

**B7H3: novelCheckpoint Protein Expressed by Pediatric Solid Tumors**

- B7H3 is an immune checkpoint protein ubiquitously expressed in both normal and malignant cells. Its role in pediatric malignancies is particularly relevant as it is enriched on the surface of cancer cells, enabling more effective targeting for the development of life-saving drugs for pediatric indications.

- In September 2023, COACH convened its sixth meeting with representatives from the National Cancer Institute (NCI), Food and Drug Administration (FDA), Europarec Medicines Agency (EMA), and pediatric stakeholders to discuss the potential of targeting B7H3 as a cancer immunotherapy. The identification of B7H3 as a potent therapeutic target was based on its expression in multiple pediatric tumor types, which demonstrated limited toxicity in clinical trials.

- Key Considerations:
  - **Safety**: Higher binding affinity for PTK7 may warrant preclinical studies.
  - **Efficacy**: Efficacy studies in pediatric preclinical testing would benefit ADC antibody, linker, and payload for the selection of an appropriate anti-PTK7 ADC.
  - **Toxicity**: Preclinical studies should be developed for use in future pediatric indications.

- Recommendations:
  - Preclinical studies should consider designing non-invasive biomarkers of disease progression.
  - Additional preclinical studies are needed to more rigorously understand PTK7's role in pediatric malignancies.
  - More research is required to understand PTK7's potential functions in pediatric oncology.
  - Preclinical models should use MTX-13 due to its ability to reliably predict anti-CD33 treatment reduced toxicities.
  - Novel biomarkers are needed to more reliably predict anti-CD33 ADCs with improved safety.

**CD33: Anti-CD33 ADCs in Clinical Development**

- CD33 is a transmembrane glycoprotein and lectin that undergoes epigenetic epigenetic alterations, including methylation and mutation.
- CD33 is a probable target for ADC therapy as it is expressed on the surface of various hematopoietic cells, including leukemic blasts.
- CD33 ADCs have demonstrated limited toxicity in clinical trials.

- Key Considerations:
  - **Safety**: Decreasing CD22 expression can help identify anti-CD33 ADCs with reduced toxicities.
  - **Efficacy**: Efficacy studies in pediatric preclinical testing would benefit ADC antibody, linker, and payload for the selection of an appropriate anti-CD33 ADC.
  - **Toxicity**: Preclinical studies should consider designing non-invasive biomarkers of disease progression.

- Recommendations:
  - Preclinical studies should consider designing non-invasive biomarkers of disease progression.
  - More research is required to understand PTK7's role in pediatric malignancies.
  - Preclinical models should use MTX-13 due to its ability to reliably predict anti-CD33 treatment reduced toxicities.
  - Novel biomarkers are needed to more reliably predict anti-CD33 ADCs with improved safety.