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Prolonged treatment of neuroendocrine carcinoma of the cervix with a PARP inhibitor based on next generation sequencing

Neuroendocrine carcinomas of the cervix are rare cancers (0.9 % of cervical cancers) (Atienza-Amores et al., 2014) with patients presenting with more advanced stage, larger tumor size, and more frequent nodal metastasis and having a significantly poorer survival than squamous or adenocarcinomas of the cervix (Chen et al., 2008). Because of the rarity there are no prospective trials and treatment is often modeled after the more common neuroendocrine small cell carcinoma of the lung. We previously reported a 58 year old patient with stage IVB disease that failed to respond to carboplatin and etoposide who was identified as having a BRCA 2 somatic mutation with Foundation One next generation sequencing. At the time of the original publication the patient had received 15 months of rucaparib therapy with stable disease. The editors requested follow-up of this patient.

Since the original publication the patient now 64 years of age has continued to receive rucaparib continuously with imaging every 3–6 months. She has now completed 74 months of therapy with completely stable disease and a performance status of 0. She does have chronic back and leg pain related to thoracic and lumbar degenerative disc disease and is treated with acetaminophen. During this time she has been working as a full time nurse and studying to be a nurse practitioner.

At the time of the original publication the use of molecular based treatment for clinical therapy was only in its infancy. Since that time the NCI match trial (molecular analysis for therapeutic choice) provided drugs for patients with biomarker expressing tumors. Since the original publication of our paper the NCI match trial has concluded and it's results have been published (O'Dwyer et al., 2023). It is important to remember that this trial was only open to patients who had failed conventional therapy or rare cancers for which there is no standard treatment. This demonstrated that while only a small percentage of patients were screened were eligible. In the case of neuroendocrine tumors 3.3 % and in the case of cervical cancers 1.6 %. Seven of the 28 arms reported to date demonstrated significant response rates varying from 14 to 50 %, with 6-month progression-free survivals of 25–68 %.

Small cell carcinoma of the cervix is a very deadly disease with mortality rates of 91 % at 3 years. Next Generation Sequencing has demonstrated recurrent somatic mutations involving MAPK, P13K/AKT/mTOR and TP53/BRCA pathways in small cell neuroendocrine carcinoma of the cervix (Xing et al., 2018). Therefore, we undertook Next Generation Sequencing of this patient's tumor which demonstrated mutation in BRCA 2 for which there were clinically available therapeutic options namely the PARP inhibitors; niraparib, rucaparib and olaparib. Genetic testing was negative for a germ-line mutation confirming our patient had a somatic mutation. No other studies utilizing target directed therapy against the BRCA mutation have been previously reported in small cell carcinoma of the cervix. The patient reported in this case report has stable disease and is progression-free at 74 months. Stable disease is quite remarkable in a disease which has such a very high mortality.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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