



# Getting *serious* about serous endometrial cancer: should we give chemotherapy in non-invasive cases?

Jennifer Mueller, Vicky Makker

Memorial Sloan Kettering  
Cancer Center, New York, New  
York, USA

## Correspondence to

Dr Vicky Makker, Memorial  
Sloan Kettering Cancer Center,  
New York, NY 10065, USA;  
makkerv@mskcc.org

Received 24 June 2020

Accepted 26 June 2020

Serous cancers are an uncommon sub-type of endometrial cancer. While they account for only 10% of newly diagnosed endometrial carcinomas, they comprise more than one-third of recurrences and 40% of endometrial cancer-related deaths.<sup>1</sup> Five-year survival rates for early- and advanced-stage serous carcinomas are 75% and 37%, respectively, compared with 86% ( $p < 0.001$ ) and 54% ( $p < 0.001$ ), respectively, for grade 3 endometrioid carcinomas.<sup>2</sup> Currently, there is no consensus regarding the optimal treatment of this rare, aggressive, and understudied uterine cancer entity.

The Cancer Genome Atlas performed comprehensive molecular profiling of 373 endometrial cancers, including serous carcinomas. The serous and serous-like tumors clustered to the 'copy number high' sub-group. Compared with endometrial tumors of the other molecular sub-groups, these tumors are defined by genomic instability, low mutational burden, frequent p53 alterations (90%), HER2 overexpression (16%–60%), and unfavorable survival outcomes. Many patients with serous endometrial carcinoma (40%–60%) will have extra-uterine metastases, even when their disease appears confined to a polyp or the endometrium.<sup>3,4</sup> As such, comprehensive surgical staging (including lymph node assessment) is a cornerstone of care. Prospective studies have examined the role of adjuvant treatment in early-stage, high-risk endometrial cancer (Gynecologic Oncology Group (GOG) 249 and 258), but <20% of the cancers in these studies were serous. Retrospective studies have contained small numbers of patients, limiting our ability to draw conclusions or generalize key findings regarding optimal practice for serous cancers.

In this issue of the *International Journal of Gynecologic Cancer*, Nasioudis and colleagues leverage the power of the US National Cancer Data Base (NCDB) to examine a cohort of more than 1700 patients with surgically staged, non-invasive serous endometrial carcinoma and evaluate the impact of adjuvant treatment (chemotherapy and/or radiotherapy) on survival.<sup>5</sup>

This study is notable for its large number of patients, lending greater statistical power to examine outcome differences in this well-defined group. The median lymph node counts were high (19), and nearly 80% of cases included a para-aortic node dissection, which suggests patients were well staged. The median follow-up approached 5 years (58 months) and nearly half of the patients were observed after surgery, which strengthens the outcomes analysis. The authors' major finding was a significant 5-year overall survival benefit for patients given chemotherapy (with or without radiotherapy) compared with no chemotherapy. This was not true for patients treated with radiation alone versus observation. No survival advantage was shown after adjusting for confounders such as age, insurance status, tumor size, comorbidities, and personal cancer history.

The results of the study suggest that patients with non-invasive serous endometrial cancer may benefit from chemotherapy but not radiotherapy. The authors have provided a well-written and appropriate critique of NCDB studies, reminding us to view their results in this context. We cannot assess the quality of surgical staging or adjuvant therapy, confirm the pathologic diagnosis, retrieve missing data, or determine progression-free and cancer-specific survival from NCDB data.

We believe the results of this study are of great interest to those in our field and should be incorporated into patient–provider discussions when considering treatment. We strongly agree with the authors' statement that we do not yet have sufficient data to uniformly recommend chemotherapy for stage I non-invasive serous endometrial cancer. We agree it is best practice to discuss chemotherapy and tailor its use after a thorough discussion between patient and provider, weighing the potential benefits of treatment against the side effects and detrimental impact to quality of life of cytotoxic therapy. In order to advocate a widespread change in practice and uniformly recommend chemotherapy in non-invasive serous endometrial cancer, we believe further prospective data are



© IGCS and ESGO 2020. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** Mueller J, Makker V. *Int J Gynecol Cancer* Published Online First: [please include Day Month Year]. doi:10.1136/ijgc-2020-001796

## Editorial

needed. The ENGOT/EN2 trial (<https://clinicaltrials.gov/ct2/show/NCT01244789>) is a prospective randomized trial examining the use of vaginal brachytherapy with and without chemotherapy in the treatment of high-risk, early-stage endometrial cancer (including serous cancers), and we eagerly await the results of this trial.

**Contributors** The authors contributed equally in writing and approving the editorial.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Provenance and peer review** Commissioned; internally peer reviewed.

## REFERENCES

- 1 Hamilton CA, Cheung MK, Osann K, *et al.* Uterine papillary serous and clear cell carcinomas predict for poorer survival compared to grade 3 endometrioid corpus cancers. *Br J Cancer* 2006;94:642–6.
- 2 McGunigal M, Liu J, Kalir T, *et al.* Survival differences among uterine papillary serous, clear cell and grade 3 endometrioid adenocarcinoma endometrial cancers: a National Cancer Database analysis. *Int J Gynecol Cancer* 2017;27:85–92.
- 3 Cancer Genome Atlas Research Network, Kandoth C, Schultz N, *et al.* Integrated genomic characterization of endometrial carcinoma. *Nature* 2013;497:67–73.
- 4 Boruta DM, Gehrig PA, Fader AN, *et al.* Management of women with uterine papillary serous cancer: a Society of Gynecologic Oncology (SGO) review. *Gynecol Oncol* 2009;115:142–53.
- 5 Nasioudis D, Roy A, EM K, *et al.* Adjuvant treatment for patients with FIGO stage I uterine serous carcinoma confined to the endometrium. *Int J Gynecol Cancer* 2020.