Prof Andreas Obermair

gynaecological oncology news

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Welcome

Happy Easter everyone! I hope you were able to take a few days off as it is important to recharge the batteries from time to time so that we can provide the highest level of service to our patients.

As always, I am keen to share emerging new treatments of gynaecological cancer with you. Knowledge and evidence should form the basis for the many important treatment recommendations we offer to our patients.

KELIM is a new way to determine if ovarian cancer patients have had a sufficient response to neoadjuvant chemotherapy, which makes them suitable for interval surgical cytoreduction surgery.

I will also introduce you to a new treatment algorithm in **cervical cancer** and how it could help to avoid poor surgical treatment decisions.

Finally, I will answer a question that I get asked by a growing number of patients: **"How urgent is my surgery?"**

I hope you will enjoy our gynaecological cancer update. As always, please feel free to be in touch if my practice can help with anything gynaecological cancer related.

Andreas Obermair

Please don't hesitate to give me a call if you wish to discuss any aspect of the enclosed or a specific patient with me.

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Predicting response to treatment for ovarian cancer – The KELIM CA125 score

Patients with advanced ovarian cancer will benefit from neoadjuvant (upfront) chemotherapy but sometimes it can be tricky to decide who responds well to chemo and should be offered surgery; and who doesn't.

Three of four patients with ovarian cancer present at advanced stages III or IV and those patients benefit from neoadjuvant chemotherapy over 3 cycles. The likelihood of responding to chemotherapy is around 85% overall. Following chemo, patients will benefit from interval cytoreductive surgery only if they respond well to neoadjuvant chemo; but if they don't respond well, they should not have surgery. Therefore assessment of response is important to make good clinical decisions.

If we falsely declare a patient did not respond to chemo, our patient will not get the chance of potentially lifesaving surgery.

If we falsely assume a patient had a good response to chemo but at laparotomy we find too much disease (incorrect information from PET CT and CA125), our patient will have an unnecessary laparotomy.

A novel and promising approach to determine the response to neoadjuvant chemo is to assess the CA125 elimination rate K (**KELIM**). We basically check if a patient dropped her CA125 by at least 1 log, equalling to a more than 90% CA125 drop since the start of chemo.

KELIM is increasingly used globally, but we need to have at least two CA125 values: one at baseline and one for assessment after neoadjuvant chemotherapy.

For example, if a patient with stage III ovarian cancer had a CA125 at diagnosis of 3000U/ml and after 3 cycles of chemo her CA125 dropped to 100U/ml, this indicates a > 90% drop in CA125, which is a marvellous response to chemo. Pending the PET CT findings, she will likely benefit from interval cytoreductive surgery.

By contrast, if the same patient had a CA125 drop to only 1500U/ml, I would be very suspicious that she has had a suboptimal response to neoadjuvant chemo. The chance that the PET CT shows significant residual disease is high. The patient will likely not benefit from a laparotomy and debulking surgery.

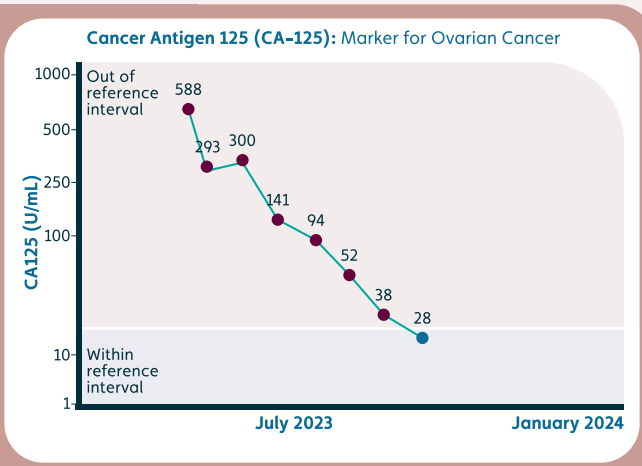
In a retrospective study from the United States enrolling 217 patients with Stage III-IV high grade serous ovarian cancer, a low KELIM CA125 response was linked to worse outcomes, including shorter survival and higher risk of disease progression. Patients with a great KELIM CA125 response had an increased progression-free survival by 6 months, double the platinum-free interval (13 months vs 7.6 months) and a 15% higher 5-year overall survival.

Importantly, KELIM suggests that the rate of decline in CA125 during treatment is more important than the actual level of the marker. This indicates the KELIM score could help identify patients who may not benefit from standard treatment and could benefit from alternative therapies.

In a recent review of seven studies with more than 12,000 patients combined (including six randomized clinical trials, a meta-analysis database and a national cancer registry), the results consistently showed that the CA125 elimination rate is a predictor of the chances of successful interval cytoreductive surgery, the platinum-free interval (the time between the completion of platinum-based chemotherapy and the recurrence of ovarian cancer), and overall survival. It also provides insights into how effective certain maintenance treatments are.

In my practice I have recently started using this new score calculated during neoadjuvant chemotherapy to provide an indication whether debulking surgery is likely beneficial to the patient or not.

** Sourced from https://pubmed.ncbi.nlm.nih.gov/37191644/*



This is a CA125 graph of a patient with stage IV ovarian cancer. Her initial CA125 was 588U/ml. After 3 cycles of chemo, her CA125 fell to only 141U/ml, which I felt was insufficient. Ideally, it would have been below 58 to make her a great candidate for interval surgical cytoreduction.

Together with the medical oncologist, we decided to continue with chemo, after several more cycles of chemo, her CA125 dropped to 28U/ml.

She had interval cytoreduction without any residual tumour left behind. Great outcome – at least in the short term!

Can aspirin help reduce risk of developing ovarian cancer?

The potential role of aspirin in preventing ovarian cancer is an area of intense, ongoing research. Strong evidence indicates that regular and frequent use of aspirin, particularly on a daily or near-daily basis, may have a protective effect against the occurrence of ovarian cancer.

In a recent study in **JAMA Network Open,** researchers aimed to investigate if taking aspirin frequently can reduce the risk of ovarian cancer, and if this effect is influenced by a person's genetic makeup.

The researchers combined information from eight different studies conducted in the US, UK and Australia combining 4,476 ovarian cancer patients and looked at how often people took aspirin and their genetic information. Frequent use of aspirin was defined across the studies as daily or most days of the week for six months or longer. They then used this information to see if there was a connection between taking aspirin frequently and the risk of developing ovarian cancer, and if this connection was influenced by a person's genes.

The researchers found that taking aspirin regularly lowered the risk of ovarian cancer by 13%. This was found for most types of ovarian cancer, including the more aggressive subtypes. The researchers also found that a person's genes do not seem to affect the protective effect of aspirin.

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Aspirin and its use after diagnosis

I was a Chief Investigator in the Ovarian cancer Prognosis And Lifestyle (OPAL) study, and part of its findings have been recently published in the **Journal of The National Cancer Institute.** The study aimed to see if nonsteroidal anti-inflammatory drugs (NSAIDS), such as aspirin, have any influence on the recurrence of ovarian cancer disease and overall patient survival. The study included more than 900 Australian women diagnosed with ovarian cancer from 2012 to 2015. We asked them how often they used NSAIDs. Participants were followed for up to five years postdiagnosis.

In our study frequent use (defined as 4 days per week or more) of NSAIDs, including aspirin, after a diagnosis of ovarian cancer was associated with improved survival, particularly in women with stage III or IV disease. The findings suggest an average additional survival of 2.5 months during the five years following diagnosis. While this may not seem substantial, it holds significance in the context of ovarian cancer. About 75% of patients are detected in advanced stages with limited treatment options, making any extension in survival noteworthy.

While these results sound promising, introducing aspirin is not straight forward. Aspirin, like any medication, comes with potential risks, including gastrointestinal bleeding and haemorrhagic stroke. These risks need to be carefully weighed against the potential benefits when considering aspirin for cancer prevention. Future studies should determine specifically the benefits and harms of aspirin maintenance treatment.

I often recommend low-dose aspirin after any gynaecological cancer type if patients tolerate it well. It is cheap, mostly well tolerated and an increasing number of studies detect a survival benefit.

"How urgent is my surgery?"

At the end of 2023 I was looking after some patients without private health insurance who were keen to expedite their treatment. "How urgent is my surgery?" is a very reasonable question that patients in those situations ask.

- Surgery for low-grade endometrial cancer is less urgent than high-grade endometrial cancer (clear cell cancers, uterine serous cancers, malignant mixed Mullerian tumours/MMMT) or uterine sarcomas, which should be performed as soon as possible.
- Treatment for biopsy-confirmed cervical cancer should also be considered urgent.
- Initial treatment for advanced ovarian cancer (ascites, omental caking) is urgent.
- Treatment for vulvar cancer that is biopsy-proven should be expedited because otherwise the risk of spread increases.

Less urgent conditions include the majority of ovarian cysts as well as precancerous lesions on the cervix (CIN) and the vulva (VIN).

Cervical cancer – change in surgical management

Two key changes in cervical cancer surgery will be adopted in Australia in 2024

Evidence on novel surgical approaches has been published recently and will have significant impact on patient's surgical recovery and long-term wellbeing. These changes will come into effect in Australia this year.

The first change is that selected patients diagnosed with cervical cancer will no longer require a radical hysterectomy (with a parametrial margin) but they are well treated with a simple, standard hysterectomy.

The SHAPE trial: Based on a recent study (SHAPE), which was presented for the first time at conferences in 2023, I decided to change the clinical decision making in surgical treatment of cervical cancer. The SHAPE trial was led by my colleague Marie Plante from Quebec in Canada. She was wondering if, for certain patients with cervical cancer, a standard hysterectomy would be sufficient and patients could be spared a radical hysterectomy and its adverse effects (bladder dysfunction, sexual quality of life). This international group of researchers found that patients with small tumours and superficial tumour invasion into the cervix (based on MRI) had the same survival outcomes when they were given a radical or a standard hysterectomy. These patients still need to have their lymph nodes checked.

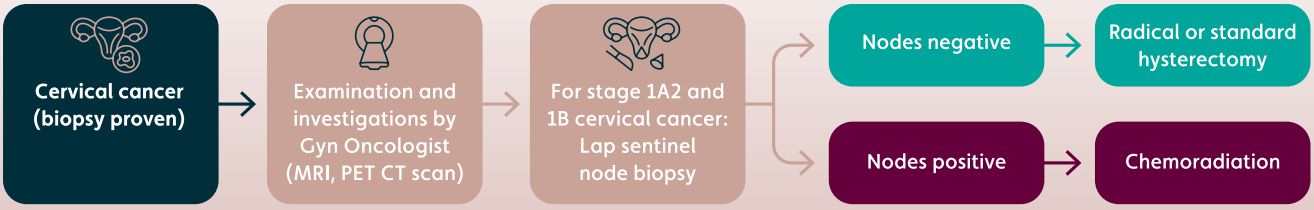
The challenge of this trial is that these results only apply to a very specific group of patients and not all patients with cervical cancer: it applies to only those with tumours less than 2 cm and superficial invasion into the cervix. If these specifics are misunderstood and patients uncritically receive a standard hysterectomy (instead of a radical hysterectomy), it could be risky for patients.

What I learned from this: Patients with small and innocuous cervical cancers that formally just had to be regarded as stage 1B, can expect great survival outcomes with less radical surgery. Patients will definitely continue to benefit from gynaecological oncology input.

The second change is about the risk of pelvic lymph node metastasis. We routinely perform PET CT scans for patients with cervical cancer prior to surgery. However, PET CT comes at a risk of false negative findings in up to 15% of patients. For that reasons **Sentinel Node Biopsy,** that only removes 1 or 2 nodes on each side, has been established for the treatment of cervical cancer only last year. The procedure is done laparoscopically with near-infrared technology and ICG and in my practice we do the procedure regularly for patients with endometrial cancer.

I propose that patients who are suitable for a cervical cancer hysterectomy have a laparoscopic sentinel node biopsy first and only when the nodes come back clear, they will proceed to a radical or standard hysterectomy depending on their risk profile as a separate, second procedure. Patients with positive sentinel nodes, should be spared a hysterectomy (radical or standard) but I will refer them to definitive chemoradiation treatment instead.

Personalise treatment: While this will be very difficult to implement in the **public hospital s**ystem (because of a chronic lack of operating time), in the **private hospital** system it will give patients better outcomes because only patients who really should have a hysterectomy will have one. Patients with negative sentinel nodes can be spared chemoradiation and its side effects; whereas patients with positive sentinel nodes, will go on to have chemoradiation without the need for an unnecessary hysterectomy.



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