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Successful treatment of refractory lung adenocarcinoma harboring a germline *BRCA2* mutation with olaparib: A case report

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Abstract

BACKGROUND

In recent years, targeted therapy and immunotherapy have become important treatment strategies for patients with non-small cell lung cancer (NSCLC). However, the clinical evidence for successful off-label use of targeted drugs for patients with NSCLC following progression on multiple lines of treatment is still lacking.

CASE SUMMARY

We describe a 62-year-old male patient with a right lung adenocarcinoma who harbored an *EGFR* exon 19 deletion mutation. He received gefitinib combined with six cycles of vinorelbine, cisplatin, and recombinant human endostatin as the first-line therapy. Then gefitinib was administered in combination with recombinant human endostatin as maintenance therapy, resulting in a progression-free survival (PFS) of 14 mo. Chemoradiotherapy was added following progression (enlarged brain metastases) on maintenance treatment. Unfortunately, the brain lesions were highly refractory and progressed again after 15 mo, at which time next-generation sequencing (NGS) of 1021 cancer-related genes was performed using peripheral blood to identify potential actionable mutations. NGS revealed that the patient harbored a *BRCA2* germline mutation, the *EGFR* exon 19 deletion mutation disappeared, and no additional targetable genetic variant was detected. Therefore, the patient received olaparib combined with gefitinib and recombinant human endostatin, with a rapid and long-lasting clinical response (PFS = 13.5 mo).

CONCLUSION

This is a rare case of lung adenocarcinoma in a patient with a *BRCA2* germline mutation who had long-term benefit from olaparib combination treatment, suggesting that NGS-based genetic testing may render the possibility of long-term survival in NSCLC patients after disease progression.

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Core Tip: The clinical evidence for successful off-label use of targeted drugs for lung adenocarcinoma patients following progression on multiple lines of treatment is still lacking now. Herein, we describe the identification of a germline *BRCA2* mutation in a lung adenocarcinoma patient. The patient had multiple refractory brain metastases and received olaparib combined with gefitinib and recombinant human endostatin following progression on multiple lines of treatment, with a progression-free survival of 13.5 mo. This case provides unequivocal clinical evidence for the off-label use of olaparib in lung adenocarcinoma patients with a *BRCA* mutation after disease progression.

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INTRODUCTION

Lung cancer is one of the most common malignancies with high morbidity and mortality rates worldwide. In recent years, immunotherapy and targeted therapy have made great progress in non-small cell lung cancer (NSCLC), which is the most common type of lung cancer. However, post-progression effective therapy for NSCLC is still lacking. One highly potential strategy is to identify alternative therapeutic options. Next-generation sequencing (NGS)-based genetic testing, which provides abundant genetic information on cancer including both germline and somatic gene mutations, has resulted in more individualized therapeutic strategies for NSCLC.

BRCA2 is a tumor suppressor gene that encodes a protein involved in the DNA homologous recombination repair (HRR) pathway to maintain genome stability. A *BRCA2* germline mutation increases the risks of a variety of malignancies, including a 50%-60% increased risk of breast cancer and a 30% increased risk of ovarian cancer[1]. It is also associated with an increased risk of breast cancer and prostate cancer in males [2,3]. In addition, studies have shown that the HRR genes including *BRCA2* may be involved in the tumorigenesis of lung cancer[4]. Multiple clinical studies have confirmed that patients with *BRCA1/2*-mutated cancer, including breast cancer, ovarian cancer, and prostate cancer, may be sensitive to poly(adenosine diphosphate-ribose) polymerase (PARP) inhibitors[5-7]. PARP inhibitors are a novel class of anticancer drugs, which take advantage of synthetic lethality and induce cell death by exploiting a defect in DNA repair. Currently, the US Food and Drug Administration has approved four PARP inhibitors for various indications: Olaparib for ovarian cancer, metastatic breast cancer, fallopian tube cancer, and primary peritoneal cancer, niraparib and rucaparib for ovarian cancer, fallopian tube cancer, and primary peritoneal cancer, and talazoparib for metastatic breast cancer. However, the efficacy of PARP inhibitors in patients with tumors that are not commonly associated with germline *BRCA1/2* mutations remains to be explored. The results from multiple basket trials suggested that patients harboring the same molecular abnormalities may benefit from targeted therapy independent of tumor origin[8]. Although some studies have suggested that the PARP inhibitors talazoparib and olaparib both had synergistic activity with gemcitabine in lung cancer cell lines[9], and that *BRCA2*-mutant lung cancer organoids responded to olaparib[10], there is still a lack of clear clinical evidence to support that NSCLC patients with a *BRCA2* gene mutation respond to targeted therapies. In this paper, we present a case of *BRCA2* germline mutation positive, refractory lung adenocarcinoma with durable response and tolerable toxicities to olaparib combined with gefitinib and recombinant human endostatin, with a progression-free survival (PFS) up to 13.5 mo.

CASE PRESENTATION

Chief complaints

In September 2019, a 62-year-old Chinese man presented to hospital for treatment because of multiple progression of brain metastases from lung adenocarcinoma without an effective therapy.

History of present illness

In March 2017, the patient presented with cough and blood-tinged sputum. He underwent bronchoscopy at another hospital and was diagnosed with lung adenocarcinoma. In order to seek further treatment, he came to our hospital and was diagnosed with a T2N0M1 (stage IV) adenocarcinoma of the right lung with focal squamous cell differentiation, and multiple brain metastases. An *EGFR* exon 19 deletion mutation was identified. Therefore, the patient received gefitinib 250 mg/d, and was given six courses of chemotherapy with the vinorelbine plus cisplatin (NP) regimen and recombinant human endostatin, and achieved a partial response. Then gefitinib was given in combination with recombinant human endostatin as maintenance therapy. Bilateral frontal lobe and temporal lobe metastases were observed after 14 mo, and 4 mo later, the bilateral frontal lobe metastases were enlarged. The patient was given oral temozolomide for four courses on the basis of maintenance therapy, but had progressive disease. Magnetic resonance imaging (MRI) showed supratentorial and infratentorial brain metastases. To identify potentially actionable mutations, NGS-based genetic testing of 1021 cancer-related genes was performed using peripheral blood. A germline mutation in *BRCA2* was found (NM_000059.3, c.6816_6820del AAGAG, p.G2274Afs*17), and the *EGFR* exon 19 deletion mutation disappeared. The patient was then treated with intensity-modulated radiation therapy, and the supratentorial and infratentorial brain metastases were reduced.

History of past illness

No past illnesses were documented.

Personal and family history

The patient had no known comorbidities or family history and had a 30-year smoking history.

Physical examination

No abnormal indicators were observed on physical examination. His Eastern Cooperative Oncology Group performance status score was 2.

Laboratory examinations

Examinations of serum tumor markers showed that carcinoembryonic antigen, neuron-specific enolase, cytokeratin fragment antigen 21-1, progastrin-releasing peptide, and cancer antigen 125 were 1.96 µg/L (reference range: < 3 µg/L), 5.31 µg/L (reference range: < 12 µg/L), 0.75 ng/mL (reference range: < 4 ng/mL), 9.46 pg/mL (reference range: < 45 pg/mL), and 3.18 U/mL (reference range: < 30 U/mL), respectively.

Imaging examinations

On September 6, 2019, the patient underwent MRI. The long T1 and long T2 signals from nodules of various sizes were found in the supratentorial and infratentorial brain parenchyma, and the largest lesion was located in the left frontal lobe with a diameter of approximately 1.0 cm (Figure 1A). Small patchy and slightly longer T1 and slightly longer T2 signals were observed in bilateral paraventricles and bilateral basal ganglia. The sulcus was not widened and the ventricular system was not dilated.

Further diagnostic work-up

To determine potential therapeutic methods, the patient underwent genetic testing of 1021 cancer-related genes using peripheral blood (Geneplus-Beijing, Beijing, China) for the second time, and a somatic *ASXL1* mutation and the previous germline *BRCA2* mutation were identified (Table 1).

Table 1 Somatic mutation and germline mutation detected by next-generation sequencing

Somatic mutation				
Gene	Transcript	c.HGVS	p.HGVS	Allele frequency
<i>ASXL1</i>	NM_015338.5	c.2247C[4>3]	p.V751Lfs*21	0.6%
Germline mutation				
Gene	Transcript	c.HGVS	p.HGVS	Homozygous/heterozygous
<i>BRCA2</i>	NM_000059.3	c.6816_6820delAAGAG	p.G2274Afs*17	Heterozygous

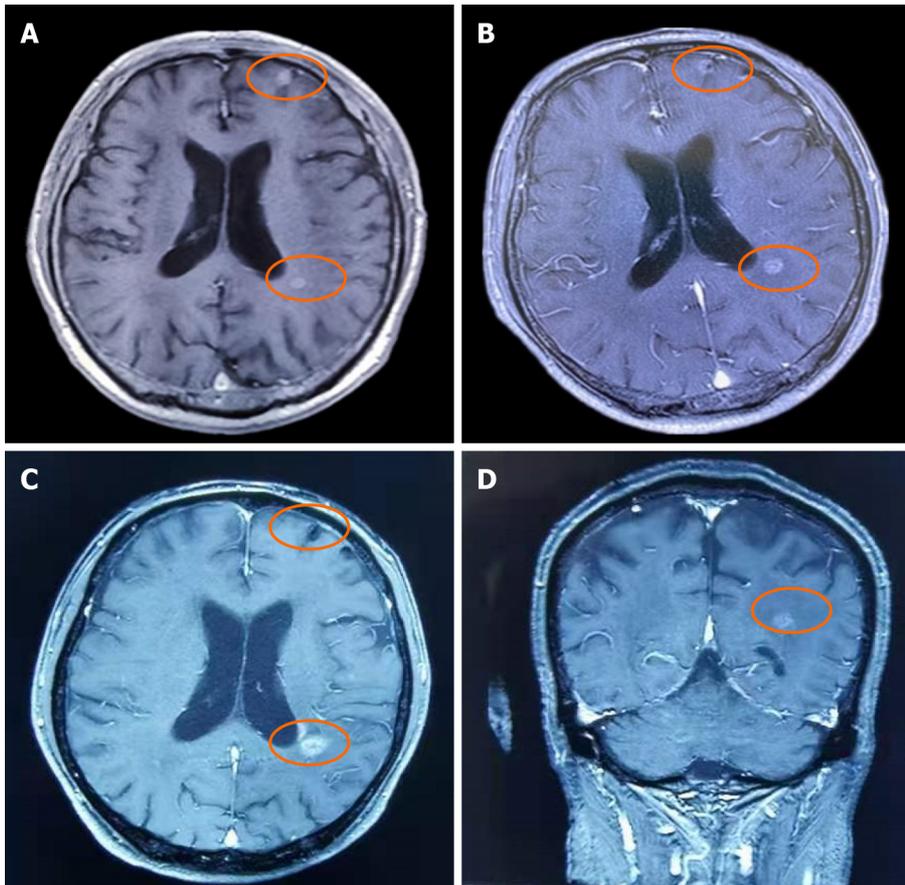


Figure 1 Changes in brain metastases after olaparib treatment. A: The lesion before olaparib treatment; B: At 7 mo after treatment; C: At 13.5 mo after treatment; D: At 13.5 mo after treatment.

FINAL DIAGNOSIS

A germline *BRCA2*-mutated right lung adenocarcinoma with focal squamous cell differentiation and multiple brain metastases.

TREATMENT

Since September 24, 2019, the patient has been receiving oral olaparib at a dosage of 300 mg twice daily, on the basis of maintenance therapy with gefitinib plus recombinant human endostatin.

OUTCOME AND FOLLOW-UP

In the course of treatment, the brain metastases were under control and maintained the

same size as 2 mo previously. At the end of March 2020, MRI showed a slight reduction of the left frontal lobe metastases, with the largest being approximately 0.8 cm in diameter. There was also a cavity in the middle of the metastases (Figure 1B). Furthermore, his Eastern Cooperative Oncology Group performance status score changed from 2 to 1. From April to May 2020, the patient was unable to purchase the drug due to the impact of the coronavirus disease 2019 outbreak and opted to be treated only with gefitinib. From June 2020, he was treated with oral olaparib and gefitinib plus recombinant human endostatin. In late August 2020, his brain metastases appeared to be enlarged; thus, temozolomide was added to the treatment regimen. In early November 2020, imaging revealed enlargement of bilateral cerebral hemisphere metastases and the appearance of new metastases. The largest lesion was located near the left posterior horn of the ventricle and was about 1.1 cm × 0.9 cm in size (Figure 1C and D), which was evaluated as progression, and PFS on olaparib combined with gefitinib and recombinant human endostatin was 13.5 mo. In addition, the patient's primary lung cancer has remained consistently well-controlled since diagnosis. No adverse events associated with the use of olaparib were observed.

DISCUSSION

Olaparib, a PARP inhibitor, has been proven to be effective in patients with *BRCA*-mutant breast, ovarian, prostate, and pancreatic cancers[5-7,11]. The STUdy19 trial showed that patients with *BRCA*-mutated ovarian cancer gained great benefit from olaparib[5]. Among patients with *HER2*-negative metastatic breast cancer and a germline *BRCA* mutation, olaparib monotherapy provided significant benefit over standard therapy[6]. Another study showed that of 16 prostate cancer patients with mutations in DNA damage repair genes, 14 (88%) had a response to olaparib, including all 7 patients with loss of DNA damage repair genes[7]. A study also confirmed that *BRCA2*-mutant lung cancer organoids responded to olaparib[10]. In the present report, the patient with an adenocarcinoma of the right lung harboring an *EGFR* exon 19 deletion mutation received olaparib plus gefitinib and recombinant human endostatin following progression after multiple lines of treatment, as NGS revealed a *BRCA2* germline mutation. Brain metastases in this refractory lung adenocarcinoma patient were successfully controlled.

In this study, the *BRCA2*-mutated lung adenocarcinoma patient benefited from olaparib combined with gefitinib and recombinant human endostatin with a relatively long survival following progression on multiple lines of treatment. One study found [12] that niraparib (a PARP inhibitor) combined with bevacizumab (an anti-angiogenic drug) significantly improved PFS compared with niraparib alone [median PFS 11.9 mo *vs* 5.5 mo; adjusted hazard ratio 0.35 (95% confidence interval: 0.21-0.57), *P* < 0.0001] for platinum-sensitive recurrent ovarian cancer, suggesting that PARP inhibitors combined with anti-angiogenic drugs may increase sensitivity to PARP inhibitors. In this study, the combination of olaparib and an anti-angiogenic drug also led to a good outcome. We observed that the patient had a cavity in the middle of the brain metastases after initiation of olaparib treatment. We suspected that the metastatic lesions were killed and the tumor tissue expelled, or insufficient neovascularization led to necrosis due to insufficient blood supply, resulting in cavitation. As this tumor cavity was formed after the use of olaparib, it may have been related to olaparib treatment, or the synergistic effect of olaparib and other drugs.

CONCLUSION

We present a lung adenocarcinoma patient with a *BRCA2* mutation who had long-lasting benefit following treatment with olaparib plus gefitinib and recombinant human endostatin. This case provides unequivocal clinical evidence for the off-label use of the PARP inhibitor olaparib in lung adenocarcinoma patients with *BRCA* mutations after disease progression.

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REFERENCES

- 1 **Roy R**, Chun J, Powell SN. BRCA1 and BRCA2: different roles in a common pathway of genome protection. *Nat Rev Cancer* 2011; **12**: 68-78 [PMID: [22193408](#) DOI: [10.1038/nrc3181](#)]
- 2 **Li D**, Kumaraswamy E, Harlan-Williams LM, Jensen RA. The role of BRCA1 and BRCA2 in prostate cancer. *Front Biosci (Landmark Ed)* 2013; **18**: 1445-1459 [PMID: [23747895](#) DOI: [10.2741/4191](#)]
- 3 **Rizzolo P**, Silvestri V, Tommasi S, Pinto R, Danza K, Falchetti M, Gulino M, Frati P, Ottini L. Male breast cancer: genetics, epigenetics, and ethical aspects. *Ann Oncol* 2013; **24** Suppl 8: viii75-viii82 [PMID: [24131976](#) DOI: [10.1093/annonc/mdt316](#)]
- 4 **Lee MN**, Tseng RC, Hsu HS, Chen JY, Tzao C, Ho WL, Wang YC. Epigenetic inactivation of the chromosomal stability control genes BRCA1, BRCA2, and XRCC5 in non-small cell lung cancer. *Clin Cancer Res* 2007; **13**: 832-838 [PMID: [17289874](#) DOI: [10.1158/1078-0432.CCR-05-2694](#)]
- 5 **Hodgson DR**, Dougherty BA, Lai Z, Fielding A, Grinsted L, Spencer S, O'Connor MJ, Ho TW, Robertson JD, Lanchbury JS, Timms KM, Gutin A, Orr M, Jones H, Gilks B, Womack C, Gourley C, Ledermann J, Barrett JC. Candidate biomarkers of PARP inhibitor sensitivity in ovarian cancer beyond the BRCA genes. *Br J Cancer* 2018; **119**: 1401-1409 [PMID: [30353044](#) DOI: [10.1038/s41416-018-0274-8](#)]
- 6 **Robson M**, Im SA, Senkus E, Xu B, Domchek SM, Masuda N, Delaloge S, Li W, Tung N, Armstrong A, Wu W, Goessl C, Runswick S, Conte P. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. *N Engl J Med* 2017; **377**: 523-533 [PMID: [28578601](#) DOI: [10.1056/NEJMoa1706450](#)]
- 7 **Mateo J**, Carreira S, Sandhu S, Miranda S, Mossop H, Perez-Lopez R, Nava Rodrigues D, Robinson D, Omlin A, Tunariu N, Boysen G, Porta N, Flohr P, Gillman A, Figueiredo I, Paulding C, Seed G, Jain S, Ralph C, Protheroe A, Hussain S, Jones R, Elliott T, McGovern U, Bianchini D, Goodall J, Zafeiriou Z, Williamson CT, Ferraldeschi R, Riisnaes R, Ebbs B, Fowler G, Roda D, Yuan W, Wu YM, Cao X, Brough R, Pemberton H, A'Hern R, Swain A, Kunju LP, Eeles R, Attard G, Lord CJ, Ashworth A, Rubin MA, Knudsen KE, Feng FY, Chinnaiyan AM, Hall E, de Bono JS. DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer. *N Engl J Med* 2015; **373**: 1697-1708 [PMID: [26510020](#) DOI: [10.1056/NEJMoa1506859](#)]
- 8 **Cocco E**, Scaltriti M, Drilon A. NTRK fusion-positive cancers and TRK inhibitor therapy. *Nat Rev Clin Oncol* 2018; **15**: 731-747 [PMID: [30333516](#) DOI: [10.1038/s41571-018-0113-0](#)]
- 9 **Jiang Y**, Dai H, Li Y, Yin J, Guo S, Lin SY, McGrail DJ. PARP inhibitors synergize with gemcitabine by potentiating DNA damage in non-small-cell lung cancer. *Int J Cancer* 2019; **144**: 1092-1103 [PMID: [30152517](#) DOI: [10.1002/ijc.31770](#)]
- 10 **Kim M**, Mun H, Sung CO, Cho EJ, Jeon HJ, Chun SM, Jung DJ, Shin TH, Jeong GS, Kim DK, Choi EK, Jeong SY, Taylor AM, Jain S, Meyerson M, Jang SJ. Patient-derived lung cancer organoids as *in vitro* cancer models for therapeutic screening. *Nat Commun* 2019; **10**: 3991 [PMID: [31488816](#) DOI: [10.1038/s41467-019-11867-6](#)]
- 11 **Tacconi EM**, Lai X, Folio C, Porru M, Zonderland G, Badie S, Michl J, Sechi I, Rogier M, Matía García V, Batra AS, Rueda OM, Bouwman P, Jonkers J, Ryan A, Reina-San-Martin B, Hui J, Tang N, Bruna A, Biroccio A, Tarsounas M. BRCA1 and BRCA2 tumor suppressors protect against endogenous acetaldehyde toxicity. *EMBO Mol Med* 2017; **9**: 1398-1414 [PMID: [28729482](#) DOI: [10.15252/emmm.201607446](#)]
- 12 **Mirza MR**, Ávall Lundqvist E, Birrer MJ, dePont Christensen R, Nyvang GB, Malander S, Anttila M, Werner TL, Lund B, Lindahl G, Hietanen S, Peen U, Dimoula M, Roed H, Ør Knudsen A, Staff S, Krog Vistisen A, Bjørge L, Mäenpää JU; AVANOVA investigators. Niraparib plus bevacizumab vs niraparib alone for platinum-sensitive recurrent ovarian cancer (NSGO-AVANOVA2/ENGOT-ov24): a randomised, phase 2, superiority trial. *Lancet Oncol* 2019; **20**: 1409-1419 [PMID: [31474354](#) DOI: [10.1016/S1470-2045\(19\)30515-7](#)]



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