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Letter to the Editor

An exceptional response to olaparib in relapsed and refractory BRCA2 mutated non-small cell lung cancer in hereditary breast–ovarian cancer syndrome

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Dear Editor,

Poly (ADP-ribose) polymerase inhibitors (PARPi) have demonstrated impressive efficacy in BRCA-mutated gynecological malignancies.[1,2] Several lines of evidence now support that the DNA Damage repair (DDR)-deficient populations that benefit from PARPi go far beyond BRCA deficiency. Non-small cell lung cancer (NSCLC), the most common cause of death due to cancer worldwide, displays frequent DDR defects, the most frequent being ERCC1. This defect leads to platinum and PARPi sensitivity. Beyond ERCC1, DDR defects leading to platinum sensitivity widely overlap with those underlying PARPi sensitivity.[3,4] Here, we report a case of 47-year-old doctor with no known comorbidites and family history of ovarian cancer in mother at 63 years and unknown primary squamous cell carcinoma with submandibular lymph node (LN) in sister at 42 years of age. He had hoarseness of voice in December 2016 which was evaluated to have squamous cell carcinoma lung with metastatic paratracheal and aortopulmonary LN after radical treatment with definitive radiotherapy of 59.6 Gy/28# with 6# weekly paclitaxel + carboplatin completed on January 26, 2017, followed by adjuvant 6 cycles of gemcitabine and cisplatin till May 20, 2017. He developed 1.5 cm × 1.2 cm enhancing lesion in the right posterior parietal lesion within 1 month of completion of therapy. He was treated with gamma knife (June 30, 2017) 25 gy for the brain metastasis which recurred with the size of 5 cm × 5.4 cm × 4 cm along with new cervical LN and soft tissue deposit in trapezius in January 2018. Excision of brain metastasis and whole-genome sequencing was performed on a biopsy from a metastasis and blood which revealed deleterious gene mutation in exon 2 of breast cancer 1 (BRCA1) (c.68_69delAG, p.Glu23ValfsTer17) confirming risk of hereditary breast and ovarian cancer syndrome (dated February 4, 2018 MedGenome Labs Private Ltd, Bengaluru, India and ACTREC Genetic Lab, Kharghar). He was then started on olaparib 300 mg twice daily from 10th February and response positron emission tomography-computed tomography suggest resolution in the lesion in R occipital lesion, mass deposit in trapezius and bilateral cervical Lymph node. On follow up he had sustained response till January 2019 when he developed oligometastatic right supraclavicular LN recurrence which was treated again with radical chemotherapy with cisplatin and definitive radiation to supraclavicular fossa with

(Continue on page 12...)

(Letter to the editor continue from page 6...)

Table 1: Trials demonstrating efficacy of Olaprib in solid tumors with breast cancer mutation

Study	Year/status	Drug	Cancer type	Results
Wainberg *et al*.[5]	2014/ongoing	BMN673	SCLC	PFS 7.4 weeks recommended phase 2 dose 1 mg/d (*n*=11)
Owonikoko *et al*.[6]	2014/ongoing	Veliparib	SCLC	Unconfirmed Outcomes (*n*=7)
Molife *et al*.[7]	2013/ongoing	Rucaparib	Solid tumors (2 lung)	3 patients has stable disease for >12 weeks BRCA unknown
Rajan *et al*.[8]	2012/completed	Olaparib	Solid tumors	2/21 patients had response. Awaited results
Appleman *et al*.[9]	2012/completed	Veliparib	Advance solid tumors (15 lung)	PR seen in 11 patients (2 lung 2 melanoma 2 breast 2 urothelial , 2 unknown primary) Stable disease in 35 patients

SCLC=Small-cell lung cancer, PFS=Progression-free survival, BRCA=Breast cancer, PR=Partial response

olaparib continued. As continued research into hazard ratio pathways and mutations within NSCLC emerge, new uses for PARP inhibition can be applied [Table 1]. These therapies have proven to be well tolerated on oral administration, making a compelling rationale for the continued study of these agents in lung cancer.[10]

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Conflicts of interest

There are no conflicts of interest.

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References

1. Ledermann J, Harter P, Gourley C, Friedlander M, Vergote I, Rustin G, *et al.* Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer. N Engl J Med 2012;366:1382-92.
2. Gelmon KA, Tischkowitz M, Mackay H, Swenerton K, Robidoux A, Tonkin K, *et al.* Olaparib in patients with recurrent high-grade serous or poorly differentiated ovarian carcinoma or triple-negative breast cancer: A phase 2, multicentre, open-label, non-randomised study. Lancet Oncol 2011;12:852-61.
3. O'Sullivan CC, Moon DH, Kohn EC, Lee JM. Beyond breast and ovarian cancers: PARP inhibitors for BRCA mutation-associated and BRCA-like solid tumors. Front Oncol 2014;4:42.
4. Alexandrov LB, Stratton MR. Mutational signatures: The patterns of somatic mutations hidden in cancer genomes. Curr Opin Genet Dev 2014;24:52-60.
5. Wainberg ZA, Rafii S, Ramanathan RK, Mina LA, Byers LA, Goldman RC, *et al.* Safety and antitumor activity of the PARP inhibitor BMN673 in a phase 1 trial recruiting metastatic small-cell lung cancer (SCLC) and germline BRCA-mutation carrier cancer patients [abstract]. J Clin Oncol. 2014;32(5s). Abstract 7522.
6. Owonikoko TK, Dahlberg SE, Sica GL, Wagner LI, Wade JL 3rd, Srkalovic G, *et al*. Randomized phase II trial of cisplatin and etoposide in combination with veliparib or placebo for extensive-stage small-cell lung cancer: ECOG-ACRIN 2511 Study. J Clin Oncol 2019;37:222-9.
7. Molife LR, Roxburgh P, Wilson RH, Gupta A, Middleton MR, Michie TR, *et al.* A phase I study of oral rucaparib in combination with carboplatin.10.1200/jco.2013.31.15_suppl.2586 Journal of Clinical Oncology 2013;31:2586.
8. Rajan A, Carter CA, Kelly RJ, Gutierrez M, Kummar S, Szabo E, *et al.* A phase I combination study of olaparib with cisplatin and gemcitabine in adults with solid tumors. Clin Cancer Res 2012;18:2344-51.
9. Appleman LJ, Beumer JH, Jiang Y, Puhalla S, Lin Y, Ramalingam TK, *et al.* A phase I study of veliparib (ABT- 888) in combination with carboplatin and paclitaxel in advanced solid malignancies. 10.1200/jco.2012.30.15_suppl.3049 Journal of Clinical Oncology 2012;30:3049.
10. A Randomised Phase II Trial of Olaparib Maintenance Versus Placebo Monotherapy in Patients with Chemosensitive Advanced Non-Small Cell Lung Cancer. Available from: https://clinicaltrials.gov/ct2/show/NCT01788332. [Last accesed on 2019 Apr 24].

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