



## Looking for New Strategies for Gynecological Cancer

**Margarita S Alfie<sup>1</sup> and Adrian P Hunis<sup>2\*</sup>**

<sup>1</sup>*Argentine Institute of Diagnosis and Treatment (IADT), Member of ASCO, Member of ESMO, Argentina*

<sup>2</sup>*School of Medicine, Universidad de Buenos Aires (UBA), Emeritus Member of ASCO, Argentina*

**\*Corresponding Author:** Adrian P Hunis, School of Medicine, Universidad de Buenos Aires (UBA), Emeritus Member of ASCO, Argentina.

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In order to achieve better results in survival, new strategies try to cover that need not meet in gynecological cancers.

At the ASCO Annual Meeting several works for ovarian cancer will be presented.

The Surgical treatment without residual disease is associated with better survival and prognosis. Additional strategies to achieve complete response were evaluated in the abstracts session.

Folate receptor  $\alpha$  is overexpressed in a number of solid tumours, such as ovarian.

Pafolacianine sodium is a fluorescent marker made of near-infrared dye and a ligand that allows it to bind to receptors overexpressed in ovarian cancer cells. When injected, the agent binds to folate receptors and will illuminate when used under near-infrared light. This mechanism of action allows for greater confidence that surgery resulted in a complete resection. Pafolacianine sodium injection is injected as a single-dose intravenous infusion prior to surgery.

The use of pafolacianine sodium injection in combination with intraoperative near-infrared fluorescence imaging to detect additional lesions not detected by palpation and normal white light alone, were the objective of study and met its primary endpoint, intraoperatively identifying additional cancer not planned for resection in a statistically significant number of patients [1].

The Peritoneal Cancer Index is a Strong Predictor of Incomplete Cytoreductive Surgery in Ovarian Cancer and the use of this

index allows defining when it's necessary neoadjuvant treatment. In patients with initially unresectable stage IIIC/IV ovarian, tubal or peritoneal high-grade serous carcinoma with median Peritoneal Cancer Index at 24 (range 7-39) it was used Pembrolizumab adding to neoadjuvant carboplatin-paclitaxel chemotherapy. The combination with immunotherapy increase the optimal debulking rate, assessed by Complete Resection Rate after Interval Debulking Surgery [2].

What it's the optimal duration of maintenance bevacizumab with primary epithelial ovarian (fallopian tube or peritoneal cancer)?

GOG-0218 established the addition of BEV 15 mg/kg every 3 weeks for 15 months to standard front-line chemotherapy for advanced ovarian cancer. In the phase 3 ENGOT/GCIG trial showed that the use of 30 months Bevacizumab is not better than 15 months, neither improved PFS and OS [3].

In patients with platinum agnostic recurrent ovarian cancer, the use of the antibody-drug conjugate mirvetuximab soravtansine, given with bevacizumab showed durable responses mainly in patients with strong expression of folate receptor alpha.

What is platinum agnostic ovarian cancer? as patients either platinum resistant or platinum with sensitive disease for whom a non-platinum based doublet would be appropriate [4].

New treatment options are being tested in patients with resistance to PARP inhibitors: Adavosertib, the Wee1 Inhibitor; it was tested with or without Olaparib: it showed objectives responses

but the toxicity grade 3/4 caused in some cases the reduction of dose or suspension of the treatment. Additional analyses are ongoing to clarify clinical benefit [5].

Unfortunately we had little news for cervix cancer treatment.

The OUTBACK trial was described in the Plenary Session.

The objective of the study was to evaluate the benefit of adjuvant treatment in patients with locally advanced cervical cancer after chemoradiation.

The administration of 4 cycles of carboplatin and paclitaxel after standard cisplatin-based chemoradiation showed no benefit in OS and PFS in women with locally advanced cervical cancer (FIGO 2018 EIB1-2, EII, EIIIB y EIVA) [6].

### What's news about endometrial cancer?

The TOTEM study was presented in which intensive versus minimalist follow-up is compared in patients with endometrial cancer. The main objective was to demonstrate OS benefit. The intensive exam showed advantage in detecting earlier asymptomatic relapses but did not improve OS [7].

The Pi3K-Akt-mTOR signaling pathway is a possible target of treatment. Vistusertib is a small-molecule ATP competitive inhibitor of both mTORC1 and mTORC2 complexes. The combination with anastrozole showed in phase 1/2 Victoria study in patients with recurrent oestrogen or progesterone (ER and/or PR) positive advanced/metastatic endometrial carcinoma clinical benefits. More studies are needed to define its usefulness [8].

Finally, results in a cohort of Uterine Cancer patients with ERBB2 or ERBB3 amplification, overexpression or mutation treated with Pertuzumab +Trastuzumab was reported from the Targeted Agent and Profiling Utilization Registry (TAPUR) study, showing antitumor activity in this study population [9].

### Gynecological cancers

#### Continues seeking new therapeutic strategies

- Neoadjuvant immunotherapy in ovarian cancer
- Pafolacianina binds to overexpress folate receptors identifying more lesion to achieve complete response
- Mirvetuximab soravtansine with bevacizumab in platinum agnostic recurrent ovarian cancer

- Adavosertib, the Wee1 Inhibitor, it was tested with or without Olaparib in patients with resistance to PARP inhibitors
- Vistusertib is inhibitor of both mTORC1 and mTORC2 complexes, with anastrozole in recurrent endometrial cancer.

### Take Home Point

#### Continue reaffirming

- Maintenance treatment for 15 cycles with bevacizumab in ovarian cancer
- The intensive exam did not improve OS in endometrial cancer
- The administration of 4 cycles of carboplatin and paclitaxel after standard cisplatin-based chemoradiation showed no benefit in OS and PFS in women with locally advanced cervical cancer.

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