# *In Vivo* Studies of New Bcr-Abl Inhibitors Based on Purine Scaffold as Potential Drugs For CML Treatment

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## Abstract:

In the search for new Bcr-Abl inhibitors that can overcome drug resistance in clinical use, such as imatinib, we report the results of an in vivo study of a new purine derivative with promising properties. The hit compound, COS-5C, was selected from in vitro studies to in vivo studies, as this compound showed potent inhibition of Bcr-Abl and antiproliferative effects on chronic myeloid leukemia (CML) cell lines sensitive and resistant to imatinib. A nanoemulsion of COS-5C (NEM- COS-5C) was then developed, and to evaluate antitumor efficacy in a CML model, a cell line-derived xenograft (CDX) model was established by subcutaneous implantation of KCL-22 cells into NSG mice. Tumor cells were mixed with matrigel and injected subcutaneously into NSG mice. The animals were intraperitoneally administered 10 mg/kg NEM-COS-5C for 14 days. The tumor response was assessed longitudinally through volume measurements, and the results indicated that NEM-COS-5C diminished the size of the tumors compared to imatinib and control. This model enables the in vivo validation of new Bcr-Abl inhibitors for CML and provides a translational platform for future preclinical evaluation.

## Keywords:

Bcr-Abl, TKI, in vivo studies, chronic myeloid leukemia, purine derivatives.