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BBI608 inhibits cancer stemness and reverses cisplatin resistance in NSCLC

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Abstract

Non-small cell lung cancer (NSCLC) is the most common cause of cancer-related deaths worldwide. While partial or complete tumor regression can be achieved in patients, particularly with cisplatin-based strategies, these initial responses are frequently short-lived and are followed by tumor relapse and chemoresistance. Identifying the root of cisplatin resistance in NSCLC and elucidating the mechanism(s) of tumor relapse, is of critical importance in order to determine the point of therapeutic failure, which in turn, will aid the discovery of novel therapeutics, new combination strategies and a strategy to enhance the efficacy of current chemotherapeutics. It has been hypothesized that cancer stem cells (CSCs) may be the initiating factor of resistance. We have previously identified and characterized an aldehyde dehydrogenase 1 CSC subpopulation in cisplatin resistant NSCLC. BBI608 is a small molecule STAT3 inhibitor known to suppress cancer relapse, progression and metastasis. Here, we show that BBI608 can inhibit stemness gene expression, deplete CSCs and overcome cisplatin resistance in NSCLC.