Ovarian cancer is treacherous and crafty. Laying low and silently spreading, the tumour thrives undetected. When it’s finally identified, the tumour is often advanced and is a formidable challenge to treat. Its aggressiveness leaves women with a five-year survival rate of anywhere between 12-42%, taking 150,000 lives annually worldwide. For this, it is known as the ‘Silent Killer’. A promising new therapy for this cruel cancer has been developed by clinicians and scientists including Academician of the Russian Academy of Sciences, Prof Lev Ashraphyan and Associate academician of the Russian Academy of Sciences, Prof Vsevolod Kiselev from Institute of Gynecologic Oncology and Mammology of Acad. V.I.Kulakov National Medical Research Centre of Obstetrics, Gynecology and Perinatology, the Ministry of Health of Russia, and Ekaterina Muyzhnek from the pharmaceutical company, ImiGroup, and Academician of the Russian Academy of Sciences, Prof Gennady Sukhikh from Acad. V.I.Kulakov National Medical Research Centre of Obstetrics, Gynecology and Perinatology, the Ministry of Health of Russia.

**TENACIOUS TUMOURS**

Treatment for ovarian cancer has changed little since the late 1990s. The standard treatment involves surgery to remove as much of the tumour as possible (maximal cytoreductive surgery) followed by a cocktail of platinum-based drugs and taxanes (chemotherapy), aimed at killing cancer cells. One would think that attacking the tumour from all angles would wipe it out for good; yet this is not the case. Within 6 – 24 months after the treatment, 60-80% of patients relapse and further cycles of chemotherapy are required. Unfortunately, chemotherapy doesn’t kill all the cancer cells; some are resistant to the drugs. When a drug attempts to kill a cancer cell, it has no effect on resistant cancer cells and they stay alive. Once the resistant cells start multiplying they form chemoresistant tumours, which can’t be destroyed, leading to medical complications and early deaths. The need for more effective treatments has never been more urgent.

In recent years, targeted anti-tumour drugs known as ‘Breakthrough Therapies’ have been made widely available. With a catch phrase like that, we should all be jumping for joy. For some, targeted therapy has helped extend patients’ lives for months. This truly sounds like a breakthrough so why is there a growing scepticism about targeted therapies amongst researchers and clinicians?

Imagine this, you have a rubbish bin in your house but you don’t understand rubbish collection days so you keep filling it with rubbish. As the pile gets bigger you squash it down and pack it in, trying to contain it, but one day you know that if you don’t figure out the collection day the rubbish will take over your house. Now, imagine the rubbish bin is a tumour and the human trying to control the waste is the targeted therapy. According to the original via targeted therapies aimed to decrease tumour size and, eventually, eliminate the tumour. Actually, it turns out that targeted therapies are unable to get rid of the tumour. The main positive effect of targeted drugs is usually less about decreasing tumour size than achieving prolonged stabilisation of tumour management process. Like the human not understanding collection days, if scientists don’t figure out how to get rid of the tumour, or rather to remove tumour’s source (its root system) instead of reducing its size, the patient could relapse. Another drawback is that over time, tumours develop resistance to the monotargeted drugs, just like their predecessors, so the positive effects don’t last long. Targeted therapies cannot be used alone or even in combination with conventional chemotherapy to effectively fight ovarian cancer. For the next generation of cancer therapies, a better understanding of chemoresistant and recurrent ovarian tumours is needed to help promote patients’ survival.

**THE NEXT CHAPTER**

It’s not all doom and gloom. In recent years there has been a huge effort to understand tumour recurrence and resistance. A recent scientific breakthrough in cancer research involves the discovery of a population of hardy cancer cells, known as cancer stem cells, or CSCs. Research into this rare population of immortal cells suggests they are responsible for chemoresistance and recurrent tumours in many different cancers, including ovarian cancer. This discovery has opened up a whole new opportunity for cancer research scientists, who over the last decade, have been searching and developing new drugs to destroy CSCs.

Astonishing findings reveal that combining conventional chemotherapy with ovarian CSCs inhibitors is essential for tackling the tumour. In the first round of chemotherapy the bulk of ovarian tumour cells are eliminated but hardy, chemoresistant CSCs survive the treatment. While the symptoms for the patient disappear, CSCs silently grow into tumours. At recurrence the patients have large tumours full of CSCs that cannot be destroyed with chemotherapy. can begin to uncover more effective anti-cancer treatments.

**BACK TO NATURE**

Today, natural agents play a dominant role in the discovery of leads for the development of drugs against many human diseases, especially cancer. Currently, over 60% of anti-cancer drugs are derived in one way or another from natural sources, with the rest being artificially synthesised.

In the recent study led by Academicians Lev Ashraphyan and Vsevolod Kiselev and their colleagues, compounds of natural origin were used in a clinical trial to identify their effectiveness in treating...
**Figure 2:** Multiple anti-cancer activity of indole-3-carbinol (I3C), 3,3’-diindolylmethane (DIM), and epigallocatechin-3-gallate (EGCG) in advanced ovarian cancer dramatically increased median overall survival by one and a half times and 5-year overall survival increased from 37% to 67%.

...therapy with I3C and EGCG in advanced ovarian cancer dramatically increased median overall survival by one and a half times and 5-year overall survival increased from 37% to 67%.

**Bio**

Lev Ashraphyan:
A highly regarded gynecologic oncologist and a surgeon in gynecologic cancers, Honoured Doctor of the Russian Federation, Director, Institute of Gynecologic Oncology and Mammology of Acad. V.I. Kulakov National Medical Research Centre of Obstetrics, Gynecology and Perinatology, the Ministry of Health of Russia (Moscow). Academician of the Russian Academy of Sciences, Professor, MD. A member of Russian and foreign Associations of gynecologists and gynecologic oncologists. President of Russian Association of specialists in the treatment of female reproductive system tumours.

Vsevolod Kiselev:
A highly regarded clinician-scientist, specialist in molecular biology, molecular medicine and biotechnology. Deputy Director, Institute of Gynecologic Oncology and Mammology of Acad. V.I. Kulakov National Medical Research Centre of Obstetrics, Gynecology and Perinatology, the Ministry of Health of Russia (Moscow). Associate academician of the Russian Academy of Sciences, Professor, D. Biol. Sci. Twice winner of Russian Government Award in Science and Engineering, a laureate of the International Prize Galen (Prix Galien Russia), a winner of the National Prize to the best doctors of Russia “Vocation”.

Ekaterina Muyzhnek:
Chief Scientific Officer, Joint-Stock Company “IlmixGroup”, PhD (Biochemistry, Biol. Faculty, V.Lomonosov Moscow State University). A winner of the Russian Academy of Medical Sciences Prize.

Gennady Sukhikh:
Honoured Scientist of the Russian Federation, Director, Acad. V.I. Kulakov National Medical Research Centre of Obstetrics, Gynecology and Perinatology, the Ministry of Health of Russia (Moscow). Academician of the Russian Academy of Sciences, Professor, MD.

**References**

We believe it depends on two points: the speed at which available information on this new treatment approach would be distributed in public space and on the ability of oncologists (who are known as the most conservative clinicians) to accept current ideas and knowledge and their desire to apply them in clinical practice. But importantly, safety, affordability, simple peroral usage, and clinically proven efficacy of the preparations used in the trial could give a hope for a long happy life to large number of oncological patients and their relatives with no participation of physicians if they aren’t ready yet.

**Personal Response**

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**Research Objectives**

The research is focused on an effective and safe approach of maintenance therapy for advanced ovarian cancer that is both inexpensive and affordable.