WAGO 2025 ANNUAL MEETING
ORAL ABSTRACT

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Treatment Outcomes with Ipilimumab and Nivolumab Combination in Recurrent Neuroendocrine Cervical Cancer: a Neuroendocrine Cervical Tumor Registry (NeCTuR) study

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Objectives
Neuroendocrine carcinomas of the cervix (NECC) are rare and aggressive. Given limited effective treatment options and no established standard of care in the recurrent setting, treatments for small cell lung cancer are often utilized given their histologic similarity. Published case reports highlight prolonged or complete responses to ipilimumab and nivolumab (ipi/nivo) in NECC, however these may be subject to publication bias. The purpose of this study was to evaluate treatment outcomes with ipi/nivo in a larger series of patients with recurrent NECC.

Methods
A retrospective analysis from the NeCTuR Cervical Tumor Registry of all patients with recurrent NECC treated with a combination of ipi/nivo was performed. The primary outcome was overall response rate (ORR). Overall Survival (OS) and treatment-related toxicities were assessed as secondary outcomes.

Results
Twelve patients were included. Median age at diagnosis was 37 years. Eight patients (66.6%) had advanced stage (III-IV) disease at diagnosis. All patients received 1mg/kg of ipilimumab and 3mg/kg of nivolumab, but schedules varied. Ipi/nivo was used after a median of 2 (range 1-7) prior lines of systemic therapy with 16.7% receiving prior immunotherapy. Mismatch repair testing was performed in four tumors and all were proficient (pMMR) with low tumor mutational burden (< 10 mutations/Mb). PD-L1 was positive (Combined Positive Score (CPS) >1) in 60% (3/5 tumors). The ORR was 16.7% (2/12 patients), with one current complete response (CR) after 26 months follow up, and one partial response (PR) still on therapy at 6 months. The patient with the CR had a pMMR, PDL-1 positive tumor with prior exposure to immunotherapy. The patient with a PR had a PD-L1 negative tumor. The median OS was 6 months (IQR 3-27 months). Eleven patients were evaluable for toxicity and of these, 10/11 (90.9%) had grade 1 or 2 toxicity and 1/11 (9.1%) had a grade 3 toxicity (see table).

Conclusions
Although in the largest retrospective series to date, the ORR with ipi/nivo was modest at 16.7%, it is similar to response rates for established therapies commonly used for recurrent disease in other cancers. Importantly, the observed responses were profound and durable, and seen in PD-L1 positive and negative tumors, and in those with prior immunotherapy. As numbers remain small, further data is needed.

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