Immunotherapy in combination points to paradigm shift in the treatment of cervical cancer

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Ana Oaknin, Principal Investigator of VHIO's Gynecological Malignancies Group. Credit: VHIO

With an estimated 570,000 cases and 311,000 deaths in 2018 worldwide,

cervical cancer currently ranks as the fourth most frequently diagnosed cancer and the fourth leading cause of cancer death in women. Furthermore, patients suffering from recurrent and metastatic disease face a dismal prognosis with few therapeutic options available. The need to identify and develop more effective treatment opportunities against this tumor type is therefore critical.

Set to first-outing during a Proffered Paper Session on Gynecological Cancers, interim results from a combination cohort study of the phase I/II investigational immune-therapy trial to assess the safety and effectiveness of nivolumab, and nivolumab in combination against virus-associated tumors -Checkmate 358- signpost next steps towards doing just that.

Presented by first author Ana Oaknin, Principal Investigator of VHIO's Gynecological Malignancies Group, and Chair of the ESMO Congress 2019's Gynecological Cancer Track, this cohort paired nivolumab with ipilimumab for the treatment of patients with recurrent or metastatic cervical cancer, with or without prior systematic therapies, and irrespective of PD-L1 expression.

"Importantly, the only treatment option for these patients in the second line setting is pembrolizumab. This immune-based therapy hones in on and blocks the PD-L1 protein found on the surface of T-Cells. Only those individuals whose tumors express PD-L1 are eligible to receive this treatment," said Ana Oaknin.

She continued, "In order to explore novel treatment avenues and thus provide fresh hope for all of our patients, Checkmate 358 has been designed to tackle virus-associated cancers, irrespective of PD-L1 expression status."

Patients who had received prior previous systemic therapy or not were

randomized to either combination A, receiving nivolumab plus ipilimumab, or B, with this same combination followed by subsequent therapy with nivolumab. While results showed clinical benefit in both combinations, the objective response rate (ORR) was significantly higher in B, particularly in those patients who had not received prior therapy (46% vs 32%).

Median overall survival (OS) with current first-line standard of care is around 17 months. While median OS has not yet been reached with this novel immunotherapy combination, strikingly, among those patients who received regimen B after failing to respond to platinum-based therapy, OS is 25 months.

For patients receiving the nivolumab and ipilimumab combination without previous treatments for metastatic disease, OS rate was 83% vs 38% for those who had.

"Not only do these results reflect the increasing promise of immunotherapeutics administered in combination, they also show improved efficacy for those patients who have very few therapeutic options available. As importantly, results were particularly encouraging in chemotherapy-naïve patients. Our results therefore represent a crucial forward step towards a new standard of care, warranting further investigation in an extended population," concluded Ana.

These present findings also confirm the promise of nivolumab recently reported by the study's monotherapy cohort. Co-authored by Ana Oaknin, results published in the *Journal of Clinical Oncology* evidenced the safety and efficacy of treating patients with recurrent and metastatic cervical, vaginal or vulvar virus-associated cancers with nivolumab alone.

More information: LBA62 - Efficacy and safety of nivolumab (Nivo)

+ ipilimumab (Ipi) in patients (pts) with recurrent/metastatic (R/M) cervical cancer: Results from CheckMate 358.

R. Wendel Naumann et al. Safety and Efficacy of Nivolumab Monotherapy in Recurrent or Metastatic Cervical, Vaginal, or Vulvar Carcinoma: Results From the Phase I/II CheckMate 358 Trial, *Journal of Clinical Oncology* (2019). DOI: 10.1200/JCO.19.00739