SGN-B6A Induces Immunogenic Cell Death as an Additional Mechanism of Action

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SGN-B6A Induces Immunogenic Cell Death

- SGN-B6A is an investigational vedotin antibody-drug conjugate (ADC) directed to integrin beta-6 that is currently being evaluated in a phase I study (NCT04389632)
- SGN-B6A is comprised of the humanized antibody h2A2, highly specific for integrin beta-6 over other beta integrins, paired with the vedotin ADC technology that delivers the potent cytotoxin MMAE

SGN-B6A Displays Anti-tumor Activity in BxPC3 and HPAFII Xenograft Models

- Other vedotin ADCs delivering the clinically validated MMAE payload (including those ADCs based on the antibodies brentuximab, enfotuximab, liscutzimab, and adituzumab) have shown to induce immunogenic cell death (ICD) in preclinical models [1-5] and have demonstrated promising clinical activity in combination with immunotherapy [6-8]
- Here, we present data to support immunogenic cell death as an additional mechanism of action for SGN-B6A

SGN-B6A Induces Apoptosis and ICD Markers In Vitro

- SGN-B6A induces apoptosis and cell cycle translocation of calreticulin, a marker associated with ICD, and may enhance antitumor immunity

SGN-B6A Induces ER Stress In Vitro

- The Endoplasmic Reticulum (ER) is a key organelle that has evolved complex signaling cascades to help maintain its homeostasis when undergoing stress. This process is known as the unfolded protein response (UPR) or UPR
- Alternatively, IREα can independently contribute to apoptosis via activation of JNK
- Phosphorylation of JNK (pJNK) and eIF2α (p-eIF2α) are two downstream markers of ER stress

Conclusions

- SGN-B6A exhibits hallmarks of inducing immunogenic cell death in both in vitro and in vivo assays
- We have previously reported similar predictive findings for other vedotin ADCs that have also shown promising clinical combination data with immune checkpoint inhibitors [1-8]
- SGN-B6A is currently being evaluated as monotherapy in NSCLC, HNSCC, EBCS, and other tumors in a phase I study (NCT04389632)
- This work provides additional preclinical rationale for exploring SGN-B6A in combination with immune checkpoint inhibitors in the clinic

References