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Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

Adjuvant Cytotoxic and Targeted Therapy

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Adjuvant Cytotoxic and Targeted Therapy

- **Versions 2002–2017:**
  Harbeck / Jackisch /Janni / Loibl / Lux/ von Minckwitz / Möbus / Müller / Nitz / Schneeweiss / Simon / Schütz / Solomeyer / Stickeler / Thomssen / Untch

- **Version 2018:**
  Thill / Untch

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Subtype-specific Strategies for Systemic Treatment

	AGO
■ If chemotherapy is indicated due to tumor biology consider systemic treatment before surgery (neoadjuvant)	++
■ HR+/HER2- and „low risk”	
▪ Endocrine therapy without chemotherapy	++
■ HR+/HER2- and „high risk”	
▪ Conventionally dosed AT-based chemotherapy	++
▪ Dose dense chemotherapy	++
▪ Followed by endocrine therapy	++
■ HER2+	
▪ Trastuzumab (plus Pertuzumab neoadjuvant at high risk)	++
▪ Sequential A/T-based regimen with concurrent T + H	++
▪ Anthracycline-free, platinum-containing regimen	+
▪ Anthracycline-free, taxane-containing regimen	+
■ Triple-negativ (TNBC)	
▪ Conventionally dosed AT-based chemotherapy	++
▪ Dose dense chemotherapy	++
▪ Neoadjuvant platinum-containing chemotherapy	+

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Adjuvant Chemotherapy without Trastuzumab: Overview

	Oxford		
	LoE	GR	AGO
▪ Anthracycline / taxane based chemotherapy	1a	A	++
▪ If anthracyclines cannot be given			
▪ Docetaxel plus cyclophosphamide	1b	B	+
▪ Paclitaxel mono weekly	1b	B	+/-
▪ CMF	1a	A	+/-
▪ Dose-dense therapy	1a	A	++
▪ Low dose maintenance chemo	1b	B	-

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Colleoni et al., J Clin Oncol 2016, 34: 3400-8

rand. phase 3-study of IBCSG: trial 22-00

n = 1086 pat., HR neg.,

DFS as primary endpoint

OP -> adj. CT -> R -> Cyclophos. 50 mg p.o. cont. plus
Mtx 2.5 mg 2 x tgl. p.o. d 1 + 2, q1w
versus
control (nil)

Results:
FU 6.9 yrs.,
n.s. DFS difference,
more side effects (14% WHO3/4) in the CM-arm

Recommended Conventional Regimens for Adjuvant Chemotherapy

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		Oxford LoE	Oxford GR	Oxford AGO
Anthracycline / taxane based regimen				
▪ *EC q3w x 4 → P_{ac} q1w x 12		2b	B	++
▪ AC q3w x 4 → Pac q1w y 12		1b	A	++
▪ AC → D	$A_{60}C$ q3w x 4 → D_{100} x 4	1b	A	+
▪ *EC → D	$E_{90}C$ q3w x 4 → D_{100} x 4	1b	B	+
▪ DAC	$D_{75}A_{50}C$ q3w x 6	1b	A	+
Anthracycline-free regimen				
▪ DC corresponds to EC → D	D_{75} C_{600} x 6	1b	B	+
▪ DC >> 4 x AC	$D_{75}C_{600}$ x 6	1b	B	+
▪ Pac mono	P_{80} q1w x 12	1b	B	+/-
▪ CMF		1a	A	+/-

* Extrapolated from doxorubicin trials

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Recommended Dose-dense and / or Dose-escalated, Sequential Adjuvant Chemotherapy *

	Oxford		
	LoE	GR	AGO
Dose-dense regimen			
▪ E_{90}-Pac_{175}-C_{600} q2w	1b	A	++
▪ AC q2w x4 → Pac q2w x 4	1b	B	++
▪ EC q2w x4 → Pac q2w x 4	1b	A	++
▪ EC q2w x4 → Pac q1w x 12	1b	B	++
Dose-dense and dose-escalated regimen (N ≥ 4+)			
▪ E_{150}-Pac_{225}-C_{2500} q2w	1b	A	++

* G-CSF obligatory

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Adjuvant Chemotherapy
Other Drugs

	Oxford		
	LoE	GR	AGO
▪ Capecitabine containing regimen in TNBC	1a	B	+/-
▪ Platinum containing regimen in TNBC	5	D	+/-
▪ 5- Fluorouracile added to EC/AC	1b	A	--

Adjuvant Treatment with Trastuzumab +/- Pertuzumab

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	Oxford		
	LoE	GR	AGO
Trastuzumab	1a	A	++
▪ **Trastuzumab + Pertuzumab**			
▪ **N+ and / or HR-**	1b	B	+
• **N- and HR+**	1b	B	+/-
▪ **Trastuzumab in node-negative disease (if chemotherapy is indicated)**			
▪ **10 mm**	1a	A	++
▪ **> 5–10 mm**	2b	B	+
▪ **≤ 5 mm**	2b	B	+/-

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Adjuvante Therapie mit Trastuzumab

	Oxford LoE	Oxford GR	Oxford AGO
Start of treatment			
▪ Simultaneously with taxanes	1a	A	++
▪ Sequentially up to 3 months after chemotherapy	1b	B	+
▪ S.c. = i.v.	1b	B	++
Duration			
▪ For 1 year	1b	A	++
▪ For 2 years	1b	A	-
▪ For 0.5 years	1b	A	+/-

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Adjuvant Trastuzumab
Cardiac Monitoring for CHF

Oxford LoE: 5 **GR: D** **AGO: ++**

Before start of trastuzumab

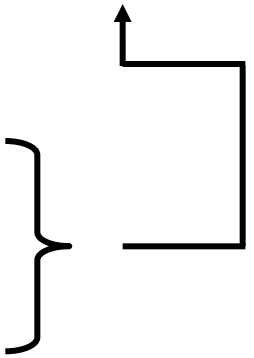
- History, physical examination (edema, hepatomegaly)
- Echocardiography (alternative to MUGA)

During trastuzumab

Regular assessment of

- Heart rate increase > 15% above individual base level
- Body weight increase ≥ 2 kg/week
- Cardiac signs and symptoms

Assessment of LVEF



3 monthly assessment of LVEF

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Adjuvant Treatment with Trastuzumab +/- Pertuzumab: Chemotherapy regimen

	Oxford LoE	Oxford GR	AGO
Trastuzumab simultaneously with			
▪ With paclitaxel / docetaxel after AC / EC	1b	A	++
▪ With P q1w 12 x without A in pT < 2 cm, pN0	2b	B	+
▪ With docetaxel and carboplatin	1b	A	+
Trastuzumab + Pertuzumab simultaneously with			
▪ With anthracyclines	2b	B	+/-
▪ With taxanes dose-dense	2b	B	+*
Radiotherapy concurrent with Trastuzumab	2b	B	+

* Study participation recommended

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Adjuvant Therapy with Other Targeted Agents

	Oxford		
	LoE	GR	AGO
▪ Lapatinib	1b[a]	B	-
▪ (delayed adjuvant treatment)	1b	B	-
▪ Lapatinib + Trastuzumab	1b[a]	B	-
▪ Neratinib after 1 year of Trastuzumab			
▪ HR+	2b	B	+/-
▪ HR-	2b	B	-
▪ Bevacizumab	1b	B	--

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Biosimilars
Genaral Considerations

Biosimilars, used for treatment (i.e. Trastuzumab) and supportive care of breast cancer (i.e growth factors) must be approved after passing the stringent development and validation processes required by EMA, FDA or other similarly strict authority, before used in daily practise.*

* **Thill M et al. Einführung und Verwendung von biosimilaren Antikörpern in der Therapie des Mammakarzinoms. Geburtshilfe Frauenheilkd 2018; DOI: 10.1055/s-0043-118761**