2022-RA-1546-ESGO POTENTIAL APPROACH TO OVERCOME CHECKPOINT INHIBITOR RESISTANCE IN A LONG-TERM SURVIVOR PATIENT WITH RECURRENT ENDOMETRIAL CARCINOMA

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10.1136/ijgc-2022-ESGO.339

Introduction/Background The adjuvant treatment of endometrial carcinoma is constantly evolving. The introduction of checkpoint inhibitors in the therapy of recurrent endometrial carcinoma marked a milestone in the clinical outcome. Nevertheless, there is a need to develop possible treatment strategies to overcome a checkpoint inhibitor resistance.

Methodology

Results We present a case of 79-year-old patient diagnosed with endometrioid endometrial carcinoma in 2010. Laparoscopically assisted vaginal hysterectomy with salpingo-oophorectomy and systematic pelvic and paraaortic lymphadenectomy was performed, and the carcinoma was classified as pT1b G2 R0 L0 V0 FIGO IB. Two years later a vaginal stump recurrence was resected, macroscopically tumor free. Five years after initial diagnosis, the patient presented with pulmonary metastasis. Chemotherapy was started with weekly paclitaxel and carboplatin for twelve cycles. Moreover, the patient underwent combined radio-chemotherapy in June 2016. Six months later the patient was first diagnosed with cerebral metastasis, stereotactic radiation was followed by MPA for 10 months. In November 2017 due to the third local recurrence, a laparotomy with resection of the tumor from the pelvic wall and the iliac vessels was performed and letrozol therapy was initiated until January 2020. A pathological examination confirmed an EEC – p53 wt, hormone receptor positive and a microsatellite instability with loss of PMS2 and MLH1. In 2020 the patient presented infiltration of the bladder. Immunotherapy with checkpoint inhibitor was initiated but the tumor showed image morphological progression after 9 months. Due to the progression the addition of lenvatinib was recommended. Under this combination therapy the tumor showed a stable disease ever since in total of 21 months and with some lesions to partial response.

Conclusion The combination of checkpoint inhibitor and a tyrosine kinase inhibitor is a potential approach to overcome checkpoint inhibitor resistance. Further clinical trials are warranted.

2022-RA-1547-ESGO PRIMARY LEIOMYOSARCOMA OF FEMALE GENITAL TRACT: SALAH AZAIEZ INSTITUTE EXPERIENCE

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10.1136/ijgc-2022-ESGO.340

Introduction/Background Leiomyosarcomas of the gynecological tract (LMS) are heterogeneous group of mesenchymal gynecological cancers with unspecific but dismal prognosis since they generally spread even in early stages.

Methodology We conducted a retrospective study of all female with LMS treated at our institution during the previous 22 years. Clinicopathological information, therapies, and results were all documented.

Results Data were collected from 16 women. The median age at diagnosis was 51 years old (31–77 yo). 50% of patients were menopausal. Bleeding was the most common symptom, followed by pelvic discomfort. Ten patients had uterine leiomyosarcoma, three had cervix leiomyosarcoma, and three had vaginal leiomyosarcoma. The average size of the tumor was 6.4 cm (3–10 cm). There were no evidence of distant metastasis in all patients. As an initial treatment, fifteen patients had surgery, while one patient received extemal beam radiation followed by brachytherapy. Adjuvant chemotherapy was administered to four patients, while adjuvant radiation was administered to seven. Six patients were diagnosed with LMS grade 1, three with grade 2, and seven with grade 3. The average duration of follow-up was 61 months. Full remission was obtained in nine cases while five suffered from a progressive disease course and two had locoregional recurrence. Seven patients died.

Conclusion The relative rarity of LMS, as well as its clinical variety, inhibit studies aiming at improving understanding of the disease and makes establishing the best therapy challenging.

2022-RA-1550-ESGO THERAPEUTIC EFFECT OF T-CELL-DERIVED NANOVESICLES IN ENDOMETRIAL CANCER

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10.1136/ijgc-2022-ESGO.341

Introduction/Background T cell therapy, including adoptive T cell transfer and immune checkpoint blockades, is a remarkable advance in cancer immunotherapy, but its therapeutic effect on solid tumors is limited. A main cause of the low efficacy is T-cell exhaustion by immunosuppressive mechanisms of solid tumors, which are mainly mediated by PD-L1. To address some of the challenges faced by the current cancer mmunotherapy, we developed human T-cell-derived nanovesicles using a perfusable vascular network hydrogel with culturing patient tissues.

Methodology Human T-cell-derived nanovesicles produced by the serial extrusion of human cytotoxic T cells through membranes with nanosized pores that inhibit T-cell exhaustion and exhibit antitumoral activity maintained in the immunosuppressive tumor microenvironment are presented.

Results Similar to cytotoxic T cells, human T-cell-derived nanovesicles can be targeted at tumors via T-cell-membrane-originated proteins and kill cancer cells by releasing anticancer molecules such as granzyme B. Unlike cytotoxic T cells, human T-cell-derived nanovesicles are resistant to immunosuppressive molecules (e.g. PD-L1) of cancer cells by scavenging PD-L1, thereby preventing cytotoxic-T-cell exhaustion. Human T-cell-derived nanovesicles successfully inhibit tumor growth in a 3D human endometrial cancer chip using a perfusable vascular network hydrogel with culturing the same patients' tissues. Indeed, human T-cell-derived nanovesicles exhibit higher therapeutic efficacy than an immune checkpoint blockade in endometrial treatment.

Conclusion We propose to present these aspects of the human T-cell-derived nanovesicle to eventually improve the current cancer immunotherapy strategy and overcome the tumor's immunosuppressive mechanisms.

Int J Gynecol Cancer: first published as 10.1136/ijgc-2022-ESGO.341 on 20 October 2022. Downloaded from http://ijgc.bmj.com/ on April 23, 2024 by guest. Protected by copyright.