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St. Gallen Konsensusmeeting

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Interdisziplinäres Brustzentrum

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Rational Recommendations – Personalizing the Approach to Treatment of Women with Early Breast Cancer

Consensus & Controversy

Surgery

Surgery of the Primary

When considering breast conserving surgery the following factors are contraindications

- **Multi-focal disease**

  Relative **Y:42,6% N:53,2% A:4,3%**

  Absolute **Y: 6,7% N:88,9% A:4,4%**

- **Multi-centric disease**

  Relative **Y:76,9% *N:15,4%* A:7,7%**

  Absolute **Yes No A**

- **Tumour close to nipple**

  Relative **Y:42,6% N:53,2% A:4,3%**

  Absolute **Y: 0% N:95,9%**

Surgery of the Primary

When considering breast conserving surgery the following factors are relative contraindications:

- **Family history** *Y:4,1%* N:95,9% A:0%
- **BRCA1 positivity** Y:54,3% N:43,5% A:2,2%
- **BRCA2 positivity** *Y:51,1%* N:46,8% A:2,1%
- **Involved margins after repeated excisions (including DCIS)**

  Y:95,9% N: 2,0% A:2,0%
- **Unfavourable biology on gene expression/sequencing**

  Y:6,3% N:93,8% A:0%
- **Contraindications to breast irradiation that should follow breast conserving surgery**

  Y:93,8% N: 4,2% A:2,1%

Surgery of the Primary

Is skin-nipple sparing mastectomy an acceptable treatment without RT?

Y:66,7% N:21,4% A:11,9%

ONLY if margin toward nipple is tumour-free and immediate reconstruction planned

Y:55,3% N:15,8% A:28,9%

Surgery of the Primary

- **Should MRI be routine for patients with newly diagnosed disease (to assist decision on BCS)?**

  Y:10,2% N:89,8% A:0%

- **In women undergoing breast conserving surgery the minimum appropriate surgical margin is**
  - **No ink on invasive tumor? Y:72,9% N:20,8% A: 6,3%**
  - **1 mm clearance (invasive)? Y:48,1% N:25,9% A:25,9%**
  - **3 mm clearance (invasive)? Y: 7,7% N:30,8% A:61,5%**
  - **5 mm clearance (invasive)? Y: 4,7% N: 9,3% A:86,0%**
  - **2 mm clearance (DCIS)? *Y:41,5%* N:53,7% A: 4,9%**
  - **Dependent on tumor biology? *Y:18,4%* N:77,6% A: 4,1%**

Surgery of the Axilla

In patients with macrometastases in 1-2 sentinel nodes, completion axillary dissection can safely be omitted following:

- **Mastectomy (no radiotherapy planned)**

  Y:4,3% N:91,3% A: 4,3%

- **Mastectomy (radiotherapy planned)**

  Y:39,1% N:50,0% A:10,9%

- **Conservative resection and radiotherapy**

  Y:72,7% **N:20,5% A:6,8%**

Surgery of the Axilla

In patients otherwise undergoing breast conserving surgery, completion axillary dissection is necessary if :

- ***Clinical*** **N1 ?** ***Y:67,4%*** **N:26,1% A:6,5%**
- **3 or more positive SLNs? Y:95,1% N: 4,9% A: 0%**
- **Nodal status (eg. N 4+) needed for chemotherapy choice? Y:59,1% N:38,6% A:2,3%**

Radiotherapy

RT: Conserved Breast Irradiation

- **Is there a group not requiring RT as part of BCT?**

  Y:68,2% N:27,3% A:4,5%

- **Should «short course» RT (e.g. 40Gy in 15 fractions) be offered as a standard?**

  Y:59,2% N:30,6% A:10,2%

- **Is «short course» RT as above an option if boost is also planned?**

  Y:77,8% N:4,4% A:17,8%

Radiation Therapy: After Mx

Should post Mx RT be standard for patients with:

- N+ ≥4? Y:95,3% N:2,3% A:2,3%
- N+ 1 to 3: all patients? Y:29,8% N:63,8% A:6,4%
- N+ 1 to 3 with adverse pathology? Y:61,7% N:31,9% A:6,4%
- N+ 1 to 3 at young age (< 40 yr)? Y:55,1% N:40,8% A:4,1%
- pN0 after axillary dissection but < 8 nodes examined? Y:6,5% N:89,1% A:4,3%
- Positive sentinel node biopsy but no axillary dissection? Y:63,8% N:25,5% A:10,6%

Pathology

Pathology

For practical purposes, distinction between 'Luminal A' and 'Luminal B' (Her2 Neg) tumors can be:

- **made by ER, PR alone?** *Y: 6,1%* **N:91,8%** **A:2,0%**
- **made by ER, PR and Ki-67?** **Y:72,9%** **N:27,1%** **A: 0%**
- **made with grade 3 as a substitute for high Ki-67?**

  Y:36% **N:64,0%** **A: 0%**

- **only safely determined by molecular diagnostics?**

  Y:34% *N:60%* **A: 6%**

•only safely determined by laboratories participating in quality assurance programs?

Y:88,9% **N:8,9%** **A: 2,2%**

Pathology: Subtypes

- **Intrinsic subtypes may influence whether or not chemotherapy is used in the adjuvant regimen?**

  Y:88,9% N:6,7% A:4,4%

  - **If yes, multi-gene expression array profiling is <u>required</u> for subtype definition?**

    Y:22,0% N:70,0% A:8,0%

  - **Yes, but clinicopathologic definition of 'subtype' (e.g. St Gallen 2011) is sufficient for this purpose?**

    Y:53,1% N:38,8% A:8,2%

- **Choice of cytotoxic therapy regimen should be influenced by intrinsic subtype?**

  Y:27,7% N:68,1% A:4,3%

Multi-Gene Signatures

Would you ask for one of the multigene signatures (after clinicopathological assessment) :

- **–in nearly all cases independently of the 'intrinsic subtype'?**

  Y: 0% N:97,6% A:2,4%

- **–in nearly all ER and/or PgR positive ' (HER2-neg) cases?**

  Y:20,8% N:79,2% A: 0%

- **–in nearly all 'Luminal B' (HER2-neg) but not 'Luminal A' cases?**

  Y:44,4% N:51,1% A:4,4%

- **–in N-neg. ER positive ' (HER2-neg) cases?**

  Y:56,8% N:43;2% A:0%

- **–in N-pos. ER positive ' (HER2-neg) cases?**

  Y:22,2% N:77,8% A:0%

Multi-Gene Signatures

In an endocrine-responsive* cohort:

- **Does 21 gene RS *predict* Chemotherapy (ChT) response?**

  Y: 78% N:12% A:10%

- **Does PAM-50 predict ChT response?**

  Y:29,5% N:40,9% A:29,5%

- **Does 70 gene signature predict ChT response?**

  Y: 25% N:25% A:54,2%

- **Does EPClin predict ChT response?**

  Y:10,6% N:57,4% A:31,9%

*** i.e. any expression of ER and/or PgR**

Multi-Gene Signatures

In an endocrine-responsive cohort*, selection of patients who might forego chemotherapy can be partially based on:

• **21 gene RS**	**Y:88,1%**	**N:7,1%**	**A:4,8%**
• **PAM-50**	**Y:28,6%**	**N:50%**	**A:21,4%**
• **70 gene signature**	**Y:40,4%**	**N:44,7%**	**A:14,9%**
• **EPClin**	**Y:21,7%**	**N:50%**	**A:28,3%**

*** i.e. any expression of ER and/or PgR**

Molecular Diagnostics

- **In an endocrine-responsive cohort*, molecular diagnostics can be omitted if:**
- **Chemotherapy would not be given anyway because:**
  - **T size ≤ 1 cm?** **Y:83,9%** **N:12,9%** **A:3,2%**
- **Chemotherapy would be given anyway because:**
  - **T size (e.g. > 5 cm)?** **Y:52,4%** **N:40,5%** **A:7,1%**
  - **Inflammatory BC?** **Y:93,8%** **N: 4,2%** **A:2,1%**
  - **1-3 nodes+?** **Y:26,3%** **N:71,1%** **A:2,6%**
  - **≥ 4 nodes+?** **Y:91,5%** **N: 6,4%** **A:2,1%**
  - **Grade 3?** **Y:30,6%** **N:65,3%** **A:4,1%**
  - **Low ER% (e.g. 5%)** **Y:55,8%** **N:44,2%** **A: 0%**
  - **Young age (e.g.< 35)** **Y:24,4%** **N:75,6%** **A: 0%**

*** i.e. any expression of ER and/or PgR**

Endocrine Therapies

Endocrine Therapy:
Establishing Standards for Premenopausal

- **Tam alone as default?** **Y:83,3%** **N:16,7%** **A:0%**

- **Tamoxifen duration should be extended to 10 years in all patients remaining premenopausal?**

  Y:42,9% **N:49,0%** **A:8,2%**

  some patients **Y:88,9%** **N: 8,9%** **A.2,2%**

- **Ovarian function suppression (OFS) should be added to Tam:**
  - **In all patients** **Y:14,9%** **N80,9%** **A:4,3%**
  - **In the young (e.g. < 40 yr)**

    Y:40,9% **N:50%** **A:9,1%**

Chemotherapies

Chemotherapy
Basic Questions

Factors arguing for inclusion of ChT are:

- **Histological grade 3 tumor ?**
  Y:84,4% **N:13,3%** **A:2,2%**
- **Ki-67 high** ***Y:75,5%*** **N:14,3%** **A:10,2%**
- **Low hormone receptor status?**
  Y:81,6% **N:12,2%** **A:6,1%**
- **Positive HER2 status?** **Y:91,8%** **N: 8,2%** **A: 0%**
- **Triple negative status?** **Y:98,0%** **N: 0%** **A:2,0%**

Chemotherapy
Basic Questions

Factors arguing for inclusion of ChT are (continued):

- **High 21 gene RS (e.g. >25)? Y:93,9% N: 4,1% A:2,0%**
- **70 gene High-Risk? Y:63,3% N:30,6% A:6,1%**
- **Any positive node? Y:32,7% N:67,3% A: 0%**
- **> 3 positive nodes? Y:93,9% N: 6,1% A: 0%**
- **Lymphovascular invasion? Y:32,0% N:64,0% A: 4%**
- **Young age (e.g. < 35 yr)? Y:46,0% N:54,0% A: 0%**

Chemotherapy
Luminal A

- **Is Luminal A phenotype less *responsive* to chemotherapy?**

  Y:83,3% N:10,4% A:6,3%

- **Is chemotherapy less *useful* if added to endocrine therapy for pts. with Luminal A phenotype?**

  Y: No A

- ***Is less intensive chemotherapy such as AC4 or CMF6 or TC4 adequate if chemotherapy is considered in Luminal A disease?***

  Y:61,7% N:25,5% A:12,8%

- **Should chemotherapy be added for high risk (based on tumour volume)?**

  Y:60,0% N:22,9% A:17,1%

Chemotherapy

Luminal B (HER2 negative)

- **Is Luminal B subtype by itself sufficient to prescribe chemotherapy?**

  Y:61,2% N:38,8% A:0%

- **Is Ki-67 useful in defining Luminal B subtype?**

  Y:72,9% N:20,8% A:6,3%

- **If Ki-67 is used, which threshold should be used for defining Luminal B subtype:**

- ≥ 14%?	**Y:23,9%**	**N:37,0%**	**A:39,1%**
- ≥ 20%?	**Y:29,5%**	**N:13,9%**	**A:56,8%**
- ≥ 25%?	**Y:13,3%**	**N: 6,7%**	**A:80,0%**
- ≥ 30%?	**Y:**	**No**	**A**

Chemotherapy

Luminal B (HER2 negative)

- **If given, the ChT regimen should contain anthracyclines rather than CMF?**

  Y:70,5% N:80,9% A:11,4%

- **Should the regimen contain taxanes?**

  Y:56,5% N:26,1% A:17,4%

- **Should chemotherapy extend for at least 6 courses?**

  Y:50,0% N:34,8% A:15,2%

- **Should dose-dense ChT be preferred when chemotherapy is indicated?**

  Y:19,1% N:68,1% A:12,8%

Anti-HER2 Therapies

Anti-HER2 Therapy

- **Minimum T size (invasive diameter) requiring trastuzumab :**
  Vote for: 10 mm: 10% 5 mm:72,5% any:17,5%
- **Trastuzumab if given should be concurrent with taxane**
  Y:87,2% N:8,5% A:4,3%
- **Trastuzumab if given may be concurrent with anthra.**
  Y:14,3% N:85,7% A:0%
- **Trastuzumab (+/- endocrine therapy) if ChT contra-indicated?**
  - **ER positive Y:50% N:50% A:0%**
  - **ER negative Y: 75% N:25% A**
- **Preferred duration of trastuzumab if given:**

Vote for	< 1 yr	1 yr	> 1 yr

Neo-Adjuvant Systemic Therapies

Neo-Adjuvant Systemic Therapy
Chemotherapy

- **Should the only aim of neoadjuvant chemotherapy be to facilitate subsequent local therapies?**

  Y:50,9% N:45,3% A:3,8%

- **After pCR to neoadjuvant chemotherapy, subsequent adjuvant chemotherapy:**
  - **Should be given?** Y: 4,1% N:95,9% A: 0%
  - **If so, should include the same agents?**

    Yes No A

- **After failure to achieve pCR with neoadjuvant chemotherapy, subsequent adjuvant chemotherapy:**
  - **Should be given?** Y:10,0% N:82,5% A
  - **If so, should include different agents?**

    Yes No A

Neo-Adjuvant Systemic Therapy
Endocrine Therapy

- **Is neoadjuvant endocrine therapy alone a reasonable option for postmenopausal patients with *highly endocrine-responsive* disease (e.g. strongly positive receptors, low proliferation)?**

  Y:93,8% N:2,1% A:4,2%

  - **If yes, for which duration (choose one)?**
  - **3-4 months** **Y:11,1%**
  - **4-8 months** **Y:26,7%**
  - **Maximal response** **Y:62,2%**