Combining anti-HER3 antibody, HMBD-001, with EGFR inhibition and chemotherapy may improve treatment outcomes in squamous NSCLC.

**Background and rationale**

Squamous non-small cell lung cancer (sqNSCLC) accounts for ~30% of NSCLC, with poor prognosis, suggesting a significant unmet need for effective treatments beyond standard-of-care (SOC) therapies.

- Environmental insults generate common genetic aberrations, such as an amplification of Chr 3p and loss of Chr 3p, which are hallmark features of early oncogenesis in squamous cell carcinoma.
- Chr 3q amplification leads to increased transcriptional activity.
  - TP63, which directly promotes HER3 ligand (NRG1)
  - SOX2, which directly promotes EGFR expression
- **Chou YT, et al. Stem Cells. 2013;31(12):2607-2619.**

These findings propose a unified hypothesis of etiology and tumorigenesis in squamous cell carcinoma, highlighting the role of anti-HER3 therapeutics in squamous NSCLC.

**Squamous NSCLC cell lines are dependent on HER3 instead of EGFR.**

**Combining HMBD-001 with cetuximab results in potent and sustained antitumor activity in PIK3CA amplified sqNSCLC models.**

**Conclusion**

- Common genetic alterations that increase HER3/NRG1 and EGFR signaling are frequently observed in squamous cell carcinoma.
- sqNSCLC is more dependent on HER3 than EGFR, therefore, the inhibition of HER3, either alone or in combination with EGFR inhibition and chemotherapy, could have broad applicability in the treatment of sqNSCLC.
- Inhibition of HER3 signaling with HMBD-001, a potentially best-in-class anti-HER3 antibody, results in potent antitumor activity in sqNSCLC as a monotherapy.
- Combining HMBD-001 with EGFR inhibition and docetaxel could further improve efficacy in the treatment of PIK3CA amplified sqNSCLC.
- Hummingbird Bioscience has initiated two Phase Ib studies in the second half of 2023, one of which is in PIK3CA amplified squamous NSCLC (NCT05910827).