Activity of SGN-B6A in Patient-Derived Xenograft Models of Non-Small Cell Lung Cancer

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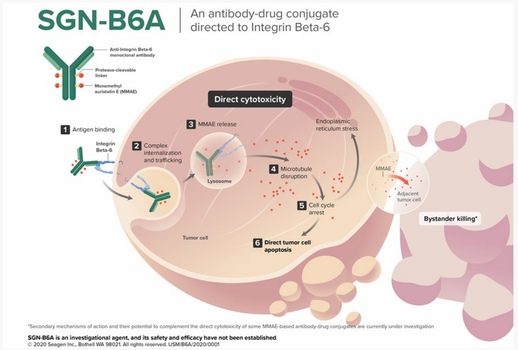
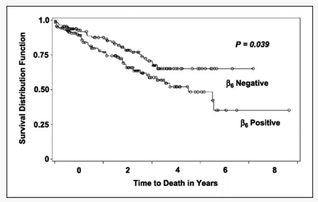
Antibody-Drug Conjugate SGN-B6A

- SGN-B6A is an investigational antibody-drug conjugate (ADC) targeting integrin beta-6 that is currently in a Phase I study (NCT04389632)
- The targeting component of SGN-B6A is the humanized anti-integrin beta-6 antibody h2A2, paired with the vedotin ADC technology that delivers the potent cytotoxin MMAE



Integrin Beta-6 is a Promising Carcinoma Target

- Member of the integrin family of adhesion protein isoforms that exist as alpha-beta heterodimers
  - Beta-6 forms exclusive heterodimers with alpha-v
- Role in tissue remodeling & repair
  - Activates transforming growth factor-beta
  - Regulates motility through extracellular matrix ligands
- Constitutively expressed at low levels in several epithelial tissues, upregulated in tissue repair response
- Tumors exploit remodeling function to promote invasiveness and metastasis
  - Promotes epithelial to mesenchymal transition
  - Promotes metastasis through inhibition of anoikis
- High expression is a poor prognostic indicator in multiple cancer types, including non-small cell lung cancer (NSCLC):



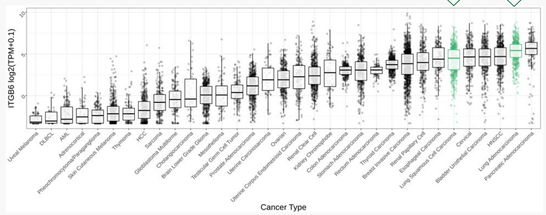
Anissa N. Elayadi *et al.* Cancer Res 2007; 67:5889-5895.

Integrin beta-6 positivity was determined by IHC staining using an undisclosed anti-integrin beta-6 antibody clone and a tumor microarray of 293 NSCLC samples (180 adenocarcinomas, 107 squamous cell carcinomas, 6 adenosquamous carcinomas) for which patient outcomes were known. Scores of 0 or 1 were considered negative, scores of 3 or 4 were considered positive. By these methods and metrics, the authors considered 54% of the samples to be positive. Survival times in positive and negative patients were compared using a long-rank test.

Integrin Beta-6 is Strongly Expressed in NSCLC

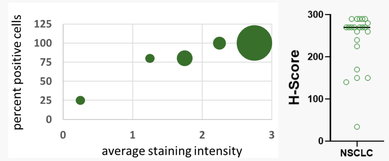
RNASeq (The Cancer Genome Atlas)

- **Lung squamous cell and adenocarcinomas are among the tumors with highest antigen expression**

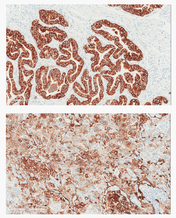


Immunohistochemistry (IHC)

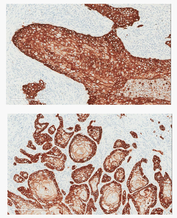
- **High and uniform expression was observed by IHC in a study of 22 NSCLC samples** (Mosaic Laboratories, Lake Forest CA)
  - High staining intensity and prevalence may indicate this method is more sensitive than previously reported integrin beta-6 IHC results



Adenocarcinoma examples

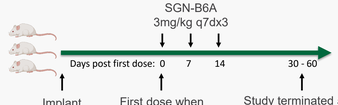


Squamous cell carcinoma examples



Evaluating SGN-B6A in NSCLC PDX Models

- Patient-derived xenograft (PDX) study performed at Champions Oncology
  - 18 models represent both adeno and squamous histologies
  - Selected to span a range of integrin beta-6 expression



Analysis of results

Best response 'waterfall' plots

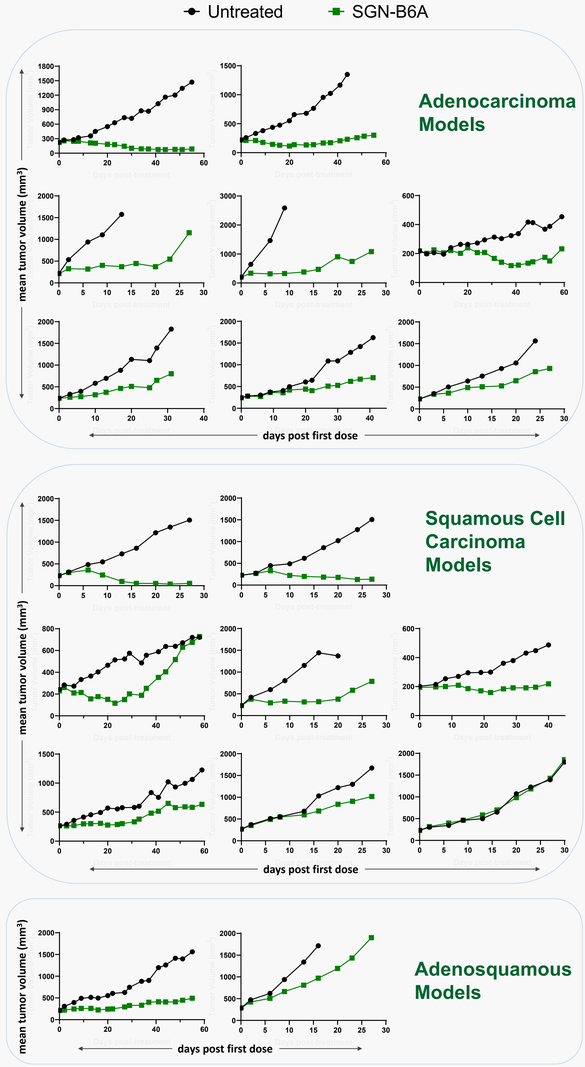
The waterfall plots depict the average of the percent tumor volume change for each model in which T_x is the smallest tumor volume achieved or for growing tumors the first measurement post final dose and T_i is the initial tumor volume at dosing **($100 * ((T_x-T_i)/T_i)$)**

Tumor growth inhibition plots

Percent tumor growth inhibition (TGI) is determined by normalizing the growth of treated **(T)** and control **(C)** animals, **b** denotes the tumor volume at best response. **($100 x [1-(T_b-T_i)/(C_b-C_i)]$)**

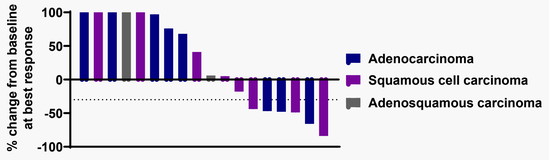
SGN-B6A Exhibited Robust Antitumor Activity in PDX Models of NSCLC

Model growth curves, grouped by histology

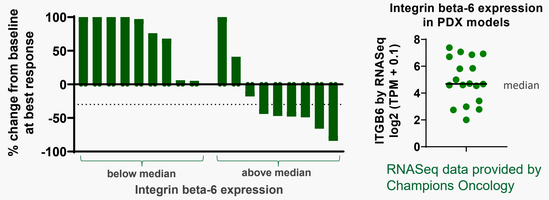


SGN-B6A induced >30% tumor volume reduction in 6 / 18 models (33%)

- **Similar responses in squamous cell and adenocarcinoma**

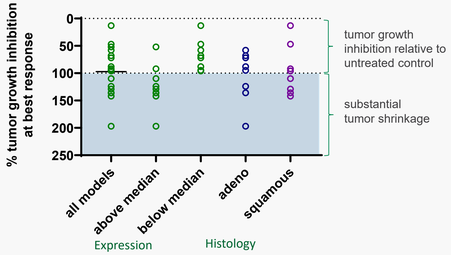


- **Models with above-median integrin beta-6 expression (by RNASeq) were more likely to respond to treatment**



RNASeq data provided by Champions Oncology

- **Models that did not show tumor regression did respond with growth delay**



Conclusions

- **SGN-B6A is a novel vedotin ADC currently in a Phase 1 study in multiple tumor types, including NSCLC**
- **In patient-derived xenograft models of NSCLC, SGN-B6A exhibited broad activity**
  - **Best responses were observed in models with higher integrin beta-6 expression by RNASeq**
  - **Activity was similar between adenocarcinoma and squamous cell carcinoma models**
- **These results support further clinical investigation of SGN-B6A in the ongoing Phase I study (NCT04389632)**

DISCLOSURES: All authors are employees and shareholders of Seagen Inc.

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