-confirmed, metastatic or unresectable TNBC, clear cell renal cell carcinoma, colorectal cancer, head and neck cancer, NSCLC, or ovarian cancer
  - Ovarian cancer may have platinum-sensitive or platinum-resistant and/or platinum-refractory tumors
- Patients must have tumor progression after standard therapy who have no options for standard therapies
- ECOG PS 0 or 1

Key Exclusion Criteria

- Active systemic yeast infection within 4 weeks before study treatment
- Prior hospitalization for asthma during past year
- CNS metastases except for disease that is asymptomatic, stable, and has not required steroids for at least 14 days prior to study treatment
- Medical condition requiring corticosteroids (> 10 mg daily oral prednisone or equivalent) or other systemic immunosuppressive therapy within 28 days before starting study treatment, except for intermittent or sporadic use of inhaled or topical steroids
- Use of an investigational agent within 28 days prior to starting study treatment

BIOMARKER ASSESSMENT

- Screening fresh tissue biopsy is optional. Archival tumor sample may be submitted.
- Serial blood collection for all subjects
- Assess potential association between baseline biomarkers expression and BDC-3042 ± anti-PD-1 anti-tumor activity
- Pro-inflammatory cytokines and chemokines to be evaluated
- Assess additional exploratory biomarkers in tumor tissue and blood related to tumor and immune biology by such methods as gene expression profiling, mutational, protein and tissue image analysis

SUMMARY

- BDC-3042 is a novel agonist antibody targeting an immune-activating receptor expressed on TAMs known as Dectin-2
- Nonclinical studies with BDC-3042 have demonstrated its potential to reprogram TAMs and elicit anti-tumor activity as a novel immunotherapeutic approach for diverse human cancers[2]
- BBI-20233042 is a phase 1/2, first-in-human, four-part trial evaluating BDC-3042 ± anti-PD-1 in patients with metastatic or unresectable TNBC, clear cell renal cell carcinoma, colorectal cancer, head and neck cancer, NSCLC, or ovarian cancer (NCT06052852)
- Enrollment in dose escalation is ongoing in the United States