Seribantumab

Cat. No.:	HY-P99268
CAS No.:	1334296-12-6
Target:	EGFR; Apoptosis
Pathway:	JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Apoptosis
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

Seribantumab (MM 121) is a fully human IgG2 monoclonal antibody that targets HER3. Seribantumab blocks the activation of epidermal growth factor receptor (ErbB) family members and its downstream signal. Seribantumab inhibits neuregulin 1 (NRG1) fusion-dependent tumorigenesis in vitro and in vivo in breast, lung and ovarian patient-derived cancer models[1].

In Vitro

Seribantumab (0.1 nmol/L-10 μmol/L; 96 h) dose-dependently inhibits two cell lines that harbor NRG1 rearrangements (MDA-MB-175-VII, DOC4-NRG1 fusion and LUAD-0061AS3, SLC3A2-NRG1 fusion) with IC_{50} values of 0.02, 1.4, 45.2 and 203 μmol/L for MDA-MB-175-VII, LUAD-0061AS3, MCF-7 and HBECp53 cells, respectively[1].

Seribantumab (0.1, 1, and 10 μmol/L; 24-48 h) effectively inhibits growth of tumor cell lines that harbor NRG1 fusions or NRG1 amplification[1].

Seribantumab (0-0.5 μmol/L; 96 h) largely suppresses growth of NRG1-b1-stimulated MCF-7 cells[1].

Seribantumab (0-10 μmol/L; 48 h) induces apoptosis of cells harboring NRG1 rearrangements[1].

Seribantumab (0-10 μmol/L; 1 h) inhibits phosphorylation of downstream mediators in cells with NRG1 alterations[1].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Apoptosis Analysis[1]

Cell Line:	MDA-MB-175-VII and LUAD-0061AS3 cell lines
Concentration:	0-10 μmol/L
Incubation Time:	48 hours
Result:	Dose-dependently increased caspase 3/7 activity and induced apoptosis of NRG1 fusion-positive breast and lung cancer cell lines.

Western Blot Analysis[1]

Cell Line:	LUAD-0061AS3 and HBECp53-CD74-NRG1 cell lines
Concentration:	0, 0.001, 0.01, 0.1, 1 and 10 μmol/L
Incubation Time:	1 hour
Result:	Inhibited the phosphorylation of EGFR, HER2, HER3, HER4, AKT and STAT3 in LUAD-0061AS3 cells. Completely inhibited HER3, AKT, p70S6K and STAT3, and reduced phosphorylation of HER2, EGFR and HER4 to a lesser extent in HBECp53-CD74-NRG1 cells.

In Vivo

Seribantumab (0.6-1 mg; i.p. twice weekly for once) reduces tumor growth in non-small cell lung cancer (NSCLC) patient-derived xenograft (PDX) mice model with a higher efficacy than afatinib, blocks phosphorylation of growth modulators and induces expression of apoptosis markers in vivo[1].

Seribantumab (1-10 mg; i.p. twice weekly for once) eliminates the vast majority of tumor cells and causes no significant change in overall animal health or weight in High-grade serous ovarian cancer (HGSOC) mice model[1].

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Animal Model:	Immunocompromised mice with LUAD-0061AS3 PDX tumors implanted[1]
Dosage:	0.6, 0.75 and 1 mg
Administration:	Intraperitoneal injection; 0.6, 0.75 and 1 mg for once
Result:	Effectively reduced tumor growth of mice and time- and dose-dependently reduced phosphorylation of HER2, HER3, AKT, and ERK1/2. Induced the expression if proapoptotic protein, BIM.

REFERENCES

[1]. Odintsov I, et al. The Anti-HER3 mAb Seribantumab Effectively Inhibits Growth of Patient-Derived and Isogenic Cell Line and Xenograft Models with Oncogenic NRG1 Fusions. Clin Cancer Res. 2021 Jun 1;27(11):3154-3166.

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