Antibody-Drug Conjugates (ADCs) in Gynaecological Cancers

What they are, how they work, and what's currently available in Europe

What are ADCs?

Almost all modern cancer treatments aim to kill tumour cells while preserving healthy tissue. For gynaecological cancers (such as of the ovary, fallopian tube, peritoneum, cervix or endometrium), we now have a new class of medicines: **antibody-drug conjugates (ADCs)**.

An ADC is like a Trojan Horse for cancer cells:

- **The "antibody"** part are lab-created proteins that mimic the body's immune response. Instead of recognising foreign invaders like bacteria or viruses, they specifically recognise a marker (target) on the surface of cancer cells.
- **The "payload"** is a potent cancer-killing drug, usually a chemotherapy.
- **The "linker"** connects the antibody to the payload and ensures the drug is released once inside the cancer cell.

Put simply, the antibody acts as a guide for the medicine, directing it to the correct location. Once it binds to the target on the surface of the cancer cell, the cell absorbs the antibody-drug conjugate (ADC). Inside the cell, the linker breaks down, releasing the potent drug from the antibody. As ADCs specifically attack tumour cells, they should leave healthy cells more intact than classical chemotherapy does.

Because ADCs use an antibody as a disguise to sneak a harmful drug inside the cancer cells, they are also known as Trojan horses.

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ESGO European Network of Gynaecological Cancer Advocacy Groups

Why does this matter for gynaecological cancers?

Because some gynaecological tumours express unique targets (markers) on their cells, ADCs offer a way to deliver stronger treatment with potentially fewer side-effects than giving "strong chemo" everywhere. That means ADCs provide more treatment options for women whose cancers have returned or progressed, or who have fewer options left.

Important note

ADCs are not magic cures. They are newer treatments, used when other standard treatments have been tried or are not suitable. Also, not every patient will be eligible (because the target must be present on the tumour, which is not always the case). If you are a patient, your doctor may talk to you about whether the tumour expresses the right marker, and whether an ADC might help.

How do ADCs work?

Let's follow a step-by-step cartoon style explanation (you could imagine a small graphic here):

1. The antibody part flies through the bloodstream and attaches to the cancer cell which displays the target – like a homing device.
2. The whole ADC (antibody + drug) is taken inside the cancer cell (internalised).
3. Inside the cell, the linker is cut or broken and the drug (payload) is released.
4. The drug does its job: it interferes with the cell's machinery (for example microtubules or DNA) and triggers the cell to die or stop dividing.
5. Healthy cells that do not have the target are less likely to take in the ADC, so they are less affected (in theory) than with regular chemotherapy.

What are the benefits and limitations?

Benefits

- More targeted delivery of the "strong stuff" (cytotoxic drugs) to the tumour.
- Possibility of fewer side effects compared with non-targeted chemotherapy.
- New treatment options where few existed before.

Limitations

- The tumour must express the target (marker) — otherwise the ADC won't "home in".

- Some side-effects still occur (and may be different from classic chemotherapy).
- Not yet a standard treatment in most settings: often used only when other treatments have been tried first.
- The access and national approval processes vary across Europe.
- ADCs are expensive drugs, more expensive compared to classical chemotherapy.

What this means for you

If your gynaecological cancer has recurred or progressed, your tumour may be tested and you may be asked if you are interested in exploring treatment with an ADC.

It is useful to know:

- What marker your tumour expresses
- What previous treatments you have had
- Whether a clinical trial is available

Currently approved ADCs in Europe

A small number of ADCs are already approved in Europe for use in certain gynaecological cancers. These treatments are directed at specific markers found on some ovarian-related and cervical tumours, and they offer additional options for people whose cancer has returned or no longer responds to earlier therapies. Whether an ADC is suitable depends on factors such as the marker your tumour expresses and what treatments you have already had.

At the same time, several new ADCs are being developed. Researchers are exploring different targets and new types of payloads, including options that may one day help in endometrial cancer. Many of these potential treatments are currently being tested in clinical trials, with the aim of expanding the choices available in the future.

Looking ahead:
What's next, and what you can ask your doctor

What's coming

- More ADCs are being tested in clinical trials for gynaecological cancers. We hope this will lead to more ADC options in the future.
- Scientists are working on **biomarker testing** (to determine which cancers test positive for which target. How much of the target is needed for the ADC to work? Does the target evolve over time and are there differences between the tumour at the time of diagnosis and when it recurs?
- Even though the indications are still quite specific, the hope is that ADC-therapy will gradually move into earlier lines or more cancer types.

- Studies are looking at possible **combination treatments** (e. g. ADCs + immunotherapy, anti-angiogenics or even chemotherapy).
- And last but not least, studies are also looking at earlier use (sooner in the disease course).

Questions you may wish to ask your doctor

- Does my tumour express the target marker?
- Am I eligible for the ADC treatment (based on prior treatments, disease state, health status)?
- What are the side-effects, how common/severe are they, and how will they be monitored?
- Is there a clinical trial of an ADC available in my country/centre?
- What is the process for accessing the ADC (approval in my country, reimbursement, cost)?
- How will this fit into my overall treatment plan (will it replace chemo, or be added to other treatments)?

Access in Europe

Even when a medicine is approved by the EMA, access may still vary by country (depending on national reimbursement decisions, hospital availability, treatment guidelines). If you live in Europe and your doctor suggests an ADC, you may wish to check with your national cancer-treatment centre or patient advocacy group about availability.

Key message

This new class of medicines (ADCs) are not a cure-all, but **a significant new option** for many women with gynaecological cancers. Asking the right questions, being informed, and working with your specialist can help you decide if they may be appropriate for you.

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ENGAGe recommends contacting your local patient association!