Tumor Biology

Abstract 2010: BTK inhibitor BGB-3111 demonstrates anti-tumor activity in solid tumor models

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Abstract

Background BGB-3111 is a novel, irreversible, second generation BTK inhibitor with better selectivity profile and DMPK property compared to ibrutinib. It has demonstrated promising anti-tumor activities in patients with advanced B cell malignancies. Given BTK is expressed in all hematopoietic lineages except for T lymphocytes, it is reasonable to explore the immune modulatory effect of BGB-3111. In this study, we sought to investigate the anti-tumor activity of BGB-3111 in solid tumor models.

Methods Cell viability was assessed with Cell Titer Glo® assay and half maximal inhibitory concentrations (IC50) were estimated. In vivo activity was assessed in subcutaneous mouse xenograft models. Treatments were administered by oral gavage and individual body weight and tumor volume was recorded twice weekly.

Results In vitro studies showed that MDA-MB-436 cells are insensitive to BGB-3111, which do not expresse BTK. In both human breast cancer MDA-MB-436 and human A431 epidermoid carcinoma subcutaneous xenograft models, the tumor cells were co-injected with peripheral blood mononuclear cells (PBMCs) of healthy donors. In MDA-MB-436 model, BGB-3111 (15 mg/kg, BID) single agent significantly induced tumor growth inhibition (TGI) of 55%, whereas showed no anti-tumor effect if no PBMCs co-injected. Furthermore, co-treatment of BGB-3111 (15 mg/kg, BID) and anti-PD-1 antibody BGB-A317 (10 mg/kg, QW) demonstrated enhanced therapeutic effect in A431 allogeneic model. Interestingly, in BCLU200 and BCLU054 NSCLC primary tumor xenograft models (without PBMC co-injection), BGB-3111 (15 mg/kg, BID) also demonstrated significant anti-tumor activity.

Conclusions In summary, BGB-3111 showed interesting activity in solid tumor models, suggesting BTK inhibitor might have potential to be used beyond hematology malignancies. .

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