

# Cancer Association of South Africa (CANSA)

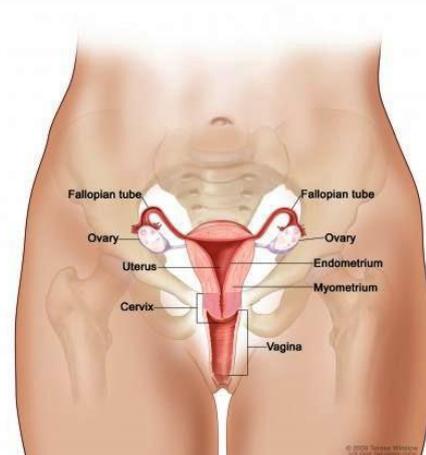


## Fact Sheet On Ovarian Cancer

### Introduction

The ovaries form part of the female reproductive organs that house the ova and are also responsible for the production of sex hormones. The ovaries are paired organs located on either side of the uterus within the broad ligament below the uterine (fallopian) tubes. Each ovary is within the ovarian fossa, a space that is bound by the external iliac vessels, obliterated umbilical artery, and the ureter. The ovaries are responsible for housing and releasing ova, or eggs, necessary for reproduction. At birth, a female has approximately 1-2 million ova, but only about 300 of these eggs will ever become mature and be released for the purpose of fertilisation.

[Picture Credit – Ovarian Anatomy]



### Ovarian Cancer

Ovarian cancer is cancer of the cells of one or both ovaries.

Cheasley, D., Wakefield, M.J., Ryland, G.L., Allan, P.E., Alsop, K., Amarasinghe, K.C., Ananda, S., Anglesio, M.S., Au-Yeung, G., Böhm, M., Bowtell, D.D.L., Brand, A., Chenevix-Trench, G., Christie, M., Chiew, Y.E., Churchman, M., DeFazio, A., Demeo, R., Dudley, R., Fairweather, N., Fedele, C.G., Fereday, S., Fox, S.B., Gilks, C.B., Gourley, C., Hacker, N.F., Hadley, A.M., Hendley, J., Ho, G.Y., Hughes, S., Hunstman, D.G., Hunter, S.M., Jobling, T.W., Kalli, K.R., Kaufmann, S.H., Kennedy, C.J., Köbel, M., Le Page, C., Li, J., Lupat, R., McNally, O.M., McAlpine, J.N., Mes-Masson, A.M., Mileshkin, L., Provencher, D.M., Pyman, J., Rahimi, K., Rowley, S.M., Salazar, C., Samimi, G., Saunders, H., Semple, T., Sharma, R., Sharpe, A.J., Stephens, A.N., Thio, N., Torres, M.C., Traficante, N., Xing, Z., Zethoven, M., Antill, Y.C., Scott, C.L., Campbell, I.G. & Goringe, K.L. 2019.

“Mucinous ovarian carcinoma (MOC) is a unique subtype of ovarian cancer with an uncertain etiology, including whether it genuinely arises at the ovary or is metastatic disease from other organs. In addition, the molecular drivers of invasive progression, high-grade and metastatic disease are poorly defined. We perform genetic analysis of MOC across all histological grades, including

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 1

benign and borderline mucinous ovarian tumors, and compare these to tumors from other potential extra-ovarian sites of origin. Here we show that MOC is distinct from tumors from other sites and supports a progressive model of evolution from borderline precursors to high-grade invasive MOC. Key drivers of progression identified are TP53 mutation and copy number aberrations, including a notable amplicon on 9p13. High copy number aberration burden is associated with worse prognosis in MOC. Our data conclusively demonstrate that MOC arise from benign and borderline precursors at the ovary and are not extra-ovarian metastases.”

### Incidence of Ovarian Cancer in South Africa

According to the outdated National Cancer Registry (2014) the following number of ovarian cancer cases was histologically diagnosed in South Africa during 2014:

Group - Females 2014	No of Cases	Lifetime Risk	Percentage of All Cancer
All females	518	1:387	1,37%
Asian females	22	1:248	3,36%
Black females	194	1:777	1,20%
Coloured females	42	1:457	1,02%
White females	260	1:134	1,58%

The frequency of histologically diagnosed cases of ovarian cancer in South Africa for 2014 was as follows (National Cancer Registry, 2014):

Group - Females 2014	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	4	18	23	73	111	161	93	30
Asian females	1	0	0	2	8	7	4	0
Black females	3	15	17	28	39	48	28	9
Coloured females	0	1	1	8	7	15	6	3
White females	0	2	4	33	56	86	64	18

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for ‘all males’ and ‘all females’, however, always reflect the correct totals.

According to **Bruni, et al.**, (2019), the burden of cervical cancer for South Africa for 2018 is estimated as:

- Annual number of ovarian cancer cases 1 371
- Annual number of ovarian cancer deaths 971

### Causes of Ovarian Cancer

It is not clear what causes ovarian cancer. In general, cancer begins when healthy cells acquire a genetic mutation that turns normal cells into abnormal cells. Healthy cells grow and multiply at a set rate, eventually dying at a set time. Cancer cells grow and multiply out of control, and they do not die. The accumulating abnormal cells form a mass (tumour).

### **Risk Factors for Ovarian Cancer**

The risk for developing ovarian cancer appears to be affected by several factors:

- The more children a woman has and the earlier in life she gives birth, the lower her risk for ovarian cancer
- Certain genes defects (BRCA1 and BRCA2) are responsible for a small number of ovarian cancer cases. Women with a personal history of breast cancer or a family history of breast or ovarian cancer have an increased risk for ovarian cancer
- Women who take oestrogen replacement only (not with progesterone) for 5 years or more seem to have a higher risk of ovarian cancer
- Birth control pills decrease the risk of ovarian cancer.
- Being infertile or having fertility treatment
- Using a coil (intra-uterine device (IUD))
- Older women are at highest risk for developing ovarian cancer. Most deaths from ovarian cancer occur in women age 55 and older
- Research suggests that the risk of ovarian cancer is slightly higher for women who:
- have medical conditions such as endometriosis
  - smoke tobacco products
  - are obese
  - are tall

### **Caution Expressed Around Consumption of Foods High in Phytoestrogens by Individuals Diagnosed with a Hormone-Sensitive Cancer**

The Cancer Association of South Africa (CANSAs) has noted:

- A statement by Memorial Sloan Kettering Cancer Center saying that "... because compounds isolated from rooibos leaves demonstrated estrogenic activity, patients with hormone-sensitive cancers should use caution before taking rooibos." (Memorial Sloan Kettering Cancer Center).
- That phytoestrogens were successfully isolated from rooibos leaves by scientists from the School of Pharmaceutical Sciences, University of Shizuoka, Japan (Shimamura, *et al.*, 2006).
- That according to Deng, *et al.*, (2010), "... there are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancer patients with hormone-sensitive disease. Based on current evidence, we propose recommendations for advising breast cancer patients, ..."
- That, according to Nelles, Hu & Prins (2011), "Early work on the hormonal basis of prostate cancer focused on the role of androgens, but more recently estrogens have been implicated as potential agents in the development and progression of prostate cancer."
- That, according to Reger, *et al.*, (2016), "Experimental studies suggest that phytoestrogen intake alters cancer and cardiovascular risk. Some urinary phytoestrogens were associated with cardiovascular and all-cause mortality in a representative sample of 5 179 participants. This is one of the first studies that used urinary phytoestrogens as biomarkers of their

dietary intake to evaluate the effect of these bioactive compounds on the risk of death from cancer and cardiovascular disease.”

CANSA, therefore, wishes to advise individuals diagnosed with the following hormone-sensitive cancers, namely: Breast Cancer, Ovarian Cancer, Endometrial Cancer, and Prostate Cancer, to:

- use caution before taking Rooibos tea and to discuss the issue around Rooibos tea consumption with their treating Oncologist prior to consuming Rooibos tea
- also use caution before taking the following high phytoestrogen-containing foods: all soy foods (including soybeans, tofu, miso, and tempeh); legumes (especially lentils, peanuts and chickpeas) and flaxseed-containing foods. Patients are advised to discuss consumption of the listed high phytoestrogen-containing foods with their treating Oncologist prior to consuming them.

### Research on Foods High in Phytoestrogens and Breast Cancer

**Deng, G., Davatgarzadeh, A., Yeung, S. & Cassileth, B.** 2010. Phytoestrogens: science, evidence, and advice for breast cancer patients. *Soc Integr Oncol.* 2010 Winter;8(1):20-30.

“There are important safety concerns associated with dietary supplements and foods rich in phytoestrogens, especially for breast cancer patients with hormone-sensitive disease. However, no consensus has been reached concerning specific dietary items that should be avoided, and safe levels of potentially problematic foods have yet to be determined. Excellent qualitative reviews of phytoestrogens and breast cancer have been published. These list agents that contain phytoestrogens and offer general cautions. Quantitative reviews, however, are needed but not yet available. Here we review quantitative data on phytoestrogens, their interaction with estrogen receptors, their bioavailability and pharmacokinetics, and their effects on breast cancer cells and animal models. We also note foods and botanicals with substances that interact with estrogen receptors and discuss the phytoestrogens they contain. Based on current evidence, we propose recommendations for advising breast cancer patients, which may also serve as a basis for the development of clinical practice guidelines.”

**Shimamura, N., Miyase, T., Umehara, K., Warashina, T. & Fuji, S.** 2006. Phytoestrogens from *Aspalathus linearis*. *Biol Pharm Bull.* 2006 Jun;29(6):1271-4.

“From the leaves of *Aspalathus linearis*, 24 known compounds and a new one, aspalalinin (25), were isolated. The structures of the compounds were determined mainly based on spectral evidence. The absolute configuration of aspalalinin was presented on the basis of X-ray analysis. Each isolate was assessed for its estrogenic activity by an estrogen ELISA assay. Compounds 12, 15, and 24 showed the estrogenic activity.”

**Patisaul, H. & Jefferson, W.** 2010. The pros and cons of phytoestrogens. *Front Neuroendocrinol.* Author manuscript; available in PMC 2011 Apr 12.

Phytoestrogens are plant derived compounds found in a wide variety of foods, most notably soy. A litany of health benefits including a lowered risk of osteoporosis, heart disease, breast cancer, and menopausal symptoms, are frequently attributed to phytoestrogens but many are also considered endocrine disruptors, indicating that they have the potential to cause adverse health effects as well.

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 4

Consequently, the question of whether or not phytoestrogens are beneficial or harmful to human health remains unresolved. The answer is likely complex and may depend on age, health status, and even the presence or absence of specific gut microflora. Clarity on this issue is needed because global consumption is rapidly increasing. Phytoestrogens are present in numerous dietary supplements and widely marketed as a natural alternative to estrogen replacement therapy. Soy infant formula now constitutes up to a third of the US market, and soy protein is now added to many processed foods. As weak estrogen agonists/antagonists with molecular and cellular properties similar to synthetic endocrine disruptors such as Bisphenol A (BPA), the phytoestrogens provide a useful model to comprehensively investigate the biological impact of endocrine disruptors in general. This review weighs the evidence for and against the purported health benefits and adverse effects of phytoestrogens.

**Rodriguez-Garcia, C., Sánchez-Quesada, C., Toledo, E., Delgado-Rodriguez, M. & Gaforio, J.J.** 2019. "Dietary guidelines universally advise adherence to plant-based diets. Plant-based foods confer considerable health benefits, partly attributable to their abundant micronutrient (e.g., polyphenol) content. Interest in polyphenols is largely focused on the contribution of their antioxidant activity to the prevention of various disorders, including cardiovascular disease and cancer. Polyphenols are classified into groups, such as stilbenes, flavonoids, phenolic acids, lignans and others. Lignans, which possess a steroid-like chemical structure and are defined as phytoestrogens, are of particular interest to researchers. Traditionally, health benefits attributed to lignans have included a lowered risk of heart disease, menopausal symptoms, osteoporosis and breast cancer. However, the intake of naturally lignan-rich foods varies with the type of diet. Consequently, based on the latest humans' findings and gathered information on lignan-rich foods collected from Phenol Explorer database this review focuses on the potential health benefits attributable to the consumption of different diets containing naturally lignan-rich foods. Current evidence highlight the bioactive properties of lignans as human health-promoting molecules. Thus, dietary intake of lignan-rich foods could be a useful way to bolster the prevention of chronic illness, such as certain types of cancers and cardiovascular disease."

### **Ovarian Cancer and Use of Talc**

There have been several lawsuits in the United States of America against the manufacturer of a popular brand of baby powder which contains talc. Retrospective research was conducted by Cramer, *et al.* (2016). They concluded that multiple studies of ovarian cancer and genital talc use have led only to consensus about possible carcinogenicity. Risks for epithelial ovarian cancer from genital talc use vary by histologic subtype, menopausal status at diagnosis, hormone therapy use, weight, and smoking. These observations suggest that oestrogen and/or prolactin may play a role via macrophage activity and inflammatory response to talc.

**Kadry Taher, M., Farhat, N., Karyakina, N.A., Shilnikova, N., Ramoju, S., Gravel, C.A., Krishnan, K., Mattison, D., Wen, S.W. & Krewski, D.** 2019.

Over the past four decades, there has been increasing concern that perineal use of talc powder, a commonly used personal care product, might be associated with an increased risk of ovarian cancer.

**OBJECTIVES:** To critically review all available human epidemiological data on the relationship between perineal use of talc powder and ovarian cancer, with consideration of other relevant experimental evidence.

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 5

**METHODOLOGY:** We identified 30 human studies for qualitative assessment of evidence, including 27 that were retained for further quantitative analysis.

**RESULTS:** A positive association between perineal use of talc powder and ovarian cancer was found [OR: 1.28 (95% CI: 1.20 - 1.37)]. A significant risk was noted in Hispanics and Whites, in women applying talc to underwear, in pre-menopausal women and in post-menopausal women receiving hormonal therapy. A negative association was noted with tubal ligation.

**CONCLUSION:** Perineal use of talc powder is a possible cause of human ovarian cancer.

### **Protective Factors for Ovarian Cancer**

There's currently nothing that can be done to prevent ovarian cancer. However, there are some things that are thought to protect against ovarian cancer. These are called protective factors. Women with protective factors may still develop ovarian cancer.

Getting enough vitamin D may reduce your risk of developing a number of cancers, including ovarian cancer – although more research needs to be done to be certain.

Research has shown that the following may be associated with a reduced risk of certain types of ovarian cancer:

- removal of the uterus (womb)
- removal of the ovaries
- having the fallopian tubes tied
- having the fallopian tubes removed
- having been pregnant
- using oral contraceptives

### **Prophylactic Oophorectomy**

Prophylactic oophorectomy may significantly reduce one's odds of developing breast cancer and ovarian cancer if one is at high risk. One should weigh the pros and cons of this cancer-prevention option in collaboration with an oncology geneticist and a medical practitioner.

#### Who can consider prophylactic oophorectomy?

Prophylactic oophorectomy is usually reserved for women with a significantly increased risk of breast cancer and ovarian cancer due to an inherited mutation in the BRCA1 or BRCA2 gene - two genes linked to breast cancer, ovarian cancer and other cancers. Women who have inherited mutations and have completed childbearing are the best candidates for this surgery.

Prophylactic oophorectomy may also be recommended if one has a strong family history of breast cancer and ovarian cancer but no known genetic alteration. It might also be recommended if one has a strong likelihood of carrying the gene mutation based on one's family history but choose not to proceed with genetic testing.

Women who are at risk, could consider this procedure as follows:

- Having a BRCA1 gene mutation: age 35 to 40
- Having a BRCA2 gene mutation: age 45 and older

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 6

## **Types of Ovarian Cancer**

The type of cell where the cancer begins determines the type of ovarian cancer you have. Ovarian cancer types include:

- Cancer that begins in the cells on the outside of the ovaries. Called epithelial tumours, these cancers begin in the thin layer of tissue that covers the outside of the ovaries. Most ovarian cancers are epithelial tumours
- Cancer that begins in the egg-producing cells. Called germ cell tumours, these ovarian cancers tend to occur in younger women
- Cancer that begins in the hormone-producing cells. These cancers, called stromal tumours, begin in the ovarian tissue that produces the hormones oestrogen, progesterone and testosterone
- The type of ovarian cancer you have helps determine your prognosis and treatment options

## **Symptoms of Ovarian Cancer**

Many ovarian cancer symptoms mimic those of less life-threatening conditions such as irritable bowel syndrome. These symptoms may include:

- Bloating
- Pelvic or abdominal pain
- Urinary urgency or frequency
- Difficulty eating or feeling full quickly

## **Further Late Stage Symptoms of Ovarian Cancer**

- Spread of the cancer to other organs
- Loss of organ function
- Fluid in the abdomen (ascites)
- Blockage of the intestines

## **Early Detection of Ovarian Cancer**

Early detection of ovarian cancer saves women's lives. No screening test exists that can test all women for ovarian cancer. The Pap test does not test for ovarian cancer; it screens for cervical cancer.

## **Diagnosis of Ovarian Cancer**

In someone showing the symptoms mentioned above, the doctor may order one or more of the following tests:

Ultrasound - Ultrasound (ultrasonography) is the use of sound waves to create an image on a video screen. Sound waves are released from a small probe placed in the woman's vagina or on the surface of her abdomen. The sound waves create echoes as they enter the ovaries and other organs. The

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 7

same probe detects the echoes that bounce back, and a computer translates the pattern of echoes into a picture.

Computed Tomography - The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine will take pictures of multiple slices of the part of your body that is being studied.

Barium Enema X-ray - This is a test to see whether the cancer has invaded the colon (large intestine) or rectum (it is also used to look for colorectal cancer). After taking laxatives the day before, the radiology technician puts barium sulphate, a chalky substance, into the rectum and colon. Because barium is impermeable to x-rays (impossible for x-rays to go through), it outlines the colon and rectum on x-rays of the abdomen.

Magnetic Resonance Imaging - MRI scans use radio waves and strong magnets instead of X-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body.

Chest X-ray - This procedure may be done to determine whether ovarian cancer has spread (metastasized) to the lungs.

Positron Emission Tomography (PET scan) - In this test, radioactive glucose (sugar) is given to look for the cancer. Because cancers use glucose (sugar) at a higher rate than normal tissues, the radioactivity will tend to concentrate in the cancer. A scanner can spot the radioactive deposits.

**Konstantinopoulos, P.A., Norquist, B., Lacchetti, C., Armstrong, D., Grisham, R.N., Goodfellow, P.J., Kohn, E.C., Levine, D.A., Liu, J.F., Lu, K.H., Sparacio, D. & Annunziata, C.M.** 2020.

**PURPOSE:** To provide recommendations on genetic and tumor testing for women diagnosed with epithelial ovarian cancer based on available evidence and expert consensus.

**METHODS:** A literature search and prospectively defined study selection criteria sought systematic reviews, meta-analyses, randomized controlled trials (RCTs), and comparative observational studies published from 2007 through 2019. Guideline recommendations were based on the review of the evidence.

**RESULTS:** The systematic review identified 19 eligible studies. The evidence consisted of systematic reviews of observational data, consensus guidelines, and RCTs.

**RECOMMENDATIONS:** All women diagnosed with epithelial ovarian cancer should have germline genetic testing for *BRCA1/2* and other ovarian cancer susceptibility genes. In women who do not carry a germline pathogenic or likely pathogenic *BRCA1/2* variant, somatic tumor testing for *BRCA1/2* pathogenic or likely pathogenic variants should be performed. Women with identified germline or somatic pathogenic or likely pathogenic variants in *BRCA1/2* genes should be offered treatments that are US Food and Drug Administration (FDA) approved in the upfront and the recurrent setting. Women diagnosed with clear cell, endometrioid, or mucinous ovarian cancer should be offered somatic tumor testing for mismatch repair deficiency (dMMR). Women with identified dMMR should be offered FDA-approved treatment based on these results. Genetic evaluations should be conducted in conjunction with health care providers familiar with the diagnosis and management of hereditary cancer. First- or second-degree blood relatives of a patient

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 8

with ovarian cancer with a known germline pathogenic cancer susceptibility gene variant should be offered individualized genetic risk evaluation, counseling, and genetic testing. Clinical decision making should not be made based on a variant of uncertain significance. Women with epithelial ovarian cancer should have testing at the time of diagnosis.

### Staging of Ovarian Cancer

Staging of ovarian cancer is done as it assists the oncologist in deciding treatment.

### Where Ovarian Cancer May Spread to in the Body

Should ovarian cancer spread (metastasise) in the body, it would most probably spread as indicated below:

Cancer Type:	Main Sites of Metastasis (Spread)
Bladder	Bone, liver, lung
Breast	Bone, brain, liver, lung
Colon	Liver, lung
Colorectal	Liver, lung, peritoneum (lining of abdomen)
Kidney	Adrenal gland, bone, brain, liver, lung
Lung	Adrenal gland, bone, brain, liver, other lung
Melanoma	Bone, brain, liver, lung, skin, muscle
Ovary	Liver, lung, peritoneum (lining of abdomen)
Pancreas	Liver lung, peritoneum (lining of abdomen)
Prostate	Adrenal gland, bone, liver, lung
Stomach	Liver, lung, peritoneum (lining of abdomen), ovaries
Thyroid	Bone, liver, lung
Uterus	Boner, liver, lung, peritoneum (lining of abdomen), vagina
Non-melanoma skin cancer	Very rare: lymph nodes, lung, bone (if in head/neck region)

### Treatment of Ovarian Cancer

Treatment for ovarian cancer usually involves a combination of surgery and chemotherapy. Less often, treatment may include radiotherapy. The type of treatment women receive depends on the type and stage of their ovarian cancer and their general health. Treatment is best managed by a gynaecological oncologist.

#### Surgery

Nearly all women who have ovarian cancer will require surgery. Sometimes, it is not possible to confirm the stage of the cancer until the surgery.

#### Chemotherapy

Chemotherapy involves using anti-cancer (cytotoxic) drugs to kill cancer cells. It is often given after surgery for ovarian cancer. In some cases, it can be given before surgery as it may help to shrink the tumour and make it easier to remove. This is called neo-adjuvant chemotherapy.

#### Radiotherapy

Radiotherapy uses high energy X-rays. Like chemotherapy, it works by targeting rapidly growing cancer cells. Radiotherapy is not often used to treat ovarian cancer. But occasionally, the

multidisciplinary team may recommend it for ovarian cancer treatment under very specific circumstances, such as treating pain and bleeding from a localised tumour mass.

**Washington, C.R., Richardson, D.L. & Moore, K.N.** 2019.

“The poly ADP ribose polymerase olaparib is currently approved in front line *BRCA*-associated epithelial ovarian cancer (EOC), platinum-sensitive recurrence agnostic to *BRCA* status and for g*BRCA* as treatment in the fourth line and beyond. Women who are diagnosed with advanced stage EOC face a formidable challenge in overcoming their disease and achieving long-term, disease-free survival. The qualifier here is disease free. EOC is largely exquisitely chemosensitive, especially in the treatment naive (first line) setting and the expectation is that the vast majority of women will complete front line platinum-based chemotherapy with a response. When unselected (not selected by *BRCA*) women are enrolled on clinical trials, the response rate among those who have measurable disease at the time of chemotherapy initiation is 48% for carboplatin/paclitaxel and 67% for carboplatin/paclitaxel plus bevacizumab. When one considers the addition of women who start chemotherapy without measurable disease, they will likely also end chemotherapy without measurable disease and the overall rate of no evidence of disease at conclusion of chemotherapy approaches 80%. Despite this, the majority of women will suffer relapse of their disease, typically within the first 3 years following completion of therapy. Once recurrent, the disease is highly treatable for many years but no longer considered curable. This review will cover indications for olaparib in ovarian cancer as well as ongoing combination trials and rationale for these combinations.”

**Wang, A., Jin, C., Tian, X., Wanag, Y. & Li, H.** 2019. Knockdown of HE4 suppresses aggressive cell growth and malignant progression of ovarian cancer by inhibiting the JAK/STAT3 pathway. *Biol Open*. 2019 Sep 2;8(9). pii: bio043570. doi: 10.1242/bio.043570.

“Human epididymis protein 4 (HE4) is well known to be a predictor of ovarian cancer clinically. HE4 is reported to play crucial roles in ovarian cancer progression and metastasis. The purpose of the present study was to explore its biological role and molecular mechanism in ovarian cancer. In our study, we found that expression levels of HE4 in tissues, serum and urine in ovarian cancer were upregulated compared to healthy and benign groups. HE4 expression was elevated in ovarian cancer cells. Knockdown of HE4 dampened cell proliferation and Ki67 expression, as well as enhanced apoptosis, caspase-3 activity and cleaved-caspase-3 expression. In addition, HE4 downregulation repressed invasion and migration capabilities of ovarian cancer cells. Western blot analyses showed that knockdown of HE4 reduced the levels of matrix metalloproteinases (MMP-2 and MMP-9) and inhibited epithelial to mesenchymal transition (EMT) in ovarian cancer cells. *In vivo* animal experiments revealed that HE4 downregulation constrained the growth of xenograft tumor. Mechanism research showed that knockdown HE4 inhibited the activity of JAK/STAT3 pathway *in vitro* and *in vivo*. In conclusion, our findings reported that knockdown of HE4 suppresses aggressive cell growth and malignant progression of ovarian cancer by inhibiting the JAK/STAT3 pathway, which provides valuable insights to contribute to develop novel HE4-targeted therapies.”

### **About Clinical Trials**

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 10

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The [South African National Clinical Trials Register](#) provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: [www.sanctr.gov.za/](http://www.sanctr.gov.za/)

### Medical Disclaimer

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.

Whilst CANSA has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.



### References and Sources Consulted or Utilised

#### American Cancer Society

<http://www.cancer.org/Cancer/OvarianCancer/DetailedGuide/ovarian-cancer-diagnosis>

<http://www.cancer.org/Cancer/OvarianCancer/DetailedGuide/ovarian-cancer-staging>

#### Australian Government, Cancer Australia

<http://canceraustralia.nbcc.org.au/ovarian-cancer/about/what-causes-ovarian-cancer>

Bruni, L., Albero, G., Serrano, B., Mena, M., Gómez, D., Muñoz, J., Bosch, F.X. & de Sanjosé, S. 2019. ICO/IARC Information Centre on HPV and Cancer (*HPV Information Centre*). Human Papillomavirus and Related Diseases in South Africa. Summary Report 17 June 2019. [Date Accessed]

#### BUPA UK

<http://www.bupa.co.uk/individuals/health-information/directory/o/ovarian-cancer?intcmp=cancer:ovarian-cancer>

#### Cancer Research UK

<http://cancerhelp.cancerresearchuk.org/type/ovarian-cancer/about/ovarian-cancer-risks-and-causes>

<http://www.cancerresearchuk.org/about-cancer/cancers-in-general/cancer-questions/primary-peritoneal-carcinoma>

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 11

## Cancer Therapy Advisor

[http://www.cancertherapyadvisor.com/gynecologic-cancer/ovarian-cancer-asco-sgo-new-guidelines-treatment/article/514573/?DCMP=ILC-CTA\\_Promo\\_082816&cpn=&hmSubId=i7VmYKZCM\\_41&NID=&dl=0&spMailingID=15280041&spUserID=MzMyODk3NTcxNTcS1&spJobID=841950477&spReportId=ODQxOTUwNDc3S0](http://www.cancertherapyadvisor.com/gynecologic-cancer/ovarian-cancer-asco-sgo-new-guidelines-treatment/article/514573/?DCMP=ILC-CTA_Promo_082816&cpn=&hmSubId=i7VmYKZCM_41&NID=&dl=0&spMailingID=15280041&spUserID=MzMyODk3NTcxNTcS1&spJobID=841950477&spReportId=ODQxOTUwNDc3S0)

Cheasley, D., Wakefield, M.J., Ryland, G.L., Allan, P.E., Alsop, K., Amarasinghe, K.C., Ananda, S., Anglesio, M.S., Au-Yeung, G., Böhm, M., Bowtell, D.D.L., Brand, A., Chenevix-Trench, G., Christie, M., Chiew, Y.E., Churchman, M., DeFazio, A., Demeo, R., Dudley, R., Fairweather, N., Fedele, C.G., Fereday, S., Fox, S.B., Gilks, C.B., Gourley, C., Hacker, N.F., Hadley, A.M., Hendley, J., Ho, G.Y., Hughes, S., Hunstman, D.G., Hunter, S.M., Jobling, T.W., Kalli, K.R., Kaufmann, S.H., Kennedy, C.J., Köbel, M., Le Page, C., Li, J., Lupat, R., McNally, O.M., McAlpine, J.N., Mes-Masson, A.M., Mileskin, L., Provencher, D.M., Pyman, J., Rahimi, K., Rowley, S.M., Salazar, C., Samimi, G., Saunders, H., Semple, T., Sharma, R., Sharpe, A.J., Stephens, A.N., Thio, N., Torres, M.C., Traficante, N., Xing, Z., Zethoven, M., Antill, Y.C., Scott, C.L., Campbell, I.G. & Gorringe, K.L. 2019. The molecular origin and taxonomy of mucinous ovarian carcinoma. *Nat Commun.* 2019 Sep 2;10(1):3935. doi: 10.1038/s41467-019-11862-x. PMID: 31477716.

Cramer, D.W., Vitonis, A.F., Terry, K.L., Welch, W.R. & Titus, L.J. 2016. The association between talc use and ovarian cancer: a retrospective case-control study in two US States. *Epidemiology*, 2016 May; 27(3):334-346. Published online 2016 Apr 1. doi: 10.1097/EDE.0000000000000434.

Deng, G., Davatgarzadeh, A., Yeung, S. & Cassileth, B. 2010. Phytoestrogens: science, evidence, and advice for breast cancer patients. *Soc Integr Oncol.* 2010 Winter;8(1):20-30.

Kadry Taher, M., Farhat, N., Karyakina, N.A., Shilnikova, N., Ramoju, S., Gravel, C.A., Krishnan, K., Mattison, D., Wen, S.W. & Krewski, D. 2019. Critical review of the association between perineal use of talc powder and risk of ovarian cancer. *Reprod Toxicol.* 2019 Aug 28. pii: S0890-6238(18)30637-3. doi: 10.1016/j.reprotox.2019.08.015. [Epub ahead of print] Review.

Konstantinopoulos, P.A., Norquist, B., Lacchetti, C., Armstrong, D., Grisham, R.N., Goodfellow, P.J., Kohn, E.C., Levine, D.A., Liu, J.F., Lu, K.H., Sparacio, D. & Annunziata, C.M. 2020. Germline and Somatic Tumor Testing in epithelial ovarian cancer: ASCO Guideline. *J Clin Oncol.* 2020 Jan 27;JCO1902960. doi: 10.1200/JCO.19.02960. [Epub ahead of print]

## Mayo Clinic

<http://www.mayoclinic.com/health/AboutThisSite/AM00057>  
<http://www.mayoclinic.org/tests-procedures/oophorectomy/in-depth/breast-cancer/art-20047337>

## Medscape

<http://www.medscape.com/viewarticle/821007>

## National Cancer Institute

<http://www.cancer.gov/clinicaltrials/learningabout/what-are-clinical-trials>  
<http://www.cancer.gov/cancertopics/factsheet.Sites-Types/metastatic>

Nelles, J.L., Hu, W-y. & Prins, G.S. 2011. Estrogen action and prostate cancer. *Expert Rev Endocrinol Metab.* 2011. May 6(3):437-451.

## NHS Choices

<http://www.nhs.uk/conditions/Cancer-of-the-ovary/Pages/Treatment.aspx>

## Ovarian Anatomy

[http://www.google.co.za/imgres?hl=en&sa=X&rlz=1T4LENN\\_enZA490ZA490&biw=1366&bih=613&tbnid=2K63IDtLkBJ8dM:&imgrefurl=http://www.cancer.umn.edu/cancerinfo/NCI/CDR62963.html&docid=AI55UkboEJR\\_M&imgurl=http://www.cancer.umn.edu/cancerinfo/NCI/Media/CDR0000609921.jpg&w=425&h=425&ei=qshWUPuXBpSWhQfm44CoBQ&zoom=1&iact=hc&vpx=758&vpy=276&dur=1562&hovh=225&hovw=225&tx=140&ty=166&sig=107310304455409594391&page=1&tbnh=122&tbnw=122&start=0&ndsp=19&ved=1t:429,r:16,s:0,i:122](http://www.google.co.za/imgres?hl=en&sa=X&rlz=1T4LENN_enZA490ZA490&biw=1366&bih=613&tbnid=2K63IDtLkBJ8dM:&imgrefurl=http://www.cancer.umn.edu/cancerinfo/NCI/CDR62963.html&docid=AI55UkboEJR_M&imgurl=http://www.cancer.umn.edu/cancerinfo/NCI/Media/CDR0000609921.jpg&w=425&h=425&ei=qshWUPuXBpSWhQfm44CoBQ&zoom=1&iact=hc&vpx=758&vpy=276&dur=1562&hovh=225&hovw=225&tx=140&ty=166&sig=107310304455409594391&page=1&tbnh=122&tbnw=122&start=0&ndsp=19&ved=1t:429,r:16,s:0,i:122)

## Ovarian Cancer Australia

<http://www.ovariancancer.net.au/treatment-support/how-is-ovarian-cancer-treated/>

---

Researched and Authored by Prof Michael C Herbst

[D Litt et Phil (Health Studies); D N Ed; M Art et Scien; B A Cur; Dip Occupational Health; Dip Genetic Counselling; Diagnostic Radiographer; Dip Audiometry and Noise Measurement; Medical Ethicist]

Approved by Ms Elize Joubert, Chief Executive Officer [BA Social Work (cum laude); MA Social Work]

January 2020

Page 12

**Ovarian Cancer National Alliance**

<http://www.ovariancancer.org/about-ovarian-cancer/detection/>

**PubMed Health.**

<http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001891/>

**Reger, M.K., Zollinger, T.W., Liu, Z., Jones, T. & Zhang, J.** 2016. Urinary phytoestrogens and cancer, cardiovascular, and all-cause mortality in the continuous National Health and Nutrition Examination Survey. *Eur J Nutr.* April 2016; 55(3):1029-1040.

**SA National Cancer Registry, 2014**

Department of Health, National Health Laboratory Service.

**Shimamura, N., Miyase, K., Warashina, T. & Fuji, S.** 2006. Phytoestrogens from *Aspalathus linearis*. *Biol Pharm Bull.* 2006 June 29(6):1271-4.

**Wang, A., Jin, C., Tian, X., Wanag, Y. & Li, H.** 2019. Knockdown of HE4 suppresses aggressive cell growth and malignant progression of ovarian cancer by inhibiting the JAK/STAT3 pathway. *Biol Open.* 2019 Sep 2;8(9). pii: bio043570. doi: 10.1242/bio.043570.

**Washington, C.R., Richardson, D.L. & Moore, K.N.** 2019. Olaparib in the treatment of ovarian cancer. *Future Oncol.* 2019 Sep 3. doi: 10.2217/fon-2019-0271. [Epub ahead of print]

**WebMD**

<http://www.webmd.com/ovarian-cancer/news/20090911/fda-oks-new-ovarian-cancer-blood-test>