Current Hematologic Malignancy Reports (2019) 14:328–336
https://doi.org/10.1007/s11899-019-00526-8

HEALTH ECONOMICS (N KHERA, SECTION EDITOR)

Emerging Role of Integrative Medicine in Hematologic Malignancies: a Literature Review and Update on Current Trends in Complementary Medical Practices in Hematologic Cancers

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Published online: 18 June 2019

Abstract

Purpose of Review This review discusses the emerging role of integrative hematology. It reinforces the growing interest of CAM among patients, and the importance of provider knowledge and participation in discussions with patients about the subject. The main question asked in this review, "Is there evidence for the use of integrative medicine practices in the field of malignant hematology?" is answered by examining current research and providing relevant summaries.

Recent Findings Data suggests that practices such as meditative movement, exercise, nutrition and supplements and touch therapy can be used for symptom alleviation, preventive measures, and novel treatment development.

Summary Integrative hematology is a needed part of complete patient care, and it is the role of providers to be knowledgeable and open to ensure patients are engaging in practices that are evidence-informed and safe. More studies are needed in the field in order to make concrete and robust recommendations.

Keywords Integrative medicine · Integrative oncology · Hematologic malignancies · Complementary medicine

Introduction

Treatment options in the field of oncology have been growing quickly in recent years with the development of treatments such as targeted therapy, immune therapy, and CAR-T. In fact, due to advanced research and treatment options, people are living longer, either cured or managed. It is estimated that, by the year 2026, there will be 20.3 million cancer survivors living in the USA [1]. Many cancer survivors are already using some sort of complementary medicine, and despite the desire to discuss complementary and alternative medicine (CAM), the majority of patients are not disclosing CAM utilization to their treating providers, which presents a safety issue [2]. What's more, there is an unmet need for symptom management in patients with hematologic malignancies and there are many non-pharmacologic techniques available to complement standard therapies that may ameliorate this unmet need.

On the spectrum of cancer diagnosis, treatment, and outcome lies quality of life. In 2017, the National Cancer Policy Forum of the National Academies of Sciences, Engineering and Medicine sponsored a workshop on post-treatment survivorship and found that psychosocial wellbeing had oftentimes been overlooked during or after cancer treatment. The review notes that patients who engaged with tools to manage symptoms such as exercise and yoga, in addition to education about their cancer, treatments, and treatment effects, fared better [3•].

Integrative medicine, and more specifically, integrative oncology, is a quickly growing field with a focus on treating the whole patient, and not only the disease. Recently, the Society of Integrative Oncology (SIO) released an official definition of integrative oncology: "integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle

This article is part of the Topical Collection on *Health Economics*

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11899-019-00526-8) contains supplementary material, which is available to authorized users.

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modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment" [4••]. It is emphasized that integrative medicine is *not* alternative medicine but works to complement conventional cancer treatment. Many patients, up to 40–50%, are already utilizing complementary and alternative therapies, but not all treatments and ventures are safe or even effective [5]. Vulnerable patients may be offered dangerous and/or expensive alternatives to standard or approved therapy, which is why practitioners in the field must be aware of the evidence-informed therapies and engage patients in conversation about the use of complementary (and not alternative) practices [6]. "Most cancer patients are not looking for cancer treatment "alternatives", but are instead interested in using additional interventions that may help improve the efficacy of conventional cancer treatments, increase their chance of survival, and/or reduce their symptom burden associated with cancer or treatments" [4••].

This review will focus on the evidence to date on the role of integrative medicine in hematologic malignancies, complementary practices (exercise, meditative movements (yoga; t'ai chi and qigong), mindfulness meditation, touch therapy (massage and Reiki), acupressure and acupuncture, nutrition and supplements), cancer-specific integrative practices (chronic lymphocytic leukemia, multiple myeloma, acute leukemia, Hodgkin and non-Hodgkin lymphoma), and conclude with a brief discussion on limitations of this review as well as importance of partnership between patients and practitioners.

Methods and Results

The question posed in preparation for this article was: *Is there evidence for the use of integrative medicine practices in the field of malignant hematology*? Sub-questions included: (1) What is integrative oncology? (2) What are some findings published within the past 5–10 years?

In order to answer these questions, a literature review that fit the following criteria was initiated: articles of randomized clinical trials, meta-analyses, systematic reviews, cohort studies, and basic science research within the last 10 years, from peer-reviewed sources, with primary focus on CAM. Keywords include "integrative medicine," "integrative oncology," and other cancer-related keywords such as hematologic diagnosis. Complementary medicine search words included "yoga," "mindfulness," "t'ai chi," and "Reiki." Literature searches were performed using PubMed, Web of Science, and Embase, as well as manual searches. The search populated 679 articles, and 423 were further extracted for more relevance. Of the 423 articles, 35 contained well-developed and oftentimes, primary research. The majority of the studies populated were novel feasibility studies, others were efficacy studies, and some were retrospective/prospective analyses. Although most studies identified were clinical, some were bench studies evaluating cytotoxic properties of plants and supplements.

A Role for Integrative Medicine in Hematologic Malignancies

Many medical subspecialties utilize integrative medicine in their practice, including hematology and oncology, though there have been more updates in guidelines of integrative oncology for solid malignancies than in hematologic malignancies. Of note, the SIO provided updated clinical guidelines in 2017 on the use of integrative therapies during and after breast cancer treatment. The report included approval for the use of meditation, yoga, and acupressure and acupuncture to manage symptoms such as stress, anxiety, and chemotherapy-induced nausea and vomiting. It recommended against the use of acetyl-L-carnitine for chemotherapy-induced peripheral neuropathy, as well as stating that there was no strong evidence in support of use of dietary supplements to manage breast cancer treatment–related side effects [7, 8]. In the field of prostate cancer, dietary interventions such as "plant-based antioxidant-rich diet with an emphasis on cruciferous vegetables, tomatoes, soy, pomegranate, and marine omega 3 fatty acids while avoiding saturated fats, including dairy" have been found to be beneficial, as well as use of Chinese medicine for the management of side effects such as hot flashes due to androgen deprivation therapy (ADT) [9].

Patients with hematologic malignancies are no different from those with solid tumors, as they too wish to become empowered and work in partnership with their physician in treating the disease and associated sequelae [5]. Evidence for integrative therapy in hematologic disease is slowly mounting in the literature (please see Appendix 1 for a summary of the more relevant studies cited in this paper).

General Complementary Practices

Exercise

Aerobic exercise has been found to have positive outcomes in patients with malignancies undergoing chemotherapy [10, 11•]. Benefits generally include improved quality of life and physical functioning [11•]. As can be expected, with harsh and prolonged treatment courses, patients become deconditioned and more challenging to tolerate subsequent treatments [12•, 13]. By engaging in aerobic exercise, patients would be able to tolerate treatment better and return to regular life faster. In fact,

"Moderate intensity exercise, up to 70-80% maximum heart rate, appears safe in patients with early and metastatic disease," though most comprehensive reviews have not included patients with findings typically seen in hematological malignancy ("studies excluded patients if they had severe comorbidities or bone metastasis, or were neutropenic, thrombocytopenic, anemic (<8g/dL) or febrile" [11•]), therefore leading to inability to give specific recommendations for the hematologic malignancy patient population (grade: moderate).

There is an up cropping of studies that focus on patients with hematologic malignancies. A Cochrane systematic review by Berganthal et al. analyzed randomized clinical trials that compared standard care for patients with hematological malignancies (ALL, AML, lymphoma, myeloma, and SCTs) versus standard care plus aerobic physical exercise [14]. They found no evidence for difference in overall survival between patients who exercised and those who received standard care only, but there was a significant difference in quality of life. Areas noted with improvement included depression, physical functioning, and fatigue [14]. Aerobic physical exercise can improve quality of life for patients with hematologic malignancies (grade: high). A post hoc analysis showed that there may be evidence that supervised aerobic exercise is associated with improved progression-free survival in lymphoma [15]. The "adjusted 5-year PFS for the supervised exercise group was 68.8% compared with 59.0% for the group that received no supervised exercise," [15] though the p value was not statistically significant ($p = 0.98$), and therefore cannot be recommended as improving PFS in patients with lymphoma. Another study, a 12-week prospective two-armed randomized control trial investigated the effects of exercise on cancer-related fatigue in post-treatment hematological cancer [12•]. The method of study included "pre-, post-, and follow-up assessments [were] conducted on outcome measures including CRF, quality of life (QoL), psychological distress, cardiovascular fitness, muscle strength (MS) and body composition" [12•]. The study concluded that combined aerobic and resistance training had statistically and clinically significant improvement in patient outcomes [12•]. They note that, because there was no continuous control group, it could not be conclusively said that the patient would recover at the same level even without the exercise intervention, but there were some patient whose exercise program was delayed by 12 weeks post-treatment and for them, "the role of exercise as the stimulus for the improvement is convincing" [12•]. Although the findings in this study were statistically significant, the sample size was only 37 patients, indicating low power and imprecision (grade: moderate). In people receiving autologous stem cell transplantation, loss of muscle mass and physical functionality is significant and there have been several studies that have evaluated exercise as an intervention to increase overall functionality before [16], during, and after the process. In a prospective longitudinal study of 40 patients between the ages of 23 and 70 undergoing autologous hematopoietic stem cell transplant for myeloma, lymphoma, and amyloidosis, a home-based exercise project in the ambulatory setting, and supervised exercise sessions when admitted, was developed [17]. The study found not only that patients could tolerate continued physical activity but also that participation was safe [17]. In contrast, the large BMT CTN study titled *Exercise and Stress management Training Prior to Hematopoietic Cell Transplantation: Blood and Marrow Transplant Clinical Trials Network*, which randomized 711 patients into four groups (self-directed exercise, self-administered stress management, neither, both), did not show a difference in overall survival, decrease in hospital days, or improvement in symptoms such as sleep quality, pain, and nausea [18]. The paper noted that possible reasons for the outcome included insufficient time to intervention initiation prior to transplant, not targeting the appropriate patient, and lack of personalization or intensity. There is currently an ongoing trial with the goal of determining the feasibility of conducting a pre-treatment RCT in myeloma patients prior to autologous stem cell transplant [19]. The results of this study (trial registration number NCT03135925) will be illuminating.

Meditative Movement (Yoga)

Meditative movement practices such as yoga have become widely practiced in the USA and are also making its way into regular practice among people with cancer [8, 20••]. Yoga is a discipline that uses breath control, meditation, and specific physical postures to promote health and relaxation. Yoga has been shown to lower anxiety levels and stress, and increase quality of life in patients with breast cancer [8]. The other potential benefits in patients with cancer include improved sleep; reduced fatigue; improved quality of life; reduced stress, anxiety, and depression; and improved cognitive function [21, 22]. There is limited data on the effects of yoga specific to hematologic malignancies, but Sprod et al. studied the effects of yoga on cancer-related fatigue in a mixed group of cancer survivors age 60 years and older (YOCAS–Yoga for Cancer Survivors) [23]. Four hundred ten participants with any type of cancer were included, with 206 randomized to intervention arm, standard care plus 4 weeks of a standardized yoga program (2 sessions per week, each session lasting 75 min), and 204 randomized to the control arm (standard care only). "Following the 4-week intervention, participants in the YOCAS © ® intervention group reported a significantly lower level of global side-effect burden as assessed using the Symptom Inventory total score compared to participants in the standard care arm ($p < 0.01$)" [23]. A big limit to this study is that "large majority of participants were white female breast cancer survivors who were relatively well educated,

limiting generalizability … [and] participants were aware of the outcomes of interest because the informed consent included both the name of the study, alluding to the research hypothesis, as well as information specific to why the study was being conducted" (grade: moderate) [23]. A Cochrane study evaluating the effectiveness (defined as reducing distress, fatigue, anxiety, depression) of yoga in addition to standard care in patients with hematologic cancers was inconclusive, stating that, "the available data provide little information about the effectiveness of yoga interventions for people suffering from hematological malignancies" [24] (grade: low). Another Cochrane review evaluated meditative practices in general, and how the practice affects the lives of people with hematological disease. The main study that was reviewed included 91 patients with newly diagnosed acute leukemia, of which 42 completed the 6-month trial. The Cochrane review cited "low quality of evidence" due to low participant numbers and missing data on study population. It concludes, "the influence of meditation practice on overall survival, fatigue, anxiety, quality of sleep, and adverse events remained unclear, as these outcomes were not evaluated in the intended trial" [25] (grade: low). Huberty et al. show that, in patients with myeloproliferative neoplasms (MPN), a 12-week home-based online yoga program is not only feasible, but preliminary results show promise for improving symptom burden [26]. Indeed, more RCTs are needed to make conclusive recommendations about the use of yoga in hematologic cancers.

Meditative Movement (T'ai Chi and Qigong)

T'ai chi and qigong are related mind and body practices integrating posture, stretching, movement, breathing techniques, and focused intent to promote general wellbeing. These techniques have been shown to improve balance and stability, and decrease fear of falling in older patients, and are also associated with improvement in cancer-specific QoL [27, 28]. A recent meta-analysis focusing on the use of t'ai chi and qigong for cancer-related symptoms and quality of life included 22 studies with a total of 1283 participants, with breast cancer, prostate cancer, lung cancer, lymphoma, and others [29•]. There were 96 patients with non-Hodgkin lymphoma. The result of the meta-analysis is that t'ai chi and qigong (TCQ) "may be effective in reducing multiple symptoms commonly experienced by cancer survivors. Statistically significant and clinically meaningful medium effect sizes in favor of TCQ were observed for symptoms of fatigue and sleep difficulty. Smaller but statistically significant effect sizes were also observed for QoL and depression, and a non-significant trend in favor of TCQ was observed for pain" [29•]. Less than 10% of the patients in the meta-analysis had a hematologic malignancy; therefore, although results were statistically significant, this limitation should be considered (grade: low).

Mindfulness Meditation

Mindfulness meditation, described as "a non-judgmental attention to experiences in the present moment," stems from Buddhist meditation traditions and teach the practitioner to regulate their attention by "maintain[ing] the focus on immediate experiences such as thoughts, emotions, body posture and sensations," and "approach one's experiences with openness and acceptance" [30]. Studies have shown that mindfulness meditation can cause neuroplastic changes in both structure and function of the brain. Changes in the anterior cingulate cortex are seen when engaged in mindfulness exercises, and engagements of the fronto-limbic networks during practice lead to improved emotion regulation and stress reduction [30]. Mindfulness meditation is also associated with reduction in chronic pain symptoms and depression [31], and popularity is growing as seen in the availability across cancer centers in the USA [2, 20••].

Touch Therapy: Massage and Reiki

Touch and massage therapy may improve nausea, fatigue, anxiety, depression, and pain [32, 33]. Although not statistically significant, a small pediatric study (23 patients; age 5–18 years) showed that acupressure-massage plus usual care in HSCT decreased symptoms of pain, fatigue and nausea, as well as reduced days of reported mucositis [34]. In fact, massage therapy has been incorporated in some adult and pediatric bone transplant units to decrease the stress and pain associated with certain procedures such as a bone marrow biopsy [35]. The availability of massage therapy in comprehensive cancer centers across the USA continues to grow, and as of 2016, 84.4% of 45 NCI-designated comprehensive cancer centers mention the availability of massage therapy in their websites [20••]. The benefits of massage therapy include provision of general comfort, improvement in quality of life, reduction in stress and anxiety, and improvement in sleep (grade: moderate) [36].

Reiki is a type of touch therapy, also known as energy healing. Research suggest benefits to relieve stress and burnout [37], and is also beneficial (decreased anxiety, improved sleep, decreased pain, improved appetite, improved mood) to those receiving chemotherapy [38]. There are few statistically significant studies on the effects (positive or negative) of Reiki in patients with hematological cancers. It is growing in popularity and, like massage therapy, is offered at many cancer centers [20••, 39]. A Portuguese study consisting of 116 patients (58 intervention, 58 control) assessed the quality of life of patients with hematologic malignancies receiving true Reiki vs. sham Reiki, which revealed Reiki is safe and

improves wellbeing [40••]. In the study, which was statistically significant, true Reiki was described as Reiki delivered by Reiki masters whereas sham Reiki (placebo) was delivered by unqualified therapists [40••].

Acupressure and Acupuncture

Acupuncture, a form of Chinese medicine, is the practice of inserting thin needles into the body along specified acupuncture points. Acupressure is the application of physical pressure by hand to acupuncture points. Both acupuncture and acupressure have been endorsed as beneficial for use in breast cancer patients for treatment-related adverse effects, specifically, nausea and vomiting. The American Society of Clinical Oncology have endorsed the clinical practice guideline put forth by the Society for Integrative Oncology that acupressure and acupuncture are recommended for reducing nausea and vomiting induced by chemotherapy [41••]. Patients with multiple myeloma undergoing high-dose melphalan followed by autologous hematopoietic stem cell transplant were randomized into two groups; one group would receive true acupuncture, and the other group would receive sham acupuncture [42••]. The results state that, "among 60 participants … true acupuncture was significantly more efficacious in reducing nausea, lack of appetite, and drowsiness at 15 days ($P = .042$, .025, and .010, respectively). Patients receiving sham acupuncture were more likely to increase pain medication use post-transplantation (odds ratio 5.31, $P = .017$)[42••]." In myeloma patients receiving bortezomib, acupuncture has also been shown to have a beneficial effect on peripheral neuropathy, especially in combination with methylcobalamin [43, 44]. When considering acupuncture and acupressure in patients with hematologic cancers, it is important to first assess for anemia, thrombocytopenia, and neutropenia. Acupuncture is invasive and although low, there is risk of infection (skin translocation) and blood-borne diseases (poor public health practices) [45]. Additionally, anemia and thrombocytopenia present high risk for bleeding and bruising with acupuncture and acupressure but a study by Lu et al. showed that, when performed by an experienced acupuncturist at an academic cancer center, using "a specific type of thin needle, mild manual stimulation administered at a shallow depth," there were no bleeding side effects even in patients with platelet counts of $< 20{,}000/\mu L$ [45]. Acupuncture and acupuncture can be beneficial to patients with hematologic malignancies by reducing nausea and fatigue (grade: high). There are studies that suggest that acupuncture may positively stimulate the bone marrow after chemotherapy but more investigations are needed [46, 47].

Nutrition and Supplements

There are a number of illnesses linked to poor diet and obesity, including diabetes and heart disease, and according to the NCI Obesity and Cancer factsheet, breast, colon, and prostate cancers are also linked [48]. Total fat intake has a positive association with CLL/SLL among women, and high trans fat intake is associated with non-Hodgkin lymphoma in women [49].

Emerging data also suggests that changes to the intestinal microbiome following adjuvant chemotherapy for breast and ovarian cancers can lead to weight gain and glucose intolerance, further emphasizing the need for continued health maintenance even after completion of cancer treatment [50]. In hematologic cancers, specifically patients who have undergone HSCT, mortality tends to be due to infection, GvHD, and relapse. Peled et al. hypothesized that components of the gut flora may be associated with relapse following allogeneic HCT. In their study comprising of 541 patients, they found that disease relapse/progression occurred less in patients with a higher abundance of the bacterial group, *Eubacterium limosum*, which has also been noted to be more predominant in the gut microbiome of centenarians, compared with younger people [51•, 52].

Body weight plays a role in the prognosis of many malignancies, including AML and ALL [53–55]. In fact, "obesity is associated with worsened prognosis after cancer diagnosis and also negatively affects the delivery of systemic therapy, contributes to morbidity of cancer treatment, and may raise the risk of second malignancies and comorbidities" [56]; it is important to maintain a healthy BMI (18.5–24.9). A post hoc analysis by Ammann et al. showed that supplementation with calcium and Vitamin D can be protective against hematologic diseases in general [57], and supplementation with fish oil not only reduce inflammation as measured by decreased C-reactive protein, but may also promote long-term survival in patients with leukemia and lymphoma receiving chemotherapy [58]. Modest supplementation with daily calcium (1000 mg elemental calcium carbonate) and vitamin D3 (400 IU) may reduce risk of hematological malignancies in older women (grade: moderate).

Medicinal Plants and Upcoming Therapies

Many commonly used and highly efficacious chemotherapies have their origins from plants and natural products. Chemotherapies such as paclitaxel/docetaxel (Pacific yew tree), etoposide (wild mandrake), vinblastine/vincristine (Madagascar periwinkle), and irinotecan/topotecan (*Camptotheca acuminate*) are well-known plant-derived treatments. Turmeric (from which curcumin is produced) has been shown to have anticancer potential in breast cancer, lung cancer, ovarian cancer, colon cancer, and melanoma, with suggested activity in leukemia and lymphoma. One mechanism of action lies in its activity against free radicals: "free radicals and oxidative stress play a significant role in the development of many disease, including cancer, and curcumin has

antioxidant effects that reduce or inhibit damage caused by free radicals" [59]. Researchers continue to investigate natural product antineoplastic properties, but there is still no high-quality evidence to recommend taking any of the listed plants with chemotherapy. See Table 1 for the table of three plants and their chemotherapeutic properties.

Cancer-Specific Integrative Practices

Integrative Care in Chronic Lymphocytic Leukemia

Vitamin D deficiency is a common global problem for which many people require supplementation. Vitamin D is important in "maintaining serum calcium and skeletal homeostasis, as well as multiple other cellular effects, including regulation of differentiation, proliferation, apoptosis, metastatic potential, and angiogenesis" [61]. A prospective observational cohort study performed in patients with CLL between the Mayo Clinic and the University of Iowa from 2002 to 2008 concluded that vitamin D insufficiency had an association with "inferior TTT and a 2-fold increased risk of death" [61]. With this knowledge, there is the potential to modify prognosis and overall survival by providing CLL patients with Vitamin D supplementation [62].

Integrative Care in Acute Leukemia

It has previously been difficult to carry out long observation studies in patients with AML, but with new targeted therapies, this is changing, and with this change, there is an increase in integrative options for patients. Green tea has been shown to decrease a wide variety of cancers in vitro and in animal models [63]. There are a few studies on APL that suggest a role for green tea (*Camellia sinensis*) catechin epigallocatechin-3-gallate (EGCG), to inhibit APL cell proliferation, but more research is needed [64]. In ALL, curcumin may be able to potentiate the effect of chemotherapeutic agents such as 6-mercaptopurinol, cyclophosphamide, vincristine, cytarabine, and L-asparaginase [65•].

Integrative Care in Multiple Myeloma

Epigenetic modifications via the silencing of cancer-related genes play a role in the development of multiple myeloma [66], and curcumin is thought to play a role in genetic modification. Many new studies are showing that curcumin, the bioactive component of turmeric, has anticancer activities including induction of apoptosis in leukemic cells through the IFIT2-dependent signaling pathways [67], and that it could inhibit the growth of myeloma cells in both a time- and concentration-dependent manner by inhibiting expression of EZH2 histone myelotransferase, a core protein in PRC2, whose over-expression is associated with hematologic malignancies [68]. Inhibition of EZH2 greatly reduces the number of viable myeloma cells [66].

Integrative Care in Hodgkin and Non-Hodgkin Lymphoma

There may be an association of high-fat diets and non-Hodgkin lymphoma (NHL). A meta-analysis by Han et al. compiled 221 published cohort and case-control studies, finding 10 relevant studies, which showed a significant association between total fat consumption and increased risk of NHL, specifically diffuse large B cell lymphoma [69]. There was less of a correlation found with SLL/CLL, T cell lymphoma, and follicular lymphoma [69]. As in CLL, vitamin D also plays a role in NHL risk reduction: "A pooled analysis of 10 studies found that higher levels of recreational sun exposure, which would be anticipated to increase vitamin D levels, was associated with a lower risk for non-Hodgkin lymphoma"[61] and low levels of serum 25(OH)D may be associated with higher incidence of NHL[61]. There is little data on single agents that may work directly against Hodgkin lymphoma.

Table 1 Plants with cytostatic and/or cytotoxic properties

Plant	Properties
Centaurea albonitens	A methanoic extract from this herbaceous flowing plant has dose-dependent cytotoxic activity in hematologic malignant cell lines without affecting normal cells, thereby having selective therapeutic potential [60•]. It leads to G0/G1 phase arrest and apoptosis in pre-B ALL NALM-6 and REH cell lines, human APL cell line (NB4), and human multiple myeloma cell line (KMM-1) [60•].
Artemisia absinthium	An ornamental plant most famous for its use as an ingredient in Absinthe, from which many promising compounds have been isolated (Quercetin, isorhamnetin, kamfrolinalol, alphapinin, limonene, and myrecene) [59]. These isolates inhibit the growth of cancer cells such as MCF-7, MB-435, SKMEL-5, and K569, and also inhibit the production of VEGF [59].
Lepidium sativum	An edible herb commonly known as garden cress or watercress, it has been shown to have cytotoxic effects on leukemia blood lines (K562), and it is rich in antioxidants and omega-3 fatty acids, which may be able to inhibit free radical damage caused by cancer cells [59].

Limitations

While there are a number of emerging research endeavors in the field of integrative oncology, the number of well-developed and statistically significant studies is low. There are gaps in the field due to a limited number of well-conducted, multi-center, and reproducible randomized trials. Additionally, publication and method bias further complicate interpreting the literature base. These limitations present challenges in making recommendations for clinical interventions.

Conclusion

Integrative oncology, a quickly growing branch in oncology, is gaining interest by patients and practitioners alike. As previously seen in fields such as palliative care and hospice, support is mounting as it is weaved into common practice. We highlight the importance of open communication on the use of CAM in order to discuss evidence-informed findings, encourage safe complementary practices with standard practice, and advise against alternative and dangerous practices. Unfortunately, there continues to be limited high-quality data for efficacy in a number of complementary medicine practices. Although some practices such as yoga, Reiki, and acupuncture have been shown to be safe for use in patients with hematologic cancers, there is heterogeneous date about the direct effects of these practices on disease. There are some statistically significant findings indicating improvement in QoL and symptoms such as fatigue, anxiety, nausea, and pain. More studies are needed, and more participation among oncology departments, in order to develop guidelines for patients with hematological malignancies and use of complementary therapies. With more studies, we may learn more preventive steps; learn to control treatment-associated symptoms such as nausea, fatigue, and stress; and learn about therapies that can adjunct efficacy of already available standard practices [70].

Acknowledgments We acknowledge Belleh Taku, PharmD, and Ahlam Saleh, MD MLS, for the help they provided towards this paper.

Compliance With Ethical Standards

Conflict of Interest Dr. Okolo has nothing to disclose.

Dr. Gowin reports personal fees from Incyte (Speaker Bureau, Scientific Advisory Board).

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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