Capmatinib hydrochloride

Cat. No.: HY-13404B

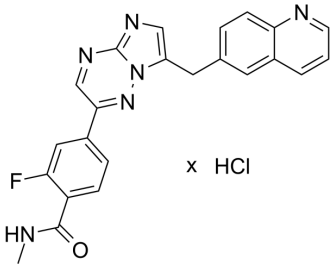
CAS No.: 1029714-89-3

Molecular Formula: $C_{23}H_{18}ClFN_6O$

Target: c-Met/HGFR; Apoptosis

Pathway: Protein Tyrosine Kinase/RTK; Apoptosis

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Capmatinib (INC280; INCB28060) hydrochloride is a potent, orally active, selective, and ATP competitive c-Met kinase inhibitor (IC_{50}=0.13 nM). Capmatinib hydrochloride can inhibit phosphorylation of c-MET as well as c-MET pathway downstream effectors such as ERK1/2, AKT, FAK, GAB1, and STAT3/5. Capmatinib hydrochloride potently inhibits c-MET-dependent tumor cell proliferation and migration and effectively induces apoptosis. Antitumor activity. Capmatinib hydrochloride is largely metabolized by CYP3A4 and aldehyde oxidase[1][2][3].

IC_{50} & Target

IC_{50}: 0.13 nM (c-MET)[1]

In Vitro

Capmatinib (INCB28060) inhibits c-MET phosphorylation with an IC_{50} value of approximately 1 nM and a concentration of approximately 4 nM inhibits c-MET more than 90%, which is reversible and the effect is significantly reduced in several hours after the compound is removed and completely disappeared by 48 hours[1].
Capmatinib (INCB28060) (0-10000 nM; 72 h) inhibits the proliferation of SNU-5, S114, H441 and U-87MG[1].
Capmatinib (INCB28060) (0.06-62.25 nM; 2h) effectively inhibits phosphorylation of c-MET as well as c-MET pathway downstream effectors such as ERK1/2, AKT, FAK, GAB1, and STAT3/5[1].
Capmatinib (INCB28060) (0.24-63 nM; over night) prevents HGF-stimulated H441 cell migration[1].
Capmatinib (INCB28060) (0.5-50 nM; 20 min) suppresses phosphorylation of both EGFR and HER-3 rapidly[1].
Capmatinib (INCB28060) (0-333 nM; 24 h) induces apoptosis in SNU-5 cells[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Cell Viability Assay[1]

Cell Line:	SNU-5, S114, H441 and U-87MG
Concentration:	0-10000 nM
Incubation Time:	72 h
Result:	Inhibited the cell viability of SNU-5 and S114, as well as the colony formation of H441 and U-87MG, with IC_{50} values of 1.2 nM, 12.4 nM, ~0.5 nM and 2 nM, respectively.

Cell Migration Assay [1]

Cell Line:	H441 (stimulated with 50 ng/mL recombinant human HGF for 24h)
Concentration:	0.24, 1, 4, 16 and 63 nM

Incubation Time:	Over night
Result:	Prevented HGF-stimulated H441 cell migration, with IC_{50} of approximately 2 nM, and less cell migration at 16 nM.

Western Blot Analysis[1]

Cell Line:	SNU-5
Concentration:	0.06, 0.24, 0.98, 3.91, 15.63 and 62.25 nM
Incubation Time:	2 h
Result:	Effectively inhibited phosphorylation of c-MET as well as c-MET pathway downstream effectors such as ERK1/2, AKT, FAK, GAB1, and STAT3/5.

Western Blot Analysis[1]

Cell Line:	H1993 cells
Concentration:	0.5, 5 and 50 nM
Incubation Time:	20 min
Result:	Suppressed phosphorylation of both EGFR and HER-3 rapidly and as effectively as the compound inhibited c-MET phosphorylation in H1993 cells.

Apoptosis Analysis[1]

Cell Line:	SNU-5 cells
Concentration:	0.017, 0.15, 1.37, 12.33, 111 and 333 nM
Incubation Time:	24 h
Result:	Effectively induced DNA fragmentation.

In Vivo

Capmatinib (INCB28060) (1-30 mg/kg; PO, twice daily, for 2 weeks) exhibits dose-dependent inhibition of tumor growth, and shows well tolerance at all doses during the treatment periods, with no evidence of overt toxicity or weight loss in U-87MG tumor mice model[1].

Capmatinib (INCB28060) (0.03-10 mg/kg; PO, single dosage) causes inhibition of c-MET phosphorylation in S114 tumor mice model[1].

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

Animal Model:	Female Balb/c nu/nu mice (inoculated subcutaneously with 5×10^6 U-87MG glioblastoma cells)[1]
Dosage:	1, 3, 10 and 30 mg/kg
Administration:	PO, twice daily, for 2 weeks
Result:	Exhibited dose-dependent inhibition of tumor growth with 35% and 76% at 1 and 3 mg/kg once daily; resulted in partial regressions in 6 of 10 U-87MG tumor-bearing mice at 10 mg/kg once daily; and showed well tolerance at all doses during the treatment periods, with no evidence of overt toxicity or weight loss.

Animal Model:	Female Balb/c nu/nu mice (inoculated subcutaneously with 4×10^6 S114 tumor cells)[1]
Dosage:	0.03, 0.1, 0.3, 1, 3 and 10 mg/kg
Administration:	PO, single dosage
Result:	Caused approximately 50% and 90% inhibition of c-MET phosphorylation at 0.03 and 0.3 mg/kg after administration of 30 min, and inhibition of phospho-c-MET exceeded 90% after 7 hours.

CUSTOMER VALIDATION

- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- J Exp Clin Cancer Res. 2022 Sep 16;41(1):275.
- Commun Biol. 2022 Nov 26;5(1):1295.
- Cancer Res Treat. 2020 Jul;52(3):973-986.
- Biochem Biophys Rep. 2020 Jan 17;21:100726.

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REFERENCES

[1]. Liu X, et al. A novel kinase inhibitor, INCB28060, blocks c-MET-dependent signaling, neoplastic activities, and cross-talk with EGFR and HER-3. Clin Cancer Res. 2011 Nov 15;17(22):7127-38.

[2]. Baltschukat S, et al. Capmatinib (INC280) Is Active Against Models of Non-Small Cell Lung Cancer and Other Cancer Types with Defined Mechanisms of MET Activation. Clin Cancer Res. 2019 May 15;25(10):3164-3175.

[3]. Dhillon S. Capmatinib: First Approval. Drugs. 2020 Jul;80(11):1125-1131.

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