Efficacy of patritumab (U3-1287), a fully human anti–human epidermal growth factor receptor 3 (HER3) monoclonal antibody, in head and neck cancer models

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ABSTRACT

To examine heregulin expression in head and neck cancer models and patient samples, and to assess the effects of patritumab and cetuximab treatment on HER3 signaling and tumor growth inhibition in vitro and in vivo, we conducted the current study.

METHODS

Heregulin expression was determined in head and neck cancer cell lines and patient samples with quantitative reverse transcription polymerase chain reaction (RT-qPCR). We compared HER3 signaling in cell lines with and without HER3 expression. HER3 expression was frequent in H&N cell lines. HRG mRNA expression was examined in H&N cell lines and patient samples. HER3 signaling was inhibited by patritumab, with additional blockage of HRG expression in HER3-positive cell lines. Patritumab and cetuximab efficacy in vivo was examined in a FaDu head and neck cancer xenograft model.

RESULTS

Patritumab and cetuximab enhanced tumor growth inhibition in vivo. Basal HER3 and AKT activation were inhibited by patritumab, with additional blockage of HRG expression in HER3-positive cell lines. Patritumab and cetuximab enhanced apoptosis, reduced proliferation in vitro, and reduced tumor cell growth in vivo.

CONCLUSIONS

Heregulin expression was frequent in head and neck cancer cell lines and patient samples. HER3 expression was associated with single-agent efficacy of patritumab and combination with cetuximab. Patritumab and cetuximab enhanced tumor growth inhibition in vivo. These data strongly support the combination of patritumab with an anti-EGFR monoclonal antibody as a promising strategy for the treatment of head and neck cancer.

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