Published OnlineFirst March 31, 2014; DOI: 10.1158/1078-0432.CCR-13-2679

Clinical Cancer Research

Letter to the Editor

Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer—Letter

Haifeng Qiu

In a recent article, Cardnell and colleagues reported that BMN 673 (a novel PARP inhibitor) exhibited striking activities in small cell lung cancer (SCLC) cell lines and xenografts, and that cellular sensitivity to BMN 673 was associated with high baseline expression of several DNA repair proteins. Furthermore, the authors also detected that greater drug resistance was observed in SCLC models with baseline activation of the PI3K/mTOR pathway (1). However, we have some concerns about these findings.

As a tumor suppressor, PTEN is frequently inactivated in human malignancies, which then activates PI3K/mTOR signaling and promotes tumor progression. In contrast to the report of Cardnell and colleagues, another recent study found that BMN 673 selectively targeted tumor cells with PTEN deficiency both *in vitro* and *in vivo* (2). In 2012, a Japanese research group reported that PTEN-deficient lung cancer cells were more sensitive to olaparib (AZD2281, another PARP inhibitor), and PTEN restoration suppressed the PI3K/mTOR pathway and induced cellular resistance to PARP inhibition (3). More findings from endometrial cancer supported that sensitivity to PARP inhibitors was PTEN dependent (4). Nonetheless, a recurrent endometrial cancer patient with PTEN deficiency responded well to olaparib (5). All these findings are in contrast to the finding of Cardnell and colleagues that SCLC cell lines with more active phosphoinositide 3-kinase (PI3K) signaling are less sensitive to BMN 673.

In summary, we believe it is necessary to clarify the association between sensitivity to BMN 673 and dysregulated PI3K/mTOR signaling, to help select patients for future clinical trials.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received September 29, 2013; revised October 29, 2013; accepted November 2, 2013; published OnlineFirst March 31, 2014.

Author's Affiliation: Department of Ob/Gyn, International Peace Maternity & Child Health Hospital of the China Welfare Institute, Shanghai Jiaotong University, Shanghai, China

Corresponding Author: Haifeng Qiu, Department of Ob/Gyn, International Peace Maternity & Child Health Hospital of the China Welfare Institute, Shanghai Jiaotong University, NO. 910, Hengshan Road, Xuhui District, Shanghai 200030, China. Phone: 86-21-64073421; Fax: 86-21-64073421; E-mail: haifengqiu120@sjtu.edu.cn

doi: 10.1158/1078-0432.CCR-13-2679

References

1. Cardnell RJ, Feng Y, Diao L, Fan YH, Masrorpour F, Wang J, et al. Proteomic markers of DNA repair and PI3K pathway activation predict response to the PARP inhibitor BMN 673 in small cell lung cancer. Clin Cancer Res 2013;19:6322–8.
2. Shen Y, Rehman FL, Feng Y, Boshuizen J, Bajrami I, Elliott R, et al. BMN 673, a novel and highly potent PARP1/2 inhibitor for the treatment of human cancers with DNA repair deficiency. Clin Cancer Res 2013;19:5003–15.
3. Minami D, Takigawa N, Takeda H, Takata M, Ochi N, Ichihara E, et al. Synergistic effect of olaparib with combination of cisplatin on PTEN-deficient lung cancer cells. Mol Cancer Res 2012;11:140–8.
4. Dedes KJ, Wetterskog D, Mendes-Pereira AM, Natrajan R, Lambros MB, Geyer FC, et al. PTEN deficiency in endometrioid endometrial adenocarcinomas predicts sensitivity to PARP inhibitors. Sci Transl Med 2010;2:53ra75.
5. Forster MD, Dedes KJ, Sandhu S, Frentzas S, Kristeleit R, Ashworth A, et al. Treatment with olaparib in a patient with PTEN-deficient endometrioid endometrial cancer. Nat Rev Clin Oncol 2011;8:302–6.

AACR American Association for Cancer Research

Clinical Cancer Research

Proteomic Markers of DNA Repair and PI3K Pathway Activation Predict Response to the PARP Inhibitor BMN 673 in Small Cell Lung Cancer––Letter

Haifeng Qiu

Clin Cancer Res Published OnlineFirst March 31, 2014.