Tarlatamab

Cat. No.:	HY-P99575
CAS No.:	2307488-83-9
Target:	Notch
Pathway:	Neuronal Signaling; Stem Cell/Wnt
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.

BIOLOGICAL ACTIVITY

Description

Tarlatamab (AMG-757) is a bispecific T-cell engager (BiTE) antibody targeting delta-like ligand 3 (DLL3). DLL3 is a target that is selectively expressed in small-cell lung cancer (SCLC) tumors, but with minimal normal tissue expression. Tarlatamab has the K_Ds of 0.64 nM and 0.50 nM for human and nonhuman primate (NHP) DLL3, respectively. Tarlatamab has the K_Ds of 14.9 nM and 12 nM for human and NHP CD3, respectively. Tarlatamab is a first-in-class HLE BiTE immuno-oncology therapy targeting DLL3 and has the potential for SCLC research[1].

In Vitro

Tarlatamab (AMG-757; 0-10 nM; 48 hours) has potent, specific cytotoxic activity against DLL3-expressing SCLC cell lines in vitro[1].

Tarlatamab (0-10 nM; 4-72 h) increased granzyme B levels and cytotoxicity over time, with maximal signal observed at 48 hours. Markers of T-cell activation or inflammation, CD69, CD71, PD-1, and PD-L1 (37-39) were upregulated[1].

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

Cell Viability Assay[1]

Cell Line:	SCLC cell lines (DMS 79, NCI-H2171, NCI-H889, SHP-77, NCI-H211,COR-L279)
Concentration:	0-10 nM
Incubation Time:	48 hours
Result:	AMG 757 effectively engaged human T cells to kill SCLC cell lines, including those with very low DLL3 expression levels.

In Vivo

Tarlatamab (AMG-757; 3 mg/kg; IP; once weekly for 3 weeks) drives tumor regression in mouse models of SCLC[1].

Tarlatamab (IP; 12 μg/kg; single dose) has a mean half-life of 234 hours (9.8 days), a mean clearance of 0.487 mL/hour/kg and a steady-state volume of distribution of 146 mL/kg in nonhuman primates (NHPs)[1].

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Animal Model:	Female NOD.Cg-PrkdcscidIl2rgtm1Sug/JicTac (NOG) mice with patient-derived SCLC tumor fragments (LXFS 1129 and LXFS 538)[1]
Dosage:	3 mg/kg
Administration:	IP; once weekly for 3 weeks

Result:	Led to 83% tumor regression and an overall significant reduction in tumor volume compared with that in mice which received a control HLE BiTE molecule in the LXFS 1129 model. Induced 98% tumor regression in the LXFS 538 model.

REFERENCES

[1]. Michael J Giffin, et al. AMG 757, a Half-Life Extended, DLL3-Targeted Bispecific T-Cell Engager, Shows High Potency and Sensitivity in Preclinical Models of Small-Cell Lung Cancer. Clin Cancer Res. 2021 Mar 1;27(5):1526-1537.

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