Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Guidelines Breast
Version 2023.1E

Complementary Therapy Survivorship

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FORSCHEN
LEHREN
HEILEN

Complementary Therapy – Hormonal Treatment and Alternatives in Breast Cancer Survivors – Survivorship

- **Versions 2002–2022:**
  Albert / Bauerfeind / Blohmer / Dall/ Fersis / Friedrich / Gerber / Göhring / Hanf / Janni / Kümmel / Lück / von Minckwitz / Nitz / Oberhoff / Rhiem / Scharl / Schmidt / Schütz / Solomayer / Thomssen

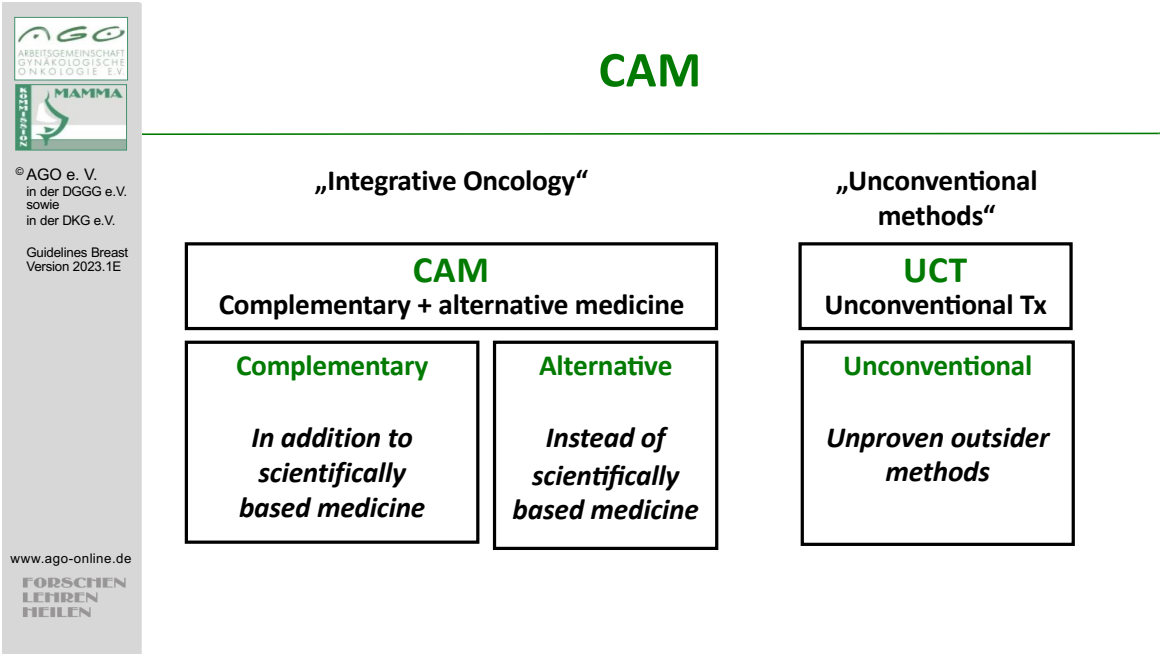
- **Version 2023:**
  Heil / Solomayer

Screened Data Sources:

Pubmed	2015 - 01/2023
ASCO	2015 – 2022
SABCS	2015 – 2022
EBCC	2015 – 2022
Cochrane library:	summary Jan. 2023

-RCT, systematic review, meta-analysis

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Komplementärmedizin in der Behandlung von onkologischen PatientInnen, Langversion 1.1, 2021, AWMF Registernummer: 032/055OL, https://www.leitlinienprogramm-onkologie.de/leitlinien/komplementaermedizin/



Komplementäre Verfahren werden parallel zur konventionellen Therapie angewendet und unterscheiden sich von alternativen Verfahren dadurch, dass sie den Wert der konventionellen Verfahren nicht in Frage stellen, sondern sich als Ergänzung verstehen

<u>Onkolleitlinienprogramm</u>

1. Witt CM et al.. A Comprehensive Definition for Integrative Oncology. J Natl Cancer Inst Monogr 2017;(52): lgx012
2. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Komplementärmedizin in der Behandlung von onkologischen PatientInnen, Langversion 1.1, 2021, AWMF Registernummer: 032/055OL, https://www.leitlinienprogramm-onkologie.de/leitlinien/komplementaermedizin/

“Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle 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.”

Good Clinical Practice

All patients should be consulted as early as possible and in the course of the process repeatedly on the interest in information complementary medical measures and, if interested, reliable sources of information should be referred.

S3 LL "Komplementärmedizin in der Behandlung von onkologischen PatientInnen"

Literatur:

1. Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF): Komplementärmedizin in der Behandlung von onkologischen PatientInnen, Langversion 1.1, 2021, AWMF Registernummer: 032/055OL, https://www.leitlinienprogramm-onkologie.de/leitlinien/komplementaermedizin/

Guidelines Breast
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General Considerations

	Oxford		
	LoE	GR	AGO
▪ **CAM instead of loco-regional interventions**	2b	B	--
▪ **CAM instead of systemic treatment**	2b	B	--

- **Patients should be asked and advised about their use of CAM modalities**
- **Diagnostic procedures in connection with complementary and alternative therapy concepts without evidence (e.g. iris diagnostics, bioresonance) should not be recommended.**
- ***During anti-cancer treatment:*** **Beware of drug interactions**

1. Guha N, Kwan ML, Quesenberry CP, et al: Soy isoflavones and risk of cancer recurrence in a cohort of breast cancer survivors: the Life After Cancer Epidemiology study. Breast Cancer Res Treat. 2009;118(2):395–405, pmid:19221874.
2. Saquib J, Parker BA, Natarajan L, et al. Prognosis following the use of complementary and alternative medicine in women diagnosed with breast cancer. Complement Ther Med. 2012 Oct;20(5):283-90. doi: 10.1016/j.ctim.2012.04.002. Epub 2012 Apr 27.
3. Smith PJ et al.. Complementary and alternative medicine use by patients receiving curative-intent chemotherapy. Asia-Pacific Journal of Clinical Oncology 2016; 12: 265–274
4. Greenlee H et al.. Association Between Complementary and Alternative Medicine Use and Breast Cancer Chemotherapy Initiation: The Breast Cancer Quality of Care (BQUAL) Study. JAMA Oncol. 2016 Sep 1;2(9):1170-6. doi: 10.1001/jamaoncol.2016.0685
5. Fremd C et al.. Use of complementary and integrative medicine among German breast cancer patients: predictors and implications for patient care within the PRAEGNANT study network. Arch Gynecol Obstet. 2017 May;295(5):1239-1245. doi: 10.1007/s00404-017-4348-2. Epub 2017 Mar 22.
6. Samuels N et al.. Unmonitored use of herbal medicine by patients with breast cancer: reframing expectations. J Cancer Res Clin Oncol 2017;143:2267–2273
7. Johnson SB et al.. Use of Alternative Medicine for Cancer and Its Impact on Survival. JNCI J Natl Cancer Inst 2018; 110(1): djx145.
8. Johnson SB et al. Complementary Medicine, Refusal of Conventional Cancer Therapy, and Survival Among Patients With Curable Cancers. JAMA Oncol. doi:10.1001/jamaoncol.2018.2487 published online July 19, 2018.

9. Johnson SB, Park HS, Gross CP et al. Use of Alternative Medicine for Cancer and Its Impact on Survival. J Natl Cancer Inst. 2018 Jan 1;110(1). doi: 10.1093/jnci/djx145.
10. Hack CC, Wasner S, Meyer J et al. Analysis of Oncological second opinions in a certified university breast and gynecological cancer center in relation to complementary and alternative medicine . Complement Med Res 2020;27(6):431-439
11. Guerra-Martin MD, Tejedor-Bueno MS, correa-Casado M. Effectiveness of Complementary Therapy in Cancer Patients: A systematic Review. Int J Environ Res Public Health 2021 Jan 24;18(3) 1017.doi:103390/ijerph18031017

Complementary Therapy
Pre- and Postoperative

	Oxford		
	LoE	GR	AGO
Preoperative:			
▪ Hypnosis (reduces anxiety, pain, nausea)	1b	B	+
Postoperative:			
▪ Acupuncture (pain relief, anxiety)	1b	B	+/-
▪ Acupuncture (nausea, vomiting)	2b	B	+
▪ Massage therapy (pain relief)	2b	C	+/-
▪ Early postoperative exercise reduces upper-limb dysfunction (beware: increased wound drainage)	1a	A	+
▪ Physical exercise			
▪ to reduce breast cancer related secondary lymphedema	1a	A	+
▪ as a prophylaxis of lymphedema	1b	B	+/-
▪ Prophylactic lymphatic drainage	1b	B	--
▪ Yoga (arm and shoulder pain)	2b	C	+
▪ Music therapy (reduces pain after mastectomy)	2b	C	+/-

Präoperativ:
Hypnosis

1. Montgomery GH, David D, Kangas M, et al. Randomized Controlled Trial of a Cognitive-Behavioral Therapy Plus Hypnosis Intervention to Control Fatigue in Patients Undergoing Radiotherapy for Breast Cancer. JCO 2014;DOI 10.12007JCO.2013.49.3437
2. Cramer H, Lauche R, Paul A, et al: Hypnosis in Breast Cancer Care: A Systematic Review of Randomized Controlled Trials. Integr Cancer Ther. 2015 Jan;14(1):5-15. Epub 2014 Sep 18.
3. Amraoui J, Pouliquen C, Fraisse J et al. Effects of a Hypnosis Session Before General Anesthesia on Postoperative Outcomes in Patients Who Underwent Minor Breast Cancer Surgery: The HYPNOSEIN Randomized Clinical Trial. JAMA 2018 Netw Open.;1(4):e181164. doi: 10.1001/jamanetworkopen.2018.1164.

Postoperative:
Acupuncture

1. Chao LF et al.: The efficacy of acupoint stimulation for the management of therapy-related adverse events in patients with breast cancer: a systematic review. Breast Cancer Res Treat 2009;118:255–267.
2. Mallory MJ et al.: Acupuncture in the postoperative setting for breast cancer patients: a feasibility study. Am J Chin Med.

2015;43(1):45-56.
3. Quinlan-Woodward J, Gode A, Dusek JA: Assessing the Impact of Acupuncture on Pain, Nausea, Anxiety, and Coping in Women Undergoing a Mastectomy. Oncol Nurs Forum. 2016 Nov 1;43(6):725-732.
4. Giron PS, Haddad CA, Lopes de Almeida: Effectiveness of acupuncture in rehabilitation of physical and functional disorders of women undergoing breast cancer surgery. Support Care Cancer. 2016 Jun;24(6):2491-6.
5. Chiu HY, Hsieh YJ, Tsai PS. Systematic review and meta-analysis of acupuncture to reduce cancer-related pain. Eur J Cancer Care (Engl). 2017 Mar;26(2). doi: 10.1111/ecc.12457. Epub 2016 Feb 7
6. Ruan QZ, Chen AD, Tran BNN integrative Medicine in Plastic Surgery: A Systematic Review of Our Literature. Ann Plast Surg 2019 April;82(49):459-468

Massage Therapy

1. Pan YQ, Yang KH, Wang YL, et al: Massage interventions and treatment-related side effects of breast cancer: a systematic review and meta-analysis. Int J Clin Oncol. 2014 Oct;19(5):829-41.
2. Lee SH, Kim JY, Yeo S et al: Meta-Analysis of Massage Therapy on Cancer Pain. Integr Cancer Ther. 2015 Jul;14(4):297-304.
3. Dilaveri CA, Croghan I, Mallory MJ, et al, Massage compared with massage plus acupuncture for breast cancer patients undergoing reconstructive surgery. J Altern Complement Med 2020 26(7):602-609

Postoperative exercise

1. McNeely ML, Campbell K, Ospina M et al.: Exercise interventions for upper-limb dysfunction due to breast cancer treatment. Cochrane Database of Systematic Reviews 2010, Issue 6. Art. No.: CD005211. DOI: 10.1002/14651858.CD005211.pub2.
2. Cavanaugh KM.: Effects of Early Exercise on the Development of Lymphedema in Patients With Breast Cancer Treated With Axillary Lymph Node Dissection. J Oncol Pract. 2011 March; 7(2): 89–93.
3. Anderson RT, Kimmick GG, McCoy TP, et al. A randomized trial of exercise on well-being and function following breast cancer surgery: the RESTORE trial. J Cancer Surv 2012;6(2):172-81
4. De Groef A, Van Kampen M, Dieltjens E, et al.Effectiveness of postoperative physical therapy for upper-limb impairments after breast cancer treatment: a systematic review. Arch Phys Med Rehabil. 2015 Jun;96(6):1140-53. doi: 10.1016/j.apmr.2015.01.006. Epub 2015 Jan 13. Review.
5. Eyigor S, Uslu R, Apaydin S, et al. Can Yoga have any effect on shoulder and arm pain an quality of life in patients with breast cancer? A randomized, controlled, single-blind trial . Complementary Therapies in Clinical Practice 2018;32:40-45.

6. Bruce J, Mazuquin B, Canaway A et al. Exercise versus usual care after non-reconstructive breast surgery (UK PROSPER) multicenter randomised controlled trial and economic evaluation. BMJ 2021;375:e066542
7. Heimann J, Onerup A, Wessman C, et al. Reovery after breast cancer surgery following recommended pre and postoperative physical activity: (PhysSURG-B) randomized clinical trial. Br J Surg 2021 Jan 27;108(1):32-39
8. Klein i, Kalichman L, Chen N et al. Effect of physical activity levels on oncological breast surgery recovery: a prospective cohort study.Scientific reports 2021;11:10432 doi:10.1038/s41598-021-89908-8

Reduction secondary lymphedema

1. Baumann FT, Reike A, Reimer V et al: Effects of physical exercise on breast cancer –related secondary lymphedema : a systematic review Br Ca res Treatment 2018; 170: 1-13

Prevention lymphedema

1. Baumann FT, Reike A, Hallek M, et al. (2018) Does Exercise have a preventive effect on secondary lymphedema in breast cancer patients following local treatment – a systemic review. Breast Care 13(5): 380–385. DOI. 10.1159/000487428
2. Ammitzbøll G, Johansen C, Lanng C, Andersen EW et al.. Progressive resistance training to prevent arm lymphedema in the first year after breast cancer surgery: Results of a randomized controlled trial. Cancer. 2019 May 15;125(10):1683-1692. doi: 10.1002/cncr.31962. Epub 2019 Jan 11.
3. Paskett ED, Le-Rademacher J, Olivieri JM et al. A randomized study to prevent lymphedema in women treated for breast cancer: CALGB 70305 (Alliance).Cancer 2021 Jan 15;127(2):291-299

Prophylactic lymph drainage

1. Devoogdt N, Christiaens MR, Geraerts I, et al: Effect of manual lymph drainage in addition to guidelines and exercise therapy on arm lymphoedema related to breast cancer: randomised controlled trial. BMJ 2011;343:d5326 doi: 10.1136/bmj.d5326
2. Li L, Yuan L, Chen X: Current Treatments for Breast Cancer-Related Lymphoedema: A Systematic Review. Asian Pac J Cancer Prev. 2016 Nov 1;17(11):4875-4883.
3. Devoogdt N, Geraerts I, Van Kampen M, et al. Manual lymph drainage may not have a preventive effect on the development of breast cancer-related lymphoedema in the long term: a randomised trial. J Physiother. 2018 Oct;64(4):245-254. doi: 10.1016/j.jphys.2018.08.007. Epub 2018 Sep 18.
4. Wanchai A, Armer JM. Manual lymphedema drainage for reducing risk for and managing breast cancer-related lympedema after

breast surgery:A systematic review. Nurs Womens Health 2021 oct;25(5):377-383.Doi 10.1016/j.nwh.2021.07.005
5. Paskett ED, Le-Rademacher J, Oliveri JM. A randomized study to prevent lymphedema in women treated for breast cancer:CALGB 70305 (Alliance).Cancer 2021 Jan15;127(2):291-299

Music therapy

1. Li, X.M., Yan H, Zhou KN, et al. Effects of music therapy on pain among female breast cancer patients after radical mastectomy: results from a randomized controlled trial. Breast Cancer Res Treat, 2011. 128(2): p. 411-9.
2. Binns-Turner, P.G., Wilson LL, et al. Perioperative music and its effects on anxiety, hemodynamics, and pain in women undergoing mastectomy. Aana j, 2011. 79(4 Suppl): p. S21-7.
3. Bradt, J., et al., Music interventions for improving psychological and physical outcomes in cancer patients. Cochrane Database Syst Rev, 2016;(8): p. Cd006911.

Complementary Treatment
While on Cancer Treatment – Impact on Toxicity I

Guidelines Breast
Version 2023.1E

During anti-cancer treatment: Beware of drug interactions	Oxford LoE	GR	AGO
▪ **Mistletoe (Viscum album)** in order to reduce side effects	1a	B	+/-
▪ **Thymic peptides** lower risk of severe infections	2a	B	+/-
▪ **Ginseng** reduces fatigue; note: interacts with cytochrome P enzymes e.g. CYP 3A4	2b	C	-
▪ **Ganoderma Lucidum** reduces fatigue, note: inhibits cytochrome P enzymes (e.g. CYP 3A4)	2b	C	-
▪ **L-Carnitine**			
▪ peripheral neuropathy	1b	B	--
▪ treatment of fatigue	1b	B	-
▪ **Melatonin** (reduces fatigue, improve sleep, depressive symptoms, cognition)	2b	B	+/-
▪ **Curcumin** adjunct to reduce radiation-induced dermatitis	1b	B	+/-
▪ **Ginger** adjunct to guideline-oriented medication to treat chemotherapy induced nausea & vomiting – beware of drug interactions	1b	C	+/-

General

1. Neuhouser ML, Smith AW, George SM: Use of complementary and alternative medicine and breast cancer survival in the Health, Eating, Activity, and Lifestyle Study. Breast Cancer Res Treat. 2016 Dec;160(3):539-546.
2. Li Y, Wang J, Lin F: A Methodology for Cancer Therapeutics by Systems Pharmacology-Based Analysis: A Case Study on Breast Cancer-Related Traditional Chinese Medicines. PLoS One. 2017 Jan 9;12(1):e0169363.
3. Farahmand L, Darvishi B, Majidzadeh-A K: Naturally occurring compounds acting as potent anti-metastatic agents and their suppressing effects on Hedgehog and WNT/β-catenin signalling pathways. Cell Prolif. 2017 Feb;50(1). doi: 10.1111/cpr.12299.
4. Cramer H, Lauche R, Klose P: Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. Cochrane Database Syst Rev. 2017 Jan 3;1:CD010802.

Mistletoe

1. Shneerson C, Taskila T, Gale N, et al: The effect of complementary and alternative medicine on the quality of life of cancer survivors: A systematic review and meta-analyses. Complementary therapies in medicine 2013;21:417-429.
2. Thronicke A, Steele ML, Grah C, et al.: Clinical safety of combined therapy of immune checkpoint inhibitors and Viscum album L. therapy in patients with advanced or metastatic cancer. BMC CAM. 2017;17:534.

3. Pelzer F, Tröger W. Complementary Treatment with Mistletoe Extracts During Chemotherapy: Safety, Neutropenia, Fever, and Quality of Life assessed in a randomized study. JAC 2018;24:954-961.
4. Ostermann T, Appelbaum S, Poier D, et al.: A Systematic Review and Meta-Analysis on the Survival of Cancer Patients Treated with a Fermented Viscum album L. Extract (Iscador) – an Update of Findings. Compl Med Res. 2019. In press.
5. Freuding M, Keinki C, Micke O, et al.: Mistletoe in oncological treatment: a systematic review : Part 1: survival and safety. J Cancer Res Clin Oncol. 2019 Mar;145(3):695-707
6. Freuding M, Keinki C, Kutschan S, et al.: Mistletoe in oncological treatment: a systematic review : Part 2: quality of life and toxicity of cancer treatment. J Cancer Res Clin Oncol. 2019;145(4):927-939.
7. Loef M, Walach H. Quality of life in cancer patients treated with mistletoe: a systematic review and meta-analysis. Compl Med Res. 2019. In press.
8. Weissenstein U, Kunz M, Oufir M, et al.: Absence of herb-drug interactions of mistletoe with the tamoxifen metabolite (E/Z)-endoxifen and cytochrome P450 3A4/5 and 2D6 in vitro. BMC Complement Altern Med. 2019;19:23.

Thymus

1. Wolf E, Milazzo S, Boehm K, et al. Thymic peptides for treatment of cancer patients. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD003993. DOI: 10.1002/14651858.CD003993.pub3.

Ginseng, Ganoderm lucidum

1. Jin X, Ruiz Beguerie J, Sze Daniel M-y et al: Ganoderma lucidum (reishi mushroom) for cancer treatment. Cochrane Database of Systematic Reviews 2012
2. Karimi N, Roshan VD: Change in adiponectin and oxidative stress after modifiable lifestyle interventions in breast cancer cases. Asian Pacific journal of cancer prevention : APJCP 2013;14:2845-2850
3. Leggett S1, Koczwara B, Miller M. The impact of complementary and alternative medicines on cancer symptoms, treatment side effects, quality of life, and survival in women with breast cancer--a systematic review. Nutr Cancer. 2015;67(3):373-91.

L-Carnitine

1. Cruciani RA, Zhang JJ, Manola J et al. L-carnitine supplementation for the management of fatigue in patients with cancer: an eastern cooperative oncology group phase III, randomized, double-blind, placebo-controlled trial. J Clin Oncol. 2012 Nov 1;30(31):3864-9
2. Hershman DL, Unger JM, Crew K et al:. Two-Year trends of Taxane-induced neuropathy in women enrolled in a randomized trial of

Acetyl-l-carnitine (SWOG S0715).j Natl Cancer Inst 2018 Jun 1;110(6) 669-676.

Melatonin

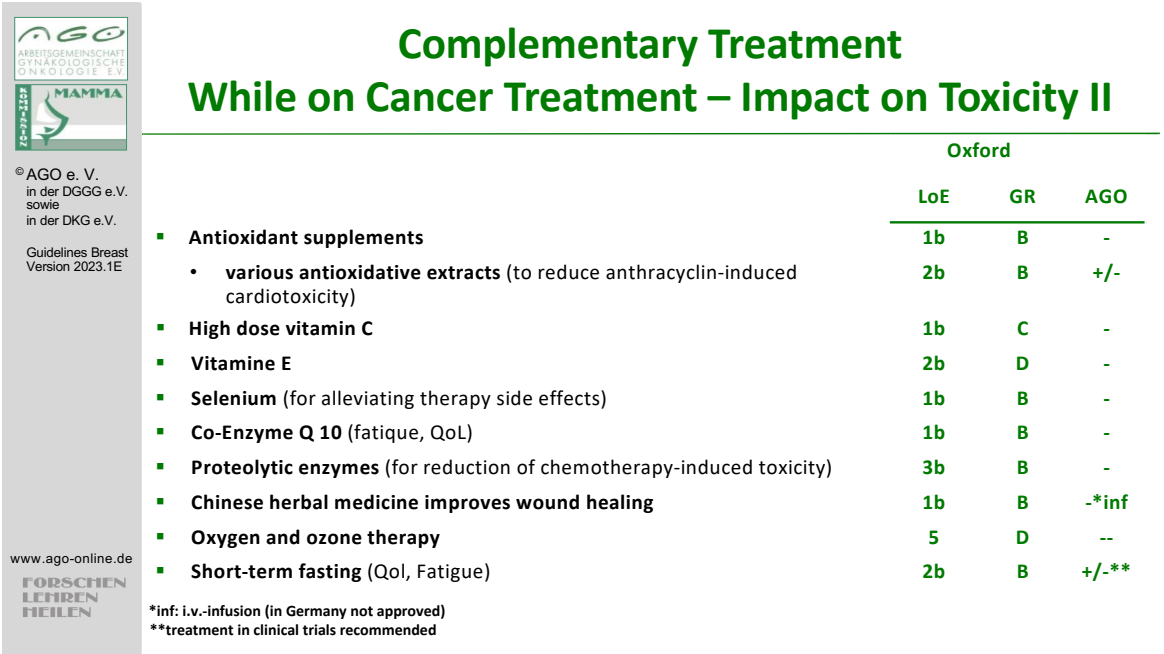
1. Li W, Chi-Hei Kwok C, Chun-Wan Chan D et al. Disruption of sleep, sleep-wake activity rhythm, and nocturnal melatonin production in breast cancer patients undergoing adjuvant chemotherapy: prospective cohort study. Sleep Med 2019;55:14-21 DOI 10.1016/j.sleep.2018.11.022
2. Zaki NFW, Sabri YM, Farouk O et al. Depressive symptoms, sleep profile and serum melatonin levels in a sample of breast cancer patients. Nature and Science of Sleep 2020;12:135-149
3. Palmer ACS, Zortea M, Souza A et al. Clinical impact on breast cancer patients undergoing chemotherapy; effects on cognition, sleep and depressive symptoms. A randomized, double-blind, placebo-controlled trial. Plos One 2020 pril 17;15(4):e0231379 doi:101371
4. Pashaki S, Mohammadian K, Afshar S et al. A randomizes controlled parallel-group trial on the effect of melatonin on fatique associated with breast cancer and its adjuvant treatment. Integr Cancer Ther 2021 Jan-Dec;20:153Doi:10.1177/4735420988343

Curcumin

1. Bandyopadhyay D: Farmer to pharmacist: Curcumin as an anti-invasive and antimetastatic agent for the treatment of cancer. Frontiers in chemistry 2014;2:113.
2. Kumar P, Kadakol A, Shasthrula P, et al: Curcumin as an adjuvant to breast cancer treatment. Anti-cancer agents in medicinal chemistry 2015

Ingwer

1. Sanaati F, Najafi S, Kashaninia Z, et al. Effect of Ginger and Chamomile on Nausea and Vomiting Caused by Chemotherapy in Iranian Women with Breast Cancer. Asian Pac J Cancer Prev. 2016;17(8):4125-9.
2. Thamlikitkul L, Srimuninnim. Efficacy of ginger for prophylaxis of chemotherapy-induced nausea and vomiting in breast cancer patients receiving adriamycin-cyclophosphamide regimen: a randomized, double-blind, placebo-controlled, crossover study. Support Care it V, Akewanlop C, et alCancer. 2017 Feb;25(2):459-464. doi: 10.1007/s00520-016-3423-8. Epub 2016 Oct 6.
3. Totmaj S, Emamat H, Jarrahi F et al. The effect of ginger (Zingiber officinale) on chemotherapy-induced nausea and vomiting in breast cancer patients: A systemativ literature review of randomized controlled trials. Phytother Res 2019 Aug:33(8):1957-65



Complementary Treatment
While on Cancer Treatment – Impact on Toxicity II

	Oxford		
	LoE	GR	AGO
▪ **Antioxidant supplements**	1b	B	-
• **various antioxidative extracts** (to reduce anthracyclin-induced cardiotoxicity)	2b	B	+/-
▪ **High dose vitamin C**	1b	C	-
▪ **Vitamine E**	2b	D	-
▪ **Selenium** (for alleviating therapy side effects)	1b	B	-
▪ **Co-Enzyme Q 10** (fatique, QoL)	1b	B	-
▪ **Proteolytic enzymes** (for reduction of chemotherapy-induced toxicity)	3b	B	-
▪ **Chinese herbal medicine improves wound healing**	1b	B	-*inf
▪ **Oxygen and ozone therapy**	5	D	--
▪ **Short-term fasting** (QoI, Fatigue)	2b	B	+/-**

*inf: i.v.-infusion (in Germany not approved)
**treatment in clinical trials recommended

General

1. Zhu L, Li L, Li Y: Chinese Herbal Medicine as an Adjunctive Therapy for Breast Cancer: A Systematic Review and Meta-Analysis. Evid Based Complement Alternat Med. 2016;2016:9469276. doi: 10.1155/2016/9469276.
2. McPherson L, Cochrane S, Zhu X:Current Usage of Traditional Chinese Medicine in the Management of Breast Cancer: A Practitioner's Perspective. Integr Cancer Ther. 2016 Sep;15(3):335-42. doi: 10.1177/1534735415607656.

Antioxidant supplements

1. van Dalen EC, Caron HN, Dickinson HO, et al: Cardioprotective interventions for cancer patients receiving anthracyclines. Cochrane Database Syst Rev 2011:Cd003917.
2. Harvie M: Nutritional supplements and cancer: Potential benefits and proven harms. American Society of Clinical Oncology educational book / ASCO American Society of Clinical Oncology Meeting 2014:e478-486.
3. The Protective Role of Phenolic Compounds Against Doxorubicin-induced Cardiotoxicity: A Comprehensive Review. Razavi-Azarkhiavi K, Iranshahy M, Sahebkar A, et al. Nutr Cancer. 2016 Aug-Sep;68(6):892-917. doi: 10.1080/01635581.2016.1187280. Epub 2016 Jun 24. Review
4. Jung AY, Cai X, Thoene K, Obi N et al. Antioxidant supplementation and breast cancer prognosis in postmenopausal women undergoing chemotherapy and radiation therapy. Am J Clin Nutr. 2019 Jan 1;109(1):69-78. doi: 10.1093/ajcn/nqy223.

5. Ambrosone CB, Zirpoli GR, Hutson AD et al. Diatery supplement use during chemotherapy and survival outcomes of patients with breast cancer enrolled in a cooperative group clinical trial (SWAG S0221). J Clin Oncol 2020 Mar 10;38(8):804-814
6. Li Y, Lin Q, Lu X et al. Post-diagnosis use of antioxidant vitamin supplements and breast cancer prognosis: A systematic review and meta analysis. Clin Breast Cancer 2021 Dec;21(6):477-485

Vitamin C

1. Heaney M, Gardner J, Karasavvas N et al.: Vitamin C antagonizes the cytotoxic effects of antineoplastic drugs. Cancer Res. 2008 Oct 1;68(19):8031-8.
2. Ma Y1, Chapman J, Levine M, et al. High-dose parenteral ascorbate enhanced chemosensitivity of ovarian cancer and reduced toxicity of chemotherapy Sci Transl Med. 2014 Feb 5;6(222):222ra18. doi: 10.1126/scitranslmed.3007154.
3. Hoffer LJ, Robitaille L, Zakarian R, et al. High-dose intravenous vitamin C combined with cytotoxic chemotherapy in patients with advanced cancer: a phase I-II clinical trial.PLoS One. 2015 Apr 7;10(4):e0120228. doi: 10.1371/journal.pone.0120228. eCollection 2015.

Selen

1. Dennert G, Horneber M. Selenium for alleviating the side effects of chemotherapy, radiotherapy and surgery in cancer patients. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD005037. DOI: 10.1002/14651858.CD005037.pub2.

Coenzym Q10

1. Lesser GJ, Case D, Stark N,et al. A randomized, double-blind, placebo-controlled study of oral coenzyme Q10 to relieve self-reported treatment-related fatigue in newly diagnosed patients with breast cancer. J Support Oncol 2013;11(1):31-42
2. Abdel-Qadir H, Ong G, Fazelzad R et al. Ann Oncol. 2017 Mar 1;28(3):628-633. doi: 10.1093/annonc/mdw671. Interventions for preventing cardiomyopathy due to anthracyclines: a Bayesian network meta-analysis.

Proteolytic enzymes and toxicity of chemotherapy

1. Petru U, Stranz B, Petru C: Effects of proteolytic enzyme therapy with Wobe Mugos against chemotherapy-induced toxicity in breast cancer patients - results of a pilot study Wien Med Wochenschr. 2010 Nov;160(19-20):513-6.

Bromelain

1. Hidaka M, Nagata M, Kawano Y, et al.: Inhibitory effects of fruit juices on cytochrome P450 2C9 activity in vitro. Biosci Biotechnol Biochem. Feb 2008;72(2):406-411.

Chinese herbal medicine and wound healing

1. Chen J, Lv Q, Yu M et al.: Randomized clinical trial of Chinese herbal medications to reduce wound complications after mastectomy for breast carcinoma. Br J Surg. 2010 Dec;97(12):1798-804

Kurzzeit-Fasten

1. Groot de S, Vreeswijk MPG, et al. the effects of short-term fasting on tolerance to (neo) adjuvant chemotherapy in Her2-negative breast cancer patients: a randomized pilot study. BMC Cancer 2015;15:652
2. Bauersfeld SP, Kessler CS, Wischnewsky M et al. The effects of short-term fasting on quality of life and tolerance to chemotherapy in patients with breast and ovarian cancer: a randomized cross-over pilot study. BMC Cancer (2018) 18:476
3. De Groot S, Lugtenberg RT, Cohen D et al. Fasting mimicking diet as an adjunct to neoadjuvant chemotherapy for breast cancer in the multicentre randomized phase 2 DIRECT trail..Nature Communication 2020;11:3083 DOI:10.1038/s4146-020-16138-3

Additional Complementary Therapy of Side Effects Related to Cancer Treatments

	Oxford		
	LoE	GR	AGO
▪ **Chinese medicinal herbs** (to treat the side effects of chemotherapy)	1b	B	-
▪ **Homoeopathic medicine** (against therapy side effects / Placeboeffect)	1b	B	+/-
▪ **Topical Silymarin (**to prevent acute dermatitis during radiotherapy)	3a	B	+/-
▪ **Massage** (to improve on fatigue, pain, anxiety, nausea)	1b	C	+/-
▪ **Transcutaneous Electrical Nerve stimulation (TENS)** (against cancer pain)	2b	D	+/-
▪ **Hydrotherapy** (for supportive skin care)	3b	C	+/-

Chinese medicinal herbs

1. Zhu L, Li L, Li Y: Chinese Herbal Medicine as an Adjunctive Therapy for Breast Cancer: A Systematic Review and Meta-Analysis. Evid Based Complement Alternat Med. 2016;2016:9469276. doi: 10.1155/2016/9469276.
2. Li S, So T, Tang G et al. chinese herbal Medicine for reducing chemotherapy-associated side-effects in breast cancer patients: A systematic review. Frontiers Oncology dec 2020;10:599C73.doi:10.3389/fonc2020.599073

Homeopathic medicines for adverse effects of cancer treatments

1. Kassab S, Cummings M, Berkovitz S, et al. Homeopathic medicines for adverse effects of cancer treatments. Cochrane Database of Systematic Reviews 2012, Issue 8. Art. No.: CD004845. DOI: 10.1002/14651858.CD004845.pub2.

Topical use of Silymarin

1. Karbasforooshan H, Hosseini S, Elyasi S et al. Topical silymarin administration for prevention of acute radiodermatitis in breast cancer patients: A randomized, double-blind, placebo-controlled clinical trial. Phytoth Res 2019 Feb;33(2):379-386. Doi:10.1002/ptr.6231

Massage

1. Shin ES, Seo KH, Lee SH, et al. Massage with or without aromatherapy for symptom relief in people with cancer. Cochrane Database

of Systematic Reviews 2016, Issue 6. Art. No.: CD009873. DOI: 10.1002/14651858.CD009873.pub3.
2. Robison JG, Smith CL. Therapeutic Massage During Chemotherapy and/or Biotherapy Infusions: Patient Perceptions of Pain, Fatigue, Nausea, Anxiety, and Satisfaction. Clin J Oncol Nurs. 2016 Apr;20(2):E34-40. doi: 10.1188/16.CJON.E34-E40.
3. Donoyama N, Satoh T, Hamano T et al., Effects of Anma therapy (Japanese massage) on health-related quality of life in gynecologic cancer survivors: a randomized controlled trial. PLoS one 2018;13:e0196638.
4. Izgu N, Metin ZG, Karadas C et al.. Prevention of chemotherapy-induced peripheral neuropathy with classical massage in breast cancer patients receiving paclitaxel: An assessor-blinded randomized controlled trial. Eur J Oncol Nurs. 2019 Jun;40:36-43. doi: 10.1016/j.ejon.2019.03.002. Epub 2019 Mar 22.

Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults: (*von Slide 16 übertragen*)

1. Paley CA, Johnson MI, Tashani O et al. Acupuncture for cancer pain in adults. Cochrane Database of Systematic Reviews 2011, Issue 1. Art. No.: CD007753. DOI: 10.1002/14651858.CD007753.pub2.
2. Hurlow A, Bennett MI, Robb KA, et al. Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults. Cochrane Database of Systematic Reviews 2012, Issue 3. Art. No.: CD006276. DOI: 10.1002/14651858.CD006276.pub3.

Hydrotherapie

1. Dalenc F, Ribet V, Rossi AB, et al. Efficacy of a global supportive skin care programme with hydrotherapy after non-metastastic breast cancer treatment: a randomized, controlled study. Eur J Cancer Care 2018;27:doi:10.1111/eec

Additional Complementary Therapy of Side Effects Related to Cancer Treatments

Acupuncture in order to improve on	Oxford LoE	Oxford GR	AGO
▪ Chemotherapy-induced nausea and vomiting			
▪ (Electro)-Acupuncture as adjunct to entiemetic treatment	1b	B	+
▪ Acupressure as adjunct to entiemetic treatment	1b	B	+
▪ Pain			
▪ Cancer pain	1b	B	+
▪ Aromatase-inhibitor – induced athralgia	1a	B	+
▪ Fatigue	1a	B	+
▪ Acupressure	1b	B	+
▪ Anxiety and depression	2b	B	+
▪ Cognitive dysfunction	5	D	+/-
▪ Menopause syndrome in Breast Cancer Patients	1b	B	+
▪ to improve on frequency and severity of hot flashes	1b	B	+/-
▪ Electro-Acupuncture to improve on sleep and hot flashes	2a	B	+
▪ Leucopenia (Moxibustion)	2b	B	+/-
▪ Treatment of chemotherapy induced polyneuropathy			
▪ prophylactically	1b	B	-
▪ therapeutically	2b	B	+/-
▪ Chronic lymph edema after Breast Cancer Treatment	2b	B	+/-

Acupuncture

1. Wu X, Chung VCh, Hui EP, et al: Effectiveness of acupuncture and related therapies for palliative care of cancer: overview of systematic reviews. Sci Rep. 2015 Nov 26;5:16776.
2. Tao WW, Jiang H, Tao XM, et al. Effects of Acupuncture, Tuina, Tai Chi, Qigong, and Traditional Chinese Medicine Five-Element Music Therapy on Symptom Management and Quality of Life for Cancer Patients: A Meta-Analysis. J Pain Symptom Manage. 2016 Apr;51(4):728-47. doi: 10.1016/j.jpainsymman.2015.11.027. Epub 2016 Feb 12. Review.
3. Lau CH, Wu X, Chung VC, et al. Acupuncture and Related Therapies for Symptom Management in Palliative Cancer Care: Systematic Review and Meta-Analysis. Medicine (Baltimore). 2016 Mar;95(9):e2901. doi: 10.1097/MD.0000000000002901.
4. Brinkhaus B, Kirschbaum B, Stockigt B, et al.: Prophylactic acupuncture treatment during chemotherapy with breast cancer: a randomized pragmatic trial with a retrospective nested qualitative study. Breast cancer research and treatment 2019, 178(3):617-628.
5. Jang S, Ko Y, Sasaki Y et al. Acupuncture as an adjuvant therapy for management of treatment-related symptoms in breast cancer:systematic review and meta-analysis (PRISMA-compliant). Medicine (Baltimore) 2020 Dec 11;99(50):e21820 doi10.1097/MD.0000000000212820
6. Xiaomeng L, Jing L, Guoxin W et al. Acupuncture for arthralgia induced by aromatase inhibitors in patientients with breast cancer: A systematic review an meta analysis. Integrative Cancer Therapies 2021;20:1-14 DOI 101177/153473542090811

Menopause syndrome

1. Salehi A, Marzban M, Zadeh AR: Acupuncture for treating hot flashes in breast cancer patients: an updated meta-analysis. Support Care Cancer. 2016 Dec;24(12):4895-4899.
2. Lesi G, Razzini G, Musti MA: Acupuncture As an Integrative Approach for the Treatment of Hot Flashes in Women With Breast Cancer: A Prospective Multicenter Randomized Controlled Trial (AcCliMaT). J Clin Oncol. 2016 May 20;34(15):1795-802. doi: 10.1200/JCO.2015.63.2893.
3. Chiu HY, Shyu YK, Chang PC: Effects of Acupuncture on Menopause-Related Symptoms in Breast Cancer Survivors: A Meta-analysis of Randomized Controlled Trials. Cancer Nurs. 2016 May-Jun;39(3):228-37. doi: 10.1097/NCC.0000000000000278.
4. Tao WW, Jiang H, Tao XM: Effects of Acupuncture, Tuina, Tai Chi, Qigong, and Traditional Chinese Medicine Five-Element Music Therapy on Symptom Management and Quality of Life for Cancer Patients: A Meta-Analysis. J Pain Symptom Manage. 2016 Apr;51(4):728-47. doi: 10.1016/j.jpainsymman.2015.11.027.
5. Chien TJ, Hsu CH, Liu CY, et al. Effect of acupuncture on hot flush and menopause symptoms in breast cancer- A systematic review and meta-analysis.
   PLoS One. 2017 Aug 22;12(8):e0180918. doi: 10.1371/journal.pone.0180918. eCollection 2017. Review.
6. Tao WW, Tao XM, Song CL. Effects of non-pharmacological supportive care for hot flushes in breast cancer: a meta-analysis. Support Care Cancer. 2017 Jul;25(7):2335-2347. doi: 10.1007/s00520-017-3691-y. Epub 2017 Apr 11.
7. Yuanqing P, Yong T, Haiqian L et al. Acupuncture for hormone therapy-related side effects in breast cancer patients: A GRADE-assessed systematic review and update. Integrative Cancer Therapy.2020;19:1-17

Chemotherapy-induced Nausea and Vomiting

1. Fonnebo V et al.: Acupuncture and acupressure in the treatment of chemotherapy-associated nausea and vomiting. www.cam-cancer.org, Updated May 21, 2009.
2. Beith JM, Oh B, Chat eld MD, et al. Electroacupuncture for nausea, vomiting, and myelosuppression in women receiving adjuvant chemo- therapy for early breast cancer: a randomized controlled pilot trial. Medical Acupuncture. 2012;24:241–248.
3. Eghbali M et al.. The effect of auricular acupressure on nausea and vomiting caused by chemotherapy among breast cancer patients. Complement Ther Clin Pract. 2016 Aug;24:189-94. doi: 10.1016/j.ctcp.2016.06.006. Epub 2016 Jul 5.

Insomnia

1. Choi TY, Kim JI, Lim HJ, et al.: Acupuncture for Managing Cancer-Related Insomnia: A Systematic Review of Randomized Clinical Trials. Integrative cancer therapies 2017, 16(2):135-146.
2. Garland SN, Xie SX, Li Q, et al.:Comparative effectiveness of electro-acupuncture versus gabapentin for sleep disturbances in breast cancer survivors with hot flashes: a randomized trial. Menopause (New York, NY) 2017, 24(5):517-523.
3. Garland SN, Xie SX, DuHamel K, et al.: Acupuncture Versus Cognitive Behavioral Therapy for Insomnia in Cancer Survivors: A Randomized Clinical Trial. Journal of the National Cancer Institute 2019.

Cognitive dysfunction

1. Tong T, Pei C, Chen J et al. Efficacy of Acupuncture Therapy for Chemotherapy-Related Cognitive Impairment in Breast Cancer Patients. Med Sci Monit. 2018 May 8 [revised 2018 Jan 1];24:2919-2927. doi: 10.12659/MSM.909712.

Fatigue

1. Smith C, Carmady B, Thornton C et al. The effect of acupuncture on post-cancer fatigue and well-being for women recovering from breast cancer: a pilot randomised controlled trial. Complement Ther Clin Pract. 2013;19(1):32-5.
2. Ling WM, Lui LY, So WK, et al: Effects of acupuncture and acupressure on cancer-related fatigue: a systematic review. Oncol Nurs Forum. 2014 Nov 1;41(6):581-92.
3. Mao JJ, Farrar JT, Bruner D et al. Electroacupuncture for fatigue, sleep, and psychological distress in breast cancer patients with aromatase inhibitor-related arthralgia: a randomized trial. Cancer. 2014;120(23):3744-51.
4. Zick SM, Sen A, Wyatt GK, et al. Investigation of 2 Types of Self-administered Acupressure for Persistent Cancer-Related Fatigue in Breast Cancer Survivors: A Randomized Clinical Trial. JAMA Oncol. 2016 Nov 1;2(11):1470-1476. doi: 10.1001/jamaoncol.2016.1867.
5. Zhang B, Dong JN, Sun P, et al. Effect of therapeutic care for treating fatigue in patients with breast cancer receiving chemotherapy. Medicine (Baltimore). 2017 Aug;96(33):e7750. doi: 10.1097/MD.0000000000007750.
6. Zhang Y, Lin L, Li H, et al. Effects of acupuncture on cancer-related fatigue: a meta-analysis. Support Care Cancer. 2017 Nov 11. doi: 10.1007/s00520-017-3955-6.

Pain

1. Garcia MK, McQuade J, Haddad R, et al. Systematic review of acupuncture in cancer care: a synthesis of the evidence. J Clin Oncol. 2013 Mar 1;31(7):952-60. doi: 10.1200/JCO.2012.43.5818. Epub 2013 Jan 22. (von Slide 16 übertragen)
2. Bae K, Yoo HS, Lamoury G, et al. Acupuncture for Aromatase Inhibitor-Induced Arthralgia: A Systematic Review. Integr Cancer Ther.

2015 Nov;14(6):496-502. doi: 10.1177/1534735415596573. Epub 2015 Jul 28. (von Slide 16 übertragen)
3. Paley CA1, Johnson MI, Tashani OA, et al. Acupuncture for cancer pain in adults. Cochrane Database Syst Rev. 2015 Oct 15;10:CD007753. doi: 10.1002/14651858.CD007753
4. Chien TJ1, Liu CY, Chang YF, et al. Acupuncture for treating aromatase inhibitor-related arthralgia in breast cancer: a systematic review and meta-analysis. J Altern Complement Med. 2015 May;21(5):251-60. doi: 10.1089/acm.2014.0083. Epub 2015 Apr 27.
5. Yang GS1, Kim HJ, Griffith K et al. Interventions for the Treatment of Aromatase Inhibitor-Associated Arthralgia in Breast Cancer Survivors: A Systematic Review and Meta-analysis. Cancer Nurs. 2017 Jul/Aug;40(4):E26-E41. doi: 10.1097/NCC.0000000000000409
6. Chiu HY, Hsieh YJ, Tsai PS. Systematic review and meta-analysis of acupuncture to reduce cancer-related pain. Eur J Cancer Care (Engl). 2017 Mar;26(2). doi: 10.1111/ecc.12457. Epub 2016 Feb 7.
7. Chen L, Lin CC, Huang TW, et al. Effect of acupuncture on aromatase inhibitor-induced arthralgia in patients with breast cancer: A meta-analysis of randomized controlled trials. Breast. 2017 Jun;33:132-138. doi: 10.1016/j.breast.2017.03.015. Epub 2017 Apr 4.
8. Pan Y, Yang K, Shi X, et al.: Clinical Benefits of Acupuncture for the Reduction of Hormone Therapy–Related Side Effects in Breast Cancer Patients: A Systematic Review. Integrative cancer therapies 2018, 17(3):602-618.
9. Hershman DL, Unger JM, Greenlee H, et al.: Effect of Acupuncture vs Sham Acupuncture or Waitlist Control on Joint Pain Related to Aromatase Inhibitors Among Women With Early-Stage Breast Cancer: A Randomized Clinical Trial. Jama 2018, 320(2):167-176.
10. He Y, Guo X, May BH et al. Clinical Evidence for Association of Acupuncture and Acupressure With Improved Cancer Pain: A Systematic Review and Meta-Analysis. JAMA Oncol. 2019 Dec 19. doi: 10.1001/jamaoncol.2019.5233.

Leucopenia

1. Choi TY, Lee MS, Ernst E: Moxibustion for the treatment of chemotherapy-induced leukopenia: a systematic review of randomized clinical trials. Support Care Cancer. 2015 Jun;23(6):1819-26.

Chemotherapy induced peripheral neuropathy

1. Brami C, Bao T, Deng G Natural products and complementary therapies for chemotherapy-induced peripheral neuropathy: A systematic review. Crit Rev Oncol Hematol. 2016 Feb;98:325-34. doi: 10.1016/j.critrevonc.2015.11.014. Epub 2015 Nov 23.
2. Greenlee H, Crew KD, Capodice J et al. Randomized sham-controlled pilot trial of weekly electro-acupuncture for the prevention of taxane-induced peripheral neuropathy in women with early stage breast cancer. Breast Cancer Res Treat. 2016 Apr;156(3):453-464. doi: 10.1007/s10549-016-3759-2. Epub 2016 Mar 25.
3. Ben-Horin I, Kahan P, Ryvo L et al. Acupuncture and Reflexology for Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer.

Integr Cancer Ther. 2017 Sep;16(3):258-262. doi: 10.1177/1534735417690254. Epub 2017 Feb 2. (Haben wir die?)
4. Molassiotis A, Suen LKP, Cheng HL et al. A Randomized Assessor-Blinded Wait-List-Controlled Trial to Assess the Effectiveness of Acupuncture in the Management of Chemotherapy-Induced Peripheral Neuropathy. Integr Cancer Ther. 2019 Jan-Dec;18:1534735419836501. doi: 10.1177/1534735419836501.
5. Lu W, Giobbie-Hurder A, Freedman RA et al. Acupuncture for Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer Survivors: A Randomized Controlled Pilot Trial. Oncologist. 2020 Apr;25(4):310-318
6. Weidong Lu, Anita Giobbie-Hurder, Rachel A. Freedman et al, Acupuncture for Chemotherapy-Induced Peripheral Neuropathy in Breast Cancer Survivors: A Randomized Controlled Pilot Trial, Oncologist. 2020 Apr; 25(4): 310–318.

Chronic Lymphedema

1. Yao C1, Xu Y1, Chen L1, et al. Curr Oncol. 2016 Feb;23(1):e27-34. doi: 10.3747/co.23.2788. Epub 2016 Feb 18. Effects of warm acupuncture on breast cancer-related chronic lymphedema: a randomized controlled trial.
2. Chien TJ, Liu CY, Fang CJ: The Effect of Acupuncture in Breast Cancer-Related Lymphoedema (BCRL): A Systematic Review and Meta-Analysis. Integrative Cancer Therapies 2019, 18:1534735419866910.
3. Zayas J, Ruddy KJ, Olson JE et al, Real-world experiences with acupuncture among breast cancer survibors: a cross-sectional survey study. Support Care Cancer 2020 28(12)5833-5838
4. Jin H, XiangY, Feng Y et al. Effectiveness and safety of acupuncture moxibustion therapy used in breast cancer-related lymphedema:A systematic review and meta-analysis. Evid Based Complement Alternat Med 2020 May 11;3237451 doi10.1155/2020/3237451
5. Gao Y, Tingting M, Han M et al. Effects of Acupuncture and moxibustion on breast caner-related lymphedema: Asystematic review and meta-analysis of RCT. Integrative Cancer Therapies 2021;10:1-13 Doi:10.1177/1534735421/044107

Complementary Treatment
Mind-Body Medicine I

	Oxford LoE	GR	AGO
MBSR (Mindfulness-Based Stress Reduction) Program improves quality of life, coping strategies, attentiveness, and lowers stress, anxiety, depression, fatigue, and sleep disturbances	1a	A	+
Physical exercise / sport min. 3x/week moderate endurance training in combination with workout exercises (2x per week) improve quality of life, cardio-respiratory fitness, physical performance, sleep, pain, depression, lymphedema, and fatigue	1a	A	++

Mind-Body Medicine (MBM)

1. Charalambous A, Giannakopoulou M, Bozas E, et al: Guided Imagery And Progressive Muscle Relaxation as a Cluster of Symptoms Management Intervention in Patients Receiving Chemotherapy: A Randomized Control Trial. PLoS One. 2016 Jun 24;11(6):e0156911. doi: 10.1371/journal.pone.0156911. eCollection 2016.

MBSR

1. Huang HP, He M, Wang HY: A meta-analysis of the benefits of mindfulness-based stress reduction (MBSR) on psychological function among breast cancer (BC) survivors. Breast Cancer. 2016 Jul;23(4):568-76. doi: 10.1007/s12282-015-0604-0.
2. Lengacher CA, Reich RR, Paterson CL: Examination of Broad Symptom Improvement Resulting From Mindfulness-Based Stress Reduction in Breast Cancer Survivors: A Randomized Controlled Trial. J Clin Oncol. 2016 Aug 20;34(24):2827-34. doi: 10.1200/JCO.2015.65.7874.
3. Reich RR, Lengacher CA, Alinat CB: Mindfulness-Based Stress Reduction in Post-treatment Breast Cancer Patients: Immediate and Sustained Effects Across Multiple Symptom Clusters. J Pain Symptom Manage. 2017 Jan;53(1):85-95. doi: 10.1016/j.jpainsymman.2016.08.005.
4. Schmidt ME, Wiskemann J, Ulrich CM: Self-reported physical activity behavior of breast cancer survivors during and after adjuvant therapy: 12 months follow-up of two randomized exercise intervention trials. Acta Oncol. 2017 Jan 13:1-10. doi:

10.1080/0284186X.2016.1275776.
5. Castanhel F, Liberali R. Mindfulness-Based Stress Reduction on breast cancer symptoms: systematic review and meta-analysis. Einstein 2018;16:1-10
6. Hall DL, Luberto CM, Philpotts et al., Mind-body interventions for fear of cancer recurrence: A systematic review and meta-analysis. Psycho-Oncology 2018;1-13.
7. Haller H, Winkler MM, Klose P et al: Mindfulness-based interventions for women with breast cancer: an updated systematic review and meta-analysis. Acta oncologica (Stockholm, Sweden). 2017 Jul 07:1-12. PubMed PMID: 28686520. Epub 2017/07/08. eng.
8. Zhang Q, Zhao H, Zheng Y. Effectiveness of mindfulness-based stress reduction (MBSR) on symptom variables and health-related quality of life in breast cancer patients-a systematic review and meta-analysis. Support Care Cancer 2019;27(3):771-781. doi: 10.1007/s00520-018-4570-x. Epub 2018 Nov 28.
9. Schell LK, Monsef I, Wöckel A, et al. Mindfulness-based stress reduction for women diagnosed with breast cancer. Cochrane Database Syst Rev. 2019 Mar 27;3:CD011518.

Physical exercise

1. Cormie P, Pumpa K, Galvao DA et al. Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: a randomised controlled trial. J Cancer Surviv. 2013 Sep;7(3):413-24.
2. Forbes, C.C., et al., *Prevalence and correlates of strength exercise among breast, prostate, and colorectal cancer survivors.* Oncol Nurs Forum, 2015. 42(2): p. 118-27.
3. Furmaniak AC, Menig M, Markes MH. Exercise for women receiving adjuvant therapy for breast cancer. Cochrane Database Syst Rev. 2016 Sep 21;9:CD005001. [Epub ahead of print]
4. Mercier J, Savard J, Bernard P: Exercise interventions to improve sleep in cancer patients: A systematic review and meta-analysis. Sleep Med Rev. 2017 Dec;36:43-56. doi: 10.1016/j.smrv.2016.11.001. Epub 2016 Nov 10.
5. Steindorf K; Wiskemann J; Ulrich CM; et al: Effects of exercise on sleep problems in breast cancer patients receiving radiotherapy: a randomized clinical trial. Breast Cancer Res Treat. 2017; 162(3):489-499 (ISSN: 1573-7217)
6. Campbell, KL, et al. : Consensus Statement from International Multidisciplinary Roundtable Exercise Guidelines for Cancer Survivors. Medicine & Science in Sports & Exercise. 2019;51(11):2375–2390
7. Kreutz C, Schmidt ME, Steindorf K. Effects of physical and mind-body exercise on sleep problems during and after breast cancer treatment: a systematic review and meta-analysis. Breast Cancer Res Treat. 2019;176(1):1-15. doi: 10.1007/s10549-019-05217-9.

Epub 2019 Apr 6.

Quality of life

1. Steindorf K, Schmidt ME, Klassen O et al. Randomized, controlled trial of resistance training in breast cancer patients receiving adjuvant radiotherapy: results on cancer-related fatigue and quality of life. Ann Oncol. 2014 Nov;25(11):2237-43.
2. Schmidt ME, Wiskemann J, Armbrust Pet al. Effects of resistance exercise on fatigue and quality of life in breast cancer patients undergoing adjuvant chemotherapy: A randomized controlled trial. Int J Cancer. 2014 Dec 6. doi: 10.1002/ijc.29383. [Epub ahead of print]
3. Zeng Y, Huang M, Cheng AS et al. Meta-analysis of the effects of exercise intervention on quality of life in breast cancer survivors. Breast Cancer. 2014 May;21(3):262-74.
4. Zhang, X, Li, Y, Liu D. Effects of exercise on the quality of life in breast cancer patients: a systematic review of randomized controlled trials. Supportive Care in Cancer 2019:27(1), 9-21.

Cardio respiratory Fitness / Physical Functioning

1. Courneya KS, Segal RJ, Mackey JR et al. Effects of exercise dose and type on sleep quality in breast cancer patients receiving chemotherapy: a multicenter randomized trial. Breast Cancer Res Treat. 2014 Apr;144(2):361-9.
2. Courneya KS, McKenzie DC, Gelmon K et al. A multicenter randomized trial of the effects of exercise dose and type on psychosocial distress in breast cancer patients undergoing chemotherapy. Cancer Epidemiol Biomarkers Prev. 2014 May;23(5):857-64.
3. Courneya KS, McKenzie DC, Mackey JR et al. Subgroup effects in a randomised trial of different types and doses of exercise during breast cancer chemotherapy.Br J Cancer. 2014 Oct 28;111(9):1718-25.
4. Casla S, López-Tarruella S, Jerez Y, et al. Supervised physical exercise improves VO2max, quality of life, and health in early stage breast cancer patients: a randomized controlled trial. Breast Cancer Res Treat. 2015 Sep;153(2):371-82.
5. Jones LW et al. Exercise and Risk of Cardiovascular Events in Women With Nonmetastatic Breast Cancer. J Clin Oncol. 2016;10;34(23):2743-9. doi: 10.1200/JCO.2015.65.6603. Epub 2016 May 23**.**
6. Gebruers N, Camberlin M, Theunissen F. et al.The effect of training interventions on physical performance, quality of life, and fatigue in patients receiving breast cancer treatment: a systematic review. Supportive Care in Cancer 2019; 27(1): 109-122.

Fatigue

1. Zou LY, Yang L, He XL et al. Effects of aerobic exercise on cancer-related fatigue in breast cancer patients receiving chemotherapy: a meta-analysis. Tumour Biol. 2014 Jun;35(6):5659-67.
2. Meneses-Echávez JF, González-Jiménez E, Ramírez-Vélez R. Effects of supervised exercise on cancer-related fatigue in breast cancer survivors: a systematic review and meta-analysis. BMC Cancer. 2015 Feb 21;15:77. doi: 10.1186/s12885-015-1069-4.
3. van Waart H, Stuiver MM, van Harten WH et al. Effect of Low-Intensity Physical Activity and Moderate- to High-Intensity Physical Exercise During Adjuvant Chemotherapy on Physical Fitness, Fatigue, and Chemotherapy Completion Rates: Results of the PACES Randomized Clinical Trial. J Clin Oncol. 2015 Jun 10;33(17):1918-27.
4. Mustian KM, Alfano CM, Heckler C, et al. (2017) Comparison of Pharmaceutical, Psychological, and Exercise Treatments for Cancer-Related Fatigue: A Meta-analysis. JAMA Oncol. 1;3(7):961-968. doi: 10.1001/jamaoncol.2016.6914.
5. Hilfiker, R., Meichtry, A., Eicher, M et al. (2017). Exercise and other non-pharmaceutical interventions for cancer-related fatigue in patients during or after cancer treatment: a systematic review incorporating an indirect-comparisons meta-analysis. Br J Sports Med, bjsports-2016.
6. Lipsett A, Barrett S, Haruna F et al. The impact of exercise during adjuvant radiotherapy for breast cancer on fatigue and quality of life: A systematic review and meta-analysis. Breast. 2017 Apr;32:144-155. doi: 10.1016/j.breast.2017.02.002. Epub 2017 Feb 9.
7. Juvet LK, Thune I, Elvsaas IKØ, et al. The effect of exercise on fatigue and physical functioning in breast cancer patients during and after treatment and at 6 months follow-up: A meta-analysis. Breast. 2017 Jun;33:166-177. doi: 10.1016/j.breast.2017.04.003. Epub 2017 Apr 14.
8. Gebruers N, Camberlin M, Theunissen F, et al. The effect of training interventions on physical performance, quality of life, and fatigue in patients receiving breast cancer treatment: a systematic review. Supportive Care in Cancer 2019; 27(1), 109-122.

PNP

1. Steckmann F, Zopf EM, Lehmann HC, et al. Exercise Intervention studies in patients with PNP: a systemic review. SportsMed. 2014: DOI 10.1007/s40279-014-0207-5
2. Streckmann F, Lehmann HC, Balke M, et al., Sensorimotor training and whole-body vibration training have the potential to reduce motor and sensory symptoms of chemotherapy-induced peripheral neuropathy – a randomized controlled pilot trial. Supp Care in Cancer 2016 doi.org/10.1007/s00520-018-4531-4

Pain

1. Irwin ML, Carmel B, Gross CP, et al. Randomized exercise Trial of AI-Induced Arthralgie in Breast cancer survivors- JCO 2015;33:1104-

11011

Lymphedema

1. Baumann FG, Reike A, Reimer V et al., Effects of physical exercise on breast cancer-related secondary lymphedema: a systemic review. Breast Cancer Res Treat Doi 10.1007/s10549-018-4725
2. Baumann FT, Reike A, Hallek M, et al. Does Exercise have a preventive effect on secondary lymphedema in breast cancer patients following local treatment – a systemic review. Breast Care DOI. 10.1159/000487428

Weight change

1. Mutschler NS, Scholz C et al. Prognostic Impact of Weight Change During Adjuvant Chemotherapy in Patients With High-Risk Early Breast Cancer: Results From the ADEBAR Study. Clin Breast Cancer 2018;18(2): 175–183

Complementary Treatment
Mind-Body Medicine II

	Oxford LoE	GR	AGO
Relaxation techniques Reduction of anxiety and nausea, improvement of quality of life, reduction of psychological stress	2b	C	+/-
Yoga Improves sleep, quality of life, stress, anxiety, depression, fatigue, and sleep	1b	A	+
Qi Gong May improve quality of life, fatigue, and mood	2a	B	+/-
Tai Chi Improves quality of life, muscular strength, sleep	2a	B	+/-
Hypnosis (in combination with cognitive training) Improves fatigue and muscle weakness under radiotherapy; also reduces distress	1b	A	+

General

1. Pan Y, Yang K, Wang Y, et al.: Could yoga practice improve treatment-related side effects and quality of life for women with breast cancer? A systematic review and meta-analysis. Asia Pac J Clin Oncol. 2015 Jan 6. doi: 10.1111/ajco.12329. [Epub ahead of print]
2. Merckaert I, Lewis F, Delevallez F: Improving anxiety regulation in patients with breast cancer at the beginning of the survivorship period: A randomized clinical trial comparing the benefits of single-component and multi-component group interventions. Psychooncology. 2016 Oct 8. doi: 10.1002/pon.4294.
3. Campbell KL, Zadravec K, Chesley E et al. The Effect of exercise on cancer-related cognitive impairment and application for physical therapy: Systematic review of randomized controlled trials Phys Ther 2020 Mar 10;100(3):523-542
4. Saraswathi Y, Latha S, Niraimati K et al. Manageing Lymphedema, increasing range of motion, and quality of life through yoga therapy among breast cancer survivors: A systematic review.Int J Yoga 2021;14:3-17

Relaxation techniques

1. Abbasi B, Mirzakhany N, Oshnari A et al. The effect of relaxation techniques on edema, anxiety and depression in post-mastectomy lymphedema patients undergoing comprehensive decongestive therapy: A Clinical Trail. PLoS One 2018;13:e0190231
2. Lyman GH, Grennlee H et al. Integrative Therapies during and after Breast Cancer Treatment: ASCO Endorsement of the SIO clinical practice guideline. JCO 2018;36:2647-2655.

3. Dikmen, H. A., & Terzioglu, F. Effects of Reflexology and Progressive muscle relaxation on pain, fatigue, and quality of life during chemotherapy in gynecologic cancer patients. Pain Management Nursing 2019;20(1), 47-53.
4. Tian X, Tang R-Y, Xu LL et al. Progressive muscle relaxation is effective in preventing and alleviating of chemotherapy-induced nausea and vomiting among cancer patients: a systematic review of six randomized controlled trials. Support Care Cancer 2020; 28(9):4051-4058

Yoga

1. Chakrabarty J, Vidyasagar MS, Fernandes D, et al: Effectiveness of pranayama on cancer-related fatigue in breast cancer patients undergoing radiation therapy: A randomized controlled trial, Int J Yoga. 2015 Jan-Jun; 8(1): 47–53. doi: 10.4103/0973-6131.146062 PMCID: PMC4278135
2. Derry et.al. Yoga and self-reported cognitive problems in breast cancer survivors: a randomized controlled trial. Psychooncology. 2015 Aug;24(8):958-66.
3. Sprod LK, Fernandez ID, Janelsins MC, et al: Effects of yoga on cancer-related fatigue and global side-effect burden in older cancer survivors. J Geriatr Oncol. 2015 Jan;6(1):8-14.
4. Naciye Vardar Yagli, Ozlem Ulger. The effects of yoga on the quality of life and depression in elderly breast cancer patients. Complement Ther Clin Pract. 2015 Feb;21(1):7-10. doi: 10.1016/j.ctcp.2015.01.002. Epub 2015 Jan 29.
5. Vardar Yağlı N, Şener G, Arıkan H et al. Do yoga and aerobic exercise training have impact on functional capacity, fatigue, peripheral muscle strength, and quality of life in breast cancer survivors? Integr Cancer Ther. 2015 Mar;14(2):125-32. doi: 10.1177/1534735414565699. Epub 2015 Jan 6.
6. Rao RM, Raghuram N, Nagendra HR, et al. Effects of an integrated Yoga Program on Self-reported Depression Scores in Breast Cancer Patients Undergoing Conventional Treatment: A Randomized Controlled Trial. Indian J Palliat Care. 2015 May-Aug;21(2):174-81. doi: 10.4103/0973-1075.156486.
7. Cramer H, Lauche R, Klose P, et al. Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer. The Cochrane database of systematic reviews. 2017 Jan 03;1:CD010802. PubMed PMID: 28045199. Epub 2017/01/04. eng.
8. Dong B, Xie C, Jing X, et al. Yoga has a solid effect on cancer-related fatigue in patients with breast cancer: a meta-analysis. Breast Cancer Res Treat. 2019 Aug;177(1):5-16. doi: 10.1007/s10549-019-05278-w. Epub 2019 May 24. Review.
9. Zetzl T, Renner A, Pitting A et al. Yoga effectively reduces fatigue and symptoms of depression in patients with different types of cancer. Support Care Cancer 2020 Oct 7 doi:10.10007/s00520-020-05794-2

10. Yi LJ, Tian X, Jin YF et al. Effects of yoga on health-related quality, physical health and psychological health in women with breast cancer receiving chemotherapy: a systematic review and meta-analysis. Ann Palliativ Med 2021;10(2):1961-1975

Qigong

1. Zeng Y, Luo T, Xie H et al. Health benefits of qigong or tai chi for cancer patients: a systematic review and meta-analyses. Complement Ther Med. 2014 Feb;22(1):173-86.
2. Larkey LK, Roe DJ, Weihs KL et al. Randomized controlled trial of Qigong/Tai Chi Easy on cancer-related fatigue in breast cancer survivors. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine 2015; 49: 165-176 .
3. Fong SS, Choi AW, Luk WS: Bone Mineral Density, Balance Performance, Balance Self-Efficacy, and Falls in Breast Cancer Survivors With and Without Qigong Training. Integr Cancer Ther. 2016 Dec 1:1534735416686687. doi: 10.1177/1534735416686687.
4. Zeng Y, Xie X, Cheng ASK. Qigong or Tai Chi in Cancer Care: an Updated Systematic Review and Meta-analysis. Curr Oncol Rep 2019;21(6):48. doi: 10.1007/s11912-019-0786-2.
5. Meng T, Hu S, Cheng Y, et al. Qigong for women with breast cancer: n updateed systematic review and meta analysis. Complementary Therapies Med 2021;60:102743

Tai-Chi

1. Yan JH, Pan L, Zhang XM et al. Lack of efficacy of Tai Chi in improving quality of life in breast cancer survivors: a systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014;15(8):3715-20.
2. Larkey LK, Roe DJ, Weihs KL et al. Randomized controlled trial of Qigong/Tai Chi Easy on cancer-related fatigue in breast cancer survivors. Annals of behavioral medicine : a publication of the Society of Behavioral Medicine. 2015;49: 165-176 .
3. Pan Y, Yang K, Shi X, et al: Tai chi chuan exercise for patients with breast cancer: a systematic review and meta-analysis. Evid Based Complement Alternat Med. 2015;2015:535237.
4. Irwin M R, Olmstead R, Carrillo C et al: Tai Chi Chih Compared With Cognitive Behavioral Therapy for the Treatment of Insomnia in Survivors of Breast Cancer: A Randomized, Partially Blinded, Noninferiority Trial . J Clin Oncol. 2017 Aug 10;35(23):2656-2665. doi: 10.1200/JCO.2016.71.0285. Epub 2017 May 10**.**
5. Liu L, Tan H, Yin H et al. The effectiveness of thai chi in breast cancer patients: A systematic review and meta-analysis. Complement Ther Clin Pract 2020 Feb;38:101078.doi:10.1016/ctcp.2019.101078

Hypnosis

1. Montgomery GH, Schnur JB, Kravits K. Hypnosis for cancer care: Over 200 years young. CA Cancer J Clin. 2012 Nov 20. doi: 10.3322/caac.21165.
2. Cramer H, Lauche R, Paul A et al. Hypnosis in Breast Cancer Care: A Systematic Review of Randomized Controlled Trials. Integr Cancer Ther. 2015 Jan;14(1):5-15. Epub 2014 Sep 18.

CAM
Prevention of Recurrence / Improvement of Overall Survival I
Modifiable Lifestyle Factors

	Oxford		
	LoE	GR	AGO
▪ **Physical exercise** (equivalent to 3–5 hrs moderate walking per week) improves DFS and OS, cardio-respiratory fitness, physical functioning	2a	A	++
▪ **Reduce smoking**	2b	A	+
▪ **Reduce alcohol consumption (< 6 g/day)**	2b	A	+

Physical exercise

1. Friedenreich CM, Neilson HK, Woolcott CG, et al: Inflammatory Marker Changes in a Yearlong Randomized Exercise Intervention Trial among Postmenopausal Women. ancer Prev Res (Phila). 2012 Jan;5(1):98-108.
2. Zeng H, Irwin ML, Lu L, et al: Physical activity and breast cancer survival: an epigenetic link through reduced methylation of a tumor suppressor gene L3MBTL1. Breast Cancer Res Treat. 2012 May;133(1):127-35. doi: 10.1007/s10549-011-1716-7. Epub 2011 Aug 12.
3. de Glas NA, Fontein DB, Bastiaannet E, et al: Physical activity and survival of postmenopausal, hormone receptor-positive breast cancer patients: Results of the tamoxifen exemestane adjuvant multicenter lifestyle study. Cancer 2014;120:2847-2854.
4. Nechuta S, Chen WY, Cai H: A pooled analysis of post-diagnosis lifestyle factors in association with late estrogen-receptor-positive breast cancer prognosis. Int J Cancer. 2016 May 1;138(9):2088-97. doi: 10.1002/ijc.29940.
5. Hong, F., Ye, W., Kuo, C. H., et al.Exercise Intervention Improves Clinical Outcomes, but the “Time of Session” is Crucial for Better Quality of Life in Breast Cancer Survivors: A Systematic Review and Meta-Analysis. Cancer 2019; 11(5), 706.

Wearable technology-based physical activity

1. Blount DS, McDonough DJ Gao Z. Effect of wearable technology-based physical activity interventions on breast cancer survivors‘ physiological, cognitive, and emotional outcomes: A systematic review. J Clin Med 2021 May 8;10(9):2015. doi:10.3390/jcm10092015

Improvements in DFS and OS, prevention of recurrence

1. Zhong S, Jiang T, Ma T et al. Association between physical activity and mortality in breast cancer: a meta-analysis of cohort studies. Eur J Epidemiol. 2014 Jun;29(6):391-404.
2. Borch KB, Braaten T, Lund E et al. Physical activity before and after breast cancer diagnosis and survival - the Norwegian women and cancer cohort study. BMC Cancer. 2015 Dec 16;15(1):967. doi: 10.1186/s12885-015-1971-9.
3. Lahart IM, Metsios GS, Nevill AM, et al. Physical activity, risk of death and recurrence in breast cancer survivors: A systematic review and meta-analysis of epidemiological studies. Acta Oncol. 2015 May;54(5):635-54.
4. Patel AV, Friedenreich CM, Moore SC et al. American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and Control. Med Sci Sports Exerc 2019;51(11):2391-2402.
5. Jung, A. Y., Behrens, S., Schmidt, M et al. Pre-to postdiagnosis leisure-time physical activity and prognosis in postmenopausal breast cancer survivors. Breast Cancer Research 2019;21(1), 117.
6. Clark E, Maquire H, Cannon P et al. The effect of physical activity, fast-mimicking diet and psychological interventions on cancer survival: A systematic review and meta-analysis of randomized controlled trials. Complement Ther Med 2021 Mar;57:102654.doi:10.1016/jtim2020.2654

Smoking

1. Pierce JP, Patterson RE, Senger C et al: Lifetime cigarette smoking and breast cancer prognosis in the after breast cancer pooling project. J Natl Cancer Inst 2014;106:djt359.
2. Bérubé S, Lemieux J, Moore L: Smoking at time of diagnosis and breast cancer-specific survival: new findings and systematic review with meta-analysis. Breast Cancer Res. 2014 Apr 19;16(2):R42. doi: 10.1186/bcr3646.
3. Wang K, Li F, Zhang X:Smoking increases risks of all-cause and breast cancer specific mortality in breast cancer individuals: a dose-response meta-analysis of prospective cohort studies involving 39725 breast cancer cases. Oncotarget. 2016 Dec 13;7(50):83134-83147. doi: 10.18632/oncotarget.13366.

Alcohol

1. Larsen SB, Kroman N, Ibfelt EH: Influence of metabolic indicators, smoking, alcohol and socioeconomic position on mortality after breast cancer. Acta Oncol. 2015 May;54(5):780-8. doi: 10.3109/0284186X.2014.998774.
2. Jayasekara H, MacInnis RJ, Room R, English DR. Long-Term Alcohol Consumption and Breast, Upper Aero-Digestive Tract and

Colorectal Cancer Risk: A Systematic Review and Meta-Analysis. Alcohol Alcohol. 2015 Sep 22. pii: agv110. [Epub ahead of print]
3. Simapivapan P, Boltong A, Hodge A.:To what extent is alcohol consumption associated with breast cancer recurrence and second primary breast cancer?: A systematic review. Cancer Treat Rev. 2016 Nov;50:155-167. doi: 10.1016/j.ctrv.2016.09.010.
4. Choi YJ, Jyung SK, Lee JH. Ligth Alcohol Drinking and Risko of Cancer: A Meta-Analysis of Cohort Studies. Cancer Res Treat 2018;50:474-487.

Modifiable Lifestyle Factors

Nutrition after Breast Cancer Diagnosis
Prevention of Recurrence / Improvement of Overall Survival II

	Oxford		
	LoE	GR	AGO
▪ **Adherence to normal BMI / weight loss if overweight, irrespective of HR-status**	1a	A	++
▪ **Low fat diet** dietary counseling recommended	1a	B	+
▪ **Increased fiber intake (e.g. Flaxseed)**	2a	B	+
▪ **Adherence to general nutrition guidelines** (e.g. DGE, WCRF) similar to a Mediterranean Diet	2a	B	++
▪ **Dietary extremes**	2a	B	--

Adherence to normal body weight/BMI

1. Schwingshackl L, Hoffmann G: Adherence to Mediterranean diet and risk of cancer: an updated systematic review and meta-analysis of observational studies. Cancer Med. 2015 Dec;4(12):1933-47. doi: 10.1002/cam4.539.
2. Ferrini K, Ghelfi F, Mannucci R: Lifestyle, nutrition and breast cancer: facts and presumptions for consideration. Ecancermedicalscience. 2015 Jul 23;9:557. doi: 10.3332/ecancer.2015.557. eCollection 2015.
3. Rock CL, Flatt SW, Byers TE et al. Results of the Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) Trial: A Behavioral Weight Loss Intervention in Overweight or Obese Breast Cancer Survivors. J Clin Oncol. 2015 Oct 1;33(28):3169-76. doi: 10.1200/JCO.2015.61.1095. Epub 2015 Aug 17.
4. Ligibel JA, Cirrincione CT, Liu M2 et al. Body Mass Index, PAM50 Subtype, and Outcomes in Node-Positive Breast Cancer: CALGB 9741 (Alliance). J Natl Cancer Inst. 2015 Jun 25;107(9). pii: djv179. doi: 10.1093/jnci/djv179. Print 2015 Sep.
5. Jiralerspong S, Goodwin PJ: Obesity and Breast Cancer Prognosis: Evidence, Challenges, and Opportunities. J Clin Oncol , 2016; 34:4203-4216
6. Nechuta S, Chen WY, Cal H et al.: A pooled analysis of post- diagnosis lifestyle factors in association with late estrogen-receptor positive breast cancer prognosis. Int J Cancer. 2016 May 1; 138(9): 2088–2097. doi:10.1002/ijc.29940
7. Lauby-Secretan, B., et al.: Body Fatness and Cancer--Viewpoint of the IARC Working Group. N Engl J Med, 2016. 375(8): p. 794-8.
8. Brenner DR, Brockton NT, Kotsopoulos J: Breast cancer survival among young women: a review of the role of modifiable lifestyle

factors. Cancer Causes Control. 2016 Apr;27(4):459-72. doi: 10.1007/s10552-016-0726-5.
9. Dieli-Conwright CM, Lee K, Kiwata JL: Reducing the Risk of Breast Cancer Recurrence: an Evaluation of the Effects and Mechanisms of Diet and Exercise. Curr Breast Cancer Rep. 2016;8(3):139-150.
10. Mei L, He L, Song Y et al. Association between obesity with disease-free survival and overall survival in triple-negative breast cancer. A meta-analysis. Medicine 2018;97:19

Obesity

1. Mei L, He L, Song Y et al. Association between obesity with disease-fress survival and overall survival in triple-netative breast cancer. A meta-analysis. Medicine 2018;97:19
2. Harbourg S, Zachariae R, Olsen J et al. Overweigt and prognosis in triple-negative breast cancer patients: a systematic review and meta-analysis.NPJ Breast cancer 2021 Sep 10(:7(1):119 doi:10.1038/s41523-021-00325-6.

Low-Fat Diet

1. Makarem N, Chandran U et al. Dietary Fat in Breast Cancer Survival. Annu Rev Nutr. 2013 ; 33
2. Xing MY, Xu SZ, Shen P: Effect of low-fat diet on breast cancer survival: A meta-analysis. Asian Pacific journal of cancer prevention : APJCP 2014;15:1141-1144.
3. Dieli-Conwright CM, Lee K, Kiwata JL: Reducing the Risk of Breast Cancer Recurrence: an Evaluation of the Effects and Mechanisms of Diet and Exercise. Curr Breast Cancer Rep. 2016;8(3):139-150.
4. Chlebowski RT, Aragaki AK, Anderson GL: Low-Fat Dietary Pattern and Breast Cancer Mortality in the Women's Health Initiative Randomized Controlled Trial. J Clin Oncol. 2017 Sep 1;35(25):2919-2926. doi: 10.1200/JCO.2016.72.0326. Epub 2017 Jun 27.
5. Chlebowski R, Anderson G et al. Low-Fat Dietary Pattern and Cancer Mortality in the Women's Health Initiative (WHI) Randomized Controlled Trial, JNCI Cancer Spectrum, Volume 2, Issue 4, October 2018
6. De Cicco P, Catani MV et al. Nutrition and Breast Cancer: A Literature Review on Prevention, Treatment and Recurrence. Nutrients 2019 Jul 3;11(7).

Fiber intake

1. McQuade JL et al. Modulating the microbiome to improve therapeutic response in cancer Lancet Oncol. 2019; 20: e77-e91
2. De Cicco P, Catani MV et al. Nutrition and Breast Cancer: A Literature Review on Prevention, Treatment and Recurrence. Nutrients 2019 Jul 3;11(7).

3. Jayedi A, Emadi A, Khan TA et al Dietary fiber and survival in women with breast cancer: A dose-response meta-analysis of prospective cohort studies. Nutr Cancer 2021;73(9):1570-1580

Adherence to general nutrition – guidelines:

1. World Cancer Reasearch FundInternational/American Institue for Cancer Reasearch, Continious Update Project: Diet, Nutrition, Physical Activity, and Breast Cancer Survivors. 2014. Available at: www.wcrf.org/sites/default/files/Breast-Cancer-Survivors-2014-Report.pdf
2. Gonzales JF, Barnard ND, Jenkins DJ et al. Applying the precautionary principle to nutrition and cancer. J Am Coll Nutr 2014:33(3): 239-246.
3. Ferrini K, Ghelfi F, Mannucci R: Lifestyle, nutrition and breast cancer: facts and presumptions for consideration. Ecancermedicalscience. 2015 Jul 23;9:557. doi: 10.3332/ecancer.2015.557. eCollection 2015.
4. Toledo, E., et al., Mediterranean Diet and Invasive Breast Cancer Risk Among Women at High Cardiovascular Risk in the PREDIMED Trial: A Randomized Clinical Trial. JAMA Intern Med, 2015. 175(11): p. 1752-60
5. Biasini C, di Nunzio C, Cordani MR, et al.: Mediterranean Diet influences breast cancer relapse: preliminary results of the SETA PROJECT. Journal of Clinical Oncology, 2016 ASCO Annual Meeting (June 3-7, 2016).Vol 34, No 15_suppl (May 20 Supplement), 2016: e13039
6. Amireault, S, Fon AJ, Sabiston CM. Promoting Healthy Eating and Physical Activity Behaviors: a systematic review of multiple health behavior change interventions among cancer suvivors. American Journal of lifestyle Medicine 2016;12:184-199.
7. Schwingshackl L, Schwedhelm C: Adherence to Mediterranean Diet and Risk of Cancer: An Updated Systematic Review and Meta-Analysis. Nutrients 2017 (9) 1063; doi:10.3390/nu9101063
8. De Cicco P, Catani MV et al. Nutrition and Breast Cancer: A Literature Review on Prevention, Treatment and Recurrence. Nutrients 2019 Jul 3;11(7).
9. Hou R, Wei J et al. Healthy dietary pattern and risk and survival of breast cancer: a meta-analysis of cohort studies, Cancer causes & control 2019;30: 835-846
10. Rhee J, Mattei J, Huges M et al. Diabetes risk reduction diet score. SABSC 2020

Dietary extremes:

1. Huebner J., Marienfeld S. et al.: Counseling Patients on Cancer Diets: A Review of the Literature and Recommendations for Clinical Practice. Anticancer Res. 2014 Jan; 34(1):39-48.

2. Erickson, N., Boscheri, A., Linke, B. et al.: Systematic review: isocaloric ketogenic dietary regimes for cancer patients. Med Oncol 2017;34: 72. https://doi.org/10.1007/s12032-017-0930-5
3. Jochems SHJ, van Osch FH, Bryan RT, et al., Impact of dietary patterns and the main food groups on mortality and recurrence in cancer survivors: a systematic review of current epidemiological literature BMJ Open 2017;8:e014530.
4. Mohsen M, Katsiki N et al. Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies. European Heart Journal 2019; 40: 2870-2879

Complementary Treatment

Prevention of Recurrence / Improvement of Overall Survival III.1

Dietary Supplements – Herbal Therapies

During anti-cancer treatment: Beware of drug interactions	Oxford		
	LoE	GR	AGO
Post treatment vitamine / antioxidant supplements does not appear to be associated with increased risk of recurrence (beware of drug / treatment interactions)	2b	B	
Smokers on antioxidant supplements are at higher risk for lung cancer	1b	A	
For Prevention of BC Recurrence:			
▪ **Antioxidants**	2a	B	+/-
▪ **Vitamine supplementation in patients on a balanced diet** (esp. Vitamine C, E)	2a	B	+/-
▪ **Vitamine D (after Vit D level)**	2b	B	+/-
▪ **Soy-food** (natural source of phytoestrogenes)	2a	B	+/-
– **food or concentrates containing ≥ 100 mg) isoflavones per day**	2a	B	-
▪ **Black Cohosh** (Cimicifuga racemosa)	3b	C	+/-
▪ **Antioxidant supplements** (after completion of radiotherapy)	2b	B	+/-
▪ **Green tea**	3a	C	+/-
▪ **Selenium**	2b	B	+/-

General

1. Hervik JB, Stub T: Adverse effects of non-hormonal pharmacological interventions in breast cancer survivors, suffering from hot flashes: A systematic review and meta-analysis. Breast Cancer Res Treat. 2016 Nov;160(2):223-236.

Post treatment vitamin and/or antioxidant supplements

1. Yong L, Qimonu L, Xiaoju L et al. Post-diagnosis use of antioxidant vitamin supplements and breast cancer prognosis: Asystematic review and meta-analysis. Clin Breast Cancer 2021 Dec;21(6):477-485.
2. Cadeau C, Farvid MS, Rosner BA et al. Dietary and Supplemental Vitamin C Intake and Risk of Breast Cancer: Results from the Nurses' Health Studies. J Nutr. 2021 Dec 3:nxab407.
3. Villagran M, Ferreira J, Martorell M et al. The Role of Vitamin C in Cancer Prevention and Therapy: A Literature Review. Antioxidants (Basel). 2021 Nov 26;10(12):1894.
4. Drewe J, Bucher KA, Zahner C. A systematic review of non-hormonal treatments of vasomotor symptoms in climacteric and cancer patients. Springerplus. 2015 Feb 10;4:65. doi: 10.1186/s40064-015-0808-y. eCollection 2015.
5. Sodde VK, Lobo R, Kumar N, et al. Cytotoxic activity of Macrosolen parasiticus (L.) Danser on the growth of breast cancer cell line (MCF-7).Pharmacogn Mag. 2015 May;11(Suppl 1):S156-60. doi: 10.4103/0973-1296.157719.
6. Salarabadi A, Bidgoli SA, Madani SH. Roles of Kermanshahi Oil, Animal Fat, Dietary and Non- Dietary Vitamin D and other Nutrients in

Increased Risk of Premenopausal Breast Cancer: A Case Control Study in Kermanshah, Iran. Asian Pac J Cancer Prev. 2015;16(17):7473-8.
7. Karimi Z, Bahadoran Z, Abedini S, et al. Dietary total antioxidant capacity and the risk of breast cancer: a case-control study. East Mediterr Health J. 2015 Sep 28;21(8):564-71.
8. Carioca AA, Verde SM, Luzia LA, et al. Association of oxidative stress biomarkers with adiposity and clinical staging in women with breast cancer. Eur J Clin Nutr. 2015 Nov;69(11):1256-61.
9. Martin-Herranz A, Salinas-Hernández P. Vitamin D supplementation review and recommendations for women diagnosed with breast or ovary cancer in the context of bone health and cancer prognosis/risk. Crit Rev Oncol Hematol. 2015 Oct;96(1):91-9.

Vitamine D Supplementation

1. O'Brien KM, Keil AP, Harmon QE et al. Vitamin D Supplement Use and Risk of Breast Cancer by Race-Ethnicity. Epidemiology. 2022 Jan 1;33(1):37-47.
2. Viala M, Chiba A, Thezenas S et al. Impact of vitamin D on pathological complete response and survival following neoadjuvant chemotherapy for breast cancer: a retrospective study. BMC Cancer. 2018 Jul 30;18(1):770.
3. Gregoire AM, VoPham T, Laden F et al. Residential ultraviolet radiation and breast cancer risk in a large prospective cohort. Environ Int. 2021 Dec 8;159:107028.
4. Welsh J. Vitamin D and Breast Cancer: Mechanistic Update. JBMR Plus. 2021 Dec 10;5(12):e10582.
5. Voutsadakis JA. Vitamin D baseline levels at diagnosis of breast cancer. A systematic review and meta-analysis. Hematol Oncol Stem Cell Ther 2021;14:16-26
6. Ozmen V, Ordu C, Ilgun AS et al The effects of vitamin D replacement on pathological complete response (pCR) in breast cancer patients receiving neoadjuvant systemic chemotherapy (NAC). Breast J. 2021 Dec;27(12):902-905.
7. O'Brien KM, Sandler DP, Taylor JA et al. Serum Vitamin D and Risk of Breast Cancer within Five Years. Environ Health Perspect. 2017 Jul 6;125(7):077004.

Soy as normal part of the diet/soy concentrates

1. Fritz H, Seely D, Flower G, et al.: Soy, red clover, and isoflavones and breast cancer: A systematic review. PloS one 2013;8:e81968.
2. Wu AH, Spicer D, Garcia A, et al. Double-Blind Randomized 12-Month Soy Intervention Had No Effects on Breast MRI Fibroglandular Tissue Density or Mammographic Density. Cancer Prev Res (Phila). 2015 Oct;8(10):942-51. doi: 10.1158/1940-6207.CAPR-15-0125. Epub 2015 Aug 14.

3. Sharifi-Rad J, Quispe C, Imran M et al. Genistein: An Integrative Overview of Its Mode of Action, Pharmacological Properties, and Health Benefits. Oxid Med Cell Longev. 2021 Jul 19;2021:3268136.

Black cohosh

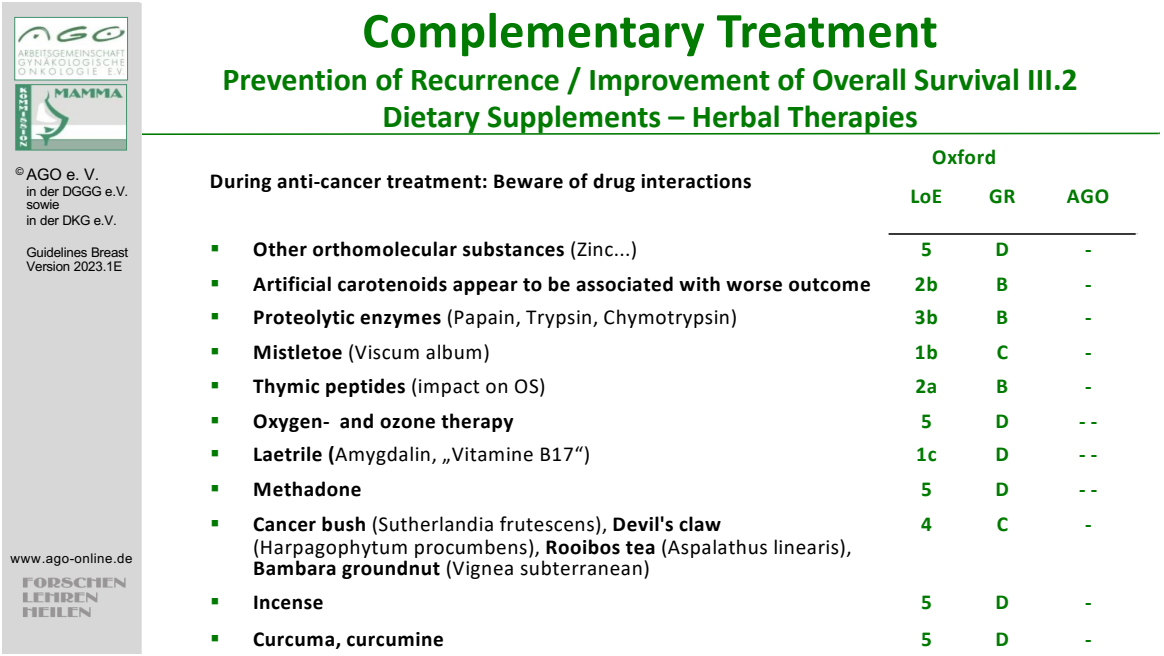
1. Fritz H, Seely D, McGowan J, et al: Black cohosh and breast cancer: A systematic review. Integrative cancer therapies 2014;13:12-29.
2. Ruan X, Mueck AO, Beer AM et al. Benefit-risk profile of black cohosh (isopropanolic *Cimicifuga racemosa* extract) with and without St John's wort in breast cancer patients. Climacteric. 2019 Aug;22(4):339-347.

Green Tea

1. Gianfredi V, Nucci D, Abalsamo A, et al. Green Tea consumption and risk of breast cancer and recurrence – a systematic review and meta-analysis of observational studies. Nutrients 2018;10;pii:E1886.
2. Najaf Najafi M, Salehi M. et al. The association between green tea consumption and breast cancer risk. A systematic review and meta-analysis. Phytother Res 2018;32:1855-1864.
3. Filippini T, Malavolti M, Borrelli F et al. Green tea (Camellia sinensis) for the prevention of cancer. Cochrane Database Syst Rev. 2020 Mar 2;3(3):CD005004.

Selenium

1. Demircan K, Bengtsson Y, Sun Q et al. Serum selenium, selenoprotein P and glutathione peroxidase 3 as predictors of mortality and recurrence following breast cancer diagnosis: A multicentre cohort study. Redox Biol. 2021 Nov;47:102145



Complementary Treatment

Prevention of Recurrence / Improvement of Overall Survival III.2

Dietary Supplements – Herbal Therapies

During anti-cancer treatment: Beware of drug interactions	Oxford LoE	Oxford GR	AGO
▪ **Other orthomolecular substances** (Zinc...)	5	D	-
▪ **Artificial carotenoids appear to be associated with worse outcome**	2b	B	-
▪ **Proteolytic enzymes** (Papain, Trypsin, Chymotrypsin)	3b	B	-
▪ **Mistletoe** (Viscum album)	1b	C	-
▪ **Thymic peptides** (impact on OS)	2a	B	-
▪ **Oxygen- and ozone therapy**	5	D	- -
▪ **Laetrile (**Amygdalin, „Vitamine B17“)	1c	D	- -
▪ **Methadone**	5	D	- -
▪ **Cancer bush** (Sutherlandia frutescens), **Devil's claw** (Harpagophytum procumbens), **Rooibos tea** (Aspalathus linearis), **Bambara groundnut** (Vignea subterranean)	4	C	-
▪ **Incense**	5	D	-
▪ **Curcuma, curcumine**	5	D	-

General

1. Hervik JB, Stub T: Adverse effects of non-hormonal pharmacological interventions in breast cancer survivors, suffering from hot flashes: A systematic review and meta-analysis. Breast Cancer Res Treat. 2016 Nov;160(2):223-236.

Orthomolecular compounds

1. Ambrosone CB, Zirpoli GR, Hutson AD et al. Diatery supplement use during chemotherapy and survival outcomes of patients with breast cancer enrolled in a cooperative group clinical trial (SWAG S0221). J Clin Oncol 2020 Mar 10;38(8):804-814
2. Li Y, Lin Q, Lu X et al. Post-diagnosis use of antioxidant vitamin supplements and breast cancer prognosis: A systematic review and meta analysis. Clin Breast Cancer 2021 Dec;21(6):477-485

Carotenoids

Proteolytic enzymes, Bromelain+Papain+Selen+Lektin bei AI-induced athralgia

1. Uhlenbruck B, Van Leendert R, Schneider B et al.: Reduced side-effects of adjuvant hormone therapy in breast cancer patients by complementary medicine. In Vivo. 2010 Sep-Oct;24(5):799-802.
2. Petru U, Stranz B, Petru C: Effects of proteolytic enzyme therapy with Wobe Mugos against chemotherapy-induced toxicity in breast

cancer patients - results of a pilot study Wien Med Wochenschr. 2010 Nov;160(19-20):513-6.

Mistletoe
1. Freuding M, Keinki C, Micke O. Mistletoe in oncological treatment: a systematic review. Journal of Cancer Research and Clinical Oncology. 2019;145:695–707

Thymus-peptides
1. Wolf E, Milazzo S, Boehm K, et al. Thymic peptides for treatment of cancer patients. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD003993. DOI: 10.1002/14651858.CD

Oxygen-therapy, ozone-therapy
1. Baeza-Noci J, Pinto-Bonilla R. Systemic Review: Ozone: A Potential New Chemotherapy. Int J Mol Sci. 2021 Oct 30;22(21):11796.

Laetrile treatment for cancer
1. Milazzo S, Ernst E, Lejeune S, et al. Laetrile treatment for cancer. Cochrane Database of Systematic Reviews 2011, Issue 11. Art. No.: CD005476. DOI: 10.1002/14651858.CD005476.pub3.

Methadone
1. Vatter T, Klumpp L, Ganser K et al. Against Repurposing Methadone for Glioblastoma Therapy. Biomolecules. 2020 Jun 17;10(6):917.

Different phytotherpeutics:
St John's Wort
1. Schellander R, Donnerer J: Antidepressants: clinically relevant drug interactions to be considered. Pharmacology. 2010;86(4):203-15. Epub 2010 Sep 8.
2. Nahrstedt A, Butterweck V: Lessons learned from herbal medicinal products: the example of St. John's Wort (perpendicular). J Nat Prod. 2010 May 28;73(5):1015-21.
3. Caraci F, Crupi R, Drago F, et al. Metabolic drug interactions between antidepressants and anticancer drugs: focus on selective serotonin reuptake inhibitors and hypericum extract. Curr Drug Metab. 2011 Jul 1;12(6):570-7.

Red clover
1. Geller SE, Shulman LP, van Breemen RB et al.: Safety and efficacy of black cohosh and red clover for the management of vasomotor symptoms: a randomized controlled trial. Menopause. 2009;16(6):1156–1166.
2. Fritz H, Seely D, Flower G et al. Soy, red clover, and isoflavones and breast cancer: A systematic review. PLoS One. 2013 Nov 28;8(11):e81968.

Dong Quai
1. Rotem C, Kaplan B: Phyto-Female Complex for the relief of hot flushes, night sweats and quality of sleep: randomized, controlled, double-blind pilot study. Gynecol Endocrinol. 2007;23(2):117-122.
2. Zhuang SR, Chiu HF, Chen SL, Effects of a Chinese medical herbs complex on cellular immunity and toxicity-related conditions of breast cancer patients. Br J Nutr. 2011 Aug 25:1-7.

Ginseng root
1. Peralta EA, Murphy LL, Minnis J, et al.: American Ginseng inhibits induced COX-2 and NFKB activation in breast cancer cells. J Surg Res. 2009 Dec;157(2):261-7.
2. Yamada N, Araki H, Yoshimura H: Identification of antidepressant-like ingredients in ginseng root (Panax ginseng C.A. Meyer) using a menopausal depressive-like state in female mice: participation of 5-HT2A receptors. Psychopharmacology (Berl). 2011 Aug;216(4):589-99.

Cancer bush, Devil‘s Claw, Rooibos Tea, Bambara Groundnut
1. Brendler T. From Bush Medicine to Modern Phytopharmaceutical: A Bibliographic Review of Devil's Claw (*Harpagophytum* spp.). Pharmaceuticals (Basel). 2021 Jul 27;14(8):726.

Incense
1. Suhail MM, Wu W, Cao A et al. Boswellia sacra essential oil induces tumor cell-specific apoptosis and suppresses tumor aggressiveness in cultured human breast cancer cells. BMC Complement Altern Med. 2011 Dec 15;11:129.

Curcuma, Curcumin
1. Sultana S, Munir N, Mahmood Z et al. Molecular targets for the management of cancer using Curcuma longa Linn. phytoconstituents:

A Review. Biomed Pharmacother. 2021 Mar;135:111078.
2. Kabir MT, Rahman MH, Akter R et al. Potential Role of Curcumin and Its Nanoformulations to Treat Various Types of Cancers. Biomolecules. 2021 Mar 7;11(3):392.