

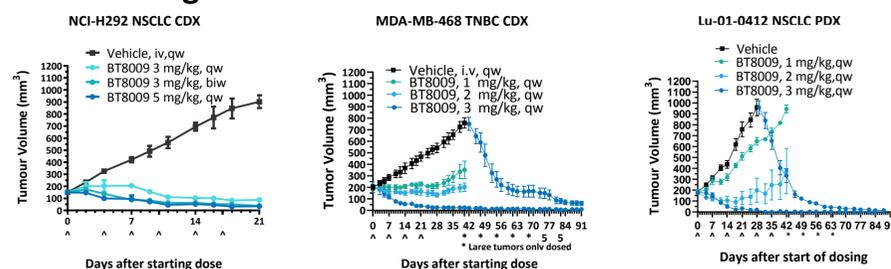
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Background:

- BT8009 is a *Bicycle*[®] Toxin Conjugate (BTC) in which a Nectin-4 binding *Bicycle* (bicyclic peptide) is conjugated through an inert sarcosine spacer chain and a cleavable linker to the antimitotic toxin MMAE.
- Nectin-4 is expressed in bladder, NSCLC, esophageal, pancreatic, ovarian and breast cancers¹⁻⁴.
- Overexpression of Nectin-4 in tumor tissue is a marker for poor prognosis¹⁻⁴.
- BT8009 is designed to have rapid tumor penetration, release and prolonged retention of MMAE in tumor and short terminal plasma half-life to reduce exposure to tissues outside of tumor.
- BT8009 exhibited a satisfactory preclinical profile supporting the initiation of a FIH study to investigate safety and efficacy in indications with evidence of Nectin-4 expression.

BT8009 in Xenograft Tumor Models



Enrollment Criteria:

Part A (Dose Escalation) Specific Inclusion Criteria

- Urothelial carcinoma naïve to Nectin-4-directed therapies; or confirmed Nectin-4 expression on fresh biopsy or archived tissue (<12 months) without intervening anti-cancer therapies or solid tumors known to frequently express Nectin-4 (pancreatic, TNBC, NSCLC, gastric, esophageal or ovarian.)

Part B Patients

- Confirmed Nectin-4 expression on fresh biopsy or archived tissue (< 12 months) without intervening anti-cancer therapies

Part C Patients

- Renal insufficiency

First-in-Human Study with a *Bicycle*[®] Toxin Conjugate targeting Nectin-4 with an MMAE cytotoxic payload. Patient enrollment ongoing.

BT8009



Primary objectives

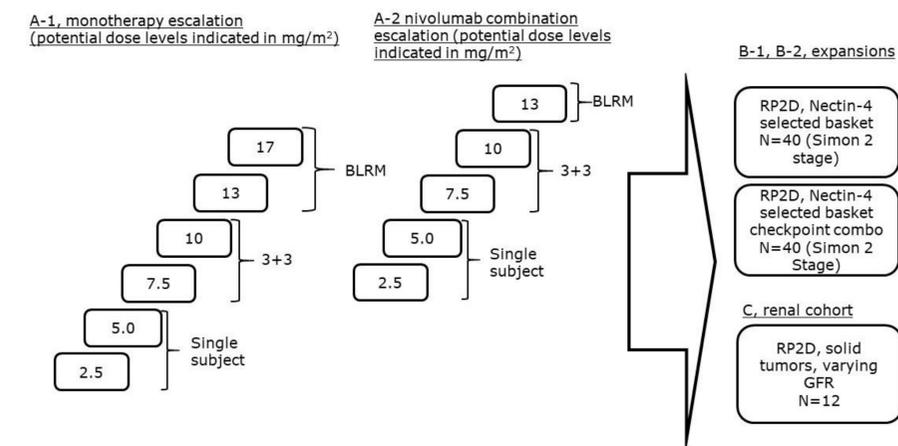
- Dose escalation
 - Safety and tolerability of BT8009 as monotherapy and in combination with nivolumab or in patients having renal insufficiency.
 - MTD and RP2D of BT8009 as monotherapy and in combination with nivolumab
- Dose expansion
 - Clinical activity of BT8009 as monotherapy and in combination with nivolumab

Secondary objectives

- Dose escalation
 - Preliminary signals of activity of BT8009 as monotherapy and in combination with nivolumab or in patients having renal insufficiency.
 - PK parameters of BT8009 and MMAE
 - Incidence of anti-drug antibody (ADA) development
- Dose expansion
 - Safety and tolerability of BT8009 as monotherapy and in combination with nivolumab
 - PK parameters of BT8009 and MMAE
 - Incidence of ADA development

Study Design

- Phase I/II, first-in-human, open-label dose-escalation study of BT8009 given as a single agent or in combination with nivolumab.
- Up to 146 patients (up to 66 in Phase I and 80 in Phase II) are expected to be enrolled in this study in approximately 20 sites globally.
- Three parts to this study:
 - Phase I: dose escalation
 - Part A-1: BT8009 monotherapy dose escalation (34 patients)
 - Part A-2: BT8009 plus nivolumab dose escalation (20 patients)
 - Phase II: dose expansion
 - Part B-1: BT8009 monotherapy dose expansion (40 patients)
 - Part B-2: BT8009 plus nivolumab dose expansion (40 patients)
- Phase I: patients with renal insufficiency (12 patients)



References

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2. M-Rabet M, Cabaud O, Josselin E, et al. (2017). Ann Oncol 28(4): 769-776.
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4. Deng H., Shi H, Chen L, et al. (2019). Cancer Cell Int 19: 106.

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