DBPR728: A kinase inhibitor targeting MYC-driven cancers

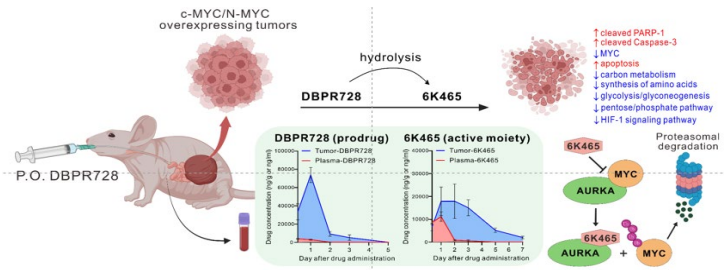
A Precision Medicine strategy for Cancers

Drug Introduction

- DBPR728 is an orally available, novel Aurora kinase A inhibitor specifically designed to suppress c-MYC and N-MYC oncoproteins.
- It demonstrates potent anti-tumor activity by effectively regressing xenograft tumors across multiple cancer types characterized by c-MYC or N-MYC amplification or overexpression.
- Key advantages include high tumor penetration and a prolonged tumor half-life, attributed to an innovative prodrug design strategy.

Drug Mechanism

- DBPR728 promotes the degradation of c-MYC and N-MYC oncoproteins by disrupting their interaction with Aurora kinase A, thereby triggering proteasome-mediated degradation.
- It exhibits synergistic anti-tumor activity when combined with everolimus, an mTOR inhibitor, in CDX models of small cell lung cancer with c-MYC or N-MYC amplification.



In Vivo Experimental / Preclinical Data

- BPR728 achieved significant tumor regression or suppression in CDX models of small cell lung cancer, triple-negative breast cancer, hepatocellular carcinoma, medulloblastoma, neuroblastoma, and pancreatic cancer.
- Its long elimination half-life enables flexible once-daily (QD), twice-a-week (BIW), three times a week (TIW) or once-weekly (QW) dosing regimens within a standard 21-day treatment cycle.
- DBPR728 outperformed alisertib, a Phase II investigational Aurora A inhibitor, across multiple xenograft models, demonstrating superior efficacy in both tumor regression and MYC oncoprotein degradation.
- At effective doses, no significant hematological toxicity was observed in mice.

Key Business Takeaways

- Strong potential as a precision medicine targeting MYC-driven cancers.
- c-MYC or N-MYC gene amplification serves as predictive biomarkers to identify patients most likely to respond, enabling a biomarker-guided patient selection strategy.
- Addresses a major unmet medical need due to the absence of direct MYC inhibitors and the inherent challenges in targeting MYC proteins.
- Offers broad expansion opportunities across multiple tumor types, with MYC alterations present in approximately 28% of all cancers.

Intellectual Properties

- PCT WO 2021/178485 (March 3, 2021); Entry countries (US, Canada, China, Japan, Korea, Europe, Australia, New Zealand)

Publications

- Discovery and Synthesis of a Pyrimidine-Based Aurora Kinase Inhibitor to Reduce Levels of MYC Oncoproteins. J. Med. Chem. 2021, 64, 7312−7330. https://doi.org/10.1021/acs.jmedchem.0c01806
- Discovery of a Long Half-Life AURKA Inhibitor to Treat MYC-Amplified Solid Tumors as a Monotherapy and in Combination with Everolimus. Mol Cancer Ther 2024, 23, 766–79. http://dx.doi.org/10.1158/1535-7163.MCT-23-0602

Contact

Pey-Yea Yang, Manager,
peyyea@nhri.edu.tw
Institute of Biotechnology and Pharmaceutical Research,
National Health Research Institutes,
Taiwan

Feb 09, 2026