Beyond Conventional Cancer Therapies

Ovarian Cancer

August 2021

A Handbook of

Integrative Cancer Care Options

and the Research Behind Them

BCCT Ovarian Cancer Handbook

Last updated August 2, 2021.

Our goal is to help you live as well as you can for as long as you can using an optimal integrative combination of conventional and complementary therapies and approaches.

Key Points

- Early detection, prompt and appropriate treatment, and general health support may greatly increase your success in treating the cancer and in maintaining quality of life.
- We summarize a protocol used at the Bastyr University Integrative Oncology Research Center for treating ovarian cancer.
- The 7 Healing Practices are the beginning point for bringing your body to health and wellness.
- Complementary therapies can be useful to enhance conventional treatment effects, improve quality of life and possibly even extend life for those with ovarian cancer.
- A number of natural products, off-label and overlooked novel cancer approaches (we call them ONCAs) and other types of therapies show benefits in three domains:
    - Treating the cancer
    - Managing side effects and promoting wellness
    - Reducing risk of both cancer onset and recurrence

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Quick Reference to Integrative Therapies

7 Healing Practices

Eating Well

- Fiber
- Green leafy vegetables
- Fish
- Higher poly- to mono-unsaturated fat ratio:
  - Snack on nuts instead of crackers or cookies
  - Favor fish over red meat
  - Add freshly ground flaxseed to food
  - Replace butter or margarine with olive and other healthy oils
- Green tea
- Organic whole soy foods, such as tempeh, miso, edamame, tofu or soy milk
- Foods high in folate: dark green leafy vegetables, fruits, nuts, beans, peas, seafood, eggs, dairy products, meat, poultry and grains

Moving More

- Physical activity, as vigorous as is comfortable

Sharing Love & Support

Engage or create your support team

- Support groups
- Supportive-expressive therapy
- Cognitive Behavioral Therapy (CBT) social skills training

Sleeping Well

Sleep 7-9 hours per night

Natural products:

- Melatonin
- L-theanine (Suntheanin)
- Valerian
- 5-HTP
- Medical cannabis and cannabinoids

Mind-body approaches:

- Cognitive Behavioral Stress Management (CBSM)
- Cognitive Behavioral Therapy for Insomnia (CBST-I)
- Mindfulness meditation
- Tai chi
- Qigong
- Yoga meditation
- Yoga
- Stress reduction practices

Body-manipulative therapies:

- Acupuncture

Managing Stress

Mind-body approaches:

- Meditation
- Relaxation techniques
- Yoga
- Music Therapy
- Tai chi
- Acceptance and Commitment Therapy (ACT)

Creating a Healing Environment

Limit chemical and radiation exposures:

- Talcum powder
- Endocrine-disrupting chemicals (EDCs) including bisphenol-A, hormone residues in meat, poultry and dairy products and some pesticides, such as organophosphates
- Asbestos
- Ionizing radiation such as x-rays

Exploring What Matters Now

Find and focus on reasons for optimism to the extent possible

Natural Products

Treating the Cancer	Managing Side Effects & Promoting Wellness
1. Combination therapy of Indole 3-carbinol (I3C) and EGCG	1. Ginger 2. Panax ginseng 3. Vitamin E 4. Medical cannabis and cannabinoids
Reducing Risk	
1. Isoflavones including genistein from soy 2. Selenium	

Off-label, Overlooked or Novel Cancer Approaches

Most of the off-label drugs here require a prescription from a licensed physician, and all require medical supervision and monitoring.

Treating the Cancer
1. Chronomodulated therapy 2. Propranolol and other beta blockers 3. Metformin 4. Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and COXII inhibitors (noting cautions) **5. Statins** (noting cautions)
Reducing Risk
1. Statins (noting cautions)

Other Approaches

Mind-body approaches for managing side effects:

- Yoga
- Hypnosis

Body-manipulative therapies for managing side effects:

- Acupuncture

Therapies using heat, sound or light for treating the cancer:

- Hyperthermia

Healthy living for treating the cancer (promoting survival) and reducing risk:

- Quit smoking tobacco

Conventional Therapies

Conventional therapies for treating the cancer and managing side effects are widely available, such as vaginal moisturizers and vaginal rings supplying low-dose estrogen to address sexual discomfort and difficulties. Ask your doctor for information.

Investigational Therapies

These therapies show promise, but **research does not yet show good evidence of effectiveness**. *(Items in bold are in more than one category.)*

Treating the Cancer
1. Bromelain **2. Intravenous vitamin C** 3. Melatonin 4. **Mistletoe** (European) 5. Turkey tail mushroom polysaccharide PSK 6. Copper chelation using tetrathiomolybdate or other chelators 7. **Massage therapy** with hypnosis and healing touch
Managing Side Effects and Promoting Wellness
1. Agaricus blazei Murill mushrooms 2. **Mistletoe** (European) 3. Curcumin 4. Glutathione **5. Intravenous vitamin C** 6. Red ginseng 7. Selenium 8. Training, relaxation and/or behavioral therapy **9. Massage therapy** 10.Short-term fasting
Reducing Risk
1. Ginkgo biloba 2. Aspirin (noting cautions)

See BCCT.ngo for more details about benefits and cautions regarding each therapy.

Many women with ovarian cancer are interested in going beyond conventional cancer therapies—that is, having an integrative approach to care that blends the best of conventional and complementary therapies. Your reading this indicates that you are likely one of these women.

Perhaps you have just been diagnosed with ovarian cancer or with a recurrence of your cancer. Now you may be embarking on surgery, chemotherapy, radiation therapy or some combination of these—maybe even all three. You are curious to see if complementary therapies or healing practices could help your treatment be more effective or bolster your resilience or prevent or manage treatment side effects.

Or maybe you've completed your treatments and you want to know what else you can do to keep the cancer from coming back or keep it at bay. Perhaps living with ovarian cancer has brought on difficult emotions, or made it hard to sleep well or challenged your relationships. Is there help for that?

Or perhaps you're dealing with advanced cancer and your conventional treatment options are slim—you ask "Are there any complementary therapies that would help me?" Or perhaps you feel you have limited time to live, and you want to bring the best quality to your life, however long that is.

So, what can I start with now? Any of the 7 Healing Practices are a good beginning in creating a body that cancer doesn't like. These practices support you through and possibly enhance your treatment. Ultimately, let your intuition guide you in choosing where to start with these healing practices. The 7 Healing Practices lead off the Integrative Therapies section of this handbook.

We have scoured the research literature to find what natural products (such as curcumin) and off-label drugs (such as metformin) might be beneficial or harmful in dealing with ovarian cancer. We have also found novel approaches such as chronomodulated treatment—scheduling your chemotherapy to coincide with your body's optimum circadian rhythms for killing cancer cells and protecting normal cells.

Optimally and safely using natural products, off-label drugs and unique administration methods happens best under the care of licensed healthcare providers who are knowledgeable and skilled in integrative cancer care. We help you explore these therapies in depth, as well as find help in putting together the options best for you.

BCCT Senior Researcher Laura Pole, RN, MSN, OCNS

Integrative Care in Ovarian Cancer

No matter where you are in your experience with ovarian cancer, there's good reason to seek integrative care: Women with ovarian cancer who followed a weekly individualized integrative medicine program during chemotherapy or palliative care had improved quality of life. They saw improvements in appetite, general well-being and ability to complete their conventional treatments. They also noted better control of symptoms such as fatigue, pain, anxiety, sleep disruption, nausea and cognitive impairment.1

Our goal is to help you live as well as you can for as long as you can using an optimal integrative combination of conventional and complementary therapies and approaches. Before investigating integrative care in ovarian cancer, we recommend reviewing integrative cancer care in general. For cancer care to be considered truly integrative, patients and their cancer treatment teams work together to find the best blend of conventional and complementary therapies that have been shown to be effective and safe.

We also recommend that you learn about your body terrain, which is your internal environment that is influenced by external factors such as the foods you eat, the chemicals around you, and the light and radiation you're exposed to. It's also influenced by internal factors such as stress hormones, sex hormones, your fitness level, your feelings of being loved, and your sense of purpose. This body terrain can influence the tumor microenvironment—the biochemical and physical interaction of cancer cancers and normal cells—in which the cancer exists, making it either more or less likely to spread. You can sometimes improve your body terrain with integrative practices. See Body Terrain and the Tumor Microenvironment.

Symptoms of Ovarian Cancer

- Abdominal pain or cramps
- Pain in the lower back or pelvis
- Abnormal vaginal bleeding or discharge
- Pain or bleeding during intercourse
- Nausea
- Loss of appetite or weight loss
- Bloating or gas
- Ascites (excess abdominal fluid)
- Fatigue
- Constipation or diarrhea
- Change in urinary frequency or urgency
- Obesity and unusual weight

Clinical Practice Guidelines

- National Comprehensive Cancer Network:
    - Professional Guidelines (Login required)
    - Guidelines for Patients: Ovarian Cancer
- American Society of Clinical Oncology: Gynecologic Cancer

Examples: Treatment Approaches from Noted Specialists and Researchers

Bastyr Integrative Oncology Care—A Naturopathic Oncology Approach

Naturopathic oncology care is complementary rather than alternative to conventional care—complementary therapies are used in conjunction with conventional treatments. Naturopathic oncologists are oriented to deliver integrative oncology care in tandem with their conventional oncology colleagues. For more information, see our discussion of naturopathic medicine and oncology at Integrative Medical Systems in Practice in the US and Canada.

BCCT advisor Leanna Standish, ND, is a fellow of the American Board of Naturopathic Oncology (FABNO) and works within the research institute of Bastyr University. Dr. Standish has been leading research studies investigating integrative therapies provided by naturopathic oncologists, as well as the costs and outcomes of that care.

A 2013 news article2 described preliminary results from the Bastyr University Integrative Oncology Research Center (BIORC) in treating 12 patients with stage 4 ovarian cancer. In looking at preventing recurrence, the researchers found that with their protocols, 83 percent of patients were still alive at three years. This is substantially higher than the 49 percent survival reported in the Surveillance, Epidemiology, and End Results Program (SEER) national data for those receiving conventional standard care (for all stages). Bear in mind, however, 12 patients is a small number—too small to conclude that these results are significant in comparison with the large SEER database.3

BIORC includes intravenous (IV) therapies. Of 46 patients, 18 received IV therapy, including IV artemisinin. At three years, a treatment effect was becoming apparent.

Bastyr University is also involved in the Canadian/US Integrative Oncology Study (CUSIOS): Advanced Integrative Oncology Treatment for Patients with Advanced Stage Cancer: A Prospective Outcomes Study, which is recruiting patients until January 2021.
Natural Products Used in the BIORC Stage 4 Ovarian Cancer Protocol

According to Neil McKinney's Integrative Naturopathic Oncology4

- Intravenous (IV) ascorbic acid
- Turkey tail mushroom (Trametes versicolor)
- Curcumin
- Bromelain
- Quercetin
- ECGC
- Helixor M mistletoe (made from apple tree mistletoe)

Integrative Oncology Program, The Oncology Service, Lin and Carmel Medical Centers, Clalit Health Services Israel

Patient Expectations in Using Complementary Approaches

One study found that patients using complementary medicine expected their gynecologic oncologist to be actively involved in the process of integration within supportive care and that complementary medicine consultations would focus on improving well-being.5

Lin and Carmel Medical Centers Haifa and Western Galilee District of Israel has an integrative oncology program. One of their leading services is integrative gynecologic oncology, based on a very close collaboration with their gynecologic oncologists. The integrative gynecologic oncology program is co-directed by Professors Eran Ben-Arye and Ofer Lavie.

According to Dr. Eran Ben-Arye, patients are referred by their gynecologic oncologists to the Integrative Oncology Program, where they begin by consulting with an integrative physician who develops a patient-specific complementary integrative medicine plan. The referring gynecologic oncologist is expected to contribute to the plan and support the patient in following it. Typical complementary therapy services:6

- Guidance on using herbs and dietary supplements
- Acupuncture and other manual-movement and body-based methods, such as acupressure, reflexology, qigong, the Paula and Feldenkrais methods
- Mind-body-spirit therapies, such as guided imagery, music therapy and spiritual care
- Anthroposophic medicine

The Integrative Oncology Program conducts research to explore the effectiveness of the patient-centered integrative model as a whole rather than a specific modality or intervention. Their studies focus on improvement in quality of life as well as improved adherence to chemotherapy protocols, mostly carboplatin and taxol.

Main findings:

- Greater chemotherapy completion: Participating in and adhering to a patient-oriented complementary integrative medicine treatment program may be linked to completion of

the planned chemotherapy regimen, as shown by a higher relative dose intensity (RDI), especially with carboplatin and paclitaxel.7

- Reduced drug use: The intervention may lower the need for drugs for managing symptoms, especially non-opioid pain relievers and anti-anxiety drugs.8
- Reduced fatigue: The intervention was associated with reduced cancer-related fatigue and improved other outcomes related to quality of life, especially among those who adhered to the regimen by having four or more treatments within 30 days of each session.9
- Reduced gastrointestinal symptoms: Breast and gynecological cancer patients experienced improved appetite, nausea/vomiting, mouth sores and/or pain, heartburn, abdominal flatulence and/or pain, and diarrhea or constipation. Greater benefit was seen in patients attending at least four treatment sessions.10 A separate study found reduced gastrointestinal concerns, with fewer chemotherapy-related hospitalizations. Including consultation with a registered dietician during complementary integrative medicine treatments led to greater reduction in nausea.11
- Improved quality of life: Improvements were seen in fatigue, physical function, role functioning, pain, drowsiness, anxiety, sleep disruption and other outcomes related to quality of life. Greater benefit was seen in patients attending at least four treatment sessions.12
- Altered patient perspective: Patients' experiencing empathy, emotional support, togetherness, and being treated as an individual seemed to generate internal processes and helped patients feel they weren't alone in their struggle. Patients felt a sense of agency, actively participating in the healing process.13

In sum, this program finds that patient-tailored complementary integrative medicine interventions may improve quality of life and well-being of patients undergoing chemotherapy and palliative care. These benefits come through both specific and non-specific mechanisms.14

Integrative Programs, Protocols and Medical Systems

- Alschuler & Gazella complementary approaches15
- Bastyr University Integrative Oncology Research Center (BIORC) protocol
- Block program16
- McKinney protocols17
- Ayurveda
- Traditional Chinese medicine18
- Traditional Korean medicine19

This guide from Ralph Moss, PhD, BCCT advisor and leading chronicler of integrative cancer treatments, shows you how to use four of the main tools that doctors use to decide on the best cancer treatments. It will help you learn why some cancer treatments that look good in clinical trials may not work for “real world” patients. It will help you answer two questions that the doctor may be hesitant to answer in the detail you need to decide about treatment:

- What are my chances of actually living longer if I take your treatment?
- What are the likely side effects, and how long will they last?

Integrative Therapies in Ovarian Cancer

7 Healing Practices: The Foundation

Let your intuition guide you in choosing where to start with these healing practices.

Any of the 7 Healing Practices are a good beginning. Eating well and moving more pack a powerful one-two punch in potentially improving treatment outcomes, enhancing quality of life and/or reducing risk of recurrence in ovarian cancer. Moreover, evidence shows that managing stress, sleeping well, creating a healing environment, sharing love and support and exploring what matters now can help women with ovarian cancer. Ultimately, let your intuition guide you in choosing where to start with these healing practices.

Eating Well

We at BCCT believe that eating well is one of the therapies that may help enhance your cancer treatments as well as restore your health, improve your quality of life and reduce your risk of recurrence. However, we emphasize that eating well alone will not likely prevent, cure or control cancer. Like every other therapy or approach included on this website, eating well is one component of an individualized integrative plan rather than a stand-alone therapy.

Treating the Cancer

The impact of diet on ovarian cancer survival:20
Higher Survival

- Higher serum levels of vitamin D (25-OH) at diagnosis
- Higher consumption of fiber
- Higher consumption of green leafy vegetables
- Higher consumption of fish
- Higher ratio of poly- to monounsaturated fat

Lower Survival

- Higher glycemic index, typically indicating a diet high in sugary and processed foods such as refined (white) wheat or rice
- Higher consumption of saturated fat

The researchers also found no association between total vitamin C, vitamin E, beta-carotene and retinol from diet plus supplements and ovarian cancer survival.21

Medline Plus recommends changes such as these to improve your poly- to monounsaturated fat ratio:22

- Snack on nuts instead of crackers or cookies
- Choose fish over red meat
- Add freshly ground flaxseed to foods
- Replace butter or margarine with healthier oils such as olive oil

Reducing Risk

Food choices are associated with ovarian cancer risk, although sometimes studies find conflicting results:23

Lower Risk

- Dietary calcium
- Tea, especially green tea[a]
- Vegetables (limited evidence)
- Whole soy and other foods containing Isoflavones
- Flavonoids
- Fiber
- Dietary folate, especially among women who consume alcohol
- Vitamin A and carotene (but results are inconsistent), stronger among women with mucinous histologic types of ovarian cancer, smokers and nondrinkers
- Omega-3 fatty acids (inconsistent results)

Higher Risk

- High glycemic load and consumption of total sugars (in African-American women)
- Consumption of whole milk, cheese or lactose (in one study of African-American women)
- Total nitrate, primarily found in processed and cured meats
- High intake of vitamin E
- Consumption of black tea (mainly for epithelial ovarian carcinoma)
- High consumption of total, saturated and trans fats, or animal and dairy fat (inconsistent evidence but generally indicating increased risk)[b]

a. No reduced risk of recurrence was found from double-brewed green tea as a maintenance intervention in women with advanced stage ovarian cancer after standard treatment.24
b. Some studies have reported an increased risk with a pro-inflammatory diet (high levels of saturated fatty acids, trans fatty acids and cholesterol),25 but two large, prospective cohort studies did not find an association.26

No significant associations are reported for red meat, eggs, fruit, vitamin D, vitamin C, coffee or four major carotenoids (alpha-carotene, beta-cryptoxanthin, lycopene and lutein). Lycopene (sources include tomatoes and other red vegetables and fruits) shows inconsistent results, but with more advantage among premenopausal women.27 See a recommendation for eating eggs in the Commentary section below.

Reduced risk was found for “an Asian diet”, but details of the diet were not reported.28

Optimizing Your Terrain

Foods can impact terrain factors to either promote or deter cancer growth and spread:

- Foods with a high glycemic index quickly raise blood sugar and may lead to chronic hyperinsulinaemia (abnormally high levels of insulin in blood), which is a potential risk factor for cancer.29
- High levels of triglyceride and low levels of HDL (high density lipoprotein, a type of cholesterol) correlate with a high severity (stage 3 or 4) of epithelial ovarian cancer.30

Moving More

Our Moving More summary has ideas on weaving this healing practice into your integrative cancer care plan.

Treating the Cancer

- Low muscle density at diagnosis and loss of muscle mass during treatment may be associated with worse survival outcomes.31
- Vigorous physical activity may benefit survival32

Managing Side Effects and Promoting Wellness

Benefits:

- Higher physical well-being for ovarian cancer patients engaging in increased moderate to strenuous physical activity during chemotherapy33
- Decreases in behavioral fatigue, cognitive fatigue and symptoms of depression, and improvements in sleep duration, sleep problems and daytime dysfunction for women who recently had surgery and completed their first cycle of adjuvant chemotherapy34

- Posttraumatic growth (positive psychological change experienced as a result of adversity and other challenges) in gynecological cancer survivors35
- Quality of life improvements in ovarian cancer survivors in a 2015 review of non-randomized studies;36 however, no effect on overall quality of life or specific aspects of quality of life (physical, emotional, social well-being and fatigue) in gynecologic cancer survivors in a 2018 review and meta-analysis37

Reducing Risk

- Risk reduction among the most active women in case–control studies but inconsistent results in cohort studies38

Managing Stress

Living with ovarian cancer can be stressful, and unmanaged stress can be harmful. Managing your responses to stressful situations and stimuli is possible and can benefit your health in many ways. Several complementary approaches promote healthy responses to stress: natural products, mind-body approaches, eating well, sleeping well and sharing love and support. See Managing Stress to explore taming stress and aiming it in a helpful direction.

Managing Side Effects and Promoting Wellness

- Improvements in quality of life and psychological flexibility as well as reduced distress, emotional disturbances, physical pain, and traumatic responses in patients receiving Acceptance and Commitment Therapy (ACT)39

Reducing Risk

- A large longitudinal study found that women with high posttraumatic stress disorder (PTSD) symptoms had a two-fold greater risk of ovarian cancer compared to women with no trauma exposure.40

Optimizing Your Terrain

- Chronic behavioral stress results in higher levels of stress hormones in tissues, greater tumor burden, and a more invasive pattern of ovarian cancer growth in mice. Tumors in stressed animals have increased formation of blood vessels (angiogenesis) and other markers of disease progression.41

Sleeping Well

Sleeping well can have profound ripple effects: reducing risk for ovarian cancer, managing stress, improving mood and energy, and modulating your immune system, to name a few.

Some lifestyle behaviors can promote quality sleep. For example, going to bed before midnight is associated with longer sleep in ovarian cancer survivors in the first six months following treatment.42 Explore this vital healing practice in BCCT's Sleeping Well summary.

Reducing Risk

- Compared to average sleepers (7-9 hours per night), long sleepers (10 or more hours per night) had an increased risk of estrogen-mediated cancers, including ovarian cancer.43

Creating a Healing Environment

If you are trying to reduce your risk of cancer recurrence, or if you are at risk for ovarian cancer, creating a healing environment may be an important part of your wellness plan. Ideas for reducing harmful exposures linked to ovarian cancer and increasing your exposure to clean air and water, nature and beneficial light are reviewed in Creating a Healing Environment.

Reducing Risk

Many environmental exposures are associated with increased risk of ovarian cancer. Reducing or eliminating these exposures in your life can reduce your risk:

- Talcum powder used in the genital area, with varying risk according to cancer subtype44
- Endocrine-disrupting chemicals (EDCs) can cause cell growth in estrogen-responsive ovarian cancer cells.45 Hundreds or even thousands of EDCs are used in consumer products, including foods and food packaging. Those with known or suspected impacts on ovarian cancer cells include these:
    - Bisphenol A (BPA)
    - Hormone residues in meat, poultry and dairy products
    - Some pesticides, such as organophosphates
    - Asbestos46
- Ionizing radiation, such as x-rays47

Sharing Love and Support

The experience of being surrounded by love, family and friends who care about you, and the kindness of strangers—including doctors and other healers who care for you—is for many a powerful experience. Sharing Love and Support guides you in this practice to light the path to your healing.

Managing Side Effects and Promoting Wellness

- Social support predicted lower psychological distress and higher psychological well-being among women with ovarian cancer.48
- Social support was associated with improved mental state and various aspects of quality of life in women with ovarian cancer undergoing chemotherapy.49

- Compared to those who felt alone, helpless and emotionally distraught, women with ovarian cancer who felt loved and supported and who kept up their morale had more combative natural killer (NK) cells—lymphocytes identified for their ability to kill tumor cells.50

Reducing Risk

- A Swedish study found a decreased risk of serous ovarian cancer in women with fewer people available for informal socializing.51 This is opposite to findings (above) that greater social support is associated with better disease outcomes after diagnosis. The authors speculate that perhaps informal socializing in a large social network may "imply stressful expectations to support others to a higher degree." Because this is the only study we could find with this result, we await further research to confirm and explain these results.

Exploring What Matters Now

Whether you approach meaning from a spiritual or religious perspective or from a practical perspective, paying attention to what matters to you now is perhaps one of the best places to start in making decisions about your care. This exploration may also improve your response to treatment, lower your distress and improve the quality of your life. Look inside BCCT's Exploring What Matters Now summary.

Treating the Cancer

- Greater decline in levels of CA-125 (a biomarker of ovarian cancer) during treatment were associated with higher levels of optimism at the start of chemotherapy.52

Managing Side Effects and Promoting Wellness

- Lower levels of distress and a positive association with health-related quality of life in epithelial ovarian cancer patients undergoing chemotherapy were seen with higher levels of optimism.53

Beyond the 7 Healing Practices: Further Integrative Therapies

Complementary Approaches in Ovarian Cancer: Involving Conventional Healthcare Providers

A 2018 review of complementary treatments for gynecologic cancer found these rates of use and communication between patients and healthcare providers:56

- Fewer than 25 percent of patients in the US received any information about complementary or alternative therapies from their physicians, nurses or other conventional medical providers.

- In Canada, most patients think their oncologists should be aware of their use of complementary or alternative therapies, but only 50 percent had informed their doctors of use.
- In a US study of ovarian patients and survivors, involving conventional healthcare providers in decisions about complementary/alternative therapies and lifestyle changes was associated with greater vitality and better emotional health.
- High adherence to a weekly patient-tailored integrative medicine program is correlated with greater rates of adherence to a conventional chemotherapy dosing protocol and improved outcomes related to quality of life:
    - Cancer-related fatigue
    - Gastrointestinal concerns (nausea, appetite)
    - Pain
    - Anxiety
    - Sleep-related problems
    - Cognitive impairment
    - General well-being

These findings included patients receiving chemotherapy and/or palliative care.

- Patients with epithelial ovarian cancer undergoing a second-line chemotherapy regimen were more likely to keep to a more “healthy” diet than those undergoing first-line treatment regimens. (A healthy diet was defined as cooking vegetables in water and increased use of rye bread, pasta, buttermilks, vegetables, fruit, oils, nuts and juices.)

Traditional Medicine Therapies

Throughout this summary, you will find examples of therapies used by and in many cases created by traditional medical systems.

Foods and herbs such as medicinal mushrooms, soy and curcumin are part of traditional systems. Evidence shows that herbs used in traditional Chinese medicine (TCM) may help in maintaining immune function in women with ovarian cancer. Mind-body practices such as mindfulness meditation and yoga also have roots in these systems. Acupuncture, another approach that is part of the Chinese and Korean medicine traditions, has helped those with ovarian cancer manage symptoms such as nausea.

“While many herbals have been shown to have anticancer properties, the research to date has been largely preclinical (in vitro), without clinical evidence of their effectiveness.”62 Here we make clear the level of evidence behind natural products.
Group 1: Good clinical evidence of efficacy & safety, easy access

Conventional treatments are readily available and are discussed below. Complementary therapies can be useful to enhance conventional treatment effects, improve quality of life and

possibly even extend life for those with ovarian cancer. Many complementary therapies—when chosen thoughtfully, reviewed with your oncology treatment team and used alongside conventional therapies—can become part of your integrative cancer care approach.

Therapies are grouped according to their effects:

- Treating the cancer
- Managing side effects and promoting wellness
- Reducing risk
- Optimizing your terrain

We present natural products in six groups:

1. Good clinical evidence of efficacy & safety, easy access
2. Good clinical evidence of efficacy & safety, limited access
3. Limited clinical evidence of efficacy but good safety, used in leading integrative programs
4. Limited clinical evidence of efficacy, or significant cautions, but potential significant benefit
5. Especially promising preclinical or emerging clinical evidence of efficacy and safety
6. Evidence of no efficacy or may be dangerous

Off-label, overlooked and novel cancer approaches (ONCAs) are grouped separately:

Group A: Good clinical evidence of efficacy
Group B: Limited clinical evidence of efficacy
Group C: Promising preclinical evidence only
Group D: Evidence of no efficacy or may be dangerous

Other integrative therapies and approaches are described but not categorized. See the full summaries as linked for more information on each of these therapies.

Treating the Cancer

Working against cancer growth or spread, improving survival, or working with other treatments or therapies to improve their anticancer action

Conventional Treatments

Some newer therapies and their outcomes:

- Pressurised intraperitoneal aerosol chemotherapy (PIPAC) is a relatively new treatment for patients with peritoneal metastases. A 2019 review found that an objective clinical response of 62–88 percent was reported for patients with ovarian cancer (median survival of 11–14 months) with PIPAC. Repeated PIPAC did not have a negative effect on quality of life.57
- Pulsed low-dose rate radiation therapy (PLDR-RT) delivers conventional radiation doses in pulses of small doses with intermittent pauses. A small study involved PLDR-RT for

patients with gynecologic and other cancers of the pelvis. Patients had undergone radiation therapy to the pelvis previously. Twenty-three patients were treated with a curative intent and 15 were treated palliatively. At one-year, 59 percent of patients treated for curative intent had a clinical, biochemical or radiographic response, and six of the 23 patients had no evidence of disease at their last follow-up. Among the patients treated palliatively, 61 percent had a clinical or radiographic response.58

- Percutaneous thermal ablation (TA) uses either heat, cold or a chemical to destroy cancerous tissue in a target organ. A special type of needle is advanced directly into a tumor within the target organ, guided by ultrasound, computerized tomography (CT) scan and/or X-ray.59 A single session was safe and highly effective in controlling local tumors in metastatic ovarian cancer.60

Sometimes adjustments in how conventional treatments are applied can impact outcomes. A 2011 retrospective analysis suggested that epidural anesthesia and analgesia for ovarian serous adenocarcinoma surgery may reduce mortality during the initial years of follow-up compared to general anesthesia (GA) and intravenous opioid analgesia.61

We recommend these resources to introduce the science and conventional therapies:

- National Cancer Institute:
    - About Cancer
    - Ovarian, Fallopian Tube, and Primary Peritoneal Cancer—Patient Version
    - Ovarian, Fallopian Tube, and Primary Peritoneal Cancer—Health Professional Version
- Cancer.net: Ovarian, Fallopian Tube, and Peritoneal Cancer

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

Combination therapy of Indole 3-carbinol (I3C) and EGCG

- Improved survival, progression-free survival, performance scores and quality of life when used prior to and during combined treatment, including neoadjuvant (prior to surgery) platinum-taxane chemotherapy, surgery, and adjuvant (supplemental) platinum-taxane chemotherapy63

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Melatonin

- Less aggressive ovarian cancer with higher serum levels of melatonin in clinical studies; in preclinical studies, effects in many cancer types including hormone-dependent cancers:64
    - Restored cancer cells' sensitivity to chemotherapy drugs (chemosensitivity)

    - Worked against cancer cell proliferation and development of new blood vessels (angiogenesis)
    - Modulated immunity
    - Induced oxidation
- Combined benefit with tamoxifen or cisplatin in preclinical and small clinical studies65
- Used in these plans and protocols:
    - Alschuler & Gazella complementary approaches66
    - McKinney protocols67

Mistletoe (Viscum album)

- No effect on survival when added to a conventional therapy in a 2019 systematic review;68 however, a significant increase in survival was found especially among ovarian cancer patients with distant metastases in a randomized clinical trial.69
- Increased survival, including when combined with other therapies (limited evidence) in a 2009 review70
- Findings from a 2017 study:71
    - Anticancer activity in both cisplatin-sensitive and cisplatin-resistant ovarian cells
    - Increased chemosensitivity to carboplatin in ovarian cancer cell lines
    - Increased sensitivity in cisplatin-resistant cells treated with carboplatin and paclitaxel
- Used in these plans and protocols:
    - Bastyr University Integrative Oncology Research Center (BIORC)
    - McKinney protocols72
- Used in traditional Chinese medicine

Shiitake mushrooms

- Partial response in a case study of a woman with recurrent cancer treated with lentinan together with adoptive immunotherapy for five months73
    - Tumor disappearance in a case study of a woman with a cisplatin-resistant tumor treated with lentinan combined with IA 5FU74
- Used in these plans and protocols:
    - Bastyr University Integrative Oncology Research Center BIORC
    - McKinney protocols75
- Used in traditional Chinese medicine

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Combinations of therapies

- Lipoic acid, hydroxycitrate and low-dose naltrexone (LDN)

    - Extended survival in some patients with advanced cancer who had failed standard chemotherapy and were offered only palliative care in a small case series76
- Oral vitamin C, vitamin E, beta-carotene, coenzyme Q10 and a multivitamin/mineral complex, plus intravenous vitamin C as an adjunct (supplement) to chemotherapy
    - Normalization of CA-125 (a biomarker of ovarian cancer) and no evidence of recurrence for more than three years after diagnosis in a case report77

Glutathione

- Better-than-expected overall survival in women with advanced ovarian cancer without significant toxicity of the auditory nerves, kidneys or peripheral nerves when used with high-dose cisplatin and carboplatin78
- Caution: “profoundly associated with chemoresistance to platinum salts” such as cisplatin and carboplatin—some of the main therapy strategies in ovarian cancer treatment79

Intravenous vitamin C

- Trends toward increased progression-free survival and improved overall survival in a small number of patients treated with high-dose IV vitamin C compared to chemotherapy80
- Notable preclinical evidence:
- Increased effects of chemotherapy drugs carboplatin and paclitaxel in mice81
- Decreased growth rates of ovarian tumors established in mice82
- Note the significant cautions in our Vitamin C summary
- Used in the Bastyr University Integrative Oncology Research Center (BIORC) protocol

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Agaricus blazei Murill mushroom

- Cytotoxic (cell-killing) effects against human ovarian cancer cells with an A. blazei extract83
- Caution: linked to severe liver dysfunction in three patients with unspecified cancers84

Ashwagandha (Withaferin A)

- Reduced likely cancer stem cells in orthotopic ovarian tumors—which are thought to lead to cisplatin resistance and recurrence of ovarian tumors—either alone or in combination with cisplatin in mice85

Astragalus

- Potentiated the effects of gemcitabine (used with breast, ovarian, non-small cell lung, and pancreatic cancers), possibly allowing for reduced dose and toxicity without sacrificing treatment effectiveness86

Combinations of therapies

- Astragalus and curcumin as an adjuvant (supplemental) treatment to cisplatinum
    - Inhibited growth of stage 1 tumors, but not stage 2 or 3 tumors, when used in mice as an adjuvant treatment to cisplatinum87 . Anticancer Research. 2015 Jun;35(6):3193-207.
- Dihydroartemisinin and curcumin
    - Synergistic antitumor effects in animals and ovarian cancer cells88

Flaxseed

- Promoted cell death (apoptosis) in ovarian tumors in hens, using both whole flaxseed and defatted flaxmeal (the lignan component)89

Lycopene supplements

- Findings from a 2017 animal study:90
    - Reduced metastatic load
    - Diminished tumor burden (tumor mass)
    - Enhanced anti-tumor effects of paclitaxel and carboplatin
    - Reduced number of proliferating cancer cells
    - Decreased expression of the ovarian cancer biomarker CA-125

Milk thistle components

- Reduced tumor volume in animals91
- Inhibited cell growth and induced cell death (apoptosis) when combined with paclitaxel92
- Anticancer effects including suppressed proliferation of ovarian cancer cells.93
- Potentiated cisplatin and doxorubicin in inhibiting cell proliferation94
- Inhibited migration and invasiveness (metastasis) and induced cell death (apoptosis) against metastatic and resistant ovarian cancer with HM015k, a silybin derivative95

Nicotinamide (a form of vitamin B3, also known as niacinamide)

- Enhanced radiation response in mice,96 with minimal effects in normal tissues, with best response when given at the time of peak plasma drug concentrations97

Quercetin

- Induced cell death (apoptosis) in lab and animal studies98
- No significant association with anticancer effects in epidemiological findings in a 2016 review99
- Inhibited growth and other anticancer effects when used with tiazofurin in cell studies100
- Suppressed metastasis in cell studies101

Selenium

- Prevented resistance to melphalan or cisplatin and enhanced efficacy of cisplatin in suppressing the growth of human ovarian tumors in animals102
- Inhibited growth of malignant cells103

Other therapies with preclinical evidence only for treating the cancer

- Amino-bisphosphonates to potentiate gammadelta T-cell immunotherapy
- Artemisinin, dihydroartemisinin and ARS4
- Calcium/Calmodulin Dependent Protein Kinase Kinase 2 (Ca2+/calmodulin (CaM)-dependent protein kinase kinase 2 (β) (CaMKK2) depletion
- Celecoxib (Celebrex)
- Conjugated linoleic acid (CLA) (About Herbs)
- Combination of curcumin and quercetin
- Curcumin
- Diindolylmethane (DIM) and other Isothiocyanates from cruciferous vegetables
- EGCG / green tea extract
- Fermented wheat germ extract
- Ginger
- Ginkgo biloba (About Herbs) (with significant cautions)
- Grape seed extract
- Indole 3-carbinol (I3C) (About Herbs)
- Iron depletion
- Isoflavones, including genistein from soy
- Jingli neixao constituents (Lonicera, Ginseng, Angelica, Atractylodes, Prunella, Pinellia, Sargassum, Laminaria, Paeoniae, Bupleurum and Poria)
- Medical cannabis and cannabinoids
- Modified citrus pectin
- Omega-3 fatty acid supplements
- Red yeast rice extract (About Herbs)
- Reishi mushrooms
- Resveratrol
- Scutellaria barbatae (About Herbs)
- Vitamin A (retinol) (About Herbs)
- Vitamin K2 (Life Extension)
- Zinc (About Herbs)

Group 6: Evidence of no efficacy or may be dangerous

Ginseng

- No effect of red ginseng on the prognosis of epithelial ovarian cancer in a small clinical trial104

Vitamin D supplements

- No evidence that vitamin D supplementation prior to diagnosis is associated with survival among women with several types of cancer, including ovarian, in a large retrospective analysis105

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

These therapies have exciting potential and/or proven benefits. However, some carry higher risks of side effects, interactions with other treatments and other adverse medical events than other therapies we review. Cautions are noted with each therapy, and we strongly encourage you to consult your doctor before using these therapies—even over-the-counter drugs—for cancer treatment. We also note whether a prescription is needed or if a therapy is not widely available.

Group A: Good clinical evidence of efficacy

May be used in integrative protocols and programs

Beta blockers

- Findings from a 2016 review:106
    - Reduced the tumor-promoting effects of catecholamines (hormones produced by the adrenal glands), especially nonselective beta blockers, in retrospective clinical studies
    - Provided a significant survival advantage, especially nonselective beta blockers
    - Sensitized malignant cells to chemotherapeutic agents, potentiating (enhancing) chemotherapy effects in preclinical studies
- Requires a prescription from a licensed physician

Chronomodulated treatment

- Enhanced control of advanced ovarian cancer while minimizing side effects with optimally timed cancer chemotherapy with doxorubicin or pirarubicin (6:00 am) and cisplatin (6:00 pm)107

Metformin

- Better survival in a case-control clinical study108
- Reduced mortality in subjects treated with metformin monotherapy (treatment only with metformin) at the time of diagnosis for ovarian/endometrial cancer or for 90 days after diagnosis in a retrospective cohort study.109
- Notable preclinical evidence:
- Altered metabolism in ovarian cancer cells, prevented tumor growth, and increased sensitivity to chemotherapy in cell and animal studies110
- Enhanced anticancer effects of olaparib in ovarian cancer cells111
- Inhibited low-grade serous ovarian cancer cells and had inhibitory effects with trametinib or 2-deoxyglucose (2DG)112

- Requires a prescription from a licensed physician

Group B: Limited clinical evidence of efficacy

May be used in integrative protocols and programs

Copper chelation using tetrathiomolybdate or other chelators

- Enhanced response to cisplatin and incremental improvement in overcoming resistance to platinum drugs in clinical use113
- Notable preclinical evidence:
- Increased uptake of cisplatin into tumors but not normal tissues, and inhibited tumor angiogenesis (creation of blood vessels) in mice114
- Enhanced cytotoxic (cell-killing) effects of doxorubicin; sensitized one cell line to mitomycin C, fenretinide, and 5-fluorouracil; and other anticancer effects115

Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and COXII inhibitors
Aspirin and other NSAIDs:

- Improved survival of serous ovarian cancer with more intensive postdiagnosis use116
- Improved ovarian cancer-specific survival with recent use of aspirin and non-aspirin NSAIDs after diagnosis in an analysis of large cohorts117
- A combination of carboplatin (chemotherapy drug) and low-dose celecoxib (NSAID) showed favorable response rates and favorable progression-free survival in heavily pretreated ovarian cancer patients with recurrent disease118
- Unclassifiable impact on mortality in one review119
- Notable preclinical evidence:
    - Phosphatidylcholine-associated aspirin (aspirin-PC) showed anticancer effects in cells and reduced ovarian cancer growth by 50 percent to 90 percent in animals, with no detectable gastrointestinal toxicity; the effect was enhanced in combination with bevacizumab (Avastin) or B20.120
    - Reduced tumor volume in mice, with diclofenac and sulindac sulphide showing the strongest activity, and combinations of diclofenac plus sulindac sulphide, diclofenac plus naproxen, sulindac sulphide plus naproxen and sulindac plus ebselen showing greater effects than single agents121
- The US Food and Drug Administration warns that ibuprofen, naproxen and ketorolac increase the risk of having a heart attack or stroke; medical supervision is strongly advised with all NSAIDs
- May require a prescription from a licensed physician

Statins

- Increased survival, especially with pre-diagnosis use122
- Associated with serious side effects including permanent muscle damage, increased incidence of diabetes and impaired cognitive function; their potential benefits in ovarian

cancer must be weighed against the risk, and they should be discontinued promptly if serious side effects occur
- Requires a prescription from a licensed physician

Group C: Promising preclinical evidence only

Dichloroacetate
- Inhibited growth and enhanced cell death (apoptosis) of ovarian cancer cells and suppressed growth of xenograft ovarian tumors in mice when used with metformin123
- Anticancer effects including blocked glycolysis (metabolism of sugar and carbohydrates) and increased cell death (apoptosis) in lab studies124
- Overcame resistance to cisplatin in ovarian cancer cells125
- Increased toxicity of selected platinum compounds (carboplatin, satraplatin, JM118, and oxoplatin), but not cisplatin, picoplatin, and oxaliplatin in cell studies126
- Caution: nerve and liver injury can be very significant; medical supervision is needed

Low-dose naltrexone
- Suppressed human ovarian cancer in mice in conjunction with opioid growth factor127
- Repressed tumor progression by reducing DNA synthesis and angiogenesis (formation of blood vessels to supply tumors), and also enhanced the effects of cisplatin in mice and cell cultures128
- Requires a prescription from a licensed physician

Noscapine
- Effective against taxane-resistant ovarian cancer with minimal neurotoxicity or immune suppression in mice129
- Inhibited proliferation of both paclitaxel-sensitive and paclitaxel-resistant human ovarian carcinoma cells130
- Increased anticancer activity of cisplatin against drug-resistant ovarian cancer cells131
- Increased cell death (apoptosis) in ovarian cancer cells132

Therapies using heat, sound or light

Hyperthermia
- Hyperthermic intraperitoneal chemotherapy (HIPEC)
- Cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is recommended by the Peritoneal Surface Oncology Group International for ovarian cancer.133
- Improved overall survival rates for both primary and recurrent epithelial ovarian cancer (EOC) in several reviews134
- Other reviews concluded that evidence to date is insufficient to support a general recommendation for use in ovarian cancer.135

- Whole-body hyperthermia
- Small clinical trials have found isolated cases of complete remission, extended survival and other benefits for ovarian cancer patients.136

Managing Side Effects and Promoting Wellness

Managing or relieving side effects or symptoms, reducing treatment toxicity, supporting quality of life or promoting general well-being

Conventional Treatments

A study of sexual activity and functioning of epithelial ovarian cancer survivors found that "low estrogen levels were significantly associated with sexual discomfort."139 Vaginal moisturizers and vaginal rings supplying low-dose estrogen are used to address sexual discomfort and difficulties. Although these are conventional therapies, they may not be included in many conventional treatment programs unless or until a patient expresses a need.

Hormone replacement therapy (HRT) is used for hot flashes and sexual discomfort that arise with ovarian cancer and treatments.

A combination regimen of megestrol acetate (MA) plus L-carnitine, celecoxib (a non-steroidal anti-inflammatory drug) and antioxidants has shown these effects:140

- Improved metabolism and inflammation as well as lean body mass, resting energy expenditure, fatigue and overall quality of life compared to MA alone
- Improved appetite and performance status (a measure of physical function) compared to MA alone

Pulsed low-dose rate radiation therapy (PLDR-RT) delivers conventional radiation doses in pulses of small doses with intermittent pauses. A small study involved PLDR-RT for ovarian and other cancers of the pelvis. Of the 50 percent of patients who reported pain at the local site before treatment, 68 percent reported an improvement in pain after PLDT-RT.141

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Curcumin

- Improved quality of life in patients with solid tumors undergoing chemotherapy treatment142

Ginger

- Reduced nausea and vomiting during chemotherapy in most but not all reviews143 —as effectively as metoclopramide but not ondansetron in one study144 —and improved response to antiemetic drugs (drugs that prevent or reduce nausea and vomiting)145

Panax ginseng

- Improved emotional functioning and decreased symptoms of fatigue, nausea and vomiting, and difficulty breathing, reduced anxiety and interference affecting quality of life and improved daytime somnolence (sleepiness) in patients with epithelial ovarian cancer (EOC)146
- No significant improvement with cancer-related fatigue, anxiety, depression, other cancer-related symptoms, quality of life and physical function among patients with advanced cancer147
- Weak evidence of reduced fatigue across illnesses and conditions, with low risk of adverse effects148
- Reduced nausea and vomiting in patients with colorectal cancer149

Vitamin E

- Reduced peripheral neuropathy in several small clinical studies, one of which used alpha-tocopherol (a form of vitamin E)150

Group 2: Good clinical evidence of efficacy & safety, limited access

Some may require a prescription, for example.

Medical cannabis and cannibinoids

- A review from the National Academies of Sciences, Engineering and Medicine reported these outcomes related to cancer:151
- Conclusive or substantial evidence that cannabis or cannabinoids are effective for treating pain in adults and chemotherapy-induced nausea and vomiting
- Moderate evidence for improvement in secondary sleep disturbances
- Limited, insufficient or absent evidence supporting improvement in appetite or anxiety
- A 2018 review and meta-analysis found no significant differences between cannabinoids and placebo for improving caloric intake, appetite, nausea and vomiting, a decrease in pain greater than 30 percent, or sleep problems in cancer patients.152
- Access varies by country or US state, with moderately easy access in some areas and very limited or no legal access in others

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Agaricus blazei Murill mushrooms

- Improved side effects: appetite, hair loss, emotional stability and general weakness in gynecologic cancer patients undergoing chemotherapy153
- Used in the Alschuler & Gazella complementary approaches154

Individualized homeopathy

- Improved total well-being, physical well-being and emotional well-being after three months of individualized treatment, at least three years after the last chemotherapy treatment, in an uncontrolled small clinical trial155
- Used in the McKinney protocols156 (Aurum muriaticum natronatum, Lachesis mutus, Lilium tigrum, Pulsatilla nigricans and Zeel)

Mistletoe (Viscum album)

- Improved pain and appetite loss, and a trend toward less neutropenia (low count of neutrophils, a type of white blood cell) in breast cancer patients157
- No effect in a review and meta-analysis of all cancer types158
- Used in the McKinney protocols159
- Used in traditional Chinese medicine

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Astragalus

- Reduced incidence and severity of chemotherapy-induced peripheral neuropathy and improved nerve function and functional performance in people with various types of cancer (mostly gastrointestinal/colorectal, but also breast and ovarian cancers), in some studies improving the response when used with western analgesics160

Combinations of therapies

- Protecton Zellactiv: selenium (200 mcg daily), vitamin E, beta-carotene, riboflavin, niacin and vitamin C
    - Decreased nausea, vomiting, diarrhea, mouth sores, hair loss, flatulence, abdominal pain, weakness, malaise or loss of appetite when used with cisplatin and cyclophosphamide chemotherapy in a pilot study161

Ginkgo biloba

- May improve the neurological side effects of cisplatin related to oxidative stress, including hearing impacts162
- Inhibited paclitaxel metabolism, potentially increasing toxic effects associated with cancer therapy163
- Cautions:
- Potential major herb–drug interactions with aspirin or warfarin, resulting in an increased risk of gastrointestinal bleeds164
- Ginkgo biloba leaf extract has been classified as a possible human carcinogen (Group 2B) by the International Agency for Research on Cancer165 , but see a discussion of that listing.
- Used in traditional Chinese medicine and Ayurveda

Glutathione

- Increased quality of life of advanced-stage ovarian cancer patients with less toxicity when used together with cisplatin166
- No effect on peripheral neuropathy when used with carboplatin and paclitaxel for ovarian and other cancers167
- Trend toward reduced neurotoxicity of cisplatin without impairing its effectiveness against tumors in women with ovarian cancer168
- Trend for neuroprotection (less toxicity to nerves) for a group receiving cisplatin at a higher dose with glutathione compared to a group with a lower dose of cisplatin and no glutathione169

Intravenous vitamin C

- Reduced chemotherapy-associated toxicity in patients with ovarian cancer170

L-glutamine

- Lower scores for severity of signs or symptoms of peripheral neuropathy, but with no effect reducing the frequency171

Red ginseng

- Improved emotional functioning and decreased symptoms of fatigue, nausea and vomiting, and labored breathing, plus reduced anxiety and interference affecting life and improved daytime drowsiness in a small clinical trial172

Selenium

- Increased white blood cell counts and reduced hair loss, flatulence, abdominal pain, weakness, malaise and loss of appetite in women with ovarian cancer undergoing chemotherapy173
- Reduced episodes and severity of radiotherapy-induced diarrhea in selenium-deficient cervical and uterine cancer patients174

- Reduced radiotherapy-induced diarrhea in patients with uterine cancer without affecting the effectiveness of the radiation therapy as shown by long-term survival175

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Quercetin

- Reduced cisplatin toxicity to kidneys without affecting impact in the tumors in animal studies176

Resveratrol

- Protected against doxorubicin-induced cardiac (heart) toxicity in lab and animal studies177

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

These therapies have exciting potential and/or proven benefits. However, some carry higher risks of side effects, interactions with other treatments and other adverse medical events than other therapies we review. Cautions are noted with each therapy, and we strongly urge you consult your doctor before using these therapies—even over-the-counter drugs—for cancer treatment. We also note whether a prescription is needed or if a therapy is not widely available.

Group C: Promising preclinical evidence only

Low-dose naltrexone

- Reduced toxicity (weight loss) associated with cisplatin in animal studies178
- Requires a prescription from a licensed physician

Metformin

- Prevented cisplatin-induced peripheral neuropathy in mice179
- Protected against cisplatin-induced cognitive impairment in mice180
- Requires a prescription from a licensed physician

Energy Therapies

Healing Touch

- No evidence of improvements in quality of life with hypnosis, therapeutic massage and healing touch with each cycle of chemotherapy181

Mind-Body, Spiritual and Consciousness-changing Approaches

Training, Relaxation and/or Behavioral therapy

- Improved overall sexual functioning and psychological distress that was maintained at a six-month follow-up182

- Improved symptoms of anxiety and personality development, but not major depression183
- Reduced anxiety, with psycho-oncology therapy slightly more effective than a single relaxation intervention in preventing depression184

Hypnosis

- Reduced pain185
- No evidence of improvements in quality of life with each cycle of chemotherapy when combined with therapeutic massage and healing touch186

Yoga

- Improved depression, negative affect (emotional state), state anxiety (anxiety in response to a specific situation), mental health and overall quality of life, with decreases in fatigue187

Manipulative and Body-Based Methods

Acupuncture

- Improved social function, but not symptoms of pain or insomnia (preliminary evidence)188
- Prevented immediate-onset vomiting following carboplatin-paclitaxel chemotherapy; as effective as the anti-nausea drug ondansetron for immediate-onset vomiting and superior to ondansetron in preventing delayed vomiting at days four and five. The acupuncture-treated group also reported less insomnia and constipation and better general quality-of-life scores.189
- Lower frequency of nausea and incidence of constipation in patients treated by chemotherapy when combined with ginger moxibustion, plus fewer side effects, lower cost, and less risk than the control therapy of intravenous tropisetron hydrochloride and dexamethasone190

Massage Therapy

- Clinical practice guidelines:
    - The 2016 American Society of Clinical Oncology clinical practice guideline for managing chronic pain in survivors of adult cancers makes a weak recommendation for using massage.191
    - The patient-education resource from the American Society for Clinical Oncology (ASCO) advises an integrative approach including massage to manage peripheral neuropathy.192
- Reduced feelings of hopelessness in ovarian cancer patients undergoing treatment193
- Reduced severity of subjective physical complaints and reduced urinary epinephrine, a marker of stress following Anma therapy (Japanese massage) in gynecologic cancer survivors194

- No evidence of improvements in quality of life with hypnosis, therapeutic massage and healing touch with each cycle of chemotherapy195
- The National Cancer Institute urges massage therapists to take precautions with all cancer patients and avoid massaging specific vulnerable areas of the body. In addition, certain patients with multiple bone metastases may be at risk for fracture during deep massage.196

Diets and Metabolic Therapies

Fasting

- Fasting from 36 hours before to 24 hours after chemotherapy (60-hour fast) improved quality of life and fatigue during chemotherapy.197
- Preliminary evidence (not yet peer-reviewed) found that a 48-hour, water-only fast at the time of each chemotherapy cycle was well tolerated without increasing weight loss, hospital admissions or chemotherapy dose reduction or delays. Patients did not see an improvement in quality of life, but the fasting patients needed only half as many treatment modifications as the nonfasting group.198
- Fasting reduced chemotherapy side effects of neutropenia (low count of white blood cells called neutrophils) and thrombocytopenia (low count of platelets) in a patient with ovarian cancer.199

Commentary: Fasting

For people having significant side effects, especially gastrointestinal, from chemo, naturopathic oncologist and BCCT advisor Lise Alschuler recommends fasting for 48 hours—from after dinner on the day before chemo, through the day of chemo and the day following chemotherapy. The chemo fast can be a water fast (which includes coconut water and vegetable broths), or you can eat up to 600 calories per day of vegetable soup and/or low-carb vegetables. She stresses the importance of your being motivated to fast, and also that fasting during chemotherapy should be cleared with your treating oncologist. You should modify or stop the fast if you become dizzy or weak (try adding boiled eggs or nuts), or if you feel worse than if you had eaten.
Eggs

Dr. Alschuler and her colleague Karolyn Gazella advise people with risk for ovarian to consider limiting egg intake to fewer than five eggs a week, while choosing eggs from free-roaming, organically fed chickens. They also advise boiling or poaching eggs, as these methods do not oxidize the yolk fat.247

Sexual Activity, Depression and Ovarian Cancer

A number of sexual difficulties can arise if ovarian cancer treatment causes hormonal changes:

- Vaginal dryness leading to painful intercourse

- Vulvodynia (pain and/or burning in the vulvar area)
- Decreased libido

Focus on survival can lead to a lack of interest in sex. Symptoms, including depression, anxiety and fatigue can also lead to sexual difficulties.

Your oncology care team should ask about changes in sexual function since your diagnosis, but if you haven't been asked about or prepared for managing potential sexual difficulties, ask your doctor about this. For providers uncomfortable with management, a number of programs in sexuality after cancer are available at tertiary care centers.137

A study of sexual activity and functioning of epithelial ovarian cancer survivors (EOCSs) found patterns regarding sexual activity, sexual pleasure and sexual discomfort:138

- Sexually active epithelial ovarian cancer survivors reported lower levels sexual pleasure and higher levels of sexual discomfort compared to the general population.
- Treatment with chemotherapy in addition to surgery compared to surgery alone was associated with more sexual discomfort.
- Higher level of sexual discomfort was associated with both lower serum levels of estradiol and sexual hormone binding globulin (SHBG).
- Greater sexual discomfort was associated with lower levels of depression. The study design did not allow researchers to determine what may drive this association.

Because sexual activity and pleasure contribute to survivors' quality of life, the researchers suggest that healthcare professionals be mindful of sexual health and function, informing and treating patients as indicated.

Reducing Risk

Reducing the risk of developing cancer or the risk of recurrence

Risk Factors

Risk factors for ovarian cancer that are generally not under a woman's control:202

- Family history of ovarian cancer or BRCA1 and BRCA2 mutation (these mutations are responsible for most family history incidence)
- Age and menopause status
- Greater genetically predicted adult height
- Greater number of menstrual cycles, influenced by early menarche, late menopause, fewer pregnancies or periods of lactation or contraceptive use
- Infertility
- Personal history of breast cancer

Lifestyle Associations
Increased Risk: Risk factors that may be influenced by a woman's lifestyle choices and behaviors:203

- Smoking tobacco with (borderline) mucinous cancers
- Use of hormone replacement therapy (estrogen plus progesterone) for serous and endometrioid ovarian cancers
- Breastfeeding is modestly associated with a decreased risk of premenopausal ovarian cancer for the mother, likely related to fewer menstrual cycles.
- Lack of physical activity (limited evidence)
- Being overweight or obese (inconsistent evidence)

An extensive meta-analysis did not find an overall association between ever-exposure to night-shift work and the risk of ovarian cancer.204 However, other evidence shows that rotating between night shifts and day or evening shifts, especially for many years, is linked to higher risk of ovarian cancer, and especially fatal cancer.205

Some initial evidence shows that the microbiome in the cervix and vagina may relate to or indicate ovarian cancer risk. Lower levels of the protective bacteria Lactobacillus in the microbiota in the cervix was associated with higher incidence of ovarian cancer or BRCA1 mutation status, especially in younger women. The research is too preliminary to draw a causal relationship, and no evidence yet shows that restoring the Lactobacillus microbiota in the cervix/vagina might lower the risk.206
Decreased Risk

Oral contraceptive use has shown a protective effect against ovarian cancer and may last several decades after use is discontinued. Use was also associated with a slightly increased risk of breast cancer, but this increase disappeared a few years after use was discontinued.207

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

These therapies may be widely used in integrative cancer protocols and traditional medical systems.

Isoflavones, including genistein from soy
Benefits of soy foods are discussed above in Eating Well

- Reduced ovarian cancer risk with higher phytoestrogen intake from both foods and supplements, and for isoflavones (a type of phytoestrogen), separately;208 however, no good evidence supports a benefit from using only soy supplements.
- Notable preclinical evidence: chemopreventive effects in animal studies209

Selenium

- Significantly reduced risk of ovarian cancer among women of African-American descent taking selenium supplements210

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Combined therapies

- Supplemental vitamin C and vitamin E
    - Reduced risk from combined vitamins C (greater than 363 mg/day) and E (greater than 75 mg/day), from both food and supplements, in a small study211
    - No evidence of reduced risk in two larger, longer studies212
    - Used in Alschuler & Gazella complementary approaches213

Intravenous, high-dose vitamin C

- Case study of therapy following surgery and chemotherapy for stage 4 ovarian cancer, with no relapse of cancer at two years after surgery.214
- Case study of two patients who added intravenous ascorbic acid to an oral high-dose antioxidant therapy (oral vitamin C, vitamin E, beta-carotene, coenzyme Q-10 and a multivitamin/mineral complex) following chemotherapy. No evidence of recurrent disease by physical examination or scan, with normal CA-125 (a biomarker of ovarian cancer) three years after diagnosis.215
- Used in the McKinney protocols216

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Ginkgo biloba

- Lower risk of ovarian cancer, especially non-mucinous types in preliminary epidemiological evidence217
- Influenced anticancer activities in human ovarian cancer cells via impacts on mechanisms and signal pathways, including pathways for cell proliferation, tumor suppression and DNA damage repair218
- Cautions:
    - Potential major herb–drug interactions with aspirin or warfarin, resulting in an increased risk of gastrointestinal bleeds219
    - Ginkgo biloba leaf extract has been classified as a possible human carcinogen (Group 2B) by the International Agency for Research on Cancer,220 but see a discussion of that listing.

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Flaxseed

- Reduced incidence of ovarian cancer in old laying hens221

Lycopene supplements

- Reduced the overall ovarian tumor incidence and the number and the size of the tumors in hens222

Other therapies with preclinical evidence only for reducing risk

- Artemisinin, artesunate, dihydroartemisinin and ARS4
- Combined therapy of lysine, proline, arginine, ascorbic acid and green tea extract
- Curcumin
- Metformin

Group 6: Evidence of no efficacy or may be dangerous

Combination therapy: vitamins A, C, E and folate

- No reduction in risk when taken either singly or in combination in an analysis of 10 cohort studies223

Oral vitamin C

- Possibly increased risk of ovarian cancer224225

Vitamin D supplements

- No association with a decreased risk of ovarian cancer in women of African-American descent226

Off-label, Overlooked or Novel Cancer Approaches (ONCAs)

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Group B: Limited clinical evidence of efficacy

Non-steroidal anti-inflammatory drugs (NSAIDs) including aspirin and COXII inhibitors

- Modestly reduced risk of ovarian cancer with aspirin use, especially long-term consistent aspirin use in observational studies; results for non-aspirin NSAID use are less clear227

- The US Food and Drug Administration warns that ibuprofen, naproxen and ketorolac increase the risk of having a heart attack or stroke; medical supervision is strongly advised with all NSAIDs
- May require a prescription from a licensed physician
- Used in the McKinney protocols228

Statins

- Reduced risk, greatest with long-term use229
- Associated with serious side effects including permanent muscle damage, increased incidence of diabetes and impaired cognitive function; their potential benefits in ovarian cancer must be weighed against the risk, and they should be discontinued promptly if serious side effects occur
- Requires a prescription from a licensed physician
- Used in the McKinney protocols230

Optimizing Your Terrain

Creating an environment within your body that does not support cancer development, growth or spread

Natural Products

Group 1: Good clinical evidence of efficacy & safety, easy access

Curcumin

- Suppressed systemic inflammation in patients with solid tumors undergoing chemotherapy treatment231

Selenium

- Reduced DNA damage232

Group 3: Limited clinical evidence of efficacy but good safety, used in leading integrative programs

Bromelain

- Anticancer activity including direct impact on the microenvironment and modulation of immune, inflammatory and hemostatic systems (systems that prevent and stop bleeding)233
- Used in these plans and protocols:
    - Bastyr University Integrative Oncology Research Center (BIORC)
    - McKinney protocols234
- Used in traditional Chinese medicine and Ayurveda

Isoflavones, including genistein from soy

- Reduced anti-inflammatory activity with genistein and daidzein (types of isoflavones) and some of their isolates235
- Used in these plans and protocols:
    - Alschuler & Gazella complementary approaches236
    - McKinney protocols237
- Used in traditional Chinese medicine

Group 4: Potential significant benefit, but either limited clinical evidence of efficacy or significant cautions

May be used in leading integrative oncology programs. Therapies in this group may need more medical oversight and surveillance.

Agaricus blazei Murill mushroom

- Increased natural killer cell activity in cervical, ovarian and endometrial cancer patients undergoing carboplatin plus VP16 (etoposide) or carboplatin plus taxol, but without significant difference in lymphokine-activated activities of killer cells and monocytes (immune cells)238
- Linked to severe liver dysfunction in three patients with unspecified cancers239

Group 5: Especially promising preclinical or emerging clinical evidence of efficacy and safety

Turkey tail mushroom polysaccarides (PSK)

- Trend toward reduced inhibition of IL-2 production (interleukin-2, a cytokine or immune protein, boosts the growth and activity of certain immune cells) with combination chemotherapy240
- Reduced inhibition of IL-2 production in patients with advanced ovarian carcinoma with combination chemotherapy241
- Trend toward increased antitumor effects of cisplatin and prolonged survival in mice242

Energy Therapies

Healing Touch

- Trends of higher levels of immune modulators (CD4, CD8 and natural killer (NK) cells) with healing touch in combination with therapeutic massage and hypnosis with each cycle of chemotherapy243

Manipulative and Body-Based Methods

Acupuncture

- Higher white blood cell counts during one cycle of chemotherapy (modest evidence)244

Massage

- Trends of higher levels of immune modulators (CD4, CD8 and natural killer (NK) cells) with therapeutic massage in combination with hypnosis and healing touch with each cycle of chemotherapy245

Mind-Body, Spiritual and Consciousness-changing Approaches

Hypnosis

- Trends of higher levels of immune modulators (CD4, CD8 and natural killer (NK) cells) with hypnosis in combination with therapeutic massage and healing touch with each cycle of chemotherapy246

Integrative Approaches and Surgery

Surgery may be part of the recommended treatment for this cancer type. We provide helpful information about how integrative approaches can coordinate with surgery.

In general, the earlier the stage of the cancer, the better the response to treatment. Unfortunately, ovarian cancer is typically diagnosed in more advanced stages, which is why treatments are less effective.

The most common primary conventional treatments for ovarian cancer are surgery, chemotherapy and targeted therapy. Radiation therapy is not typically used as a first-line treatment but may be used for small localized recurrent tumors. Hormone therapy may be prescribed for relapsed low-grade tumors.

Managing Thrombosis

Ovarian cancer brings a high risk of formation of blood clots (thrombosis).200 For prevention, BCCT advisor Dr. Keith Block provides information on modifying the terrain factor he calls hypercoagulation.201 He discusses testing, lifestyle approaches and supplements to reduce risks. For more information see chapter 17, “Blood Circulation and Cancer: The Thick and the Thin.”

Chemosensitivity Testing

In many ways, each case of cancer is unique. Your personal body terrain and tumor microenvironment, which is a combination of genes, nutritional status, stress response, circadian rhythms, fitness, microbiome, history of infectious disease, hormone levels and much more, is as unique to you as your fingerprints are. Your body and tumor may not respond exactly like others to any given treatment.

If feasible, your healthcare team can collect a live sample of tumor tissue and send it for chemosensitivity testing to identify your cancer's responses to both standard and complementary therapies. Test results can identify which chemotherapies and natural products are likely to be either most effective or ineffective or in treating the tumor.

Medical advocate and BCCT advisor Gwen Stritter, MD, writes, "Ovarian cancer is one of the few cancers I know of where oncologists will do chemosensitivity testing right after initial diagnosis." Indeed, the National Comprehensive Cancer Network (NCCN) guideline for ovarian cancer says that a number of their member institutions use chemotherapy/resistance and other biomarker tests to help select chemotherapy when multiple chemotherapy options are available.

However, the National Comprehensive Cancer Network (NCCN) states that the current level of evidence of using this testing is not strong, and they do not recommend such testing. The American Society of Clinical Oncology (ASCO) advises that this testing not be used in ovarian cancer except in the clinical trial setting.54 If your doctor is following the NCCN or ASCO guidelines closely, he or she is not likely to bring up this testing with you. If you'd like to consider chemosensitivity testing, you may need to take the initiative.

First, you will need to preplan. Live cells need to be prepared and shipped overnight to a special lab, and so you must discuss this with your doctor before your tumor tissue is removed. For information about this see Standard and Non-Standard Diagnostic Approaches.

Knowing how your cancer behaves may influence the type of testing and treatment used, prepare you for possible treatment side effects and guide you in steps to prevent or minimize these effects. It will help you understand and choose the complementary therapies and lifestyle approaches that may enhance your conventional treatment, manage side effects and improve your quality of your life.

BCCT advisor Dr. Keith Block relates a case of a patient with recurrent ovarian cancer with chemo-resistance and a high CA-125 level. Block's team arranged for a tumor biopsy which was assessed by the Nagourney Cancer Institute. Test results showed the tumor was sensitive to a combination of two chemotherapy drugs—even though her tumor had shown resistance to both drugs when used individually. Within two months of starting the drug combination, her CA-125 level dropped significantly and her disease stabilized. Block states he would never have come up with this combination if not for the testing.55

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