Association of ErbB/HER Biomarkers with Antitumor Activity of the anti-ErbB3/HER3 Monoclonal Antibody KTN3379 in SCCHN

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Summary

Altered regulation of the HER family of receptor tyrosine kinases (RTK) has proven to be a driver for promoting tumor growth and progression in a number of solid tumors. HER3 is a unique RTK, as it is primarily expressed and regulated in normal tissues and in normal breast tissue (UNC10). KTN3379 is a human and HER2 monoclonal antibody currently being evaluated in clinical studies. It selectively inhibits HER3 by blocking the receptor in an inactive conformation, providing evidence of its potential for activity in the context of HER2 overexpression. The anti-HER3 activity of KTN3379 is not influenced by the presence of HER3 homodimers, which are not well defined. In an in vivo study of 24 human tumor samples, KTN3379 identified 10 tumors, and 8 out of 10 tumors, resulting in a correlation with higher levels of NRG expression and KTN3379 anti-tumor activity. There was not a correlation with higher levels of NRG expression and KTN3379 anti-tumor activity in any other tumors.

Results

1 KTN3379 Inhibits Ligand-Dependent and Independent ErbB3 Signaling

- KTN3379 inhibits ligand-dependent and independent ErbB3 signaling.

2 Which Human Tumors Overexpress Neuregulin (NRG)?

- This table shows the expression levels of NRG in different human tumor types.

3 Evaluation of NRG Expression in a Cohort of Human SCCHN FFPE Tumor Samples

- This study evaluated NRG expression in a cohort of human SCCHN FFPE tumor samples.

4 Characterization of HER Expression Profile in a Cohort of Human SCCHN FFPE Tumor Samples Using VeraTag assays

- This study characterized the HER expression profile in a cohort of human SCCHN FFPE tumor samples.

5 Pairwise Comparison of VeraTag HER Assays in a Cohort of Human SCCHN FFPE Tumor Samples

- This study compared the expression levels of HER in a cohort of human SCCHN FFPE tumor samples.

6 NRG Expression Does Not Correlate with HER3 Activation in SCCHN Tumor Samples

- This study evaluated the correlation between NRG expression and HER3 activation in SCCHN tumor samples.

7 KTN3379 Anti-proliferative Activity and Biomarkers in a Panel of NRG-Expressing SCCHN Cell Lines In Vitro

- This study evaluated the anti-proliferative activity and biomarkers in a panel of NRG-expressing SCCHN cell lines.

8 Higher Levels of EGFR Dimer and Phospho-HER3 Correlate with KTN3379 Anti-tumor Activity in SCCHN Cell Lines In Vitro

- This study evaluated the correlation between EGFR dimer and phospho-HER3 levels and KTN3379 anti-tumor activity in SCCHN cell lines.

Conclusions

- SCCHN cancer has a high prevalence of NRG and HER3 family expression.
- KTN3379 treatment results in tumors with a high expression of NRG and HER3.
- This study supports the potential use of KTN3379 in SCCHN cancer patients.