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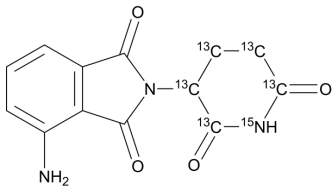
Pomalidomide-$^{15}N,^{13}C_5$

Cat. No.:	HY-10984S3
Molecular Formula:	$C_8{}^{13}C_5H_6N_2{}^{15}NO_4$
Molecular Weight:	274.16
Target:	Molecular Glues; Apoptosis; Ligands for E3 Ligase; Isotope-Labeled Compounds
Pathway:	PROTAC; Apoptosis; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Pomalidomide-$^{15}N,^{13}C_5$ is ^{15}N and ^{13}C labeled Pomalidomide (HY-10984). Pomalidomide, the third-generation immunomodulatory agent, acts as molecular glue. Pomalidomide interacts with the E3 ligase cereblon and induces degradation of essential Ikaros transcription factors.
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Pomalidomide also inhibits Whole Blood TNF-α with IC_{50} of 25 nM[2]. Exposure of lymphoma cells to Pomalidomide (CC-4047) leads to 40% decrease in cell proliferation when compared with vehicle-treated controls. Pomalidomide inhibits by 40% the DNA synthesis of Raji cells (P=0.036)[3]. In both $CD4^+$ and $CD8^+$ cells, Pomalidomide (CC-4047) is the most potent IL-2-elevator, followed by CC-6032 and CC-5013. Pomalidomide is significantly more potent than CC-5013 at elevating IL-2, IL-5, and IL-10, and slightly more potent than CC-5013 at elevating IFN-γ[4]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	The administration of Pomalidomide (CC-4047) for two consecutive days before mAb therapy enhances the antitumor activity of Rituximab and doubled the median survival of lymphoma-bearing mice. Statistically, significant differences are observed between animals treated with Rituximab versus Pomalidomide+Rituximab. The median survival time of animals treated with Pomalidomide and Rituximab is longer (median survival, 74 days; 95% CI, 70-78) than those treated with Rituximab monotherapy (median survival, 38 days; 95% CI, 26-50; log-rank test, P=0.002). The administration of CC-5013 or Pomalidomide for two consecutive days leads to a significant increase in the number of circulating NK cells as shown by flow cytometry analysis, in lymphoma-bearing SCID mice[3]. Following a 50 mg/kg PO administration of Pomalidomide (POM) to rats, unbound concentrations in blood reach a C_{max} value of 1100±82 ng/mL at 4.6±2.4 hours, with a concomitant $AUC_{(0-10)}$ value of 6800±2000 ng hr/mL. Unbound POM in the brain, however, has a C_{max} value of 430±63 ng/mL at 4.1±1.5 hours and an $AUC_{(0-10)}$ value of 2700±740 ng hr/mL, giving an unbound AUC_{brain} to AUC_{blood} ratio of 0.39±0.03. These values are consistent with excellent blood-brain-barrier penetration. The results obtained in this study are consistent with those seen in a concurrent study looking at whole brain POM content following its oral administration to mice[5]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

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