

## 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.<sup>[1,2]</sup> 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.<sup>[3,4]</sup> Here, we report a case of 47-year-old doctor with no known comorbidities 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 10<sup>th</sup> 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

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

Study	Year/status	Drug	Cancer type	Results
Wainberg <i>et al.</i> <sup>[5]</sup>	2014/ongoing	BMN673	SCLC	PFS 7.4 weeks recommended phase 2 dose 1 mg/d (n=11)
Owonikoko <i>et al.</i> <sup>[6]</sup>	2014/ongoing	Veliparib	SCLC	Unconfirmed Outcomes (n=7)
Molife <i>et al.</i> <sup>[7]</sup>	2013/ongoing	Rucaparib	Solid tumors (2 lung)	3 patients has stable disease for >12 weeks BRCA unknown
Rajan <i>et al.</i> <sup>[8]</sup>	2012/completed	Olaparib	Solid tumors	2/21 patients had response. Awaited results
Appleman <i>et al.</i> <sup>[9]</sup>	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.<sup>[10]</sup>

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#### Conflicts of interest

There are no conflicts of interest.

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