Status for nationale forsøg

Medicinsk Udvalg

A Knop

Status for nationale forsøg

(Neo)adjuverende

MASTER. A randomized, multicenter, double-blind phase III, placebo-controlled comparison of standard (neo)adjuvant therapy plus placebo versus standard (neo)adjuvant therapy plus atorvastatin in patients with early breast cancer.

Nordic Trip Trial (NTT) . A Translational Randomized Phase III Study Exploring the Effect of the Addition of Capecitabine to Carboplatine Based Chemotherapy in Early "Triple Negative" Breast Cancer

CryoPAC . Et åbent randomiseret fase 2 forsøg med kølehandske og sokker overfor ingen forebyggelse i forbindelse med adjuverende paclitaxel.

Astefania. (adj TDM1 +/- atezolizumab til HER2 pos. ptt med non-PCR efter neoadjuverende behandling.

Destiny 05. Post-neoadjuvant trastuzumab deruxtecan (T-DXd) versus T-DM1 in patients with residual invasive disease following neoadjuvant therapy. Et randomiseret fase lll forsøg hos patienter med HER2 positiv brystkræft.

ALEXANDRA . A randomized fase lll study comparing atezolizumab (Anti PD-L1 Antibody) in combination with adjuvant anthracycline/taxane-based chemotherapy versus chemotherapy alone in patients with operable triple-negative breast cancer

Metastaserende

Destiny-09. Trastuzumab Deruxtecan (T-DXd) With or Without Pertuzumab Versus Taxane, Trastuzumab and Pertuzumab in HER2-positive Metastatic Breast Cancer.

Destiny-12. At undersøge sikkerhed og effektivitet af T-DXd hos patienter med fremskreden/metastatisk HER2-positiv brystkræft med eller uden hjernemetastaser

Epik-5. A phase III, randomized study of alpelisib (ALP) plus fulvestrant (FUL) in patients with hormone receptor-positive (HR+), human epidermal growth factor receptor 2-negative (HER2-), *PIK3CA*-mutated advanced breast cancer (ABC) progressing on/after an aromatase inhibitor (AI) with a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i).

INAVO 120/Inavolisib . Phase III study evaluating the efficacy and safety of Inavolisib + Palbociclib + Fulvestrant vs Placebo + Palbociclib + Fulvestrant in patients with PIK3CA-mutant, HR+ HER2-Negative, Locally Advanced or Metastatic Breast Cancer.

PostMONARCH . Phase III study of fulvestrant +/- abemaciclib following progression om a CDK4/6i + endocrine therapy.

ImmunoBreast - A Phase Ib Study Phase Ib, open-label, single-arm, clinical study to determine the safety, tolerability and trends of efficacy of ALECSAT as an add-on therapy to standard treatment with carboplatin and gemcitabine in female patients with locally advanced inoperable or metastatic TNBC, which has received no more than two prior systemic therapies for mTNBC, max 2 prior lines for mBC (Investigator initieret)

CAPItello-292 : A Phase Ib/III Randomised Study of Capivasertib plus Palbociclib and Fulvestrant versus Placebo plus Palbociclib and Fulvestrant in Hormone Receptor-Positive and Human Epidermal Growth Factor Receptor 2-Negative Locally Advanced, Unresectable or Metastatic Breast Cancer (CAPItello-292).

Adjuverende
To nationale - et nordisk

MASTER. A randomized, multicenter, double-blind phase III, placebo-controlled comparison of standard (neo)adjuvant therapy plus placebo versus standard (neo)adjuvant therapy plus atorvastatin in patients with early breast cancer.

Nordic Trip Trial (NTT) . A Translational Randomized Phase III Study Exploring the Effect of the Addition of Capecitabine to Carboplatine Based Chemotherapy in Early "Triple Negative" Breast Cancer

CryoPAC . Et åbent randomiseret fase 2 forsøg med kølehandske og sokker overfor ingen forebyggelse i forbindelse med adjuverende paclitaxel.

Early breast cancer statin trial
the master trial

A randomized, multicenter, double-blind, placebo-controlled comparison of standard (neo)adjuvant therapy plus placebo versus standard (neo)adjuvant therapy plus atorvastatin in patients with early breast cancer

MAmmary cancer **ST**atin **ER** positive trial

Novo Nordisk Foundation

STATINS and BC-prognosis

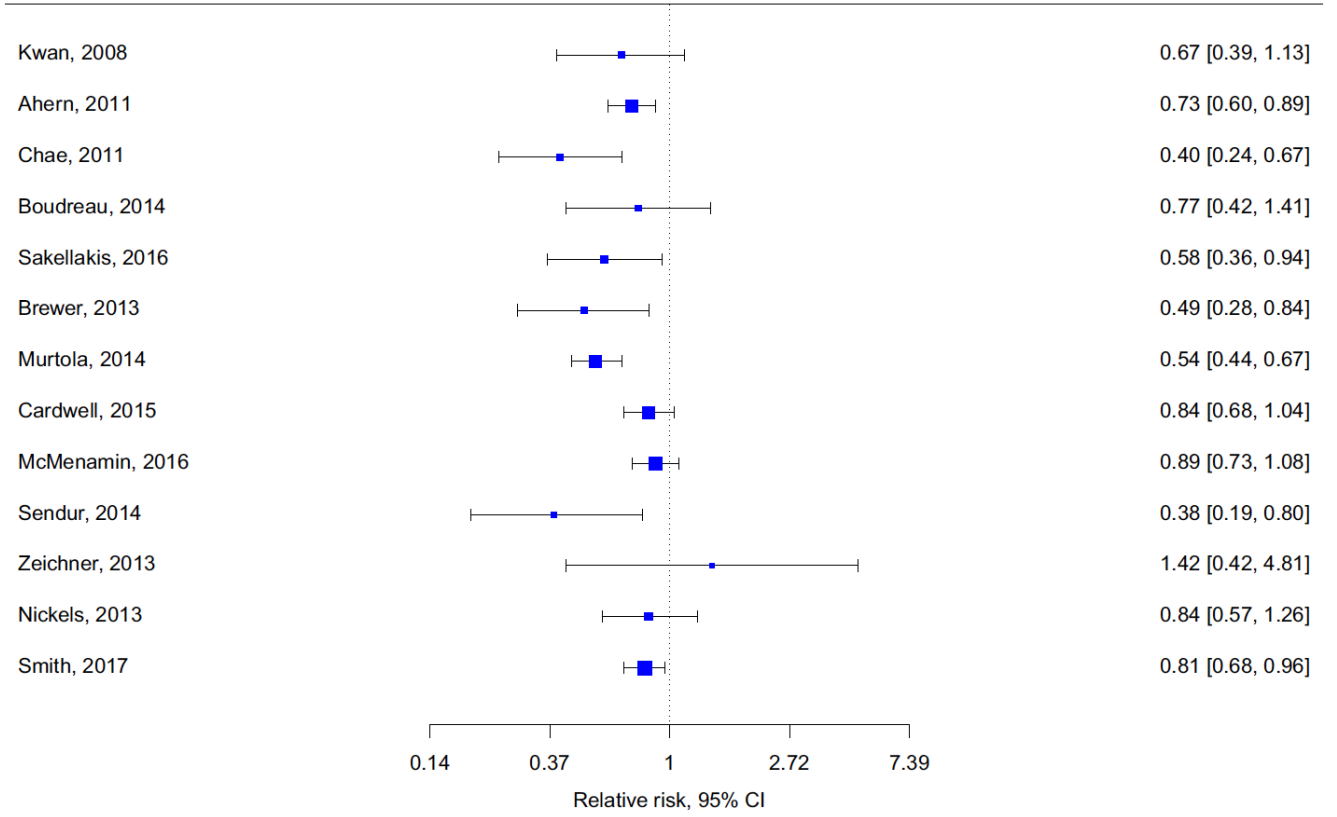


Fig. 2 *The prognostic value of statin treatment in the adjuvant breast cancer setting illustrated by a forest plot of the currently reported studies.*

Cholesterol, cholesterol lowering medication, and breast cancer outcome

Table 4. Marginal Structural Modeling Results of Initiation of CLM During Endocrine Treatment and Outcome Among All Treatment Arms

Variable	No.	HR	95% CI	*P*
No. of patients	5,944			
No. of DFS events	1,432			
No. of patients reporting CLM initiation during protocol therapy	697			
DFS model results				
Univariable weighted*		0.81	0.67 to 0.97	.02
Multivariable weighted†		0.79	0.66 to 0.95	.01
No. of BCFI events	940			
No. of patients reporting CLM initiation during protocol therapy	697			
BCFI model results				
Univariable weighted*		0.77	0.61 to 0.97	.03
Multivariable weighted†		0.76	0.60 to 0.97	.02
No. of DRFI events	729			
No. of patients reporting CLM initiation during protocol therapy	697			
DRFI model results				
Univariable weighted*		0.75	0.57 to 0.98	.04
Multivariable weighted†		0.74	0.56 to 0.97	.03

RESULT:

Patients initiating CLM had a significant improved prognosis compared to those without CLM

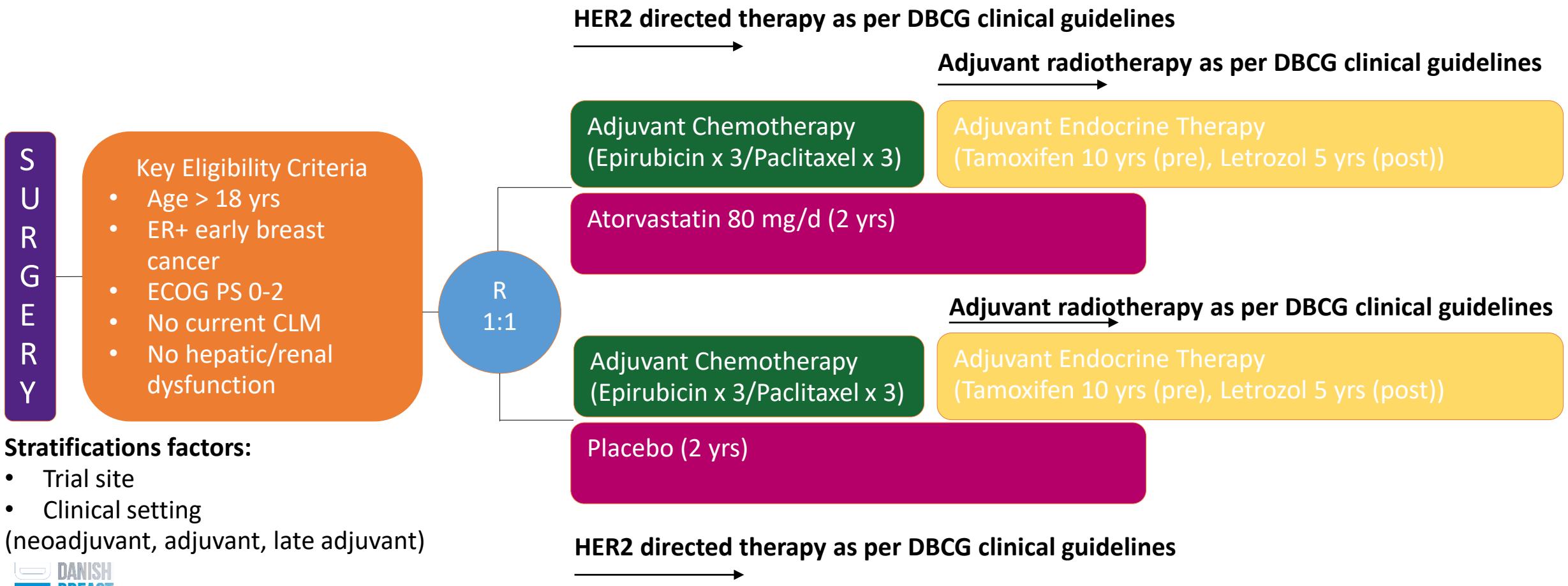
Cholesterol, Cholesterol-Lowering Medication Use, and Breast Cancer Outcome in the BIG 1-98 Study
S Borgquist et al. J Clin Oncol . 2017 Apr 10;35(11):1179-1188.

MASTER trial, Objectives

- **PRIMARY OBJECTIVE:**
- To compare invasive disease-free survival (IDFS) in patients randomized to standard (neo)adjuvant therapy plus placebo or standard (neo)adjuvant therapy plus atorvastatin

- **SECONDARY OBJECTIVES:**
- - To compare overall survival (OS), recurrence-free interval (RFI), distant recurrence-free interval (DRFI) including associations with first site of recurrence, cardiac death-free interval, and overall safety in the two treatment arms.
- - To investigate morbidity endpoints
- - To address translational endpoints

MASTER trial design, EARLY adjuvant

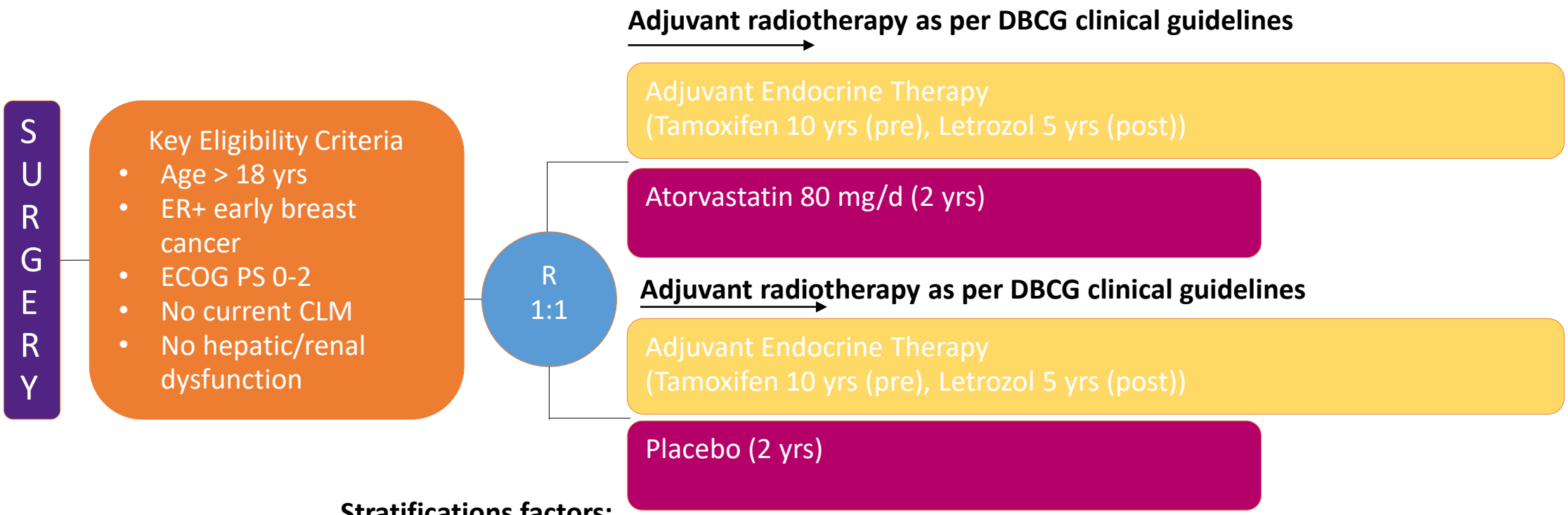


Stratifications factors:

- Trial site
- Clinical setting

(neoadjuvant, adjuvant, late adjuvant)

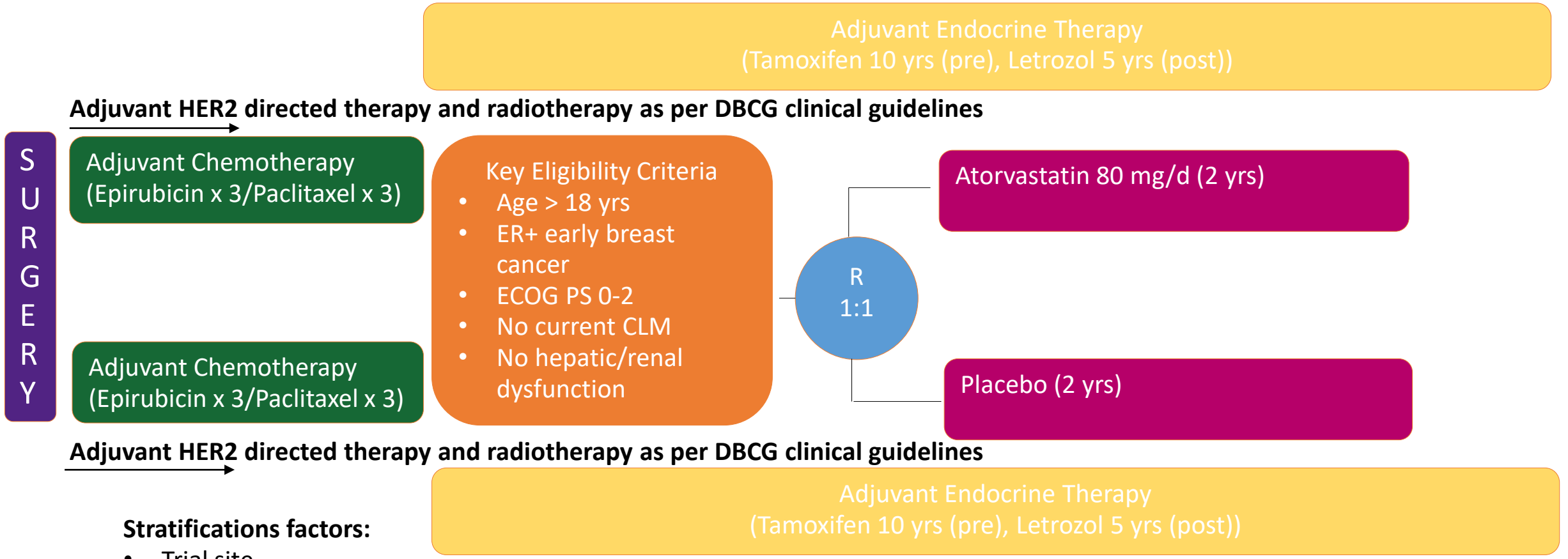
MASTER trial design, EARLY adjuvant, ET ONLY



Stratifications factors:

- Trial site
- Clinical setting (neoadjuvant, adjuvant, late adjuvant)

MASTER trial design, LATE adjuvant

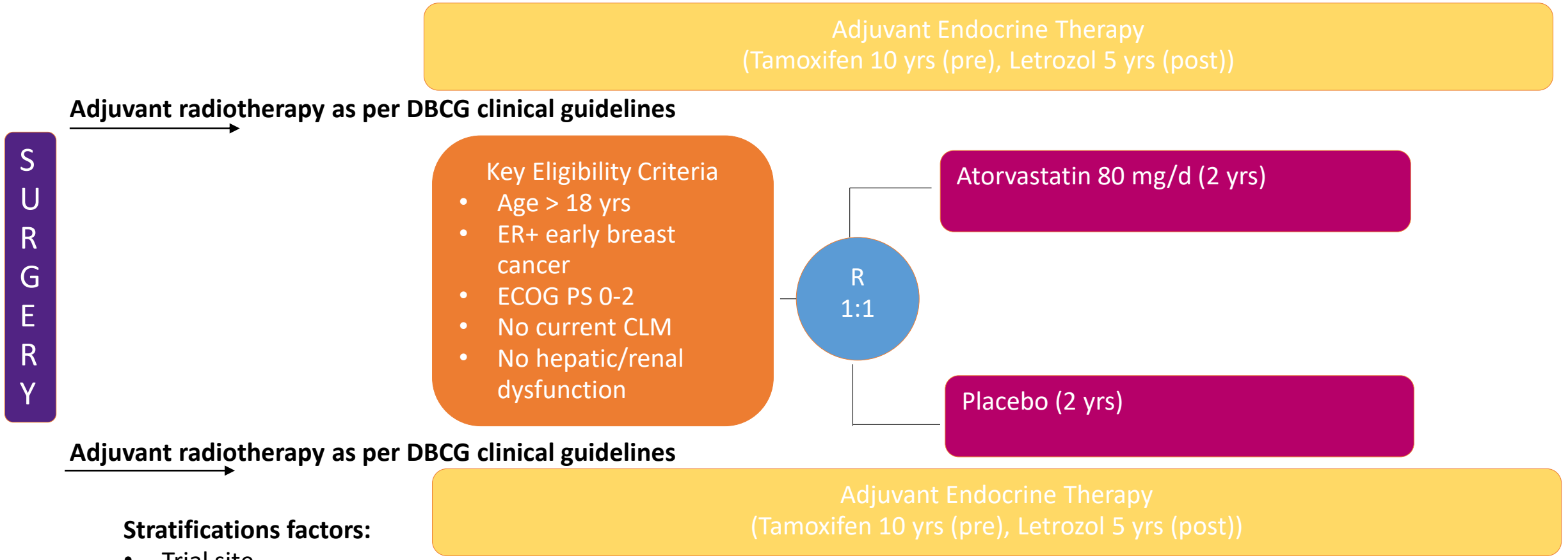


Stratifications factors:

- Trial site
- Clinical setting (neoadjuvant, adjuvant, late adjuvant)

Definition of "late entry":
randomization <u>after</u> start of adjuvant therapy,
but within three years of initiation of the endocrine treatment

MASTER trial design, LATE adjuvant, ET only



Stratifications factors:

- Trial site
- Clinical setting (neoadjuvant, adjuvant, late adjuvant)

Definition of "late entry":
randomization <u>after</u> start of adjuvant therapy,
but within three years of initiation of the endocrine treatment

MASTER trial design, OBSERVATIONAL COHORT

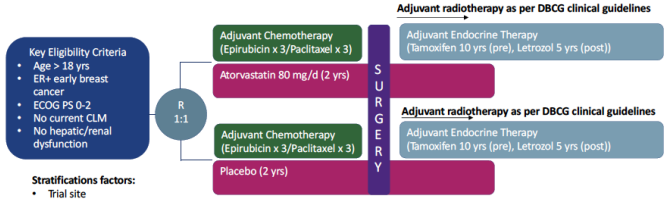
Non-randomized patient cohort on any cholesterol-lowering medication at diagnosis

Patients eligible for MASTER – any clinical setting:

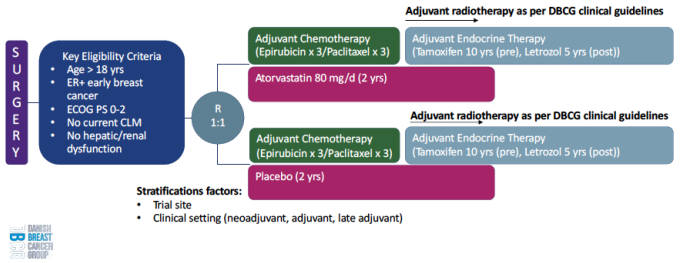
Participation in observational cohort:

1. **CRF**
2. **PRO**
3. **Blood samples**

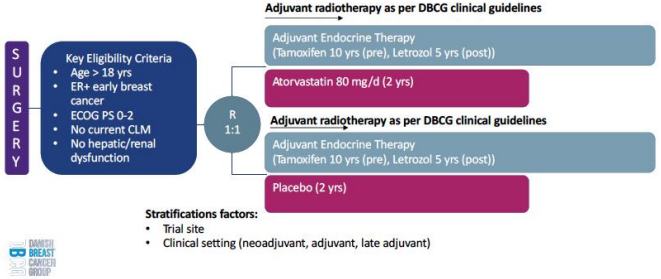
MASTER TRIAL DESIGN, NEOADJUVANT



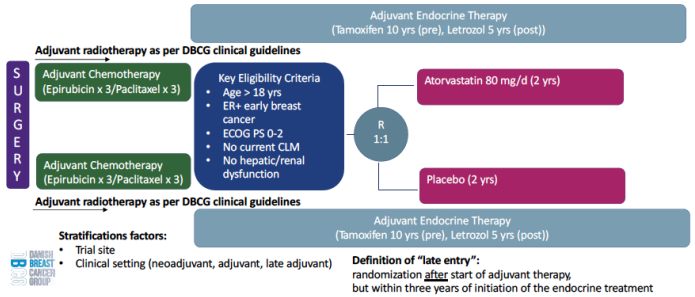
MASTER TRIAL DESIGN, EARLY ADJUVANT



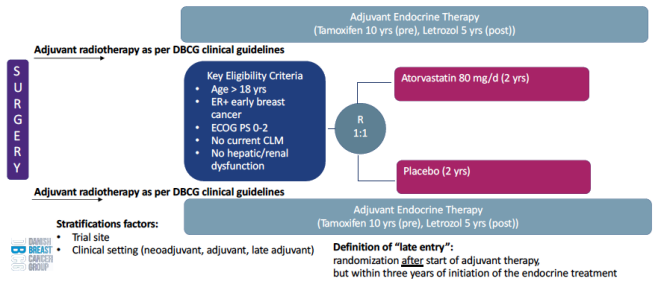
MASTER TRIAL DESIGN, EARLY ADJUVANT, ET ONLY



MASTER TRIAL DESIGN, LATE ADJUVANT



MASTER TRIAL DESIGN, LATE ADJUVANT, ET ONLY



Første patientinklusion d. 14. januar 2021

MASTER, Status pr. 01.01.2022

		2021													Strata	
		Jan	Feb	Mar	Apr	Maj	Jun	Jul	Aug						2: Adj Early	3: Adj Late
	RAND															
Rigshospitalet		-	-	-	-										1	0
Sønderborg		-	-												10	39
Esbjerg		-													2	5
Vejle															4	5
Herning															20	17
Aarhus		3													41	63
I alt		3												**12**	**78**	**129**
	SELV															
Sønderborg		-									1	3	2	17		
Vejle		-							1	1	0	0	0	2		
Aarhus		0						3	1	4	4	5	0	32		
I alt		0			4	8	6	4	7	5	8	**2**	**51**			

270

MASTER
DBCG

Status 2023

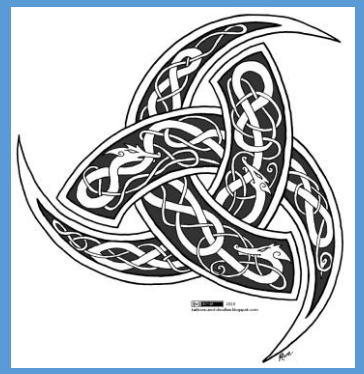
MASTER, Status pr. 01.01.2023

		2021	2022													Strata	
			Jan	Feb	Mar	Apr	Maj	Jun	Jul							Adj Early	3: Adj Late
	RAND																
Rigshospitalet		1	2	5	4											6	27
Hillerød		-	-													0	5
Odense		-														7	9
Sønderborg																16	91
Esbjerg																4	19
Vejle																4	20
Herning																44	41
Aarhus															9	80	95
I alt														**482**	**14**	**161**	**307**
	SELV																
Rigshospitalet												0	0	0	16		
Hillerød									0	1	1	2	0	4			
Odense								0	0	1	1	0	0	5			
Sønderborg							3	1	1	0	4	1	1	2	40		
Esbjerg						0	2	2	0	1	4	2	2	3	18		
Vejle				0	1	1	1	0	0	1	1	0	1	0	9		
Aarhus		32	2	1	2	2	6	2	0	3	0	2	0	1	53		
Aalborg		-	-	-	-	-	-	-	-	-	-	-	1	0	1		
I alt		51	8	3	12	9	15	8	1	5	14	7	7	**6**	**146**		

628

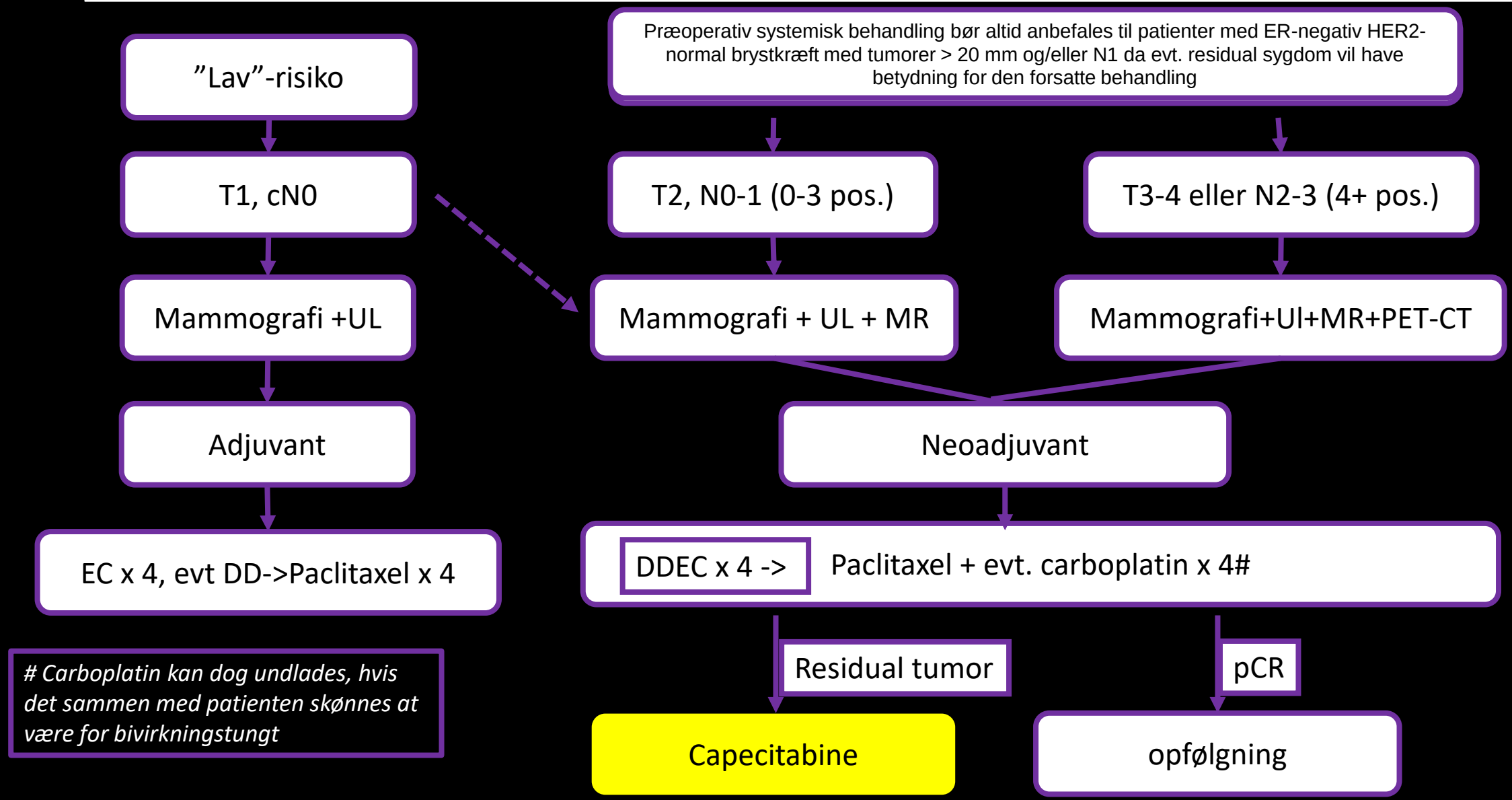
DANISH BREAST CANCER GROUP

NTT

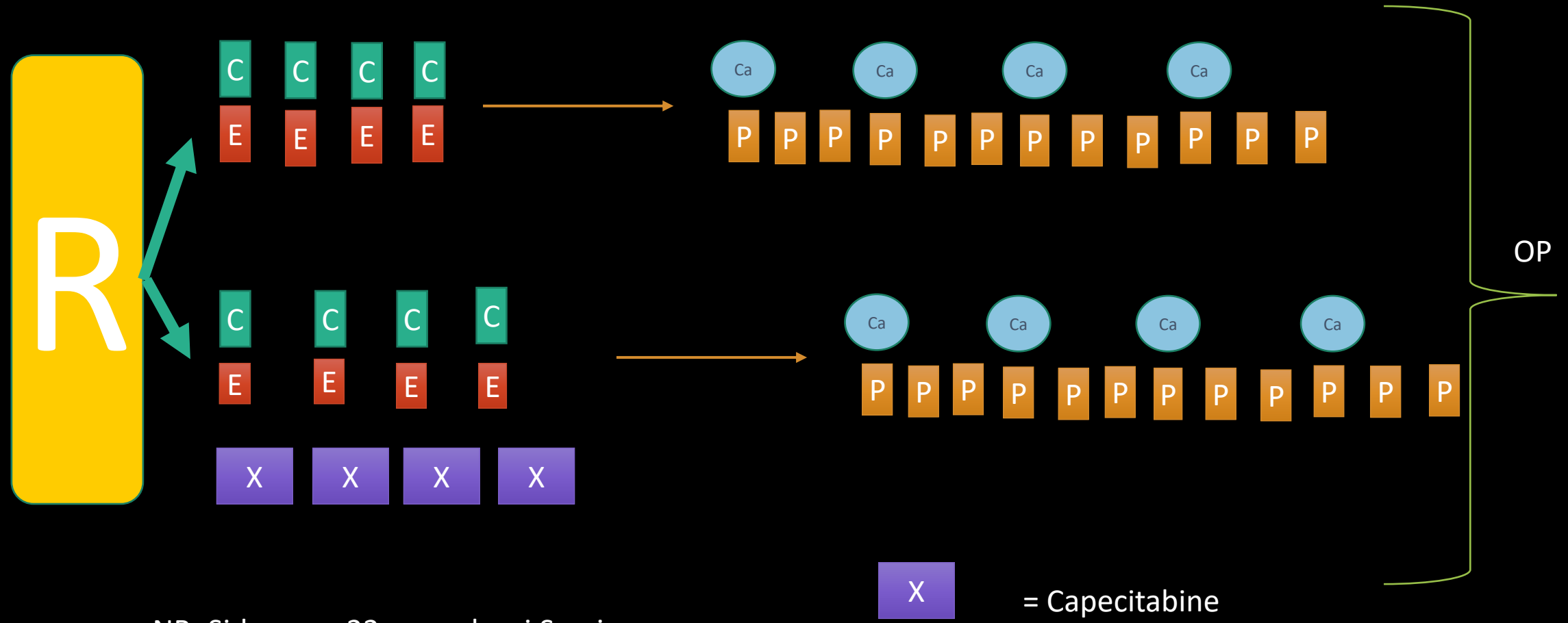


Nordic Trip/NBG-19-01, a translational randomized phase III study exploring the effect of the addition of capecitabine to carboplatinum based chemotherapy in early “triple negative” breast cancer.

Basal-like/ER÷,HER2÷



Design



NB: Siden nov 22 + pembro i Sverige

Patientantal og studieforløb

- Total 820 patienter hvoraf 250 fra Danmark
- Første patient blev inkluderet januar 2020
- Forventet dato for sidste patient afsluttet (behandling): 2024
- **Behandlingsvarighed:** 20-23 uger
- **Follow-up:** 10 år

Nordic Trip Trial

- Sverige; 18 sites (**148 pt**)
- Danmark;
  - Aalborg (screener), Vejle (screener), **Sønderborg (2 pt.)**, OUH (screener), **Næstved (4 pt.)**, **Vejle (1 pt.) RH (17 pt.)** og **Hillerød (1 pt.)**
- Finland; 1 site
- Island; 1 site

Pragmatisk studie

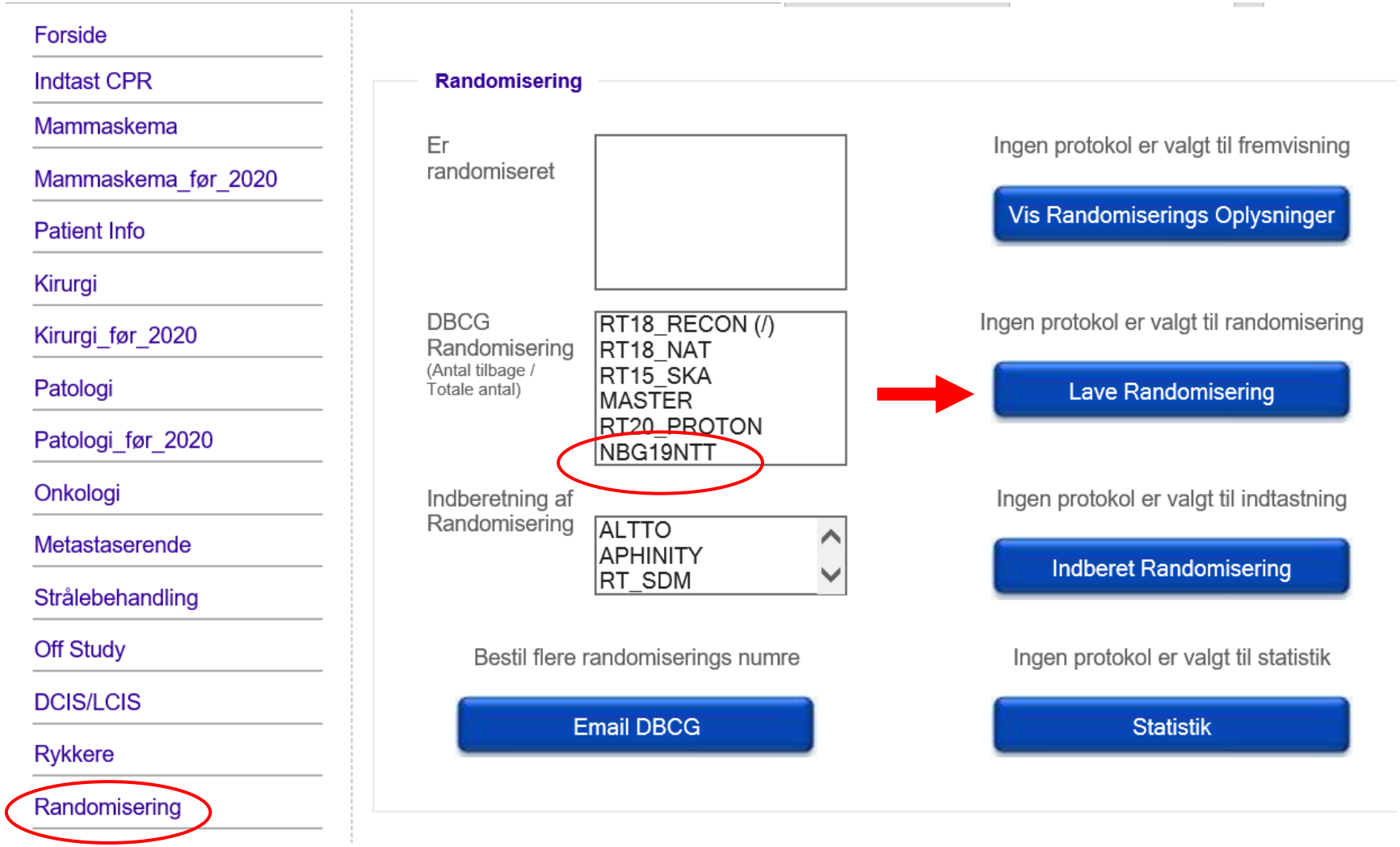
Udredning og behandling stort set ”som vi plejer”:

- Mammografi
- MR-Mammae før start, efter 2 serier og præoperativt
- PET-CT hvis node-pos
- Iodkorn mv iht alm praksis biopsi som vi plejer + biopsi til projekt
- Genetisk udredning
- Ct DNA - Genomisk Medicin på RH ansvarlig i DK

Randomisering

- Randomisering vil ske i forholdet 1:1 mellem de to behandlingsarme A og B, stratificeret for land, N-status and T-status.

DBCG-modul



The trip team

Bidrag fra DBCG

Randomisering & database
- Maj-Britt Jensen og Michael Jespersen
- DBCG er vært for databasen
- Kirurgi-, patologi-, og onkologidata overføres

Monitoring
- Ann Raaberg, DBCG

Vævsbiobank
- Anne-Vibeke Lænkholm
- Roskilde er forsøgets centrale patologiafd.

Genomisk Medicin på RH varetager forsøgsblodprøver på danske patienter

Study team i Lund
- Niklas Loman, PI og sponsor
- Åke Borg, genomisk lab., Lund
- Heidi Grill Magnusson
- Lina Zander

Laboratoriet I Göteborg
- Barbro Linderholm
- ctDNA lab. i Göteborg

CryoPac

Effects of Cryotherapy on Objective and Subjective Symptoms of Taxane-Induced Neuropathy in Patients with Early Breast Cancer.

A Randomized Prospective Controlled Trial

The incidence of CIPN with paclitaxel and docetaxel is dose dependent and occurs with higher cumulative dose and higher dose per cycle.
The incidence of taxane-associated chemotherapy-induced peripheral neuropathy ranges from **11% to 64% for docetaxel** and **57% to 83% for paclitaxel**, which in 2–33% is severe. A patient-reported outcome study found that **CIPN numbness persisted in 67%–80%** of patients for one year following the completion of paclitaxel therapy .

National status pr 5.1.2023

- **Der er aktiv inklusion på alle 4 sites**
- Nationalt har vi inkluderet 258 patienter(24% dropout).

	NOH	RH	AUH	SØNDERBORG
Åbnede for inklusion	**uge 2, 2021.**	**uge 2, 2021.**	**uge 19, 2021.**	**Uge 22, 2021.**
Antal patienter inkluderet:	**64**	**100**	**82**	**12**
Drop out/ screen failure	**22**	**20**	**18**	**2**