Biotech: Experts Believe Targeting IDO Inhibitor Alone Unlikely to Drive Efficacy, Best Utilized in Combination with CTLA-4 or PD-1 Strategies

The Jefferies Biotech team hosted an investor summit earlier this week focused on recent developments with chimeric antigen receptor (CAR) T cell immunotherapy and immune checkpoint targets. Our onco-immunology experts at the summit believe IDO is a well characterized target driving immunosuppression in the tumor environment but blocking IDO itself is unlikely to drive efficacy, and is best utilized in combination with CTLA-4/PD-1 strategies.

Newlink Genetics (NLNK) is developing two orally available IDO inhibitors for the treatment of cancer, indoximod (Phase II) and NLG919 (Phase I). Indoximod is probably more of an IDO2 inhibitor vs. targeting IDO1 and may inhibit downstream effects on WARS and mTORc. NLNK is investigating indoximod in combination trials with docetaxel (breast cancer), Provenge (prostate cancer), temozolomide (brain tumors), Yervoy (melanoma), and Abraxane (pancreatic cancer), with the bulk of the preliminary data expected in Q4'14/ Q1'15. NLNK also believes synergy between indoximod and CTLA-4 blockade inhibitors may be possible for stronger responses, which was supported in preclinical models.

NLG919 is in Phase I for solid tumors (data expected in Q4'14/Q1'15. Synergy between NLG919 and indoximod may be possible, and NLNK showed in a mouse model that significant tumor shrinkage can be achieved in combination vs. either agent alone. Furthermore, NLNK is also presenting data at the AACR meeting (Abs #1633; Monday April 7) in which the company has identified selective inhibitors of IDO1 and tryptophan 2, 3 dioxygenase (TDO). While IDO1 converts tryptophan to N-formyl-kynurenine, the catabolism of tryptophan may also occur through TDO according to literature. Both IDO1 and TDO, although functionally similar, appear structurally distinct enzymes, and therefore may represent a third class of IDO pathway compounds in NLNK's pipeline.

We also hosted a panel on chimeric antigen receptor T-cell (CAR-T) immunotherapy with a majority of companies in our panel focused on targeting CD19 antigen in B-cell malignancies. Early data has reported robust responses in patients with refractory disease, and a durable response. Key challenges include addressing cytokine release syndrome (addressed through administration of IL-6 inhibitor) and potential for off-target adverse events.

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