

REPRODUCTIVE ENDOCRINOLOGY

AS101 might prevent chemotherapy-induced infertility

The immunomodulator AS101 prevents cyclophosphamide-induced ovarian follicle loss in mice, new data reveal.

Chemotherapy with alkylating agents, such as cyclophosphamide, increases the risk of future infertility in young women with cancer. Kalich-Philosoph *et al.* used mouse models to investigate which mechanisms are responsible for follicle depletion and ovarian damage caused by chemotherapy with cyclophosphamide. In addition, they evaluated the effects of cotreatment with AS101, which also has anticancer effects.

The researchers found that cyclophosphamide attacked the ovaries of the mice by two mechanisms. “Cyclophosphamide kills actively growing ovarian follicles, and at the same time, it also activates the dormant follicles, inducing them to grow and proliferate, which makes them susceptible to the effects of the drug as well. In this way, treatment with cyclophosphamide depletes the ovarian

reserve, leading to early ovarian failure and infertility,” explains researcher Dror Meirow. The drug seemed to cause disruption of the PI3K–PTEN–Akt signalling pathway that normally maintains follicle quiescence.

By contrast, cotreatment with AS101 preserved the ovarian reserve and rescued fertility. In these mice, primordial ovarian follicles remained dormant, fewer follicles developed and less apoptosis of the growing follicles occurred.

“Understanding of the mechanism behind cyclophosphamide-induced loss of ovarian reserve will pave the way for additional research into new methods for preserving fertility in patients with cancer,” comments Meirow.

Carol Wilson

Original article Kalich-Philosoph, L. *et al.* Cyclophosphamide triggers follicle activation and “burnout”; AS101 prevents follicle loss and preserves fertility. *Sci. Transl. Med.* 5, 185ra62 (2013)