nbcg NORSK BRYST CANCER GRUPPE

Nytt fra NBCG

15.06.18

Mange tema

Diagnostikk
Kirurgi
Onkologi
Organisasjon
Studier
….
….

Organisasjon

- NBCG vil inkludere 2 fastleger utnevnt av HD/almenlegeforeningen i Styringsgruppen

NBCG - studieoversikt

https://nbcg.no/pagaende-studier-apne-for-inklusjon/

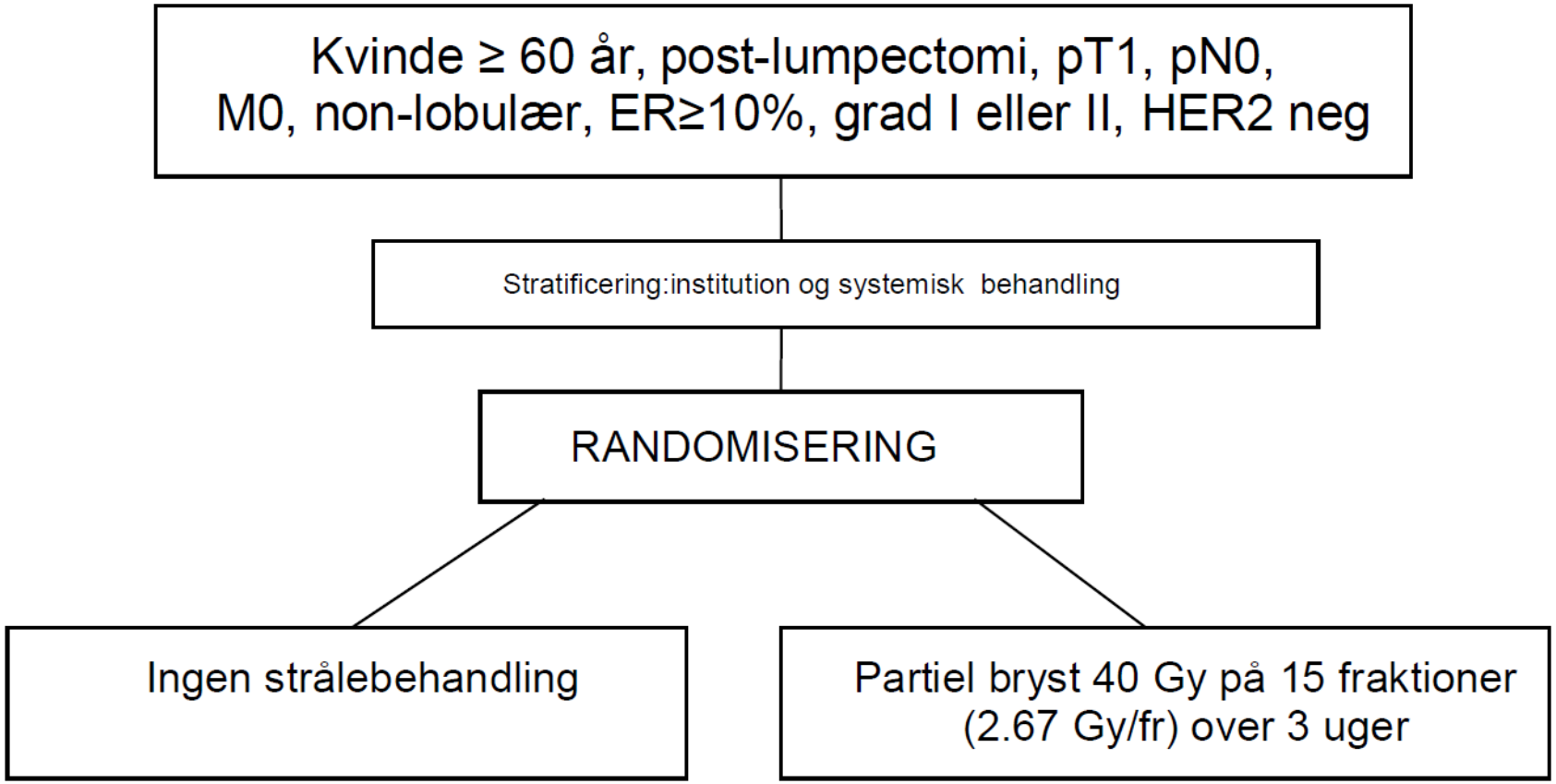
Nye studier i startgropen

DBCG RT Natural studiet:

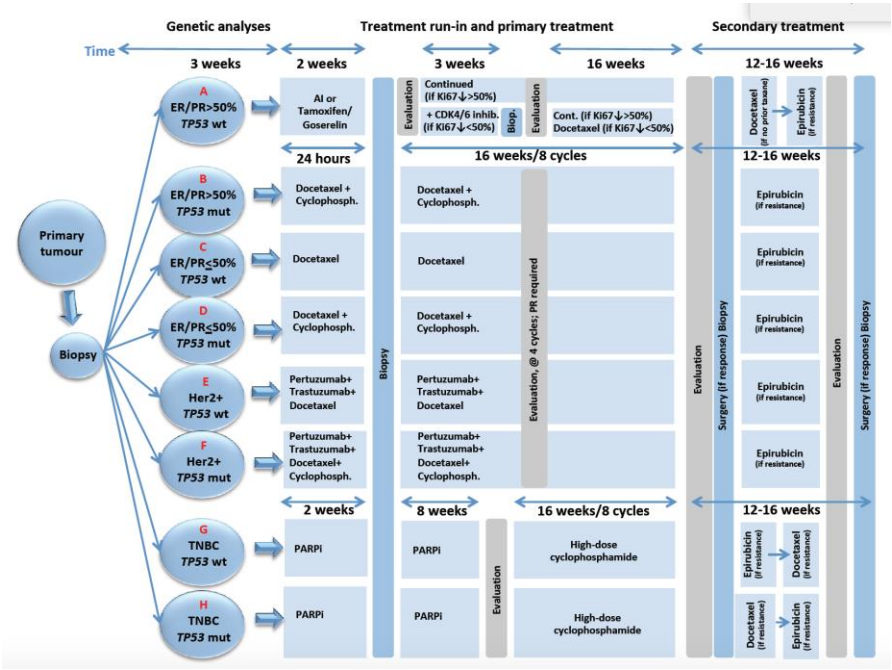
Delbryst *versus* ingen bestråling til kvinder ≥ 60 år opereret med brystbevarende operation for brystkræft:

et klinisk kontrolleret randomiseret fase III studium

Planlegges inklusjon av 928 pasienter



SUS, OUS, UNN, …. Flere?



PETREMAC - 2

Neoadjuvant studie

Overtar etter Petremac

(PI Per E. Lønning)

EMIT – studiene
Litt om status for disse litt senere i presentasjonen

Bruk av genprofilering til beslutning om adjuvant kjemoterapi

EMIT1 (implementeringsstudie)

EMIT2/OPTIMA (randomisert studie – utvidet indikasjon)

Status for vurderinger av medikamenter og metoder

- **Pertuzumab**
  - Ingen ny informasjon fra Beslutningsforum – er under arbeid
- **Palbociclib**

  Beslutning i Beslutningsforum for nye metoder (11.06.2018)
  - Delrapport 1:
    - Palbociklib (Ibrance) innføres ikke nå til kombinasjonsbehandling med aromatasehemmer av lokalavansert/metastatisk brystkreft.
    - Legemiddelet kan imidlertid inngå i fremtidige LIS-anbud. Dersom prisen i et LIS-anbud blir lik eller lavere dagens pris for ribosiklib (Kisqali) kan Palbociklib (Ibrance) innføres til kombinasjonsbehandling med aromatasehemmer av lokalavansert/metastatisk brystkreft.
  - Delrapport 2:
    - Palbociklib (Ibrance) innføres ikke til kombinasjonsbehandling med fulvestrant av lokalavansert/metastatisk brystkreft etter tidligere endokrin behandling.

Kort statusrapport for NBCR

- Ny versjon av KREMT ble klar i januar 2018
- Kurs og oppfølging onkologikoding (Rosa sløyfe)
- Videre oppfølging av radiologikoding utenfor screeningen/BDS'ene
- Datagrunnlaget for årsrapporten for 2017 er nå klart

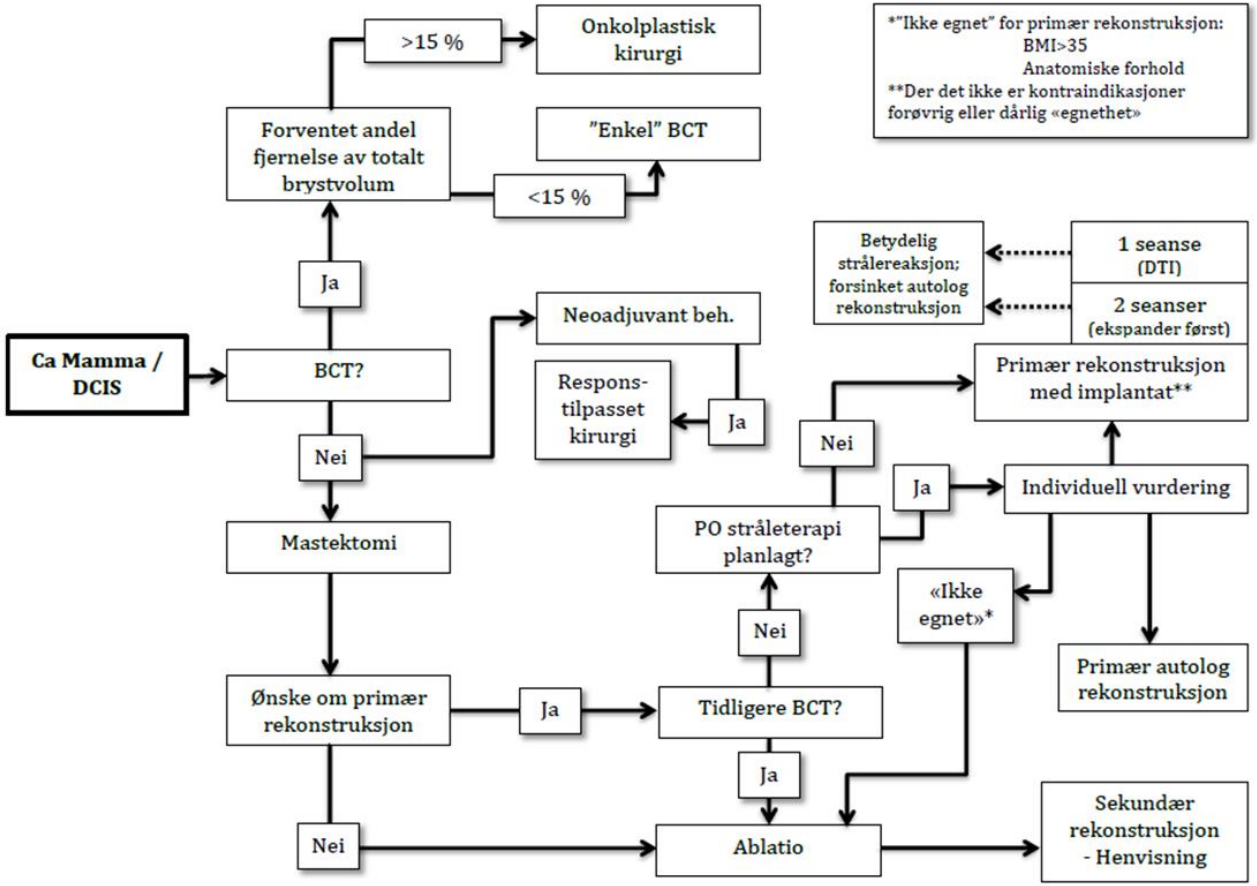
4. Utredning ved mistanke om brystkreft

Nytt kapittel i Handlingsprogrammet

Kirurgisk behandling av lokalisert sykdom

Nytt kapittel i Handlingsprogrammet

Flowskjema for kirurgiske behandlingsvalg



Adjuvant behandlingsbeslutning og genprofiler

Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline

Lyndsay N. Harris, Nofisat Ismaila, Lisa M. McShane, Fabrice Andre, Deborah E. Collyar, Ana M. Gonzalez-Angulo, Elizabeth H. Hammond, Nicole M. Kuderer, Minetta C. Liu, Robert G. Mennel, Catherine Van Poznak, Robert C. Bast, and Daniel F. Hayes

J Clin Oncol 2016

HR+/HER2-neg and NODE-negative

	INDICATION	Evidence Quality	Recommendation Strenght
OncotypeDX	YES	HIGH	STRONG
PAM50 ROR	YES	HIGH	STRONG
EndoPredict	YES	INTERMEDIATE	MODERATE
MammaPrint	YES	HIGH	STRONG

HR+/HER2-neg and NODE-positive

	INDICATION	Evidence Quality	Recommendation Strenght
OncotypeDX	NO	INTERMEDIATE	MODERATE
PAM50 ROR	NO	INTERMEDIATE	MODERATE
EndoPredict	NO	INSUFFICIENT	MODERATE
MammaPrint	NO	INTERMEDIATE	MODERATE

The NEW ENGLAND JOURNAL of MEDICINE

NEJM juni 2018
Presented on ASCO

ORIGINAL ARTICLE

Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer

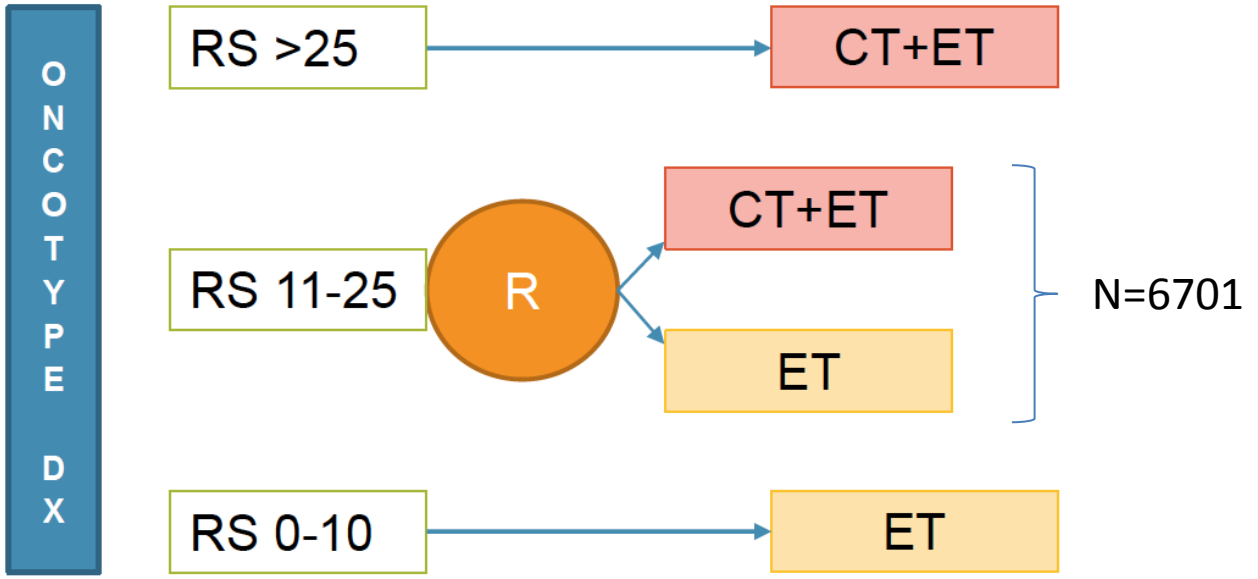
J.A. Sparano, R.J. Gray, D.F. Makower, K.I. Pritchard, K.S. Albain, D.F. Hayes, C.E. Geyer, Jr., E.C. Dees, M.P. Goetz, J.A. Olson, Jr., T. Lively, S.S. Badve, T.J. Saphner, L.I. Wagner, T.J. Whelan, M.J. Ellis, S. Paik, W.C. Wood, P.M. Ravdin, M.M. Keane, H.L. Gomez Moreno, P.S. Reddy, T.F. Goggins, I.A. Mayer, A.M. Brufsky, D.L. Toppmeyer, V.G. Kaklamani, J.L. Berenberg, J. Abrams, and G.W. Sledge, Jr.

CONCLUSIONS

Adjuvant endocrine therapy and chemoendocrine therapy had similar efficacy in women with hormone-receptor–positive, HER2-negative, axillary node–negative breast cancer who had a midrange 21-gene recurrence score, although some benefit of chemotherapy was found in some women 50 years of age or younger. (Funded by the National Cancer Institute and others; TAILORx ClinicalTrials.gov number, NCT00310180.)

TAILORx: Design

- Female 18-75
- ER and / or PR +ve
- HER2-ve
- 1.1 – 5.0 cm and any grade
- 0.6-1.0 cm and grade 2/3
- Node-negative



- primary endpoint – IDFS
- sample size based on non-inferiority of ET versus CT+ET in the 11-25 RS population

Survival analysis for the intermediate recurrence score population according to +/- chemotherapy

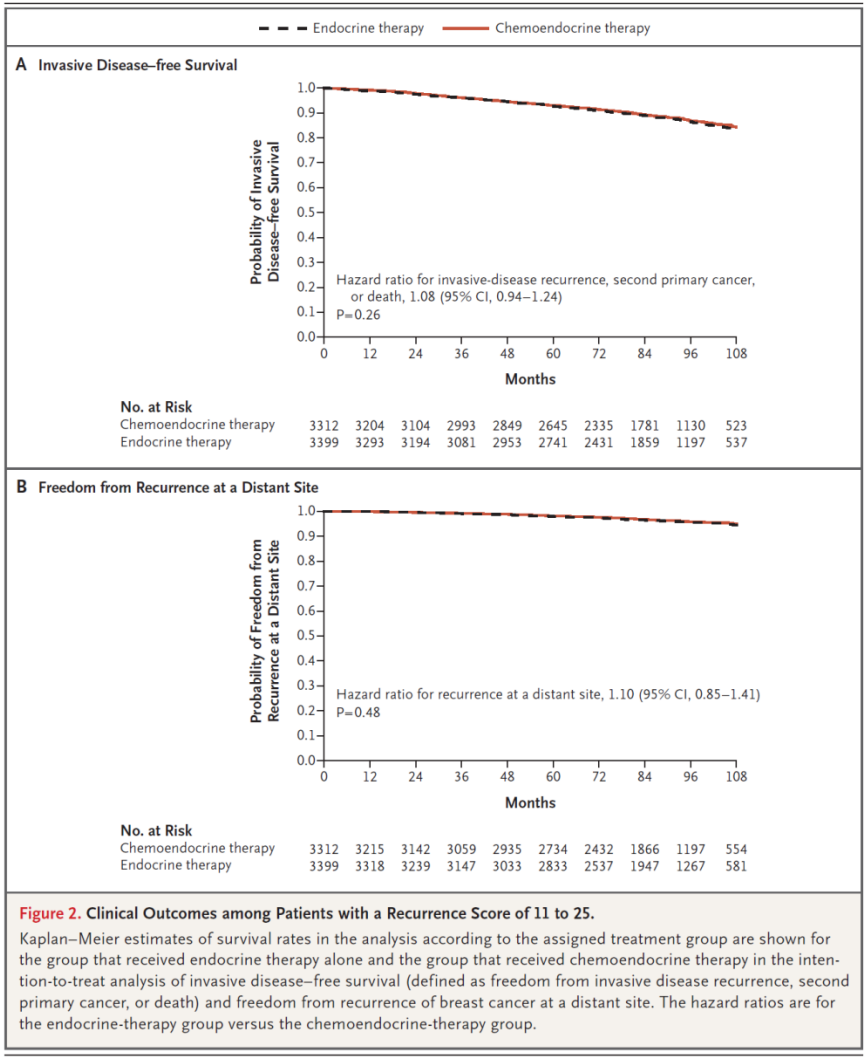


Figure 2. Clinical Outcomes among Patients with a Recurrence Score of 11 to 25.

Kaplan–Meier estimates of survival rates in the analysis according to the assigned treatment group are shown for the group that received endocrine therapy alone and the group that received chemoendocrine therapy in the intention-to-treat analysis of invasive disease–free survival (defined as freedom from invasive disease recurrence, second primary cancer, or death) and freedom from recurrence of breast cancer at a distant site. The hazard ratios are for the endocrine-therapy group versus the chemoendocrine-therapy group.

U.S. Department of Health & Human Services

DAGENS Medicin

Nyheder Karriere

ASCO | ASCO 2018 | VIDENSKAB

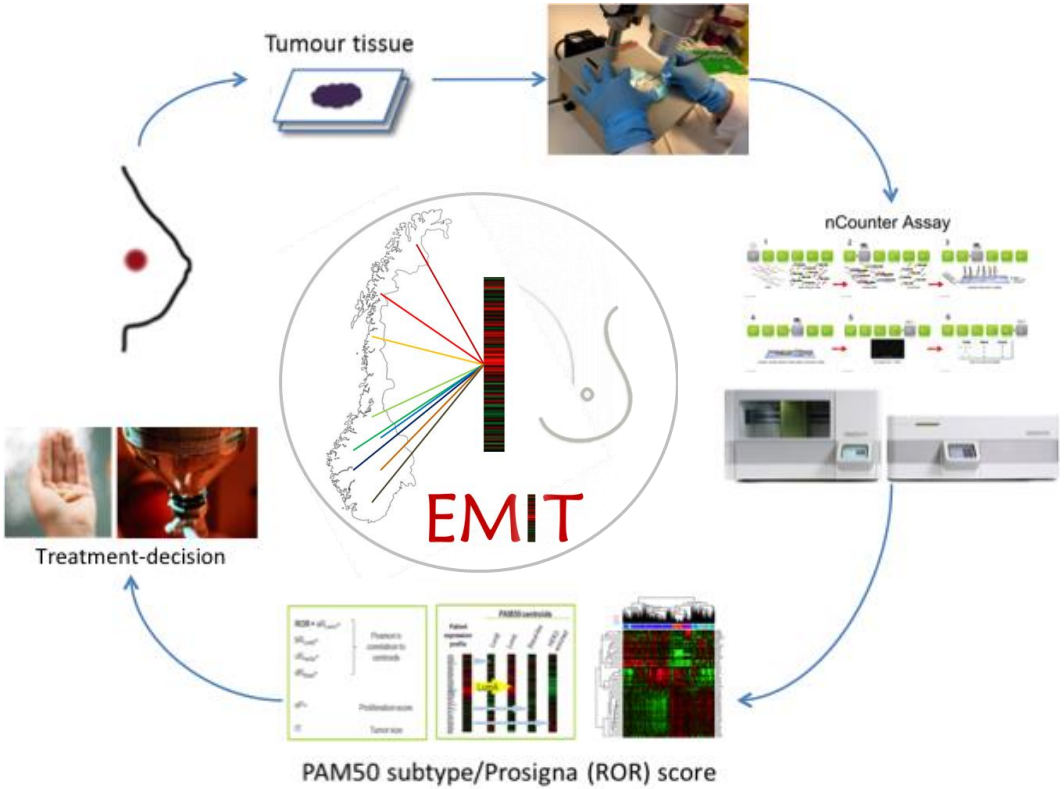
»I Danmark bruger vi kliniske histopatologiske kriterier og PAMP-50 til at vurdere, om patienter vil have gavn af kemoterapi i tillæg til antihormonel behandling. PAMP-50 kan identificere patienter med relativt fredelige tumorer, som ikke behøver kemoterapi, når der også behandles med anti-hormonelt. Det er godt at se, at USA nu også er med på vognen,« griner Claus Kamby.

Foto: Anne Mette Steen-Andersen

Stort amerikansk studie bekræfter danske DBCG-retningslinjer

NBCG – anbefaling 2017

- **Genprofiltester** (slik som Oncotype Dx/Mammaprint/ Prosigna) **kan benyttes for å klargjøre adjuvant behandlingsbeslutning ved ER+HER2- pN0 status.** Testene har god dokumentasjon for å gi prognostisk informasjon ut over tradisjonelle histopatologiske analyser og kan bidra til **beslutning om kjemoterapi bør benyttes**, innenfor selekterte pasientgrupper. Testene kan være nyttige verktøy for å skille ut pasienter med høy og lav risiko (proliferasjon) hos pasienter med ER+HER2- status, samt for å skille mellom Luminal A og Luminal B (Prosigna). Der det er aktuelt å benytte genprofiltest bør analysen gjennomføres **som ledd i et kvalitetssikringsprosjekt**, hvor analyseresultatet sammenholdes med tradisjonell histopatologi og immunhistokjemiske undersøkelser.

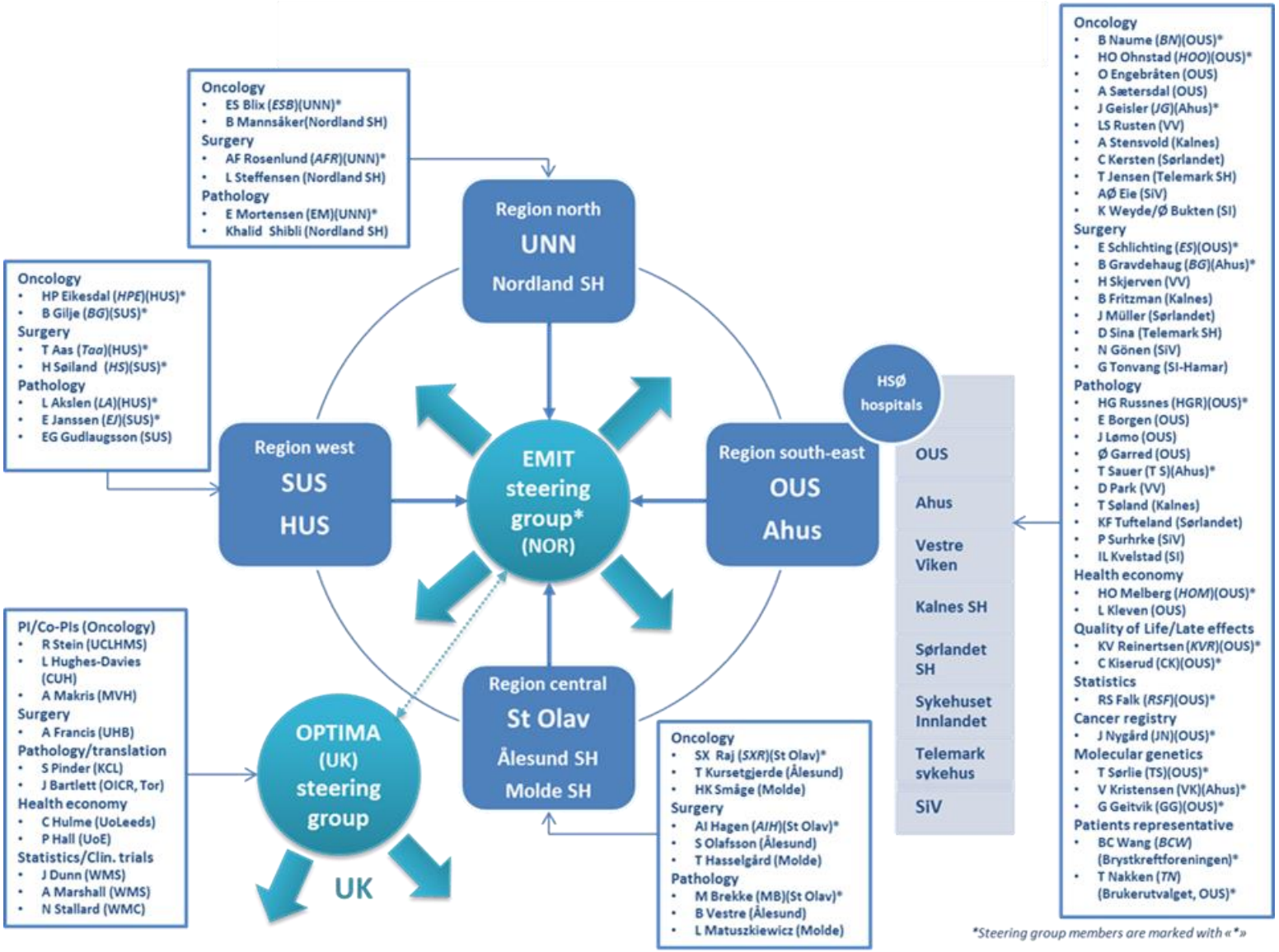


Establishment of Molecular profiling for Individual Treatment decisions in Early Breast Cancer (EMIT^{EBC})

NASJONALT PROGRAM
KLINBEFORSK

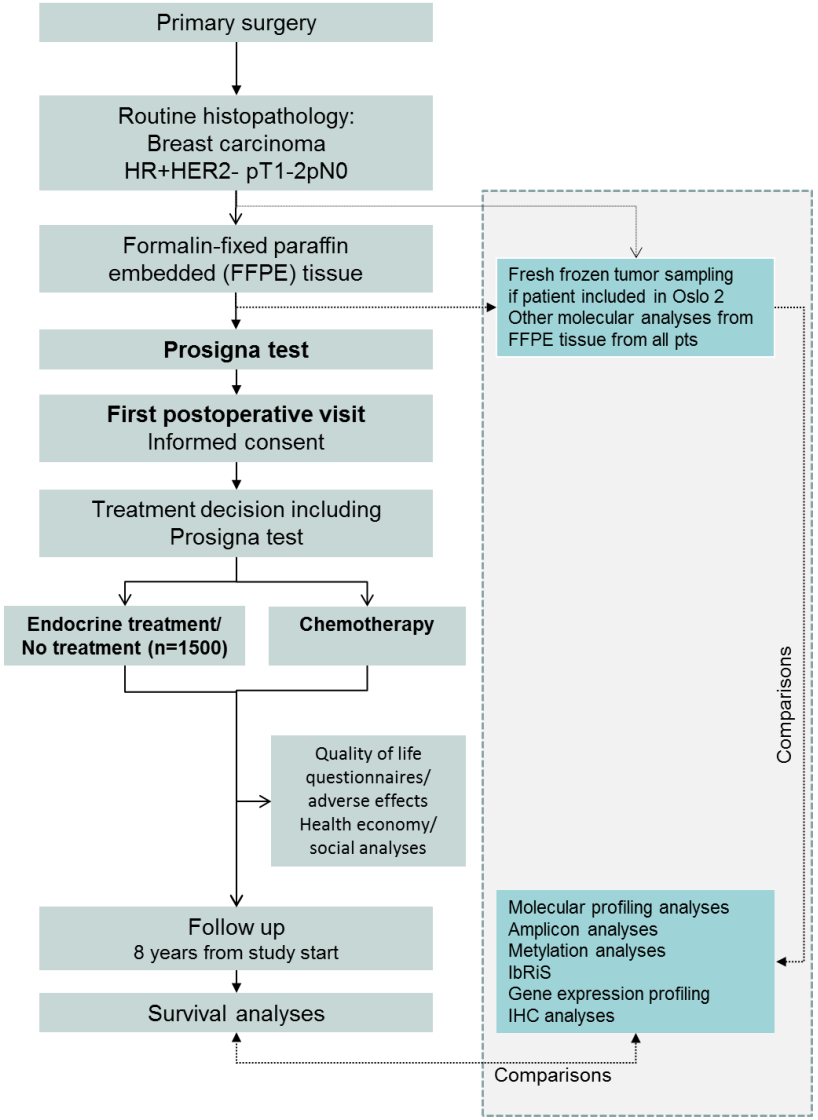
NORWEGIAN **CANCER** SOCIETY

EMIT – prosjektet (EMIT1 og EMIT2)



EMIT-1

Prospective study - Prosigna used for treatment decision in adjuvant situation among pT1-2 pN0 HR+/HER2- pts



Inclusion of 2150 patients

Expect ≥ 96% metastasis-free survival at 5 years follow up without use of chemotherapy

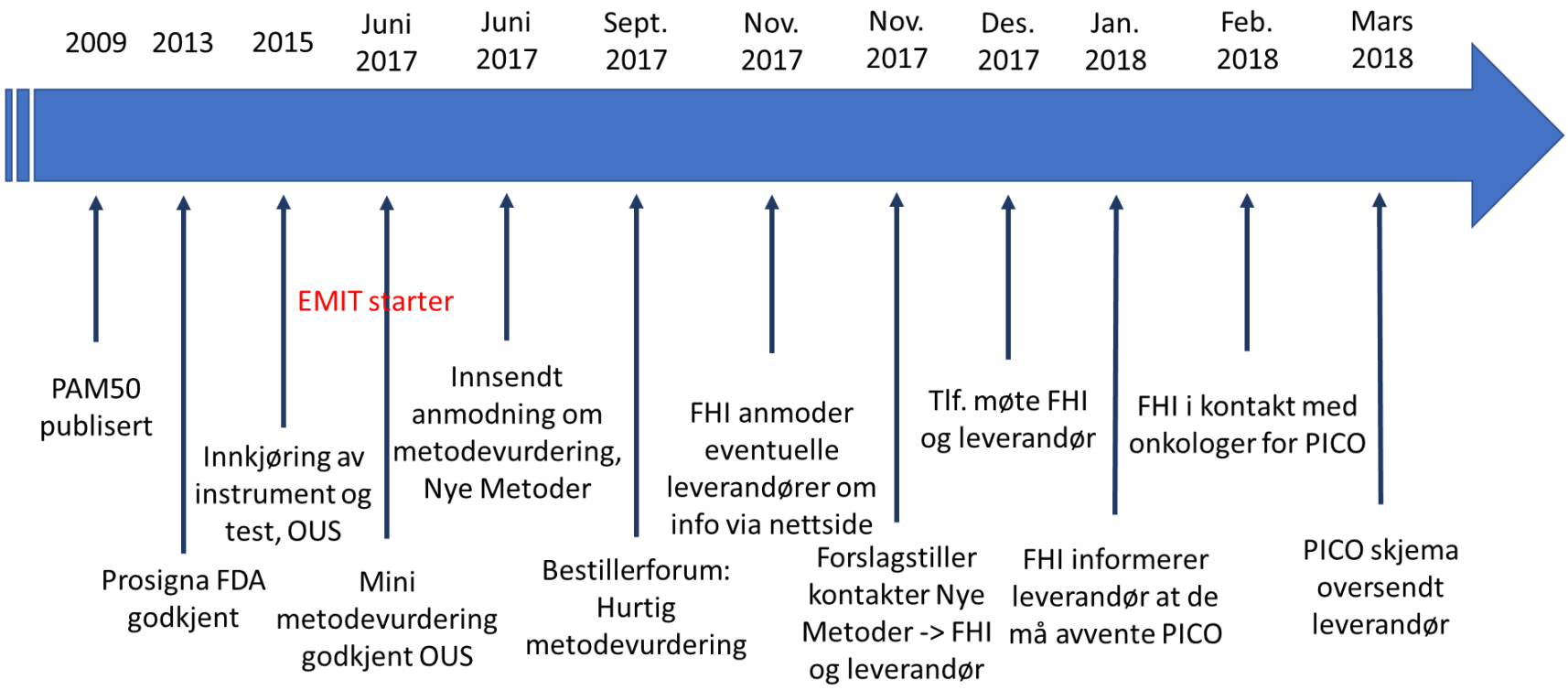
- Disease free survival and **metastasis-free survival** after 5 years follow up (8 years from study start)
- **Health care costs and benefit** for the hospitals and society using the Prosigna test, compared to the costs estimated when based on adjuvant treatment recommendations without Prosigna
- Differences in the number of patients receiving the various treatments using the Prosigna test compared to adjuvant treatment recommendations without Prosigna
- Differences in reported **quality of life** (QoL), **late effects** and **working ability/capacity** among patients receiving chemotherapy compared to those who did not receive chemotherapy (EORTC QLQ-BR23)
- The **feasibility** of the molecular classification-based treatment
- **Further refinement in subclassification** by additional molecular analyses of primary tumor

Hva er «i boks» og hva venter vi på

Beskrivelse	Resultat
Faglig vurdering Prosigna test	Inkludert i nasjonale anbefalinger; Minimetodevurdering godkjent ved OUS
Nasjonal vurdering av bruk av Prosigna test	Hurtig metodevurdering besluttet gjennomført (Folkehelseinstituttet)

EMIT

Tidslinje implementering av Prosigna test



Hva er «i boks» og hva venter vi på

Beskrivelse	Resultat
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Nasjonal vurdering av bruk av Prosigna test	Hurtig metodevurdering besluttet gjennomført (Folkehelseinstituttet)
Regional Etisk Komité	Godkjenninger foreligger

Etablering av styringsgruppe, arbeidsutvalg og overordnet organisering («på plass»)
Arbeid med budsjett og samarbeidsavtaler pågår

Oppstart EMIT-1 og EMIT-2/OPTIMA:

EMIT-2/OPTIMA i juni2018

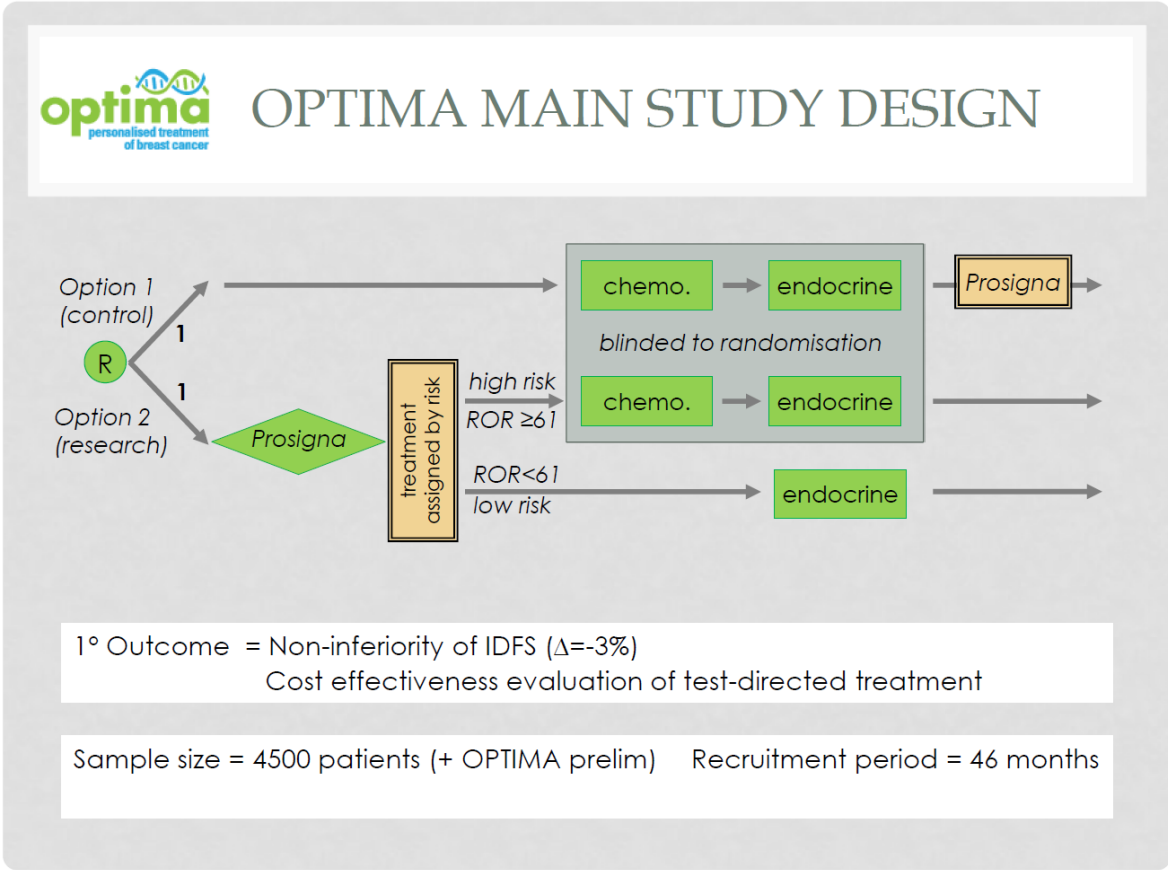
EMIT-1 avhengig av at sykehusene betaler for testen

EMIT-2 = OPTIMA
extended use of Prosigna test in pN1-2 pts

OPTIMA will disclose **predictive** value of the test:
Does pts with higher risk with low/ intermediate ROR score have any benefit of chemotherapy?

Objectives:

- To identify a method of selection that **reduces chemotherapy use** for patients with hormone sensitive primary breast cancer without detriment to recurrence and survival.
- To establish the **cost-effectiveness** of test-directed treatment strategies compared to standard practice.



NBCGs retningslinjer 2018

- Behov for presiseringer i behandlingsanbefalinger ved bruk av genprofiler?
- Presisere i handlingsprogrammet at **Genprofiltester gir kvalitativt sikrere prognostisk informasjon enn Ki67 og Grad**

HR+HER2-
Lum A-liknende
(Lav proliferasjon*, G1-2, HR>50%, og HER2-)

Ytterligere subgruppering	Generell terapi-anbefaling (1)	Generell terapi-anbefaling (2) Grunnlag for annet terapi-valg
pT1a-b pN0	Ingen behandling	
pT1c pN0 grad 1	Ingen behandling	
pT1c grad 2 pN0 pT2pN0 pT1-2pN1	Endokrin behandling Zoledronsyre ved postmenopausal status	Tumorstørrelse og omfang av lymfeknutemetastaser kan gi grunnlag for kjemoterapi (EC90 x 4)
pN2-3	EC90 x 4 etterfulgt av endokrin behandling Zoledronsyre ved postmenopausal status	Spesielt omfattende lymfeknutemetastasering kan gi grunnlag for å gi EC90 x 4 → taxan

***eller risikoscore – vurderes best ved bruk av genprofil-tester for pN0**

HR+HER2-
Lum B-liknende
(høy proliferasjon* og G2-3, - eller HR<50%)

Ytterligere subgruppering	Generell terapi-anbefaling (1)	Generell terapi-anbefaling (2) Grunnlag for annet terapi-valg
pT1a-b pN0	Endokrin behandling Zoledronsyre ved postmenopausal status	Lav HR positivitet eller høyere proliferasjonsgrad kan gi grunnlag for kjemoterapi (EC90 x 4) Individuell vurdering av grunnlag for systembehandling kan gjøres ved små pT1apN0 tumores
pT1c-pT2 pN0 **pT1-2pN1-3**	EC90 x 4 etterfulgt av endokrin behandling Zoledronsyre ved postmenopausal status	Høyere proliferasjonsgrad eller omfang av lymfeknutemetastaser kan gi grunnlag for å gi EC90 x 4 → taxan

***eller risikoscore – vurderes best ved bruk av genprofil-tester for pN0**

Bør vi behandle pasienter som i dag ikke får endokrin behandling? pT1a+bpN0 og pT1cpN0G1

Hvordan forholder vi oss til risiko for sene tilbakefall (etter 5 år)

Risiko 0-5 år

Risiko etter 5 år

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

20-Year Risks of Breast-Cancer Recurrence after Stopping Endocrine Therapy at 5 Years

Hongchao Pan, Ph.D., Richard Gray, M.Sc., Jeremy Braybrooke, B.M., Ph.D., Christina Davies, B.M., B.Ch., Carolyn Taylor, B.M., B.Ch., Ph.D., Paul McGale, Ph.D., Richard Peto, F.R.S., Kathleen I. Pritchard, M.D., Jonas Bergh, M.D., Ph.D., Mitch Dowsett, Ph.D., and Daniel F. Hayes, M.D., for the EBCTCG*

ABSTRACT

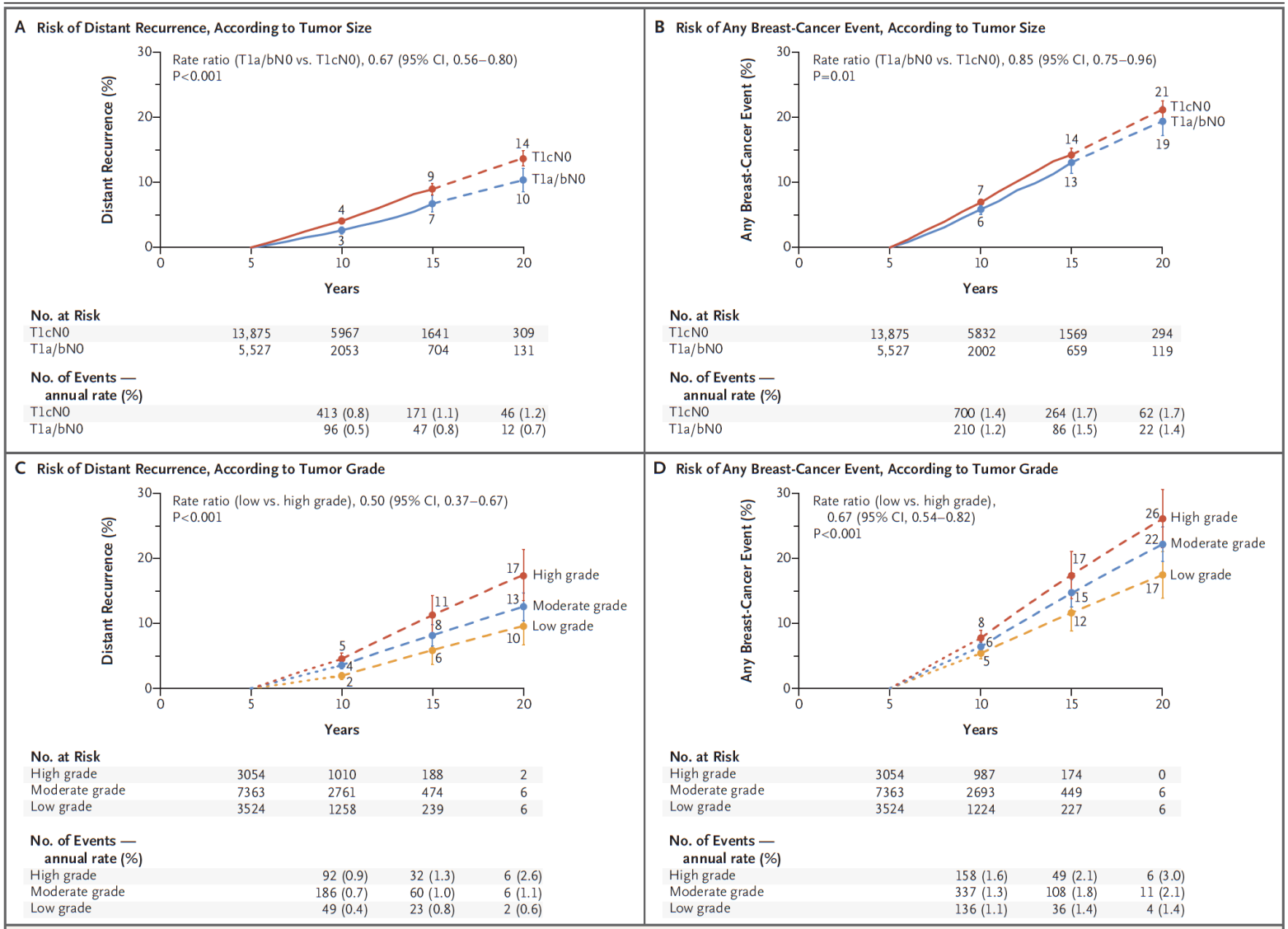
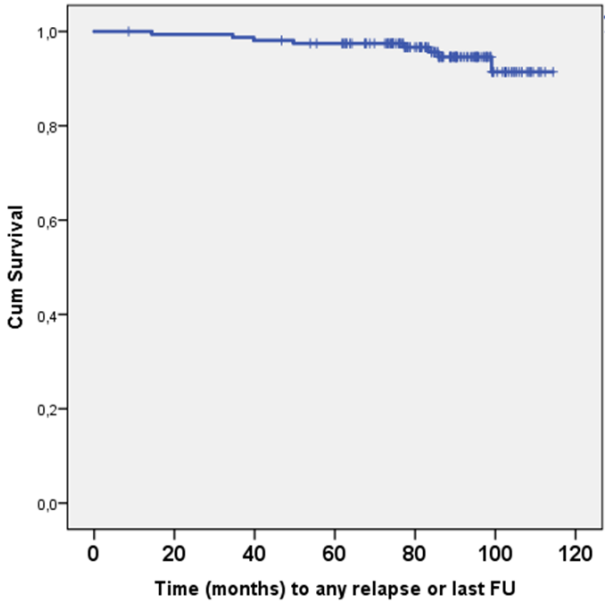


Figure 4. Association of Tumor Diameter and Tumor Grade with the Risk of Distant Recurrence or Any Breast-Cancer Event during Years 5 to 20 of the Study.

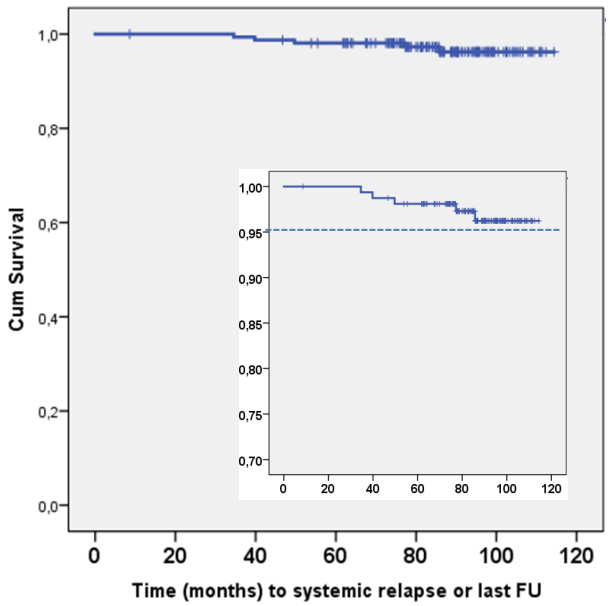
Shown are data for 19,402 women (13,941 of whom had a known tumor grade) with ER-positive breast cancer with a tumor size of 2 cm or less with no spread to lymph nodes (T1N0). All the women were scheduled to receive 5 years of adjuvant endocrine therapy and then discontinue therapy and were event-free and being followed at year 5. The findings were categorized according to tumor diameter (T1a or T1b [≤1.0 cm] vs. T1c [>1.0–2.0 cm]) and tumor grade. Panels A and C show the risk of distance recurrence during years 5 to 20 according to tumor diameter and tumor grade, respectively; Panels B and D show the risk of any breast-cancer event (distant or local recurrence or contralateral onset) during years 5 to 20 according to tumor diameter and tumor grade, respectively. The I bars indicate 95% confidence intervals. The dashed lines indicate that the event rate is for the whole 5-year period, rather than for individual years, as is otherwise shown.

HR+/HER2- Node negative
pT1b+c and pT1c G1 – survival in Oslo 1

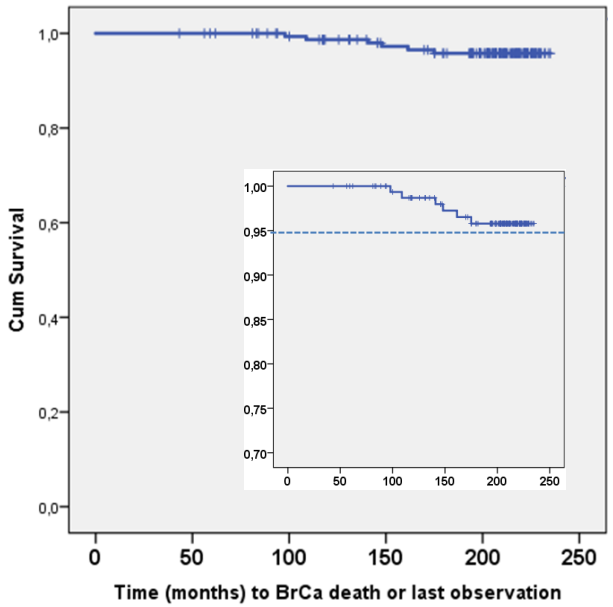
DFS



Distant DFS



BrCa specific survival*



FU DFS/DDFS: 89 mnd (median)

FU BCSS: 213 mnd (median)

6 dødsfall som følge av brystkreft, 39 totalt

Any Recurrence No=0, Yes=1

		Frequency	Percent	Valid Percent
Valid	No recurrence	151	93,2	95,0
	Recurrence Yes	8	4,9	5,0
	Total	159	98,1	100,0
Missing	System	3	1,9	
Total		162	100,0	

Systemic Recurrence no=0, yes=1

	Frequency	Percent	Valid Percent
No systemic recurrence	154	95,1	96,9
Systemic recurrence yes	5	3,1	3,1
Total	159	98,1	100,0
System	3	1,9	
	162	100,0	

Dødsårsak_kategorisert

		Frequency	Percent	Valid Percent
Valid	Alive	123	75,9	75,9
	Dead breast cancer	6	3,7	3,7
	Dead other cancer	10	6,2	6,2
	Dead non-cancer causes	23	14,2	14,2
	Total	162	100,0	100,0

Bør vi behandle pasienter som i dag ikke får endokrin behandling?
pT1a+bpN0 og pT1cpN0G1

NBCG mener ”nei”

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Integration of Clinical Variables for the Prediction of Late Distant Recurrence in Patients With Estrogen Receptor–Positive Breast Cancer Treated With 5 Years of Endocrine Therapy: CTS5

Mitch Dowsett, Ivana Sestak, Meredith M. Regan, Andrew Dodson, Giuseppe Viale, Beat Thürlimann, Marco Colleoni, and Jack Cuzick

Author affiliations and support information (if applicable) appear at the end of this article.

Published at jco.org on April 20, 2018.

Clinical trial information: ISRCTN18233230, NCT00004205.

Corresponding author: Mitch Dowsett, PhD, Ralph Lauren Centre for Breast Cancer Research, Royal Marsden Hospital, London, SW3 6JJ United Kingdom; e-mail: mitch.dowsett@icr.ac.uk.

0732-183X/18/3699-1/$20.00

ABSTRACT

Purpose

Estimating risk of late distant recurrence (DR) is an important goal for managing women with hormone receptor–positive breast cancer after 5 years of endocrine treatment without recurrence. We developed and validated a simple clinicopathologic tool (Clinical Treatment Score post–5 years [CTS5]) to estimate residual risk of DR after 5 years of endocrine treatment.

Patients and Methods

The ATAC (Arimidex, Tamoxifen, Alone or in Combination) data set (N = 4,735) was used to create a prognostic score for post–5-year risk of DR. Validity of CTS5 (ATAC) was tested in the BIG 1-98 data set (N = 6,711). Time to late DR, 5 years after finishing scheduled endocrine therapy, was the primary end point. Cox regression models estimated the prognostic performance of CTS5 (ATAC).

Results

CTS5 (ATAC) was significantly prognostic for late DR in the ATAC cohort (hazard ratio, 2.47; 95% CI, 2.24 to 2.73; $P < .001$) and BIG 1-98 validation cohort (hazard ratio, 2.07; 95% CI, 1.88 to 2.28; $P < .001$). CTS5 (ATAC) risk stratification defined in the training cohort as low (< 5% DR risk, years 5 to 10), intermediate (5% to 10%), or high (> 10%) identified 43% of the validation cohort as low risk, with an observed DR rate of 3.6% (95% CI, 2.7% to 4.9%) during years 5 to 10. From years 5 to 10, 63% of node-negative patients were low risk, with a DR rate of 3.9% (95% CI, 2.9% to 5.3%), and 24% with one to three positive nodes were low risk, with a DR rate of 1.5% (95% CI, 0.5% to 3.8%). A final CTS5 for future use was derived from pooled data from ATAC and BIG 1-98.

Conclusion

CTS5 is a simple tool based on information that is readily available to all clinicians. CTS5 was validated as highly prognostic for late DR in the independent BIG 1-98 study. The final CTS5 algorithm identified 42% of women with < 1% per-year risk of DR who could be advised of the limited potential value of extended endocrine therapy.

Grunnlag for CTS5 (= etter 5 år)

- Alder (kontinuerlig)
- Tumor størrelse i mm (kontinuerlig)
- Lymfeknutestatus
  - pN0=0
  - pN1(1+)=1
  - pN1(2-3+)=2
  - pN2=3
  - pN3=4
- Grad (I=1, II=2, III=3)

$$\text{CTS5} = 0.438 \times \text{nodes} + 0.988 \times (0.093 \times \text{size} - 0.001 \times \text{size}^2 + 0.375 \times \text{grade} + 0.017 \times \text{age})$$

Test cohort

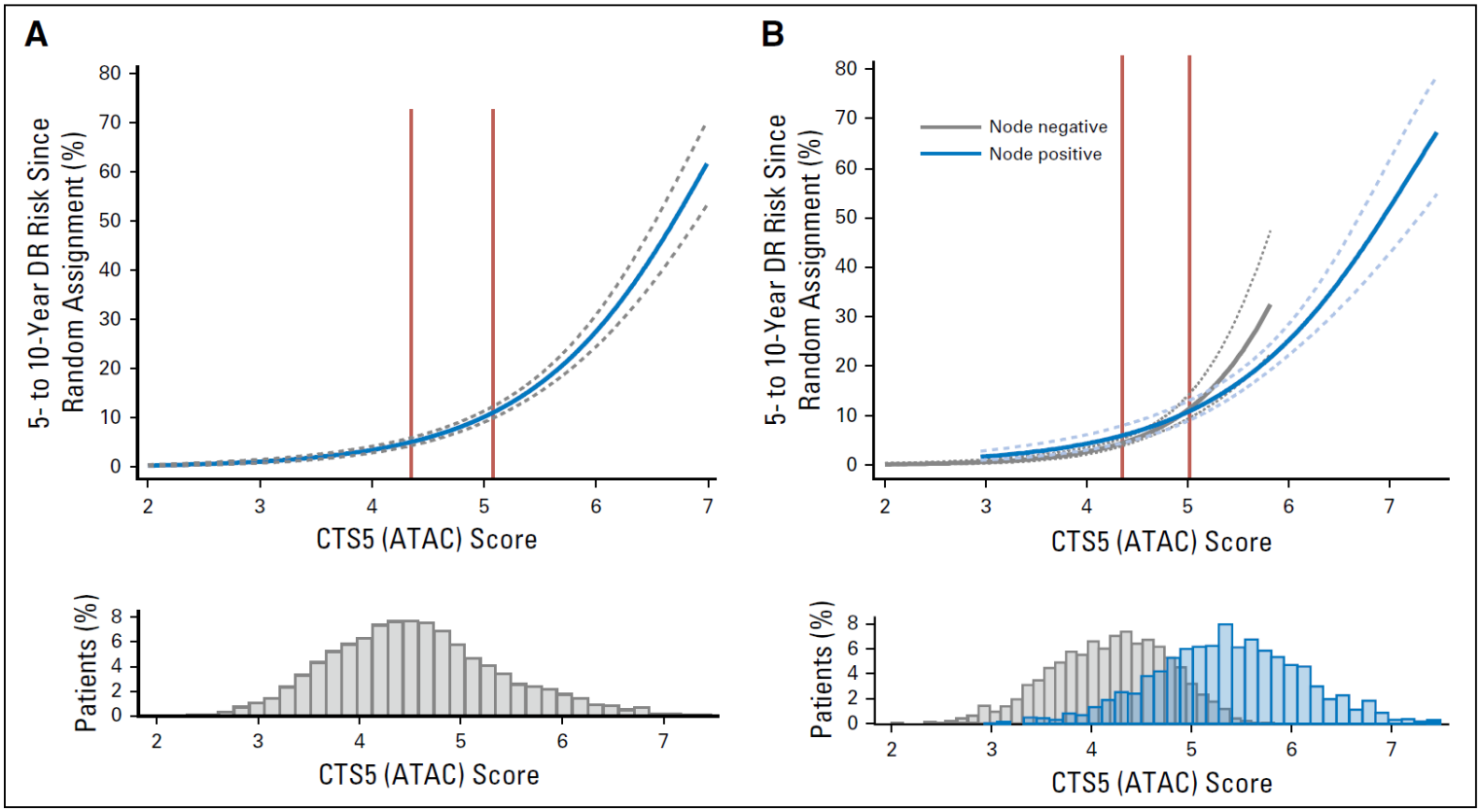


Fig 1. Predicted distant recurrence (DR) risk in years 5 to 10 since random assignment (start of adjuvant endocrine therapy) for ATAC (Arimidex, Tamoxifen, Alone or Combination) trial (A) overall population and (B) node-negative and node-positive patients. Solid vertical lines indicate cutoff points for risk groups. CTS5, Clinical Treatment Score post–5 years.

Kategoriserte risikogrupper for 5-10 års metastasefri overlevelse (ATAC^{training} - BIG1-98^{validation})

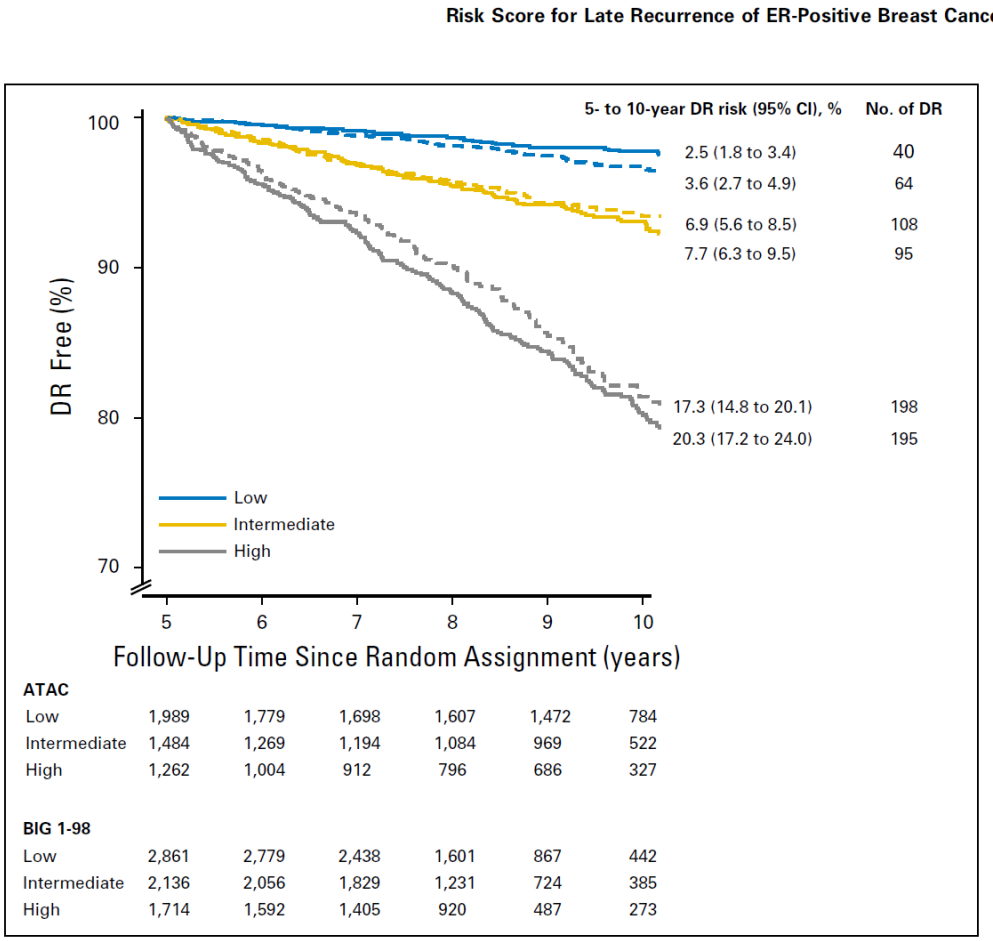


Fig 2. Kaplan-Meier curves and 5- to 10-year distant recurrence (DR) rates since random assignment for the overall population according to trial (solid lines, ATAC [Arimidex, Tamoxifen, Alone or Combination]; dashed lines, BIG [Breast International Group] 1-98).

Prediksjon av metastaserisiko ved hjelp av CTS5 score

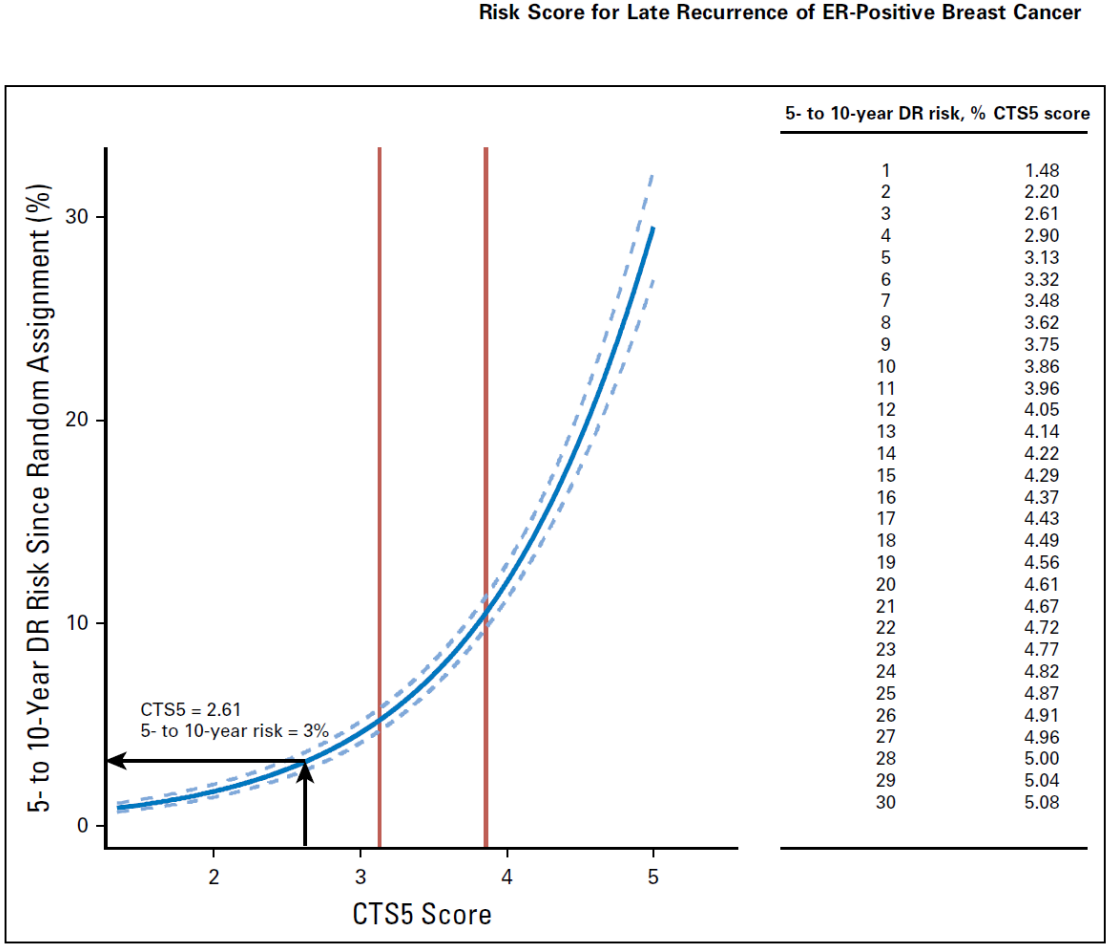


Fig 4. Predicted 5- to 10-year distant recurrence (DR) risk since random assignment and Clinical Treatment Score post–5 years (CTS5) values for the combined data set. Solid vertical lines indicate cutoff points for risk groups. Arrows indicate the CTS5 and equivalent 5- to 10-year risks of a patient age 54 years with a 12-mm, node-negative, grade 2 tumor. Using the formula CTS5 = 0.438 × nodes + 0.988 × (0.093 × size − 0.001 × size2 + 0.375 × grade + 0.017 × age), her CTS5 score is 2.61 and her 5- to 10-year risk of DR is 3%.

NBCG vil inkludere CTS5 score i Handlingsprogrammet til hjelp for beslutning om bruk av utvidet adjuvant endokrin behandling

Ovariefunksjonssuppresjon i tillegg til tamoxifen eller AI

Premenopausal adjuvant endokrin behandling

Justering av anbefaling i nytt Handlingsprogram

- Ovariefunksjonsuppresjon (OFS) med goserelin i tillegg til tamoxifen eller AI anbefales til følgende pasienter (på bakgrunn av resultatene fra SOFT/TEXT studiene):
  - Pasienter under 35 år hvor det er indikasjon for kjemoterapi. **Ved høy risikoprofil kan det være individuelt grunnlag for å gi goserelin også ved alder over 35 år, men effekten reduseres gradvis med økende alder**.
  - Ut i fra risikoprofil bør pasienter >35 år som ikke mister menstruasjonen etter kjemoterapi eller hvor menstruasjon kommer tilbake innen 8 måneder etter kjemoterapi også vurderes for OFS i tillegg til tamoxifen eller AI (AI kun aktuelt dersom OFS oppstartes og startes 6-8 uker før planlagt oppstart av AI). Vurdering av subtype brystkreft (LumA vs LumB), PgR/Ki67 og stadium kan bidra til å avklare absolutte nytteeffekter og understøtte et behandlingsvalg.

SOFT og TEXT studiene

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tailoring Adjuvant Endocrine Therapy for Premenopausal Breast Cancer

P.A. Francis, O. Pagani, G.F. Fleming, B.A. Walley, M. Colleoni, I. Láng, H.L. Gómez, C. Tondini, E. Ciruelos, H.J. Burstein, H.R. Bonnefoi, M. Bellet, S. Martino, C.E. Geyer, Jr., M.P. Goetz, V. Stearns, G. Pinotti, F. Puglisi, S. Spazzapan, M.A. Climent, L. Pavesi, T. Ruhstaller, N.E. Davidson, R. Coleman, M. Debled, S. Buchholz, J.N. Ingle, E.P. Winer, R. Maibach, M. Rabaglio-Poretti, B. Ruepp, A. Di Leo, A.S. Coates, R.D. Gelber, A. Goldhirsch, and M.M. Regan, for the SOFT and TEXT Investigators and the International Breast Cancer Study Group*

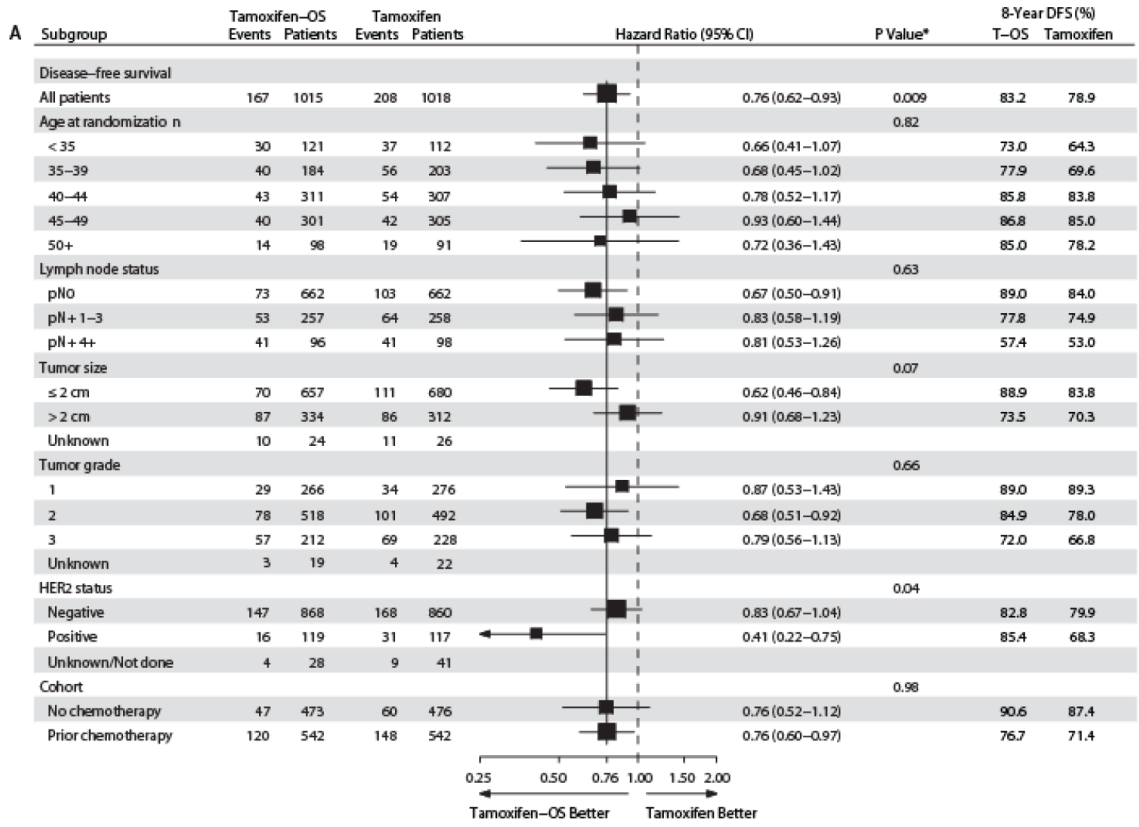
This article was published on June 4, 2018, at NEJM.org.

DOI: 10.1056/NEJMoa1803164

Tam vs TAM + OFS

Figure S2A. Results of Cox Proportional-hazards Models for the Disease-free Survival (DFS) Treatment Comparison of Tamoxifen plus Ovarian Suppression vs. Tamoxifen Alone in the SOFT Primary Analysis, among All Patients and According to Subgroups.

Median follow-up in SOFT was 8 years. The solid vertical line is placed at 0.76, the hazard-ratio estimate for all patients. The x-axis is scaled according to the natural logarithm of the hazard ratio. The size of the square is inversely proportional to the standard error of the hazard ratio.

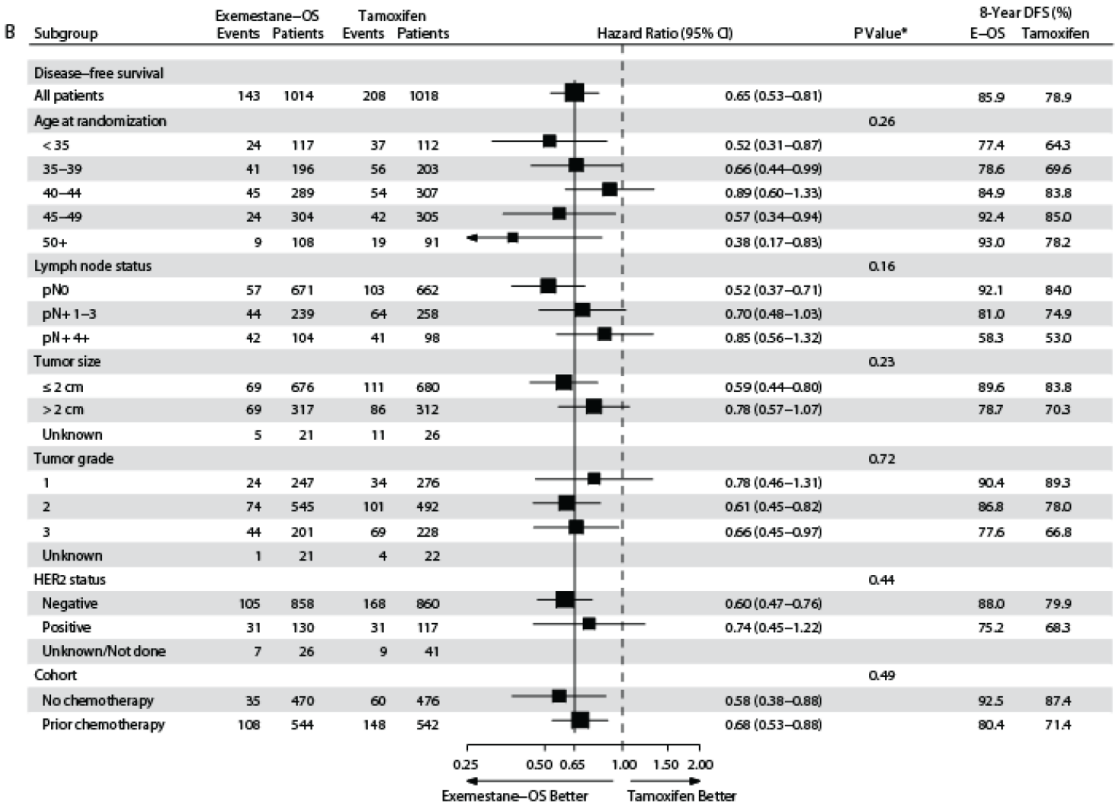


A Subgroup	Tamoxifen–OS Events	Tamoxifen–OS Patients	Tamoxifen Events	Tamoxifen Patients	Hazard Ratio (95% CI)	P Value*	8-Year DFS (%) T–OS	8-Year DFS (%) Tamoxifen
Disease–free survival								
All patients	167	1015	208	1018	0.76 (0.62–0.93)	0.009	83.2	78.9
Age at randomizatio n						0.82		
< 35	30	121	37	112	0.66 (0.41–1.07)		73.0	64.3
35–39	40	184	56	203	0.68 (0.45–1.02)		77.9	69.6
40–44	43	311	54	307	0.78 (0.52–1.17)		85.8	83.8
45–49	40	301	42	305	0.93 (0.60–1.44)		86.8	85.0
50+	14	98	19	91	0.72 (0.36–1.43)		85.0	78.2
Lymph node status						0.63		
pN0	73	662	103	662	0.67 (0.50–0.91)		89.0	84.0
pN+ 1–3	53	257	64	258	0.83 (0.58–1.19)		77.8	74.9
pN+ 4+	41	96	41	98	0.81 (0.53–1.26)		57.4	53.0
Tumor size						0.07		
≤ 2 cm	70	657	111	680	0.62 (0.46–0.84)		88.9	83.8
> 2 cm	87	334	86	312	0.91 (0.68–1.23)		73.5	70.3
Unknown	10	24	11	26				
Tumor grade						0.66		
1	29	266	34	276	0.87 (0.53–1.43)		89.0	89.3
2	78	518	101	492	0.68 (0.51–0.92)		84.9	78.0
3	57	212	69	228	0.79 (0.56–1.13)		72.0	66.8
Unknown	3	19	4	22				
HER2 status						0.04		
Negative	147	868	168	860	0.83 (0.67–1.04)		82.8	79.9
Positive	16	119	31	117	0.41 (0.22–0.75)		85.4	68.3
Unknown/Not done	4	28	9	41				
Cohort						0.98		
No chemotherapy	47	473	60	476	0.76 (0.52–1.12)		90.6	87.4
Prior chemotherapy	120	542	148	542	0.76 (0.60–0.97)		76.7	71.4

Tam vs Exe + OFS

Figure S2B. Results of Cox Proportional-hazards Models for the Disease-free Survival (DFS) Treatment Comparison of Exemestane Plus Ovarian Suppression vs. Tamoxifen Alone in SOFT, among All Patients and According to Subgroups.

Median follow-up in SOFT was 8 years. The solid vertical line is placed at 0.65, the hazard-ratio estimate for all patients. The x-axis is scaled according to the natural logarithm of the hazard ratio. The size of the square is inversely proportional to the standard error of the hazard ratio.



B

Subgroup	Exemestane–OS Events	Exemestane–OS Patients	Tamoxifen Events	Tamoxifen Patients	Hazard Ratio (95% CI)	P Value*	8-Year DFS (%) E–OS	8-Year DFS (%) Tamoxifen
Disease–free survival								
All patients	143	1014	208	1018	0.65 (0.53–0.81)		85.9	78.9
Age at randomization						0.26		
< 35	24	117	37	112	0.52 (0.31–0.87)		77.4	64.3
35–39	41	196	56	203	0.66 (0.44–0.99)		78.6	69.6
40–44	45	289	54	307	0.89 (0.60–1.33)		84.9	83.8
45–49	24	304	42	305	0.57 (0.34–0.94)		92.4	85.0
50+	9	108	19	91	0.38 (0.17–0.83)		93.0	78.2
Lymph node status						0.16		
pN0	57	671	103	662	0.52 (0.37–0.71)		92.1	84.0
pN+ 1–3	44	239	64	258	0.70 (0.48–1.03)		81.0	74.9
pN+ 4+	42	104	41	98	0.85 (0.56–1.32)		58.3	53.0
Tumor size						0.23		
≤ 2 cm	69	676	111	680	0.59 (0.44–0.80)		89.6	83.8
> 2 cm	69	317	86	312	0.78 (0.57–1.07)		78.7	70.3
Unknown	5	21	11	26				
Tumor grade						0.72		
1	24	247	34	276	0.78 (0.46–1.31)		90.4	89.3
2	74	545	101	492	0.61 (0.45–0.82)		86.8	78.0
3	44	201	69	228	0.66 (0.45–0.97)		77.6	66.8
Unknown	1	21	4	22				
HER2 status						0.44		
Negative	105	858	168	860	0.60 (0.47–0.76)		88.0	79.9
Positive	31	130	31	117	0.74 (0.45–1.22)		75.2	68.3
Unknown/Not done	7	26	9	41				
Cohort						0.49		
No chemotherapy	35	470	60	476	0.58 (0.38–0.88)		92.5	87.4
Prior chemotherapy	108	544	148	542	0.68 (0.53–0.88)		80.4	71.4

SOFT
DFS

Exe+OFS>Tam+OFS>Tam

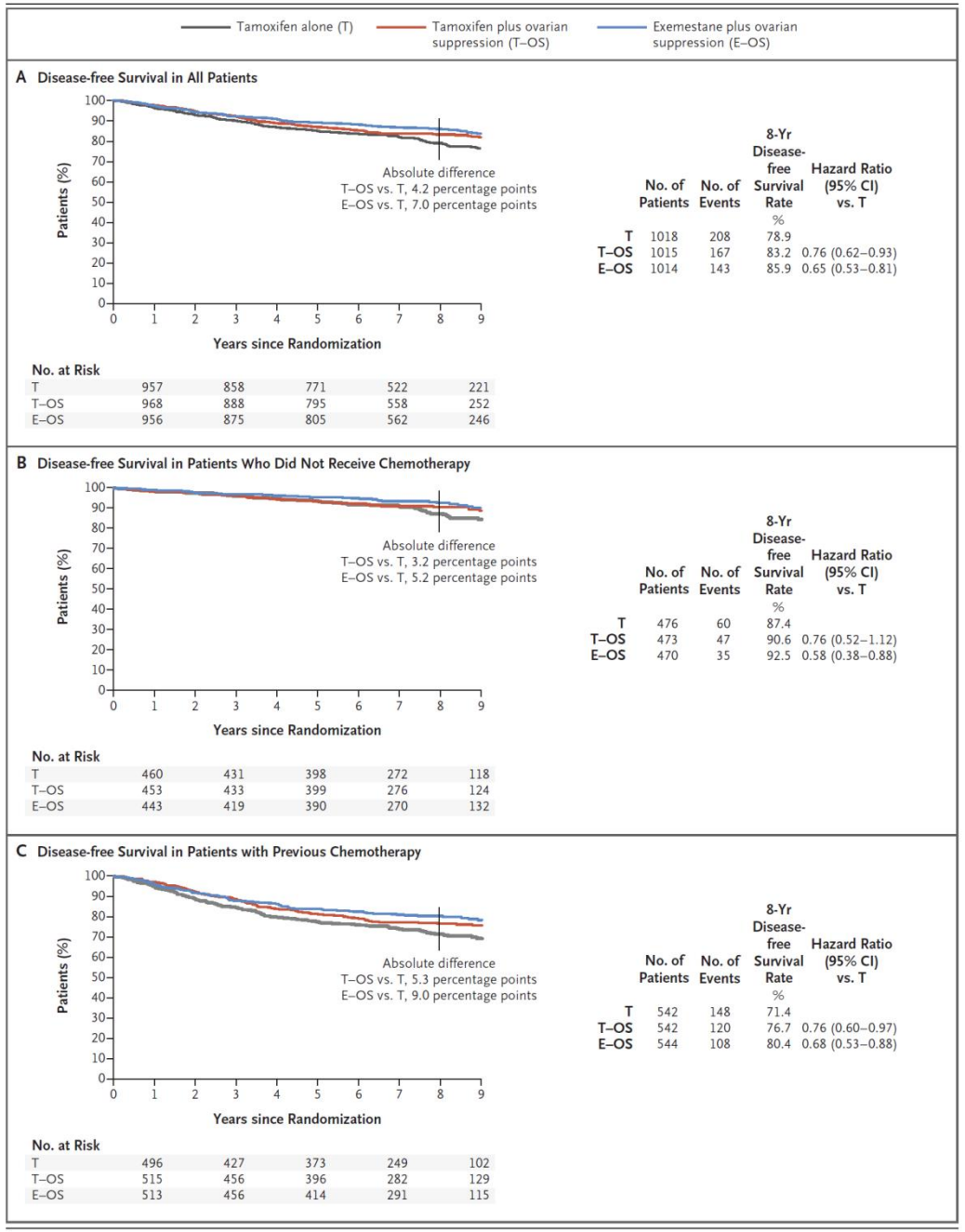


Figure 2 (facing page). Kaplan–Meier Estimates of Disease-free Survival after a Median Follow-up of 8 Years in SOFT.

Shown are Kaplan–Meier estimates of the rates of disease-free survival in SOFT according to treatment assignment — tamoxifen alone (T), tamoxifen plus ovarian suppression (T–OS), or exemestane plus ovarian suppression (E–OS) — among all the patients in the trial (Panel A) and according to chemotherapy status (Panels B and C). In Panel A, tamoxifen plus ovarian suppression resulted in a 24% lower relative risk of recurrence, a second invasive cancer, or death than tamoxifen alone (P = 0.009). In each panel, the 8-year data are highlighted by a black vertical line. The hazard ratios are for disease recurrence, a second invasive cancer, or death.

SOFT+TEXT

DDFS og DFS: Exe+OFS>Tam+OFS
OS: Exe+OFS = Tam+OFS

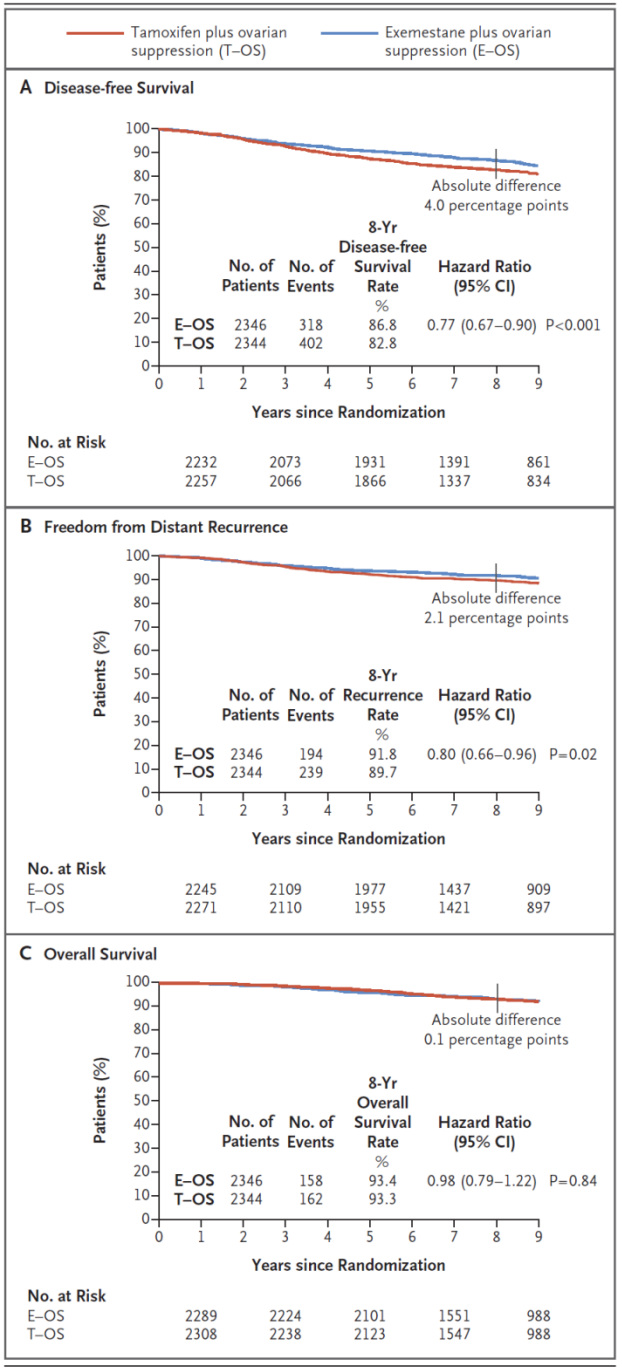


Figure 5. Kaplan–Meier Estimates of Disease-free Survival, Freedom from Distant Recurrence, and Overall Survival in the Combined SOFT and TEXT Population.

Shown are estimates of disease-free survival (Panel A), freedom from distant recurrence (Panel B), and overall survival (Panel C) among patients who received tamoxifen plus ovarian suppression (T–OS) and those who received exemestane plus ovarian suppression (E–OS) after a median follow-up of 9 years in the combined population. In each panel, the 8-year data are highlighted by a black vertical line. The hazard ratio in Panel A is for disease recurrence, a second invasive cancer, or death. In Panels B and C, the hazard ratios are for distant recurrence of breast cancer and for death, respectively. The 8-year values are based on Kaplan–Meier estimates of the time to an event.

Legges inn kommentar i Handlingsprogrammet:

Kombinasjonen Exe + OFS gav bedre DFS og DDFS enn Tam + OFS

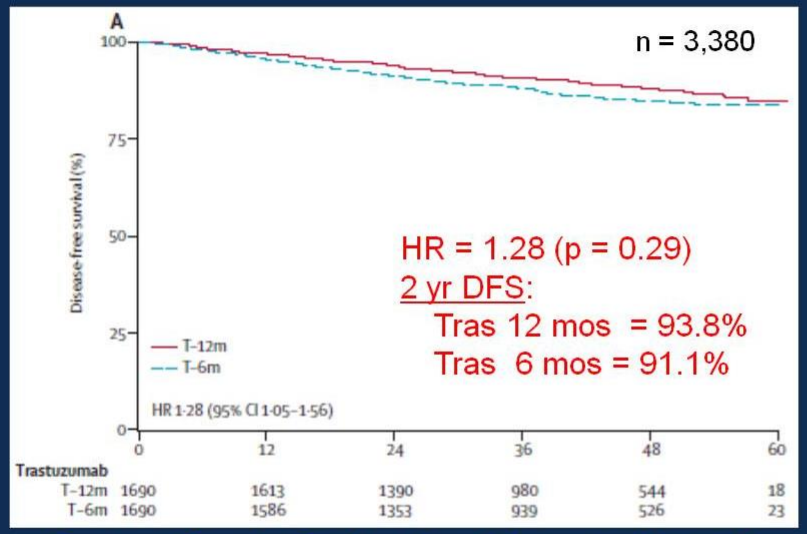
HER2 positiv brystkreft

Hvor lenge skal vi gi adjuvant trastuzumab

Studier av redusert lengde på behandling med trastuzumab

PHARE Study

Non-inferiority study; pre-specified HR 1.15



HR = 1.28 (p = 0.29)

2 yr DFS:

Tras 12 mos = 93.8%

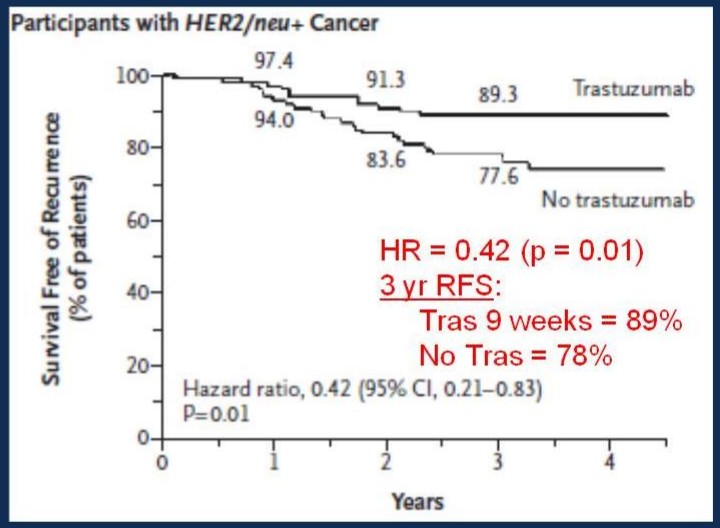
Tras 6 mos = 91.1%

6 months inferior to 12 months of trastuzumab

Pivot et al. Lancet Oncology 2013

FINHER study

Subset with HER2+ disease



HR = 0.42 (p = 0.01)

3 yr RFS:

Tras 9 weeks = 89%

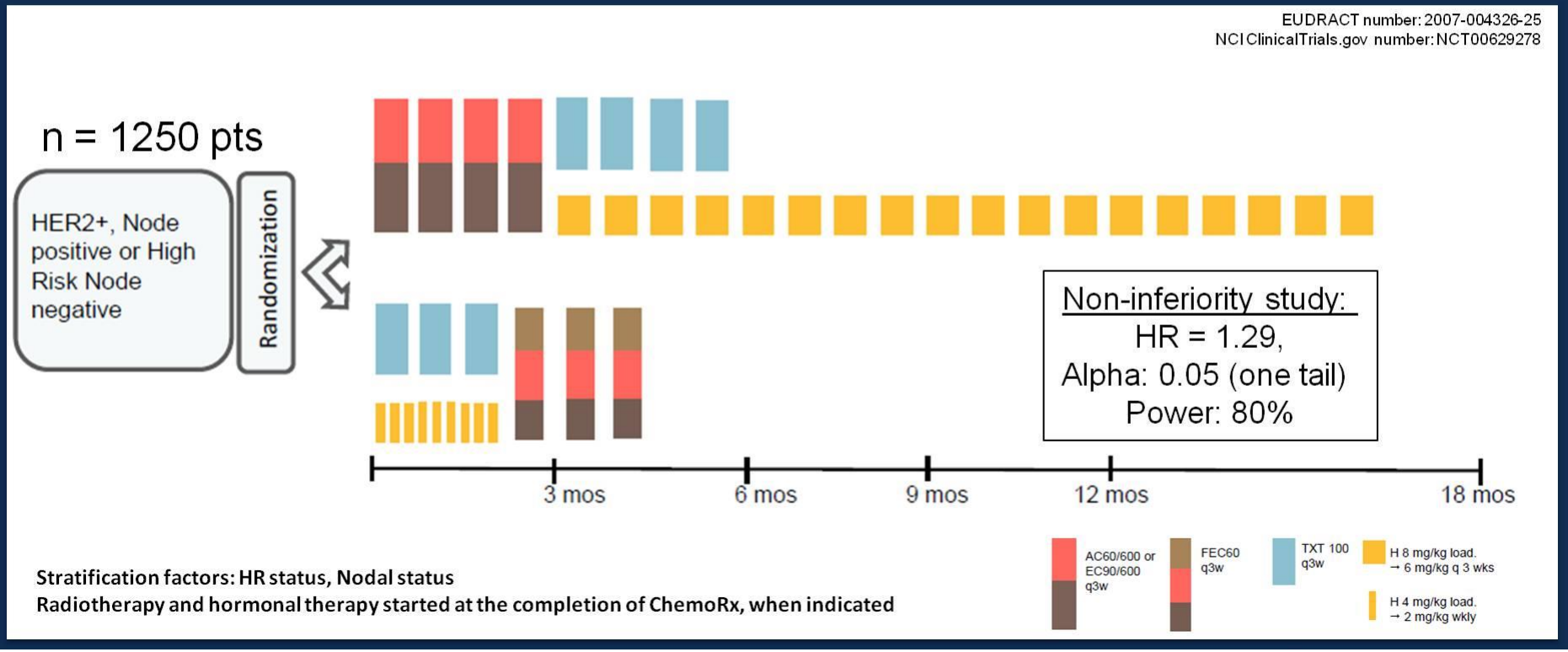
No Tras = 78%

Benefit for only 9 weeks of trastuzumab

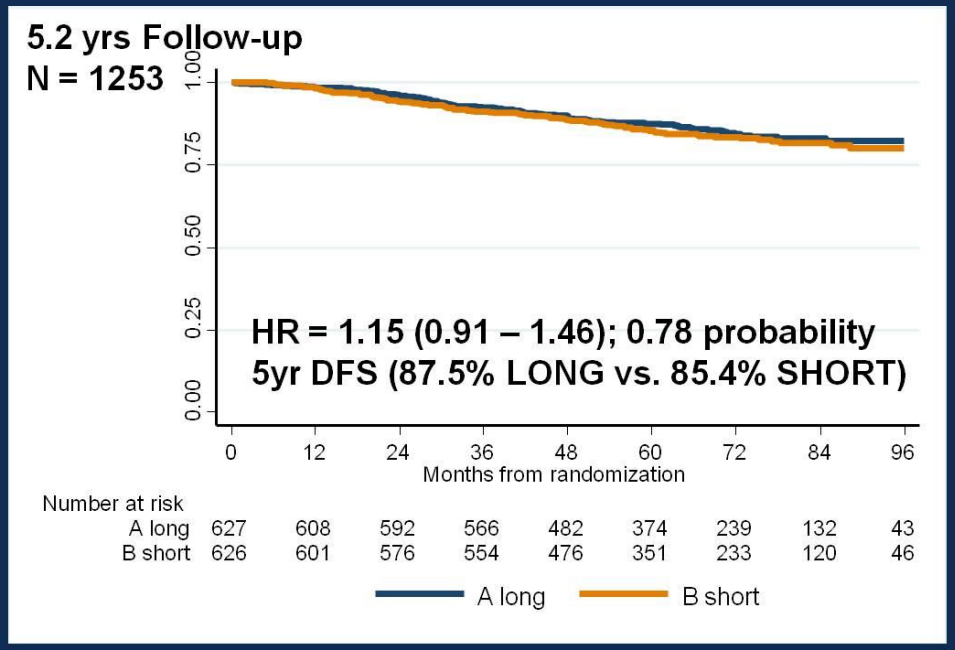
Joensuu H et al. NEJM 2006

9 uker versus 12 mnd trastuzumab

Short-HER: Study Design



SHORTHer Primary Objective of DFS



Subset Analyses:

	Ratio of HRs (90%CI)	p-value
Stage III vs I+II	**2.30** (1.35, 3.94)	**< 0.001**
Nodal status N2+N3 vs N0+N1	**2.25** (1.33, 3.83)	**< 0.001**

HR>1.0 favors LONG

No difference in 5 yr OS (95.1 vs 95%)

Studien viste ikke non-inferiority

JAMA Oncology | Original Investigation

Effect of Adjuvant Trastuzumab for a Duration of 9 Weeks vs 1 Year With Concomitant Chemotherapy for Early Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer
The SOLD Randomized Clinical Trial

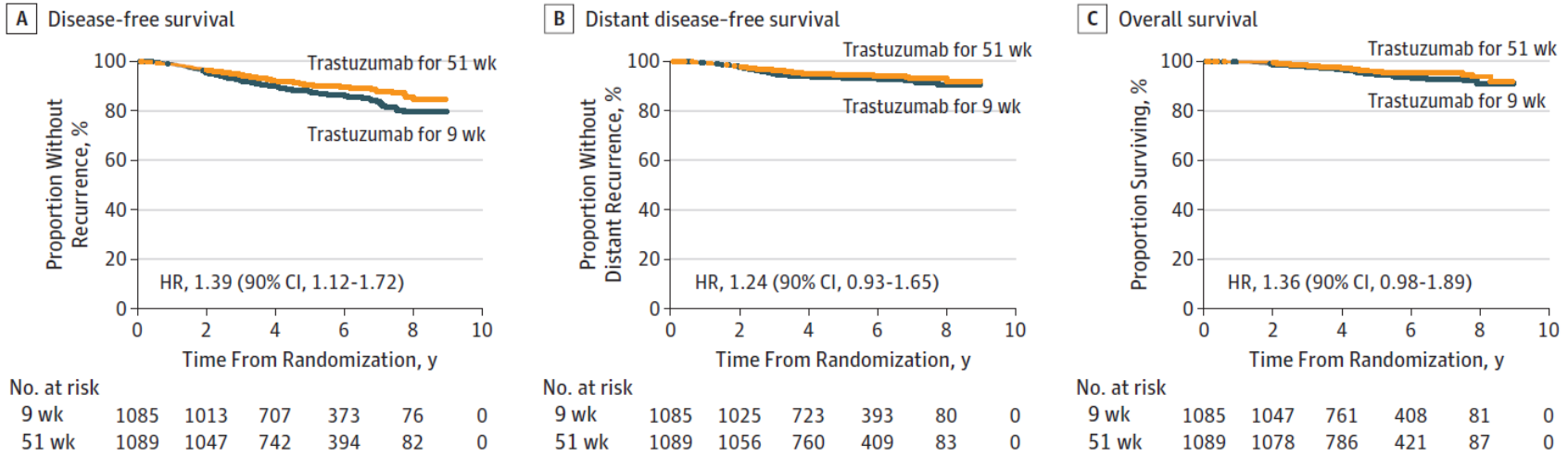
Heikki Joensuu, MD; Judith Fraser, MD; Hans Wildiers, MD; Riikka Huovinen, MD; Päivi Auvinen, MD; Meri Utriainen, MD; Paul Nyandoto, MD; Kenneth K. Villman, MD; Päivi Halonen, MD; Helena Granstam-Björneklett, MD; Lotta Lundgren, MD; Liisa Sailas, MD; Taina Turpeenniemi-Hujanen, MD; Minna Tanner, MD; Jeffrey Yachnin, MD; Diana Ritchie, MD; Oskar Johansson, MD; Teppo Huttunen, MSci; Patrick Neven, MD; Peter Canney, MD; Vernon J. Harvey, MD; Pirkko-Liisa Kellokumpu-Lehtinen, MD; Henrik Lindman, MD

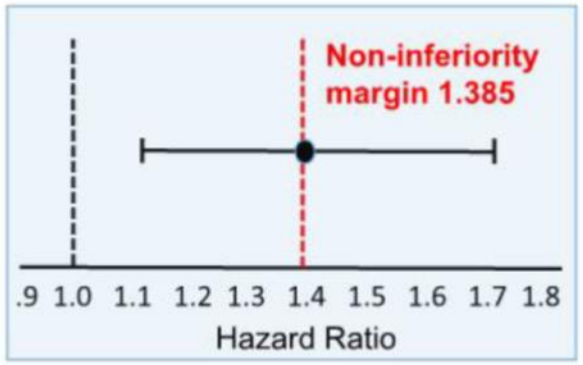
CONCLUSIONS AND RELEVANCE Nine weeks of trastuzumab was not noninferior to 1 year of trastuzumab when given with similar chemotherapy. Cardiac safety was better in the 9-week group. The docetaxel dosing with trastuzumab requires further study.

JAMA Oncol. doi:10.1001/jamaoncol.2018.1380
Published online May 31, 2018.

Survival outcomes

Figure 2. Kaplan-Meier Estimates of Survival Outcomes





PERSEPHONE (ASCO 2018)

- PERSEPHONE: 6 versus 12 months (m) of adjuvant trastuzumab in patients (pts) with HER2 positive (+) early breast cancer (EBC): Randomised phase 3 non-inferiority trial with definitive 4-year (yr) disease-free survival (DFS) results (n=4089).
- Conclusion:
  PERSEPHONE demonstrated 6months of trastuzumab as non-inferior to 12months (3% non-inferiority margin). Given cardiac and other toxicities during months 7-12 of treatment, our results would support a reduction of standard trastuzumab duration to 6 months

NBCGs konklusjon

- Persephone: 12 mnd behandling bedre for pasientene som har samme behandlingsopplegg som i Norge i dag (EC/AC etterfulgt av taxan+trastuzumab)
- Ingen endring i behandlingsanbefaling, men:
- Størstedelen av trastuzumab-effekten er knyttet til første del av behandlingen (9-26 uker) – viktig ved intoleranse/komorbiditet – vil beskrives i Handlingsprogrammet

Redusert bruk av kjemoterapi ved HER2 positive svulster med pT1 pN0 status

The NEW ENGLAND JOURNAL of MEDICINE

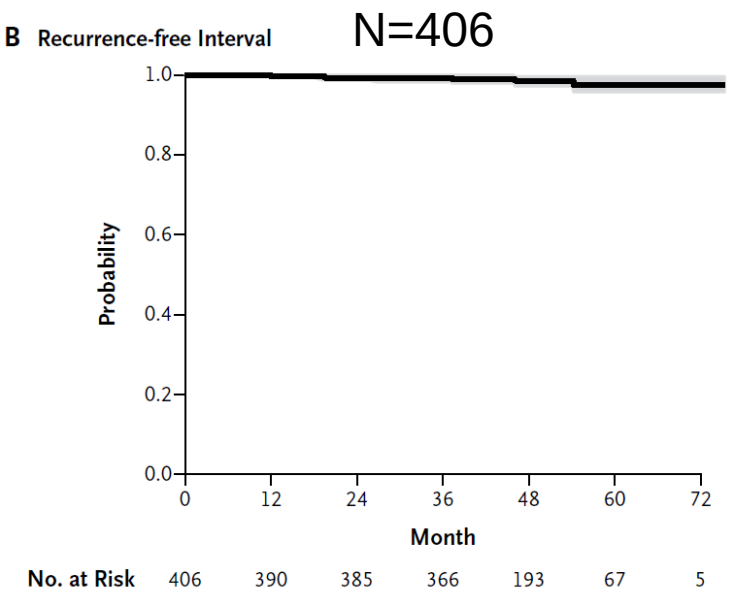
ORIGINAL ARTICLE

Adjuvant Paclitaxel and Trastuzumab for Node-Negative, HER2-Positive Breast Cancer

Sara M. Tolaney, M.D., M.P.H., William T. Barry, Ph.D., Chau T. Dang, M.D., Denise A. Yardley, M.D., Beverly Moy, M.D., M.P.H., P. Kelly Marcom, M.D., Kathy S. Albain, M.D., Hope S. Rugo, M.D., Matthew Ellis, M.B., B.Chir., Ph.D., Iuliana Shapira, M.D., Antonio C. Wolff, M.D., Lisa A. Carey, M.D., Beth A. Overmoyer, M.D., Ann H. Partridge, M.D., M.P.H., Hao Guo, M.S., Clifford A. Hudis, M.D., Ian E. Krop, M.D., Ph.D., Harold J. Burstein, M.D., Ph.D., and Eric P. Winer, M.D.

point. Six patients had a local or regional recurrence or a distant recurrence or died from breast cancer (Table 2). The 3-year rate of recurrence-free survival was 99.2% (95% CI, 98.4 to 100) (Fig. 2B).

N Engl J Med. 2015 Jan 8;372(2):134-41



6 pasienter (1.5%) med lokoregionale residiv, metastaser eller død av brystkreft i løpet av median 4 års observasjonstid

Oppdatert med 7 års FU ASCO 2017 (Abs #511)

pT1 pN0 HER2+ brystkreft

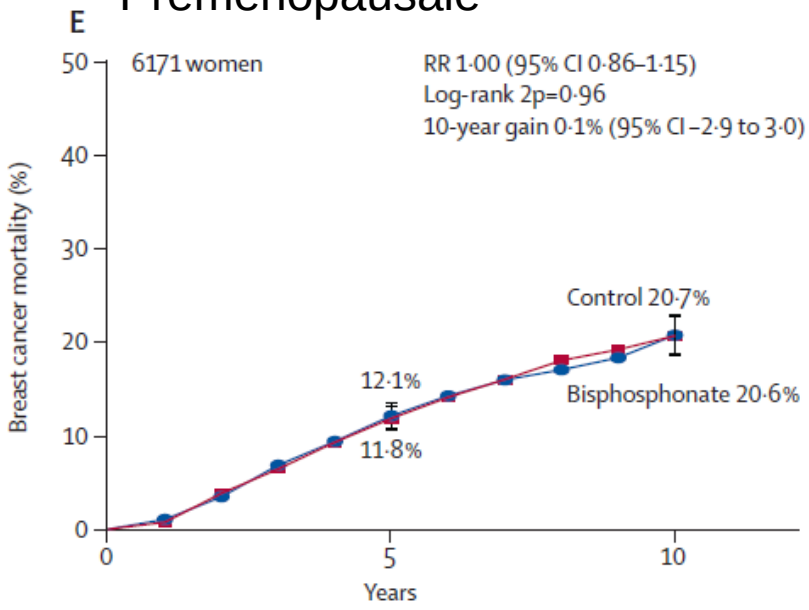
- Trastuzumab 12 mnd + paclitaxel 12 uker for de fleste
- Docetaxel 3qw 100 mg/m2 + trastuzumab kan benyttes som alternativ

Zoledronsyre i adjuvant

Ved dårlig tolerabilitet – finnes alternativ behandling?

Bedret brystkreftspesifikk overlevelse ved bruk av bisfosfonat hos postmenopausale i adjuvant behandling (HR 0.74)

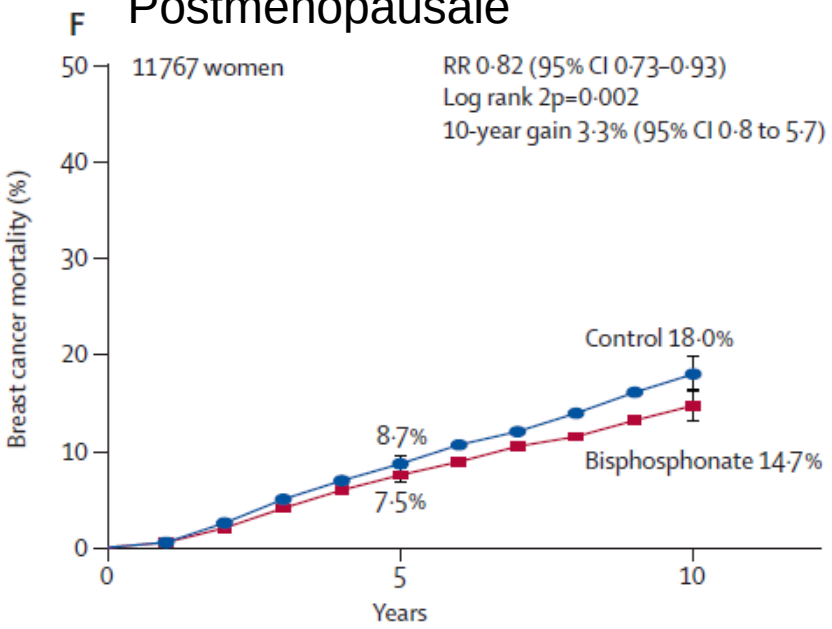
Premenopausale



Death rates (%/year: total rate minus rate in women without recurrence) and log-rank statistics

Allocation	Years 0–4	Years 5–9	Years ≥10
Bisphosphonate	2·43 (2·16–2·69)	2·26 (1·84–2·67)	1·13 (0·58–1·68)
Control	2·50 (2·22–2·79)	2·03 (1·65–2·40)	1·29 (0·71–1·88)
Rate ratio (95% CI)	0·97 (0·81–1·14)	1·10 (0·81–1·40)	0·71 (0·34–1·50)
from (O–E)/V	−3·3/130·6	5·0/50·0	−2·3/6·9

Postmenopausale



Death rates (%/year: total rate minus rate in women without recurrence) and log-rank statistics

Allocation	Years 0–4	Years 5–9	Years ≥10
Bisphosphonate	1·56 (1·41–1·72)	1·57 (1·30–1·84)	1·30 (0·34–2·26)
Control	1·74 (1·58–1·91)	2·04 (1·74–2·35)	2·73 (1·30–4·16)
Rate ratio (95% CI)	0·86 (0·72–0·99)	0·76 (0·55–0·97)	0·52 (0·18–1·44)
from (O–E)/V	−27·1/174·9	−18·0/65·0	−2·4/3·6

Category	Events/women		Bisphosphonate events		Ratio of annual event rates bisphosphonate : control	Rate ratio (CI)
	Allocated bisphosphonate	Allocated control	Log-rank O–E	Variance of O–E		
(a) Age, years (trend χ^2_1=4·9; 2p=0·03)						
<45	164/2475 (6·6%)	151/2141 (7·1%)	−0·3	71·3		1·00 (0·79–1·26)
45–54	152/3532 (4·3%)	173/3224 (5·4%)	−14·2	74·3		0·83 (0·61–1·11)
55–69	168/3314 (5·1%)	196/3022 (6·5%)	−25·1	84·4		0·74 (0·56–0·98)
≥70	13/531 (2·4%)	22/521 (4·2%)	−5·1	7·1		0·49 (0·19–1·29)

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JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Use of Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer: A Cancer Care Ontario and American Society of Clinical Oncology Clinical Practice Guideline

Sukhbinder Dhesy-Thind, Glenn G. Fletcher, Phillip S. Blanchette, Mark J. Clemons, Melissa S. Dillmon, Elizabeth S. Frank, Sonal Gandhi, Rasna Gupta, Mihaela Mates, Beverly Moy, Ted Vandenberg, and Catherine H. Van Poznak

Author affiliations and support information (if applicable) appear at the end of this article.

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ASCO Clinical Practice Guidelines Committee Approved: September 15, 2016. PEBC Report Approval Panel Approved: June 15, 2016

All work produced by the Program in Evidence-Based Care is editorially independent from the Ontario Ministry of Health and Long-Term Care.

Editor's note: This joint Cancer Care Ontario and the American Society of Clinical Oncology clinical practice guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a Data Supplement with the systematic review, a Methodology Supplement, slide sets, clinical tools and resources, is available at www.asco.org/breast-cancer-adjuvant-bisphosphonates-guideline and www.asco.org/guidelineswiki, and https://www.cancercareontario.ca/guidelines-advice/types-of-cancer/breast.

Corresponding author: American Society of Clinical Oncology, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; e-mail: guidelines@asco.org.

0732-183X/17/3518w-2062w/$20.00

ABSTRACT

Purpose

To make recommendations regarding the use of bisphosphonates and other bone-modifying agents as adjuvant therapy for patients with breast cancer.

Methods

Cancer Care Ontario and ASCO convened a Working Group and Expert Panel to develop evidence-based recommendations informed by a systematic review of the literature.

Results

Adjuvant bisphosphonates were found to reduce bone recurrence and improve survival in postmenopausal patients with nonmetastatic breast cancer. In this guideline, postmenopausal includes patients with natural menopause or that induced by ovarian suppression or ablation. Absolute benefit is greater in patients who are at higher risk of recurrence, and almost all trials were conducted in patients who also received systemic therapy. Most studies evaluated zoledronic acid or clodronate, and data are extremely limited for other bisphosphonates. While denosumab was found to reduce fractures, long-term survival data are still required.

Recommendations

It is recommended that, if available, zoledronic acid (4 mg intravenously every 6 months) or clodronate (1,600 mg/d orally) be considered as adjuvant therapy for postmenopausal patients with breast cancer who are deemed candidates for adjuvant systemic therapy. Further research comparing different bone-modifying agents, doses, dosing intervals, and durations is required. Risk factors for osteonecrosis of the jaw and renal impairment should be assessed, and any pending dental or oral health problems should be dealt with prior to starting treatment. Data for adjuvant denosumab look promising but are currently insufficient to make any recommendation. Use of these agents to reduce fragility fractures in patients with low bone mineral density is beyond the scope of the guideline. Recommendations are not meant to restrict such use of bone-modifying agents in these situations.

Additional information at www.asco.org/breast-cancer-adjuvant-bisphosphonates-guideline, www.asco.org/guidelineswiki, https://www.cancercareontario.ca/guidelines-advice/types-of-cancer/breast.

ASCO guideline keypoints/NBCGs vurdering

- Zoledronsyre eller klodronat anbefales til postmenopausale pasienter med indikasjon for systemisk adjuvant behandling
- Hva menes med postmenopausal: naturlig postmenopausal ved oppstart av systemisk adjuvant behandling eller indusert postmenopausal ved bruk av goserelin + tam eller AI hos yngre kvinner
- Amenorre etter kjemoterapi gir ikke grunnlag for adjuvant bisfosfonat
- Denosumab ved manglende tolerabilitet?
  DFS data (ut over abstracts) er ikke publisert; ASCO presenterte ABCSG18 (positiv DSF studie) og D-CARE (negativ studie): Konklusjon: foreløpig nei

Bruk av aromatasehemmer

Etter kjemoterapiindusert amenorre

Risiko for tilbakekomst av ovarialfunksjon?

OXFORD

JNCI J Natl Cancer Inst (2017) 109(12): djx074

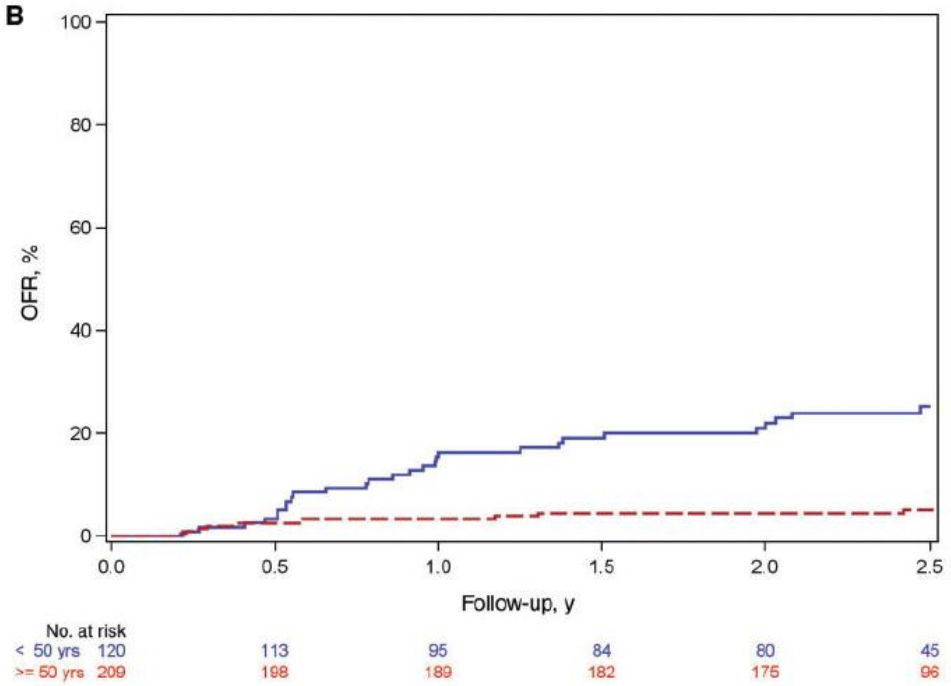
doi: 10.1093/jnci/djx074
First published online May 30, 2017
Article

ARTICLE

Ovarian Function Recovery During Anastrozole in Breast Cancer Patients With Chemotherapy-Induced Ovarian Function Failure

Irene E. G. van Hellemond, Ingeborg J. H. Vriens, Petronella G. M. Peer, Astrid C. P. Swinkels, Carolien H. Smorenburg, Caroline M. Seynaeve, Maurice J. C. van der Sangen, Judith R. Kroep, Hiltje de Graaf, Aafke H. Honkoop, Frans L. G. Erdkamp, Franchette W. P. J. van den Berkmortel, Jos J. E. M. Kitzen, Maaike de Boer, Wilfred K. de Roos, Sabine C. Linn, Alexander L. T. Imholz, Vivianne C. G. Tjan-Heijnen; on behalf of the Dutch Breast Cancer Research Group (BOOG)

Resultat



- N= 329
- 12 months after AI:
  8.1% Ovarian Failure Recovery
- 36 months after AI – 12.4%
  OFR (39 patients)

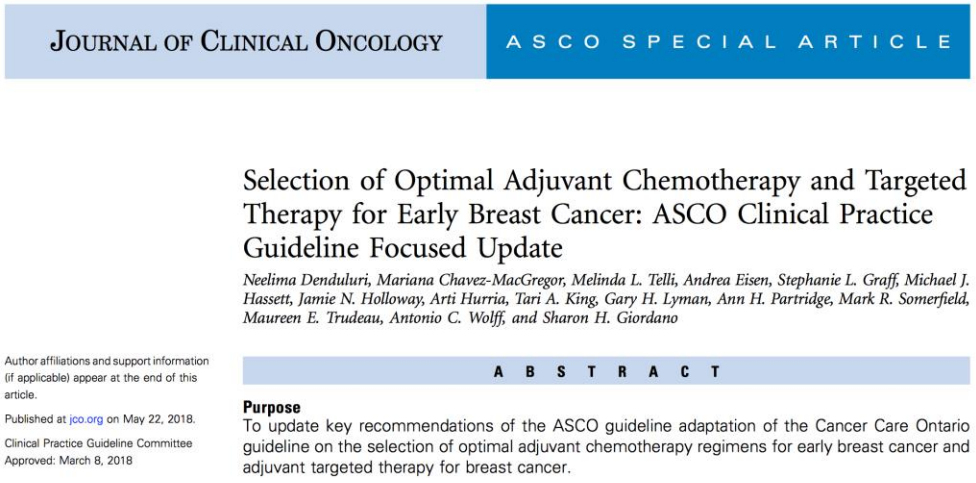
- 11 (28%) 50 years or older
- > 50 years → OFR 5.1%
- < 50 years → OFR 25.2%
- 19 of 39 (48.7%) patients reported vaginal bleeding

NBCG konklusjon (=konklusjon i artikkelen)

- **Viktig å monitorere hormonnivåer (østradiol) etter kjemoterapiindusert amenore under AI behandling, og det bør gjøres gjentatt spesielt i det første behandlingsåret**

ASCO recommendation update – adjuvant treatment

- Patients with early-stage HER2-negative breast cancer with pathologic invasive residual disease at surgery following standard anthracycline- and taxane-based preoperative therapy may be offered up to six to eight cycles of adjuvant capecitabine.
- Clinicians may add 1 year of adjuvant pertuzumab to trastuzumab-based combination chemotherapy in patients with high-risk, early-stage, HER2-positive breast cancer.
- Clinicians may use extended adjuvant therapy with neratinib to follow trastuzumab in patients with early-stage, HER2-positive breast cancer. (Neratinib causes substantial diarrhea, and diarrhea prophylaxis must be used.)



JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Clinical Practice Guideline Focused Update

Neelima Denduluri, Mariana Chavez-MacGregor, Melinda L. Telli, Andrea Eisen, Stephanie L. Graff, Michael J. Hassett, Jamie N. Holloway, Arti Hurria, Tari A. King, Gary H. Lyman, Ann H. Partridge, Mark R. Somerfield, Maureen E. Trudeau, Antonio C. Wolff, and Sharon H. Giordano

Author affiliations and support information (if applicable) appear at the end of this article.

Published at jco.org on May 22, 2018.

Clinical Practice Guideline Committee Approved: March 8, 2018

A B S T R A C T

Purpose

To update key recommendations of the ASCO guideline adaptation of the Cancer Care Ontario guideline on the selection of optimal adjuvant chemotherapy regimens for early breast cancer and adjuvant targeted therapy for breast cancer.

Create-X

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy

N. Masuda, S.-J. Lee, S. Ohtani, Y.-H. Im, E.-S. Lee, I. Yokota, K. Kuroi, S.-A. Im, B.-W. Park, S.-B. Kim, Y. Yanagita, S. Ohno, S. Takao, K. Aogi, H. Iwata, J. Jeong, A. Kim, K.-H. Park, H. Sasano, Y. Ohashi, and M. Toi

N Engl J Med 2017;376:2147-59.
DOI: 10.1056/NEJMoa1612645

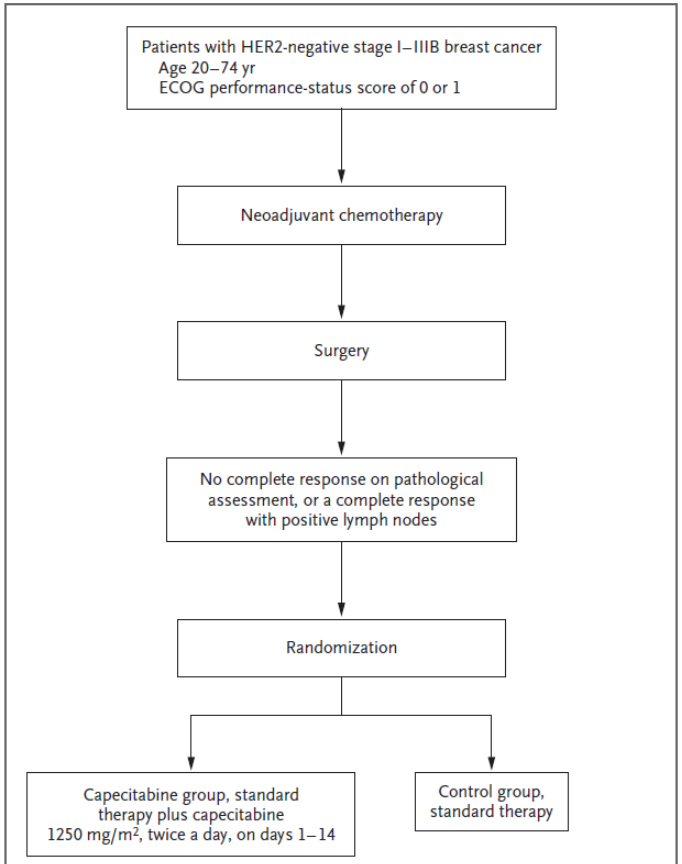


Figure 1. Trial Design.

Neoadjuvant chemotherapy involved at least four cycles of an anthracycline. However, if the anthracycline was administered for less than four cycles, one of the following four regimens could be used: fluorouracil and epirubicin (at a dose of ≥100 mg per square meter of body-surface area) and cyclophosphamide (FEC) for three cycles, followed by docetaxel at a dose of 75 mg per square meter for three cycles; FEC for three cycles, followed by docetaxel at a dose of 75 mg per square meter and cyclophosphamide at a dose of 600 mg per square meter (TC) for three cycles; TC for three cycles, followed by FEC for three cycles; or TC only for four cycles. Patients who had serious adverse events or disease progression were included if they completed at least two cycles of chemotherapy. If patients had positive lymph nodes, combined chemotherapy with an anthracycline and taxane (docetaxel or paclitaxel, as chosen by the physician) was recommended. The Eastern Cooperative Oncology Group (ECOG) performance status is scored on a scale of 0 to 5, with 0 indicating no symptoms and higher scores indicating greater disability related to tumor. Standard therapy included 5 years of endocrine therapy for hormone-receptor–positive cancer, no further systemic treatment for hormone-receptor–negative cancer, and radiotherapy if indicated. HER2 denotes human epidermal growth factor receptor 2.

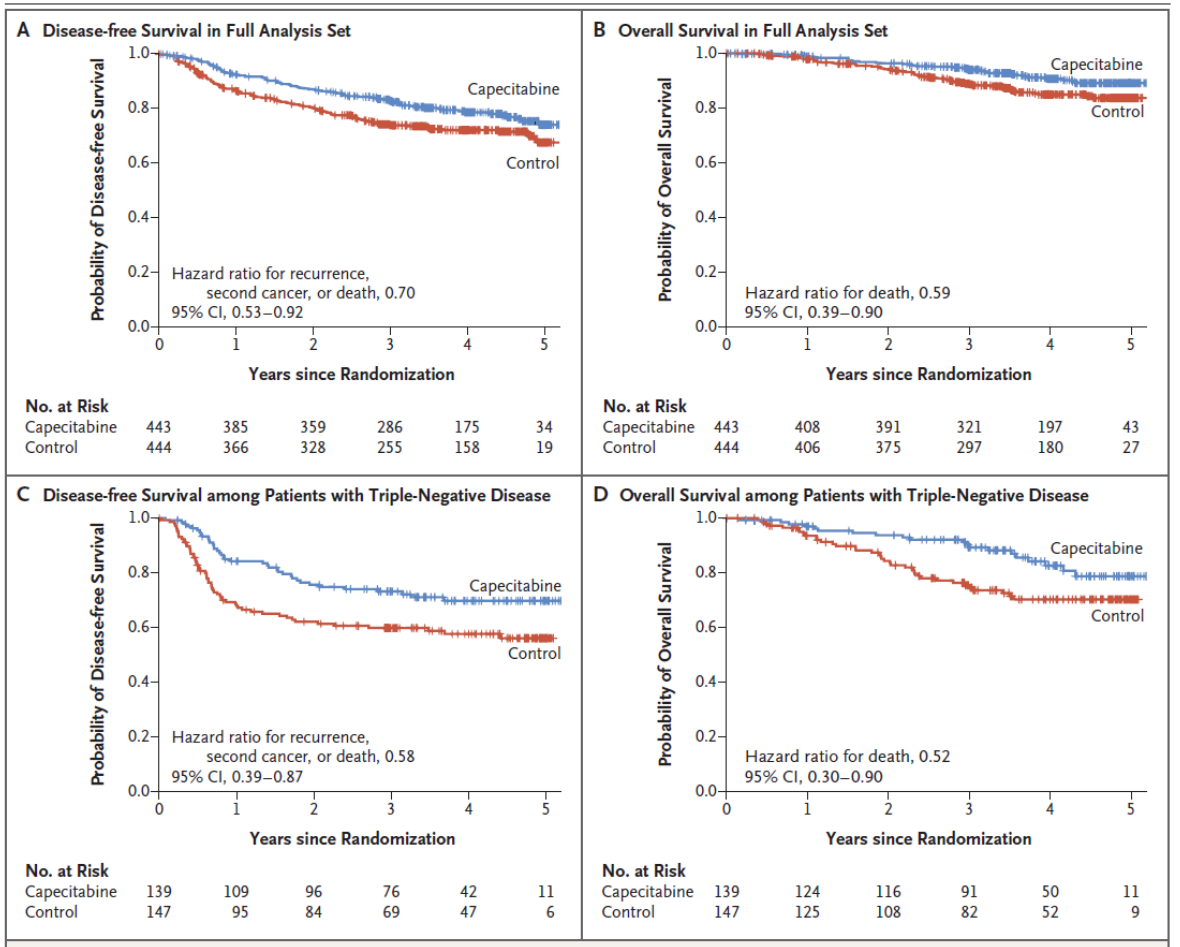


Figure 2. Kaplan–Meier Estimates of Disease-free Survival and Overall Survival.

Panels A and B show disease-free survival and overall survival, respectively, in the full analysis set (primary analysis). Tick marks indicate censored data. Panels C and D show disease-free survival and overall survival, respectively, in the subgroup of patients with triple-negative breast cancer (i.e., breast cancer that was negative for estrogen receptors, progesterone receptors, and HER2).

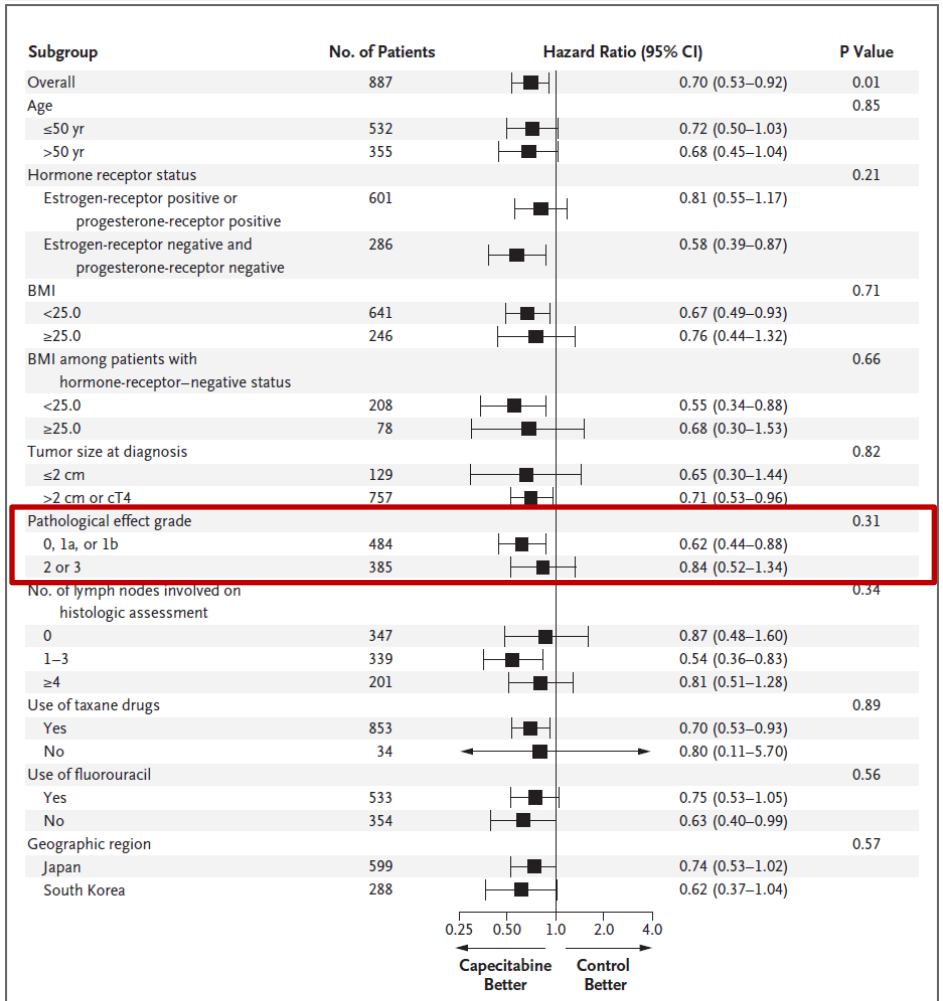


Figure 3. Subgroup Analysis of Disease-free Survival in the Full Analysis Set.

On the basis of the Cox model, prespecified subgroup analyses for background or prognostic factors were conducted to estimate hazard ratios with 95% confidence intervals and to test for interaction among subgroups with the use of two-sided P values. Post hoc subgroup analyses were conducted regarding body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) in all patients and BMI in patients with hormone-receptor–negative disease. A tumor size of cT4 indicates a tumor of any size with direct extension to the chest wall or skin. Data on tumor size were missing for one patient in the capecitabine group. The pathological effect of neoadjuvant chemotherapy was graded from 0 to 3 according to the response criteria of the Japanese Breast Cancer Society[16]: grade 0 indicates no response, grade 1a a mild response, grade 1b a moderate response, grade 2 a marked response, and grade 3 a complete response. Data on pathological effect were missing for nine patients in each group. Arrows indicate that the limits of the confidence interval are not shown.

NBCG mener

- Kun en studie som er publisert med dette behandlingsprinsipp
- Studien har vært kritisert av enkelte på grunn av blant annet manglende informasjon om/dokumentasjon av den neoadjuvante kjemoterapi
- Toksisk behandling
- Vi ønsker å avvente ytterligere studier/internasjonale gjennomganger før ny vurdering

Pertuzumab i kombinasjon med trastuzumab

Etablert i metastatisk situasjon

Hva med adjuvant situasjon?

EMA godkjenning

- Ett års behandling med Perjeta og Herceptin i kombinasjon med kjemoterapi for pasienter med HER2-positiv brystkreft med høy risiko for tilbakefall uavhengig av tidspunkt for kirurgi. Med høy risiko for tilbakefall menes
- HER2-positive pasienter med spredning til axille,
  - reduced risk of recurrence or death by 23% with the Perjeta-based regimen (HR=0.77; 95% CI 0.62-0.96, p=0.019)
- HER2-positive pasienter med HR-negativ sykdom
  - reduced risk of recurrence or death by 24% (HR=0.76; 95% CI 0.56-1.04, p=0.085)

Neoadjuvant behandling med pertuzumab (P), trastuzumab (T) og Docetaxel

5-year analysis of neoadjuvant pertuzumab and trastuzumab in patients with locally advanced, inflammatory, or early-stage HER2-positive breast cancer (NeoSphere): a multicentre, open-label, phase 2 randomised trial

Luca Gianni, Tadeusz Pienkowski, Young-Hyuck Im, Ling-Ming Tseng, Mei-Ching Liu, Ana Lluch, Elżbieta Starosławska, Juan de la Haba-Rodriguez, Seock-Ah Im, Jose Luiz Pedrini, Brigitte Poirier, Paolo Morandi, Vladimir Semiglazov, Vichien Srimuninnimit, Giulia Valeria Bianchi, Domenico Magazzù, Virginia McNally, Hannah Douthwaite, Graham Ross, Pinuccia Valagussa

Summary

Background In the primary analysis of the NeoSphere trial, patients given neoadjuvant pertuzumab, trastuzumab, and docetaxel showed a significantly improved pathological complete response compared with those given trastuzumab and docetaxel after surgery. Here, we report 5-year progression-free survival, disease-free survival, and safety.

Lancet Oncol 2016; 17: 791–800
Published Online
May 11, 2016

- P+T+Docetaxel vs T + Docetaxel: 46% vs 29% pCR

PFS and DFS

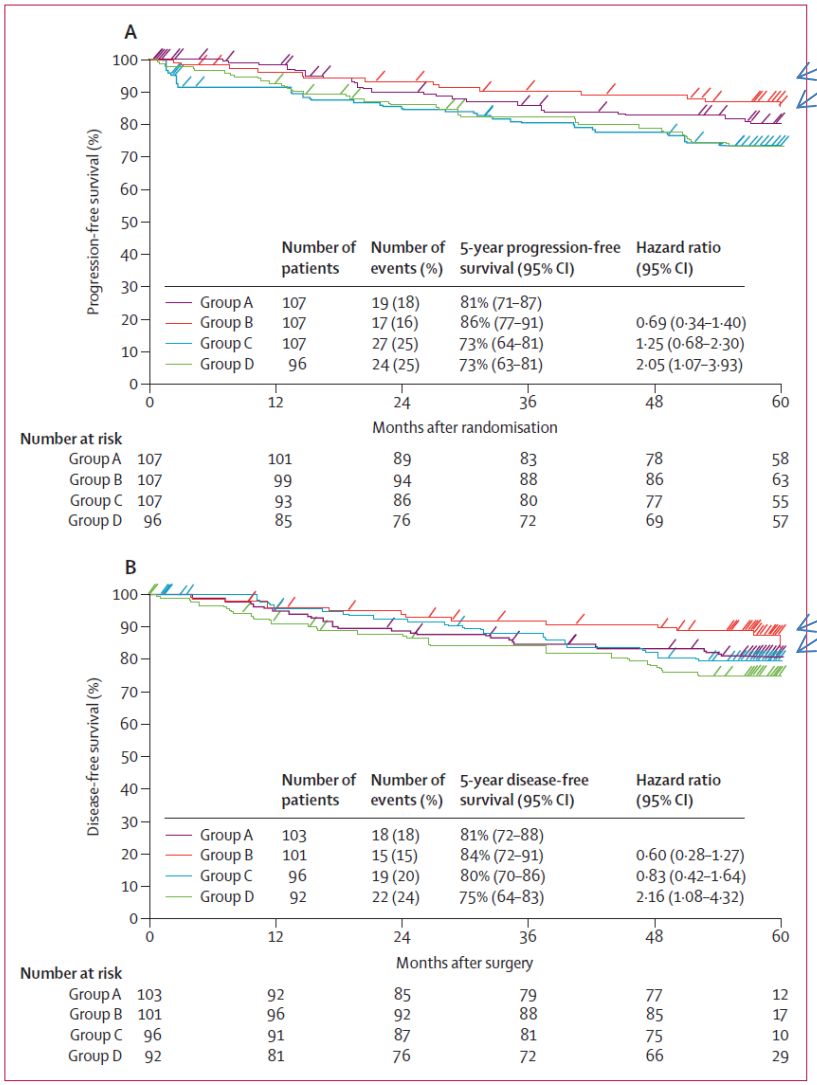


***Figure 1*: Progression-free survival and disease-free survival**
(A) Kaplan-Meier estimates of progression-free survival in the intention-to-treat population, 5 years after random assignment of the final patient. Three late events occurred in group B: two cases of progressive disease at 63 and 71 months, and one death due to an unrelated cerebrovascular accident without progressive disease at 76 months. (B) Kaplan-Meier estimates of disease-free survival in all patients who underwent surgery, 5 years after random assignment of the final patient. The hazard ratio for groups B and C is with respect to group A, whereas the hazard ratio for group D is with respect to group B. Two late events occurred in group B: one case of progressive disease at 67 months, and one death due to an unrelated cerebrovascular accident without progressive disease at 72 months. Tick marks indicate the times at which events were recorded. The Kaplan-Meier curves are truncated at 60 months (the end of scheduled follow-up). However, summary statistics shown here take into account all follow-up. Patients in group A received trastuzumab and docetaxel; group B, pertuzumab, trastuzumab, and docetaxel; group C, pertuzumab and trastuzumab; and group D, pertuzumab and docetaxel.

NBCG har følgende utgangspunkt

- Aphinitystudien viser overlevelsesgevinst, men den er beskjeden
- Tydeligst effekt hos lymfeknute positive og HR negative
- Resultatene underbygger betydningen av bruk av pertuzumab spesielt hos høyrisikopasienter som vanligvis er kandidater for neoadjuvant behandling (betydelig effekt på pCR)– hvor overlevelseskurvene (i NeoSphere) blir understøttet av Aphinity
- Pasienter med store tumores eller omfattende lymfeknutemetastaser (eller ER negative med T2 tumores) bør tilbys (neo)adjuvant behandling som inkluderer pertuzumab

Kontrollopplegget etter 5 år hos lokalavanserte – sidestilles med øvrige pasienter

Olaparib
PARP hemmer til bruk for pasienter med BRCA1/2 mutert BrCa

Status for godkjenning og hva mener vi?

Olaparib

- Er nå under vurdering av Committee for Medicinal Products for Human Use (CHMP) i EU
- Data fra OlympiAD

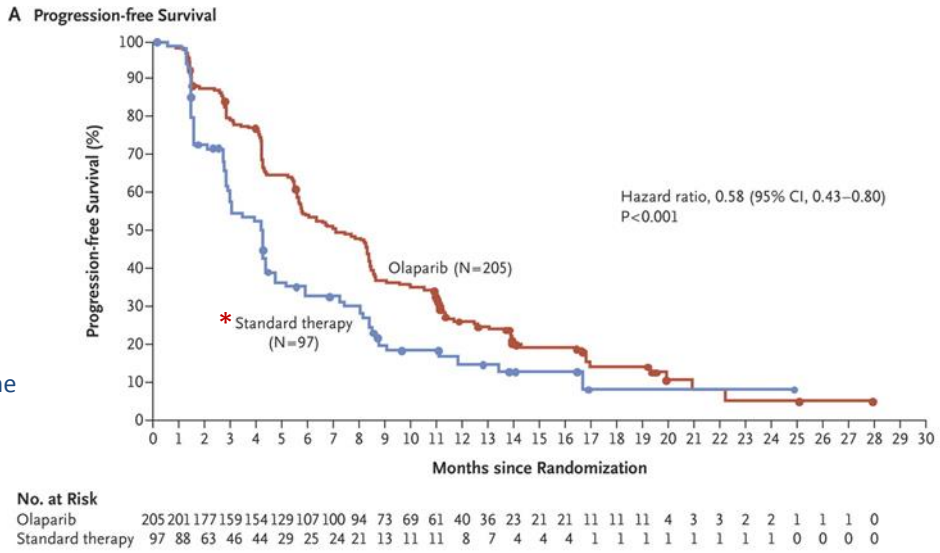
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Olaparib for Metastatic Breast Cancer in Patients with a Germline *BRCA* Mutation

Mark Robson, M.D., Seock-Ah Im, M.D., Ph.D., Elżbieta Senkus, M.D., Ph.D., Binghe Xu, M.D., Ph.D., Susan M. Domchek, M.D., Norikazu Masuda, M.D., Ph.D., Suzette Delaloge, M.D., Wei Li, M.D., Nadine Tung, M.D., Anne Armstrong, M.D., Ph.D., Wenting Wu, Ph.D., Carsten Goessl, M.D., Sarah Runswick, Ph.D., and Pierfranco Conte, M.D.

N Engl J Med 2017;377:523-33.

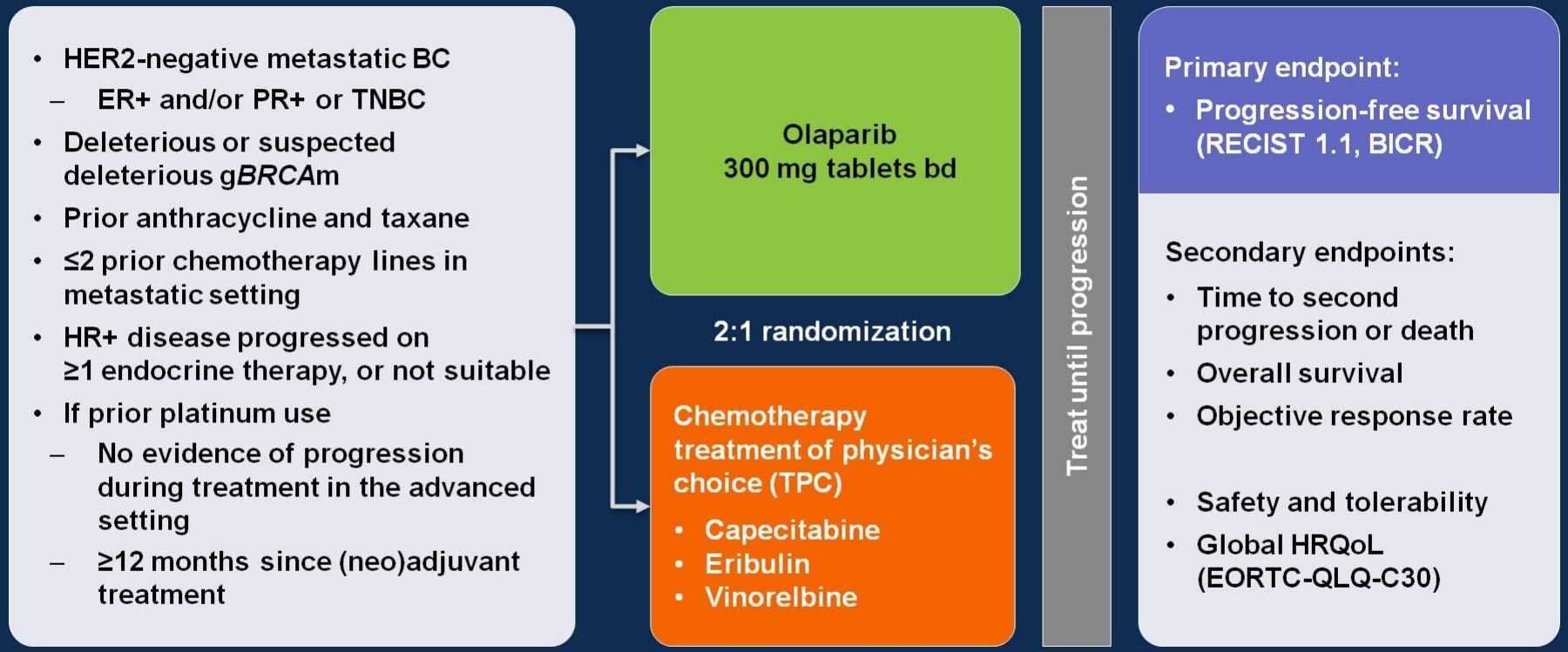


*Capecitabine,eribulin, vinorelbine

Reduserte bivirkninger sammenlignet med cellegift

Brystkreft med spredning – BRCA mutasjonsbærere (arvelig brystkreft)

OlympiAD study design



BICR, blinded independent central review; ER, estrogen receptor; HRQoL, health-related quality of life; PR, progesterone receptor; RECIST, response evaluation criteria in solid tumors; TNBC, triple negative breast cancer

Presented By Mark Robson at 2017 ASCO Annual Meeting

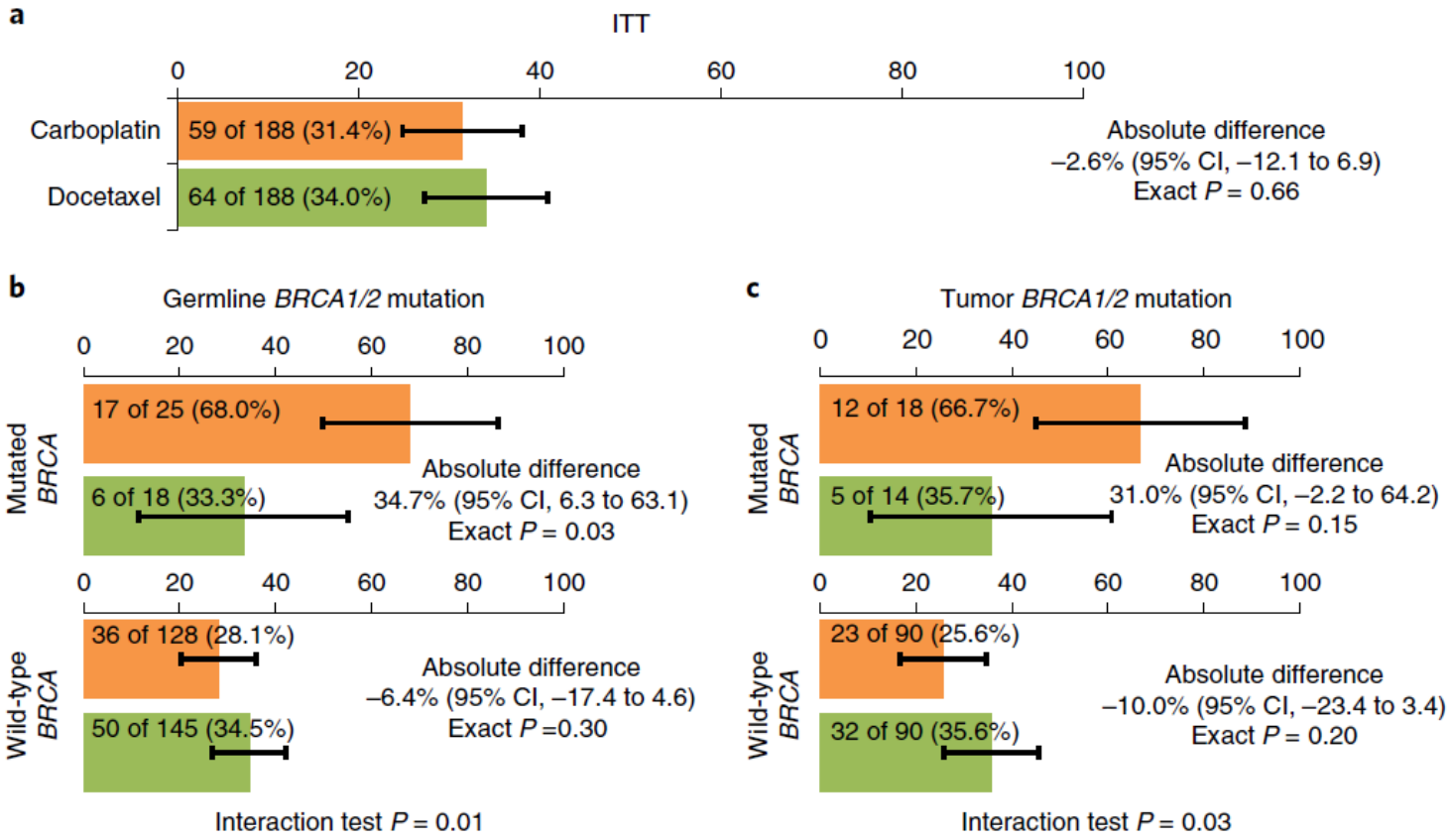
ARTICLES
https://doi.org/10.1038/s41591-018-0009-7

nature medicine

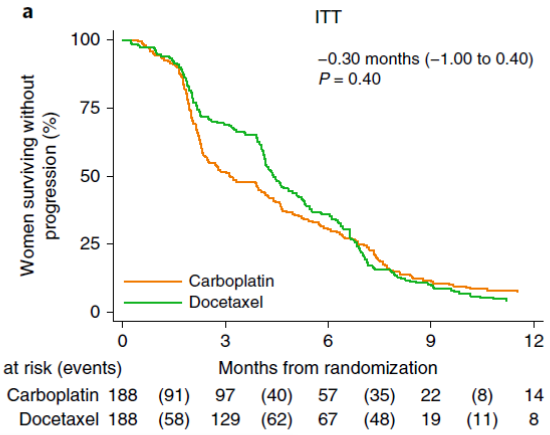
Carboplatin in *BRCA1/2*-mutated and triple-negative breast cancer BRCAness subgroups: the TNT Trial

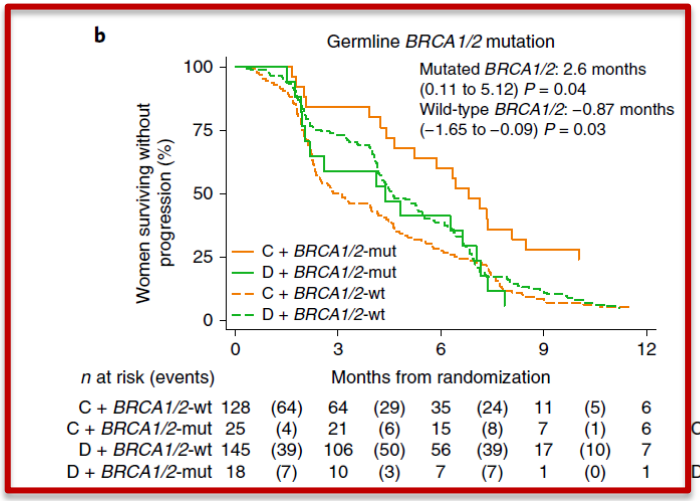
Andrew Tutt[1,2*], Holly Tovey[3], Maggie Chon U. Cheang[3], Sarah Kernaghan[3], Lucy Kilburn[3], Patrycja Gazinska[2], Julie Owen[4], Jacinta Abraham[5], Sophie Barrett[6], Peter Barrett-Lee[5], Robert Brown[7,8], Stephen Chan[9], Mitchell Dowsett[1,10], James M Flanagan[7], Lisa Fox[3], Anita Grigoriadis[2], Alexander Gutin[11], Catherine Harper-Wynne[12], Matthew Q. Hatton[13], Katherine A. Hoadley[14], Jyoti Parikh[15], Peter Parker[16,17], Charles M. Perou[14], Rebecca Roylance[18], Vandna Shah[2], Adam Shaw[19], Ian E. Smith[20], Kirsten M. Timms[11], Andrew M. Wardley[21], Gregory Wilson[22], Cheryl Gillett[4,23], Jerry S. Lanchbury[11], Alan Ashworth[24], Nazneen Rahman[25,26], Mark Harries[27], Paul Ellis[27], Sarah E. Pinder[4,23] and Judith M. Bliss[3]

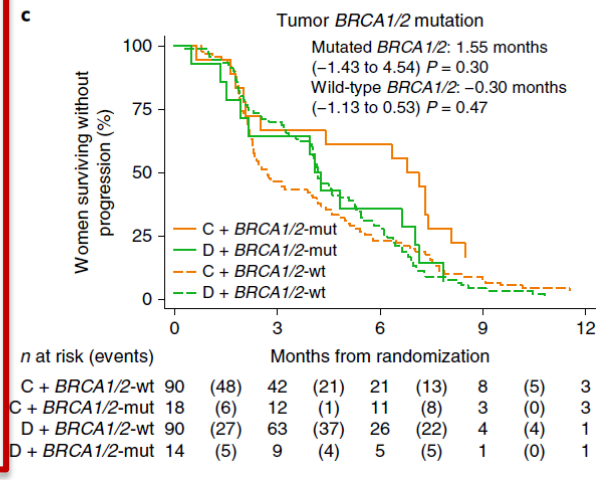
Fig. 2 | Response rates documented in the overall population and within *BRCA* subgroups. a, The absolute difference in the percentage of subjects who responded to treatment (carboplatin responders (%) – docetaxel responders (%)) between treatment groups within the overall patient population. ITT, intention to treat. **b**–**e**, The absolute differences in the percentage of subjects who responded to treatment between treatment groups with subjects stratified according to germline *BRCA1/2* mutation status (**b**), tumor *BRCA1/2* mutation status (**c**), *BRCA1* methylation status (**d**) and *BRCA1* mRNA-low



Survival analyses







NBCG forslag til anbefaling olaparib i metastatisk situasjon

- ved EMA godkjenning
  - BRCA muterte som ikke er kandidater for (eller videre bruk av) platinum kjemoterapi (Carboplatin) på grunn av komorbiditet/intolerabilitet

Takk for oppmerksomheten