The anti-HER3 monoclonal antibody seribantumab effectively inhibits growth of patient-derived and isogenic cell line and xenograft models with *NRG1* rearrangements

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Disclosure

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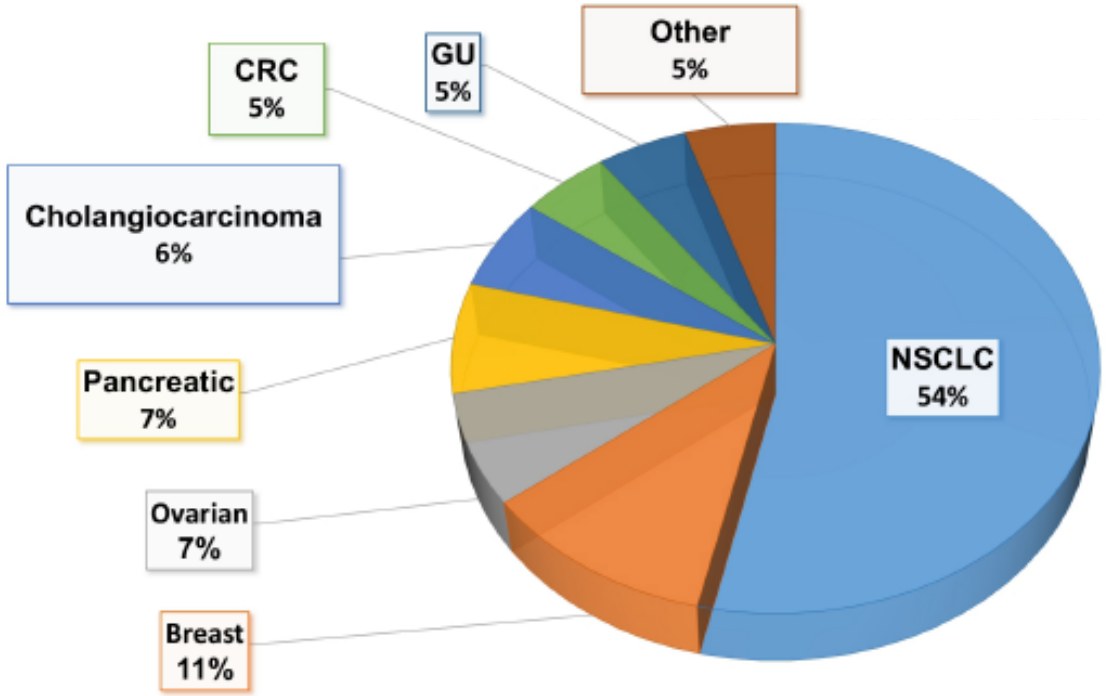
NRG1 Fusions are Present in Tumors of Diverse Origins and Activate the HER3 Pathway

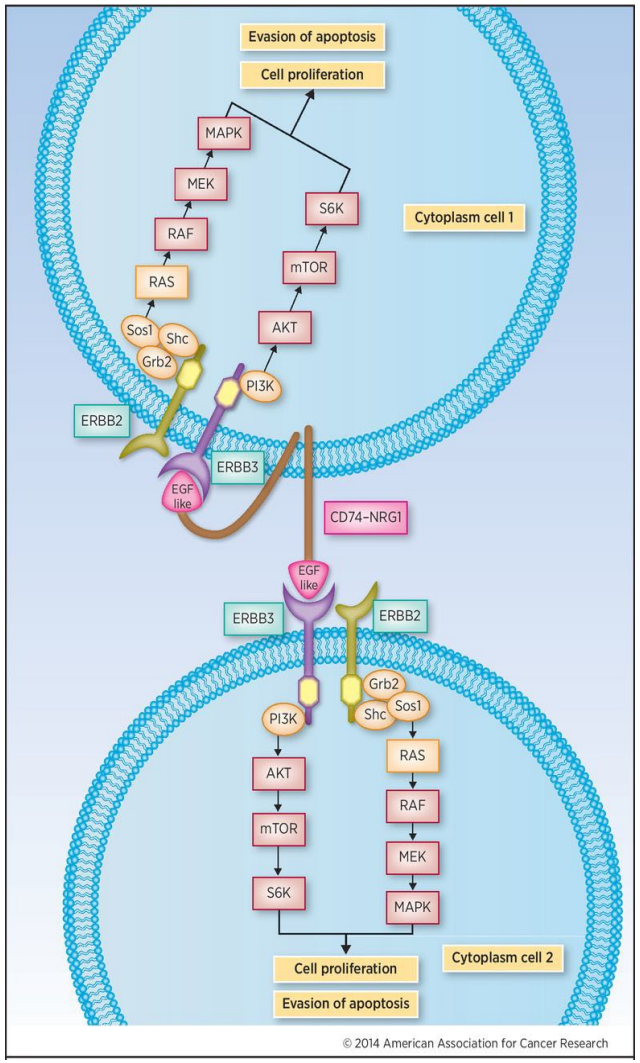
Distribution of tumor types in NRG1 fusion-positive solid tumors:



0.2% of solid tumors contain an NRG1 fusion (82/44,570)

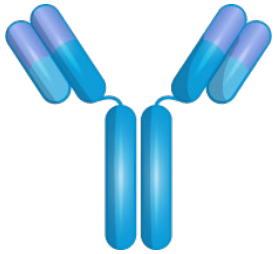
Jonna et al., ASCO 2020 Poster 1331

HER3 is a rational therapeutic target for NRG1 fusion-positive tumors



Lynnette Fernandez-Cuesta and Roman K. Thomas, CCR 2015, 21:1989-1994

Seribantumab Inhibits Growth of a Lung Cancer Patient-derived Xenograft (PDX) Model

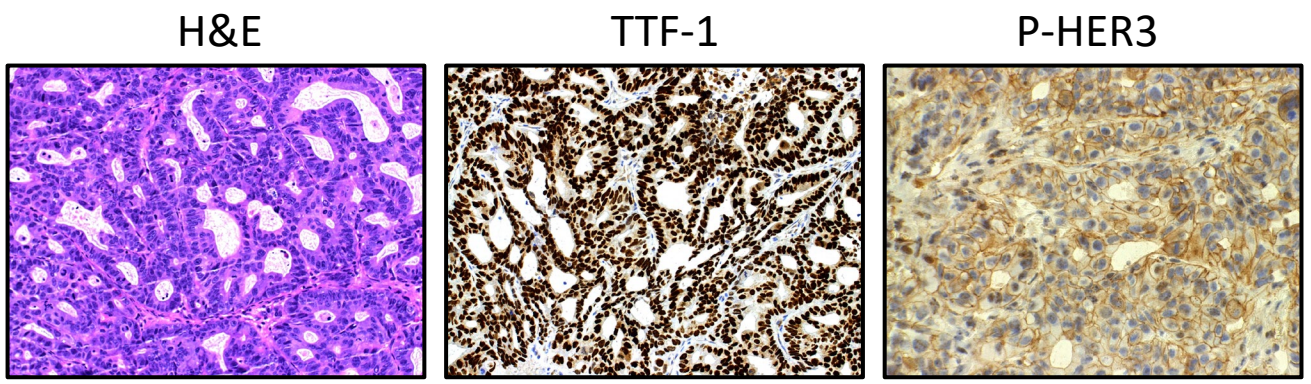


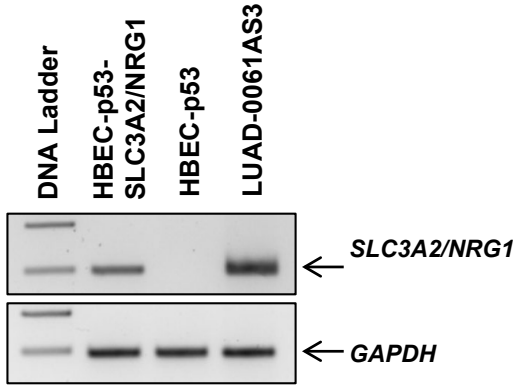
SERIBANTUMAB

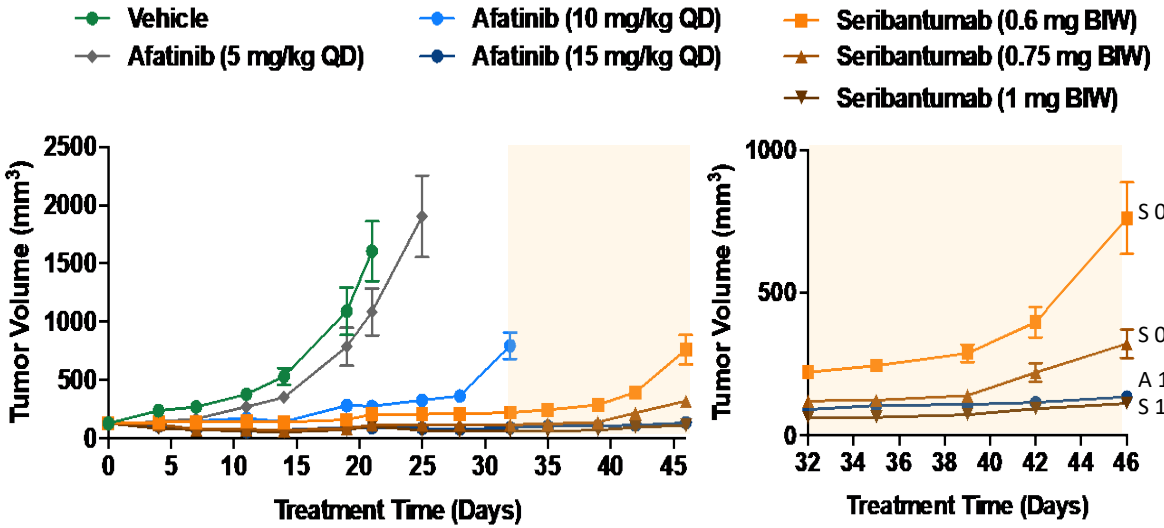
Fully Human IgG2 Anti-HER3 Monoclonal Antibody

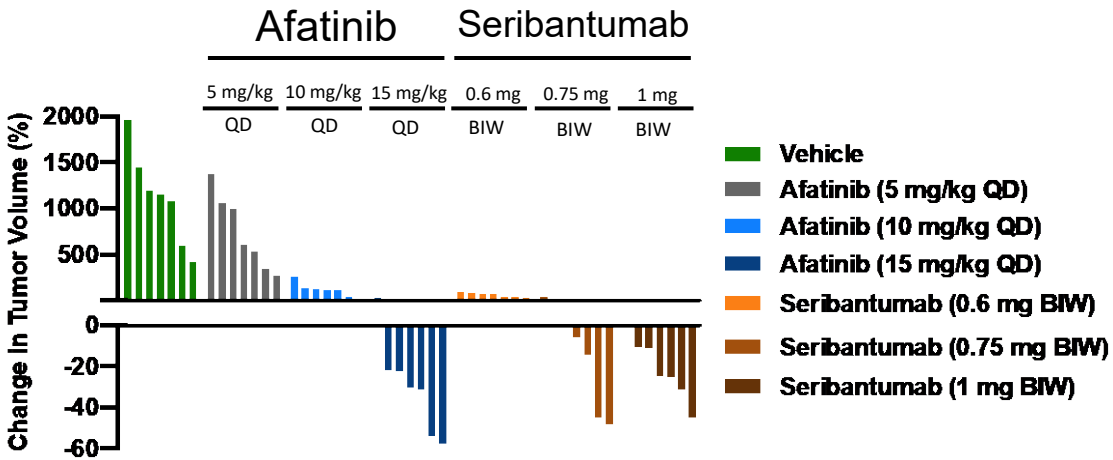
Blocks NRG1-stimulated HER3 phosphorylation

LUAD-0061AS3 – ***SLC3A2-NRG1*** rearranged invasive mucinous lung adenocarcinoma

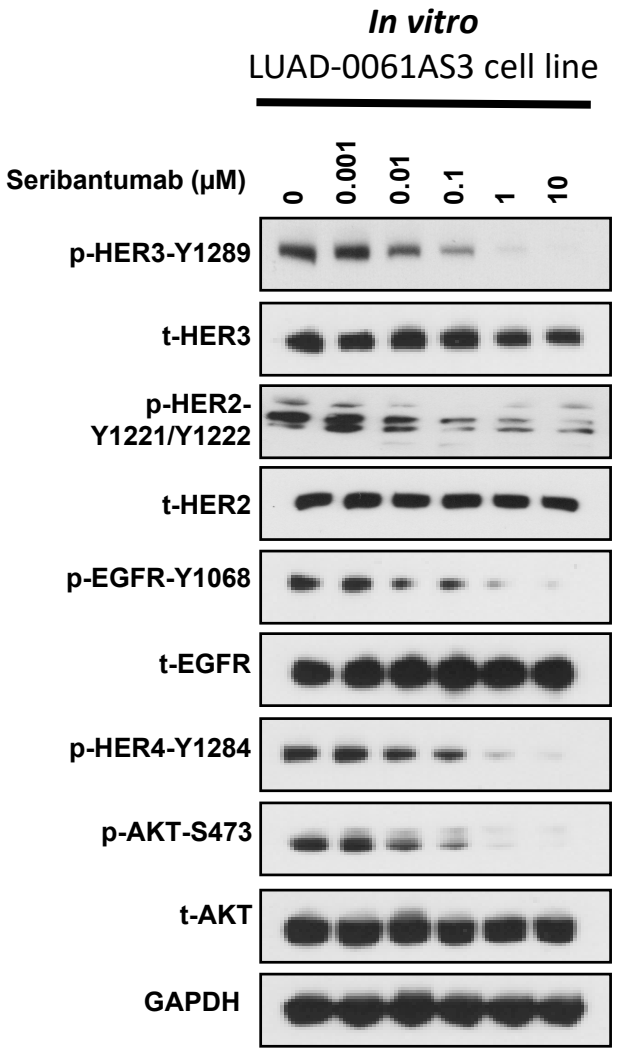


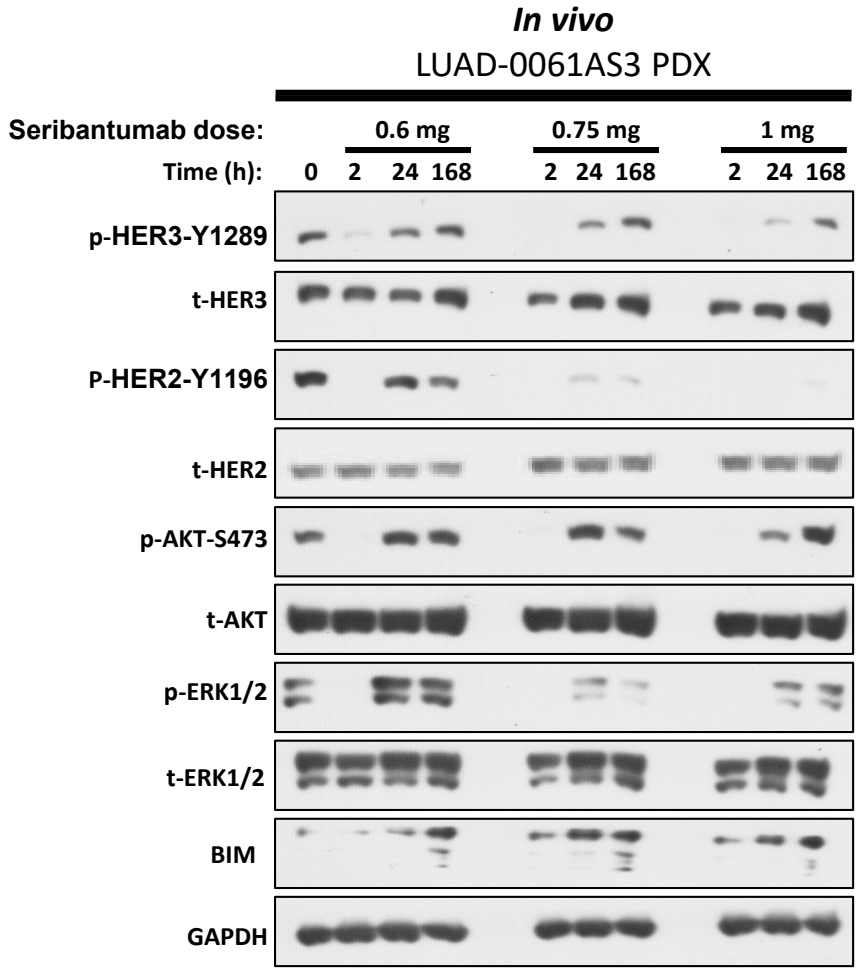






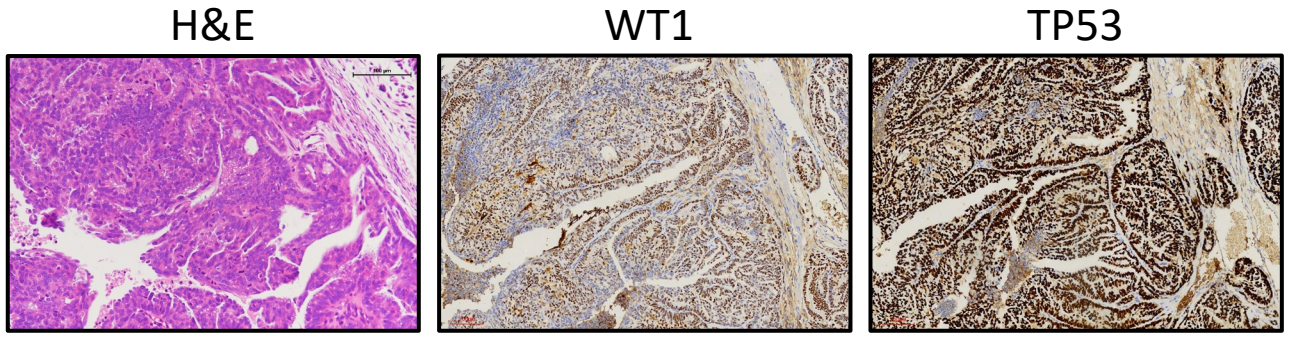
Seribantumab Inhibits Phosphorylation of ERBB Receptors and Downstream Signaling *In Vitro* and *In Vivo*

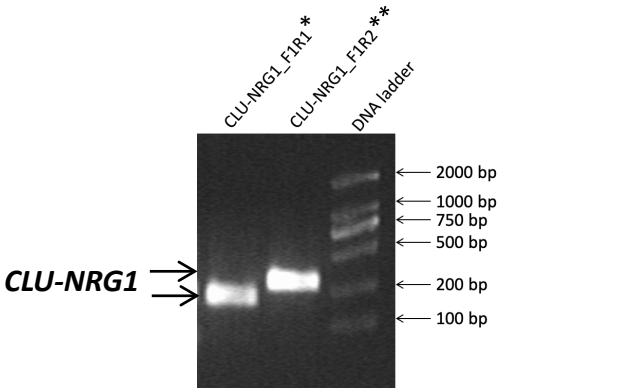




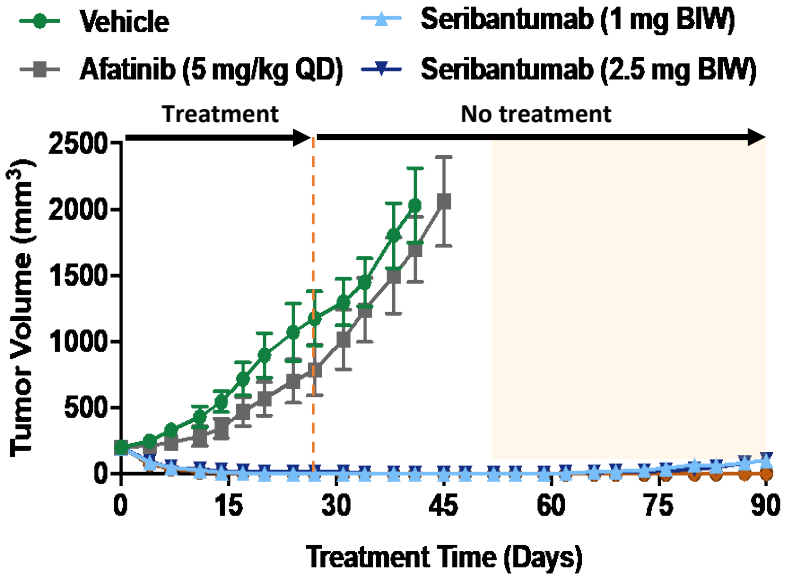
Seribantumab Inhibits Growth of a High Grade Serous Ovarian Cancer Patient-derived Xenograft model

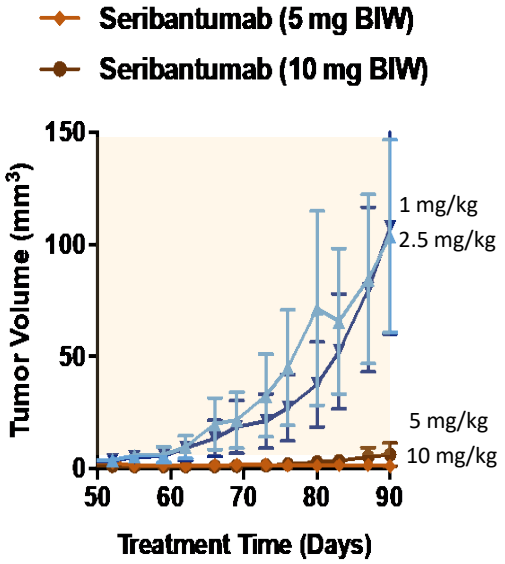
OV-10-0050 – ***CLU-NRG1*** rearranged high grade serous ovarian carcinoma

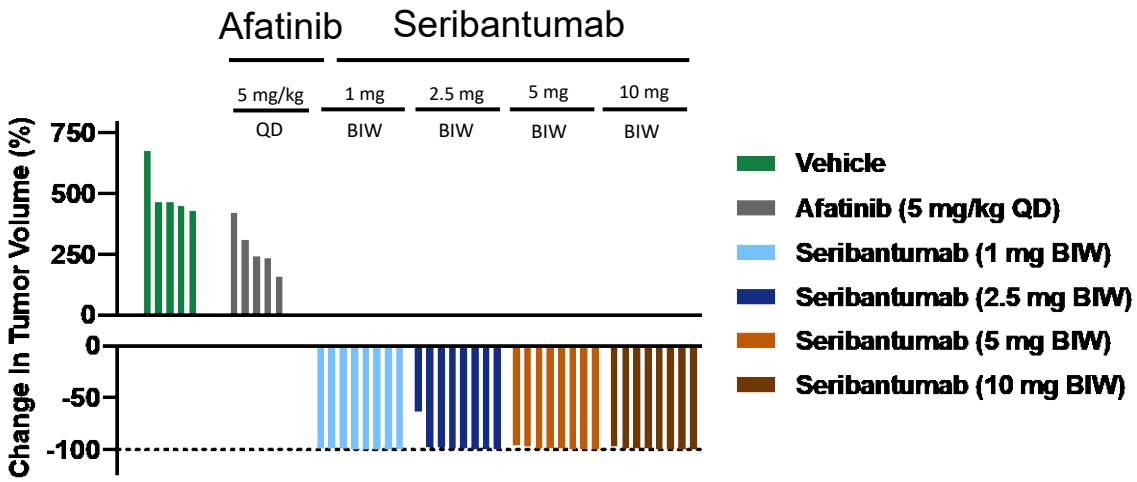




*F1R1 – CLU forward primer 1 and NRG1 reverse primer 1
**F1R2 – CLU forward primer 1 and NRG1 reverse primer 2







Summary of Results and Conclusions

- The anti-HER3 antibody seribantumab inhibited growth of lung and breast cancer cell lines harboring *NRG1* fusions.
- Seribantumab induced pro-apoptotic proteins and activated caspase 3/7 in lung and breast cancer cell lines harboring *NRG1* fusions.
- Seribantumab blocked phosphorylation of HER3, HER2, EGFR, HER4 and downstream effectors including AKT and p70S6 kinase.
- Treatment of mice bearing NRG1 fusion-positive lung and ovarian cancer PDX tumors with seribantumab resulted in 50-100% reduction in tumor volume.
- Afatinib was not effective at inhibiting growth of PDX tumors when used at the clinically equivalent dose.

These results provide a clear preclinical rationale for a tumor-agnostic trial of seribantumab in patients with *NRG1* gene fusion-positive solid tumors.

A Phase 2 trial of seribantumab in this setting is currently open and accruing patients (CRESTONE, NCT04383210).

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