TPS3655: BT5528-100 Phase I/II Study; Safety, Pharmacokinetics & Preliminary Clinical Activity of BT5528 in Patients with Advanced Malignancies Associated with EphA2 Expression (ASCO 2020)

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Background:

- BT5528 is a *Bicycle®* Toxin Conjugate (BTC), a novel class of chemically synthesized molecules, comprising a bicyclic peptide targeting EphA2 tumor antigen, linked to cytotoxin (monomethyl auristatin E [MMAE]) via a cleavable linker.
- EphA2 is overexpressed in a range of solid tumors, contributes to oncogenesis, tumor-associated angiogenesis and metastasis. Intracellular EphA2 signaling converges on pathways that are integral to cell growth, proliferation, migration and invasion.
- Increased EphA2 identified as a TKI resistance mechanism
- BT5528 mechanism of action is dependent on tumor penetration, target binding and release of MMAE payload.
- BT5528 exhibited a favorable preclinical profile with no bleeding or coagulopathy, unlike MedImmune's MEDI-547 (Annunziata, et al. Invest New Drugs 2013).
- Advantages over ADC exhibiting rapid penetration of dense tumors and decreased extra-tumor exposure.

First-in-Human (FIH) Study with a *Bicycle®* Toxin Conjugate (BTC) targeting EphA2 with an MMAE cytotoxic payload. Patient enrollment ongoing.

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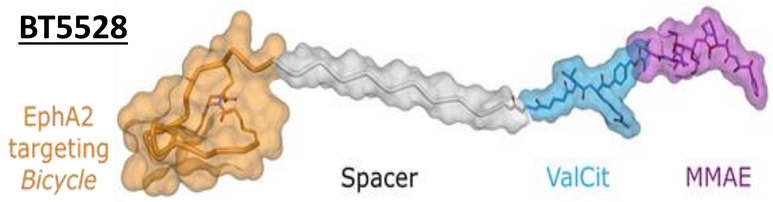
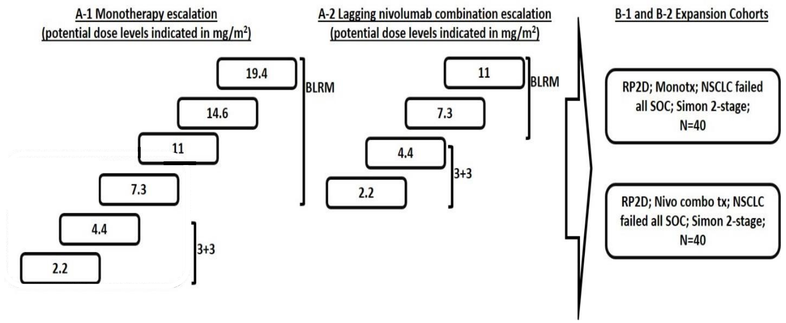
BT5528



BT5528-100 (NCT04180371) Ph I/II FIH study: Escalation Phase 1

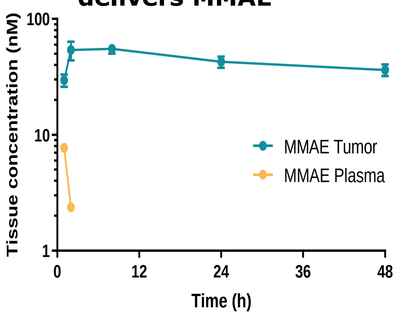
- To evaluate safety & tolerability of weekly BT5528 alone and in combination with q4w nivolumab (provided by Sponsor), and determination of RP2D
- Patients with advanced solid tumors associated with EphA2 expression after exhausting SOC options (i.e. NSCLC, TNBC, pancreatic, ovarian, gastric/upper GI, and urothelial cancers)
- At baseline must have available tumor tissue, acceptable hematologic and organ function
- Excluded if uncontrolled brain metastasis, thrombotic/ bleeding disorders, uncontrolled hypertension, CYP3A4 inhibitors; and, autoimmune disease for nivolumab cohorts
- PK serial collections on D1 and D15
- Radiologic tumor assessments q8w for response per RECIST



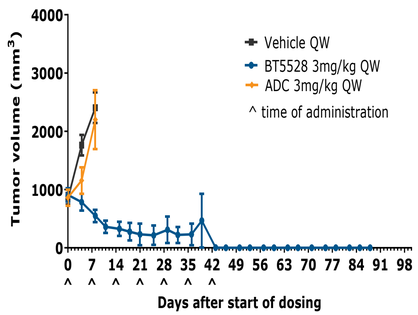
Expansion Phase 2a (part B-1 and B-2):

- Expansion cohorts to investigate efficacy (ORR and DOR) & safety of BT5528 in EphA2-enriched or -selected NSCLC populations with or without nivolumab.

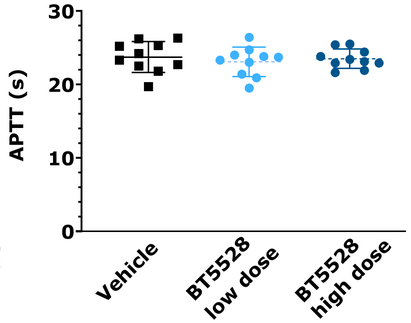
BT5528 efficiently delivers MMAE



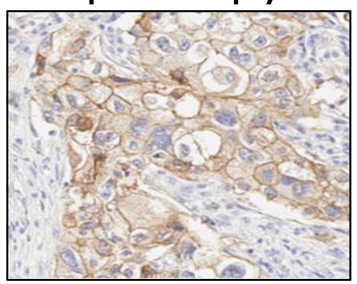
Docetaxel resistant NSCLC PDX



Preclinical aPTT



EphA2 IHC from NSCLC patient biopsy



EphA2 expression in patient samples by IHC to be presented at AACR 2020, see abstract #3302