Gynecological Issues in Breast Cancer Patients
Gynecologic Issues in Breast Cancer Patients

- **Versions 2015–2022:**
  Albert / Bauerfeind / Blohmer / Fersis / Gerber / Hanf / Huober/
  Loibl / Maas / Mundhenke / Reimer / Rody / Scharl / Thill /
  Thomssen / Witzel

- **Version 2023:**
  Fehm / Stickeler

Screened data bases:
- Pubmed 2009–2022
- ASCO 2009–2022
- SABCS 2009–2022
Endocrine responsive disease


Endocrine non-responsive disease

Endocrine responsive disease: combined treatment TAM plus low-dose-HT

Tibolone

Ospemifeme

Topical Vaginal Application:
3. Portman DJ, Gass ML; Vulvovaginal Athrophy Terminology Consensus Conference Panel. Genitourinary syndrome of menopause:
Further Medical Approaches to Reduce Menopausal Symptoms I

- Selective serotonin reuptake inhibitors and serotonin-(noradrenalin) reuptake inhibitors (SSRI-SNRI): reduce hot flashes in BC patients
  - Venlafaxine
  - Desvenlafaxine, Sertraline, Escitalopram
  - Gabapentin (patients using TAM)
  - Oxybutynine (2.5 mg / 5 mg)
  - Pregabalin
  - Clonidine 0.05-0.15 mg/die (patients using TAM)
  - MPA (i.m. 500 mg single shot) (most potent, but endocrine agent!)
  - Vitamin E
  - Omega-3 fatty acids

- Melatonin (improvement in sleep quality)
- Duloxetine (treating arthralgias while on AI)

Note: Substantial placebo-effect has been proven (23-57%) LoE 1b A +


SSRI

Venlafaxine

Desvenlafaxine

Paroxetine
Fluoxetine

Citalopram

Gabapentin

Pregabalin

Clonidin
Oxybutynin

(D) MPA (depo-) (Medroxyprogesterone acetate)

Vitamine E

Omega 3-Fettsäuren
Melatonin

Duloxetin
CAM* - Approaches to Reduce Menopausal Symptoms II
* Complementary and Alternative Medicine

During anti-cancer treatment: Beware of drug interactions!

<table>
<thead>
<tr>
<th>Treatment</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soy-derived phytoestrogens – isoflavonoids*</td>
<td>1b</td>
<td>B</td>
<td>-</td>
</tr>
<tr>
<td>Hot flushes</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Sleep disturbance</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Topical vaginal application</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Red Clover isoflavonoids*</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Hot flushes, sleep disturbance</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Flaxseed-supplementation (40 g/d) (in HR+ ≤ 10 g/d) (reduces relapses, no effect on hot flashes)</td>
<td>2b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Black Cohosh for hot flushes</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Black cohosh + St. John’s Wort (fixed combination)</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>St. John’s Wort (pharmacokinetic interference with endocrine therapy, cytotoxic drugs, and tyrosin kinase inhibitors)</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Ginseng root (Panax ginseng or P. quinquefolius)</td>
<td>1b</td>
<td>B</td>
<td>-</td>
</tr>
<tr>
<td>Bromelain + Papain + Selenium + Lectin (for AI induced joint symptoms)</td>
<td>3b</td>
<td>B</td>
<td>+</td>
</tr>
<tr>
<td>Homeopathic medicine to reduce hot flushes (consider placebo-effect)</td>
<td>1b</td>
<td>B</td>
<td>+/-</td>
</tr>
</tbody>
</table>

* might stimulate BC, especially in endocrine responsive disease


Soy- derived isoflavonoids

Red clover-derived isoflavonoids

4. Ghazanfarpour M, Sadeghi R, Latifnejad Roudsari R et al.: Effects of red clover on hot flash and circulating hormone concentrations

Flaxseed

Black cohosh (Cimicifuga racemosa) nor St John’s Wort nor Ginseng root

Sodium selenite, proteolytic plant enzymes (bromelaine and papain), and Lens culinaris lectin

Homeopathic medicine
**General Approaches to Reduce Menopausal Symptoms III - Integrative Oncology Aspects**

<table>
<thead>
<tr>
<th>General approaches:</th>
<th>Oxford</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LoE</td>
</tr>
<tr>
<td>Physical exercise</td>
<td>1a</td>
</tr>
<tr>
<td>Cognitive behavioral therapy (CBT), hypnosis</td>
<td>1a</td>
</tr>
<tr>
<td>Mind body-medicine (yoga, education, counselling, mindfulness training)</td>
<td>1b</td>
</tr>
<tr>
<td>Short interruption of endocrine therapy in case of unacceptable side effects</td>
<td>5</td>
</tr>
</tbody>
</table>

(Electro) Acupuncture

| Aromatase-inhibitor treatment induced arthralgia                                  | 1a     | B   | +   |
| Hot flushes                                                                       | 2a     | B   | +   |
| Anxiety, Depression                                                               | 2b     | B   | +   |
| Sleep                                                                             | 2a     | C   | +   |

* as in SOLE Trial


**Physical exercise**

3. Lahart IM, Metsios GS, Nevill AM et al.: Physical activity for women with breast cancer after adjuvant therapy. Cochrane...
Mind Body Medicine

Cognitive behavioral therapy, Hypnosis


Acupuncture


32940768.
Ovarian Protection with GnRHα and Fertility Preservation in Premenopausal Patients Receiving (Neo)-Adjuvant Chemotherapy (CT)

Oxidford

<table>
<thead>
<tr>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
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<tbody>
<tr>
<td>1a</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>2a</td>
<td>B</td>
<td>+/-</td>
</tr>
</tbody>
</table>

- CTx + GnRHα (preservation of ovarian function) (GnRHα application > 2 weeks prior to chemo-therapy, independent of hormone receptor status)
- CTx + GnRHα (preservation of fertility)
- Fertility preservation counselling including referral of all potential patients to appropriate reproductive specialists (further information https://fertiprotekt.com/english; S2K Guideline Fertility preservation in oncology)

Ovarian function protection

Pregnancy rates


Fertility preservation counselling

Fertility preservation and assisted reproductive therapy (ART)
- Oncological safety-

<table>
<thead>
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</table>

- Pretreatment approaches to preserve fertility
  - GnRHa
  - Cryopreservation of ovarian tissue with subsequent transplantation
  - Cryopreservation of oocytes (unfertilized / fertilized) after ovarian stimulation

- ART after (neo-)adjuvant systemic treatment

GnRH-Analogon:

Cryopreservation of ovarian tissue:
2. Rosendahl M, Greve T, Andersen CY. The safety of transplanting cryopreserved ovarian tissue in cancer patients: a review of the
Cryoconservation of oocytes after ovarian stimulation:


ART after treatment:

Oncological Safety of controlled ovarian stimulation (COS) or assisted reproductive therapy (ART)

N=15 studies including 4643 patients undergoing COS or ART (assisted reproductive therapy)

**COS before starting treatment (n=11 studies):**
- Reduced risk of recurrence RR 0.58, 95% CI 0.46-0.73
- Reduced risk of mortality RR 0.54, 95% CI 0.38-0.76
- No detrimental effect on EFS 0.76, 95% CI 0.55-1.06
  - Subgroup of HR positive pts. HR 0.36, 95% CI 0.20–0.65

**ART after treatment (n=4 studies):**
- Reduced risk of recurrence (RR 0.34, 95% CI 0.17-0.70)
- No detrimental effect EFS (HR 0.43, 95% CI 0.17-1.11).

**Conclusion:** COS at diagnosis or ART following breast cancer treatment completion does not appear to be associated with any detrimental prognostic effect in young women.


AMH:

Antrale Follicle Count:
1. Sinha N, Letourneau JM, Wald K et al: Antral follicle count recovery in women with menses after treatment with and without


FSH

1. Furlanetto J, Thode C, Huober J. et al. Changes in hormone levels (E2, FSH, AMH) and fertility of young women treated with neoadjuvant chemotherapy (CT) for early breast cancer (EBC). SABCS 2017, # 754, PD 7-09


Combined tests:

### Contraceptive Options for Women after Diagnosis of Breast Cancer

<table>
<thead>
<tr>
<th>Contraceptive Option</th>
<th>Oxford</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Barrier methods</td>
<td>5</td>
<td>D</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>▪ Sterilization (tubal ligation / salpingectomy / vasectomy)</td>
<td>5</td>
<td>D</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>▪ Non-hormonal intrauterine devices (IUDs)</td>
<td>3b</td>
<td>D</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>▪ Levonorgestrel-releasing IUDs</td>
<td>2b</td>
<td>C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>▪ Removal in newly diagnosed patients</td>
<td>4</td>
<td>D</td>
<td>+/-</td>
<td></td>
</tr>
<tr>
<td>▪ Timing methods</td>
<td>5</td>
<td>D</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>▪ Injectable progestin-only contraceptives</td>
<td>5</td>
<td>D</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>▪ Progestin-only oral contraceptives</td>
<td>5</td>
<td>D</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>▪ Combined oral contraceptives</td>
<td>5</td>
<td>D</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>▪ Options of emergency contraception</td>
<td>5</td>
<td>D</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>▪ Copper intrauterine device (Copper-IUD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>▪ Levonorgestrel, Ulipristal orally</td>
<td>5</td>
<td>D</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

### Contraception (general)


### LNG-IUDs


Emergency Contraception - Options after Diagnosis of Breast Cancer
Reviews:

Evaluation
Sexual Complaints Screener For Women:

Treatment of vaginal dryness:
Education, Group therapy, counseling:

Non-hormonal treatment:

Vaginal topic treatment
2. Cold S et al. Vaginal estrogens and risk of recurrence or death in women treated for estrogen receptor positive breast cancer, European Journal of Cancer 2015,51, S3 (Abstract)

**Laser therapy**


General recommendations

**Brief Sexual Symptom Checklist (BSSC-W)**

**Sexual Complaints Screener For Women (SCS-W)** (Langversion und Kurzversion):
Female Sexual Function Index (FSFI-19, FSFI-6):
