

Radiotherapy



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2020 SABCS Radiotherapy

- 2020 SABCS breaking news
 - Can RT be omitted in low-risk breast cancer > 65 yrs?
 - Role of a tumor bed boost in non-low risk DCIS?
- Hot topic: 1-week hypofractionated breast RT
- Messages for clinical practice



2020 SABCS: Can RT be omitted in low-risk patients > 65 yrs?

PRIME-2 trial: 10-year follow-up update



CONTEXT

Elderly patients with low risk breast cancer: level 1 evidence of impact of RT on local control after breast conserving surgery is sparse

PRIME-2 trial

≥ 65 years Low risk invasive breast cancer:

- Size < 3 cm
- pN0
- ER+ or PR+
- Excision margins ≥ 1 mm
- Unilateral
- Breast conserving surgery
- Excluded: Grade III + LVI

WBRT + endocrine treatment

Endocrine treatment only

Primary endpoint: ipsilateral breast tumor relapse

WBRT = whole breast irradiation

R



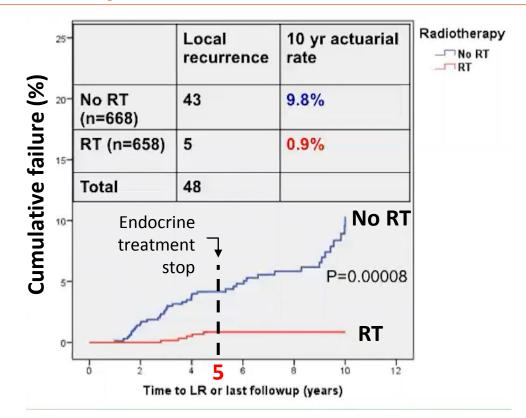
2020 SABCS: Can RT be omitted in low-risk patients > 65 yrs?

PRIME-2 trial: 10-year data



Total n = 1326 patients

Primary endpoint:
Ipsilateral breast tumor recurrence (IBTR)





2020 SABCS: Can RT be omitted in low-risk patients > 65 yrs? PRIME-2 trial: 10-year follow-up update



Secondary endpoints

Regional recurrence	RT: 0,5% No RT: 2,3% p=0,014					
Distant recurrence	No significant difference					
Contra-lateral BC	No significant difference					
New (non-breast) cancer	No significant difference					
Metastasis-free survival	No significant difference					
Overall survival	No significant difference 10-year actuarial rate: 80.5%					

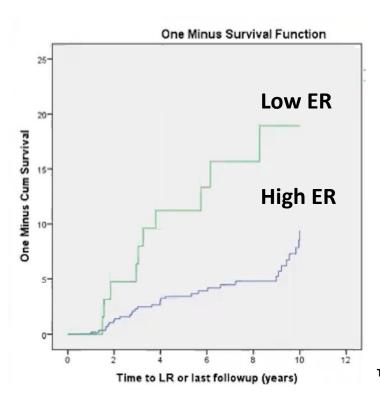


2020 SABCS: Can RT be omitted in low-risk patients > 65 yrs?

PRIME-2 trial: 10-year data



Local control by ER status in 'No RT' arm



	10-year failure rate					
High ER	<mark>9,2%</mark> (5,7%-12,7%)					
Low ER	18,8% (6,8%-30,7%)					
P-value	0,007					

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CONTEXT

Absence of high level evidence on optimal radiation dose fractionation and effect of a tumor bed boost for non-low risk DCIS

BIG 3-07/TROG 07.01 trial

Non-low risk DCIS

- Age < 50 yrs
- Age > 50 yrs + at least 1 high risk characteristic:

symptomatic presentation /
palpable tumour / multifocal
disease / size ≥1.5 cm /
intermediate or high nuclear grade /
central necrosis / comedo histology
/ surgical margin <10 mm

WBRT + boost 16 Gy/8x

WBRT without boost

Primary endpoint: ipsilateral breast tumor relapse

WBRT = whole breast radiation therapy



Α



1608 patients included Median follow-up = 6,6 years

Boost reduces local recurrence:

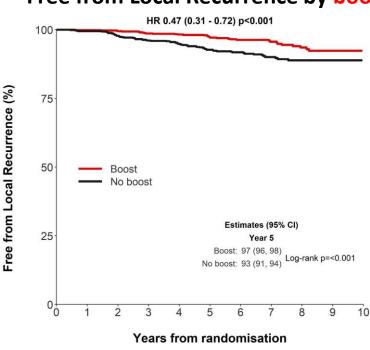
HR = 0.47 p<0.001

5-year local failure rate:

Boost: 3%

No boost: 7%

Free from Local Recurrence by boost



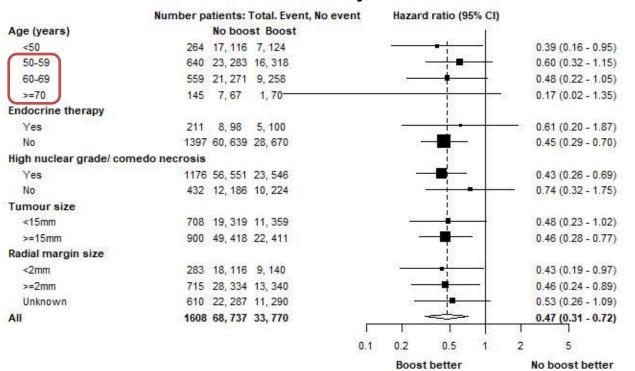
No. at risk											
Boost	803	763	748	729	692	568	404	276	181	95	3
No boost	805	776	743	721	690	566	392	247	158	91	26





Free from Local Recurrence by boost

Age > 50 yrs = 83% of included patients







Radiation toxicity

	,							
Acute	No BOOST (N=805)			ВО	OST (N=8	Р		
Grade	2	3	4	2	3	4		
Fatigue	112	7	0	131	11	1	0.25	
Radiation dermatitis	227	8	0	338	23	1	0.006	
Breast pain	90	8	0	116	10	1	0.49	
Pneumonitis	0	1	0	1	1	0	>0.99	
Late								
Breast pain	67	10	0	102	12	2	0.003	
Induration or fibrosis	44	5		99	11		<0.0001	
Telangiectasia	4	3	0	16	4	0	0.02	
Pneumonitis	Boost: increase in radiation toxicity, however grade 3/4 toxicity is low.						0.12	
Cardiac							0.21	
Second malignancy	_	-	f graue	J/4 LUXI	CILY IS I	. .	>0.99	





Additional substudy:

WBRT 50 Gy/25 fractions

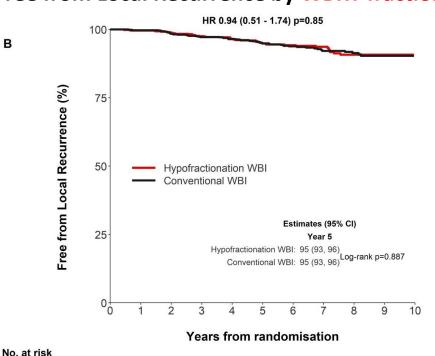
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WBRT 42,5 Gy/16 fractions

No difference between WBRT 16 fractions and WBRT 25 fractions.

* Note: WBRT dose study was partially randomized and partially the WBRT dose choice was open (multiple randomization blocks were used).

Free from Local Recurrence by WBRT fractionation



Hypofractionation WBI

Conventional WBI





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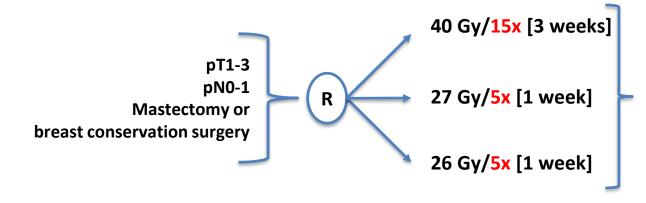
Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial



Adrian Murray Brunt*, Joanne S Haviland*, Duncan A Wheatley, Mark A Sydenham, Abdulla Alhasso, David J Bloomfield, Charlie Chan, Mark Churn, Susan Cleator, Charlotte E Coles, Andrew Goodman, Adrian Harnett, Penelope Hopwood, Anna M Kirby, Cliona C Kirwan, Carolyn Morris, Zohal Nabi, Elinor Sawyer, Navita Somaiah, Liba Stones, Isabel Syndikus, Judith M Bliss†, John R Yarnold†, on behalf of the FAST-Forward Trial Management Group



ESTRO, 2020 Lancet, 2020



+ boost if indicated.
Boost dose:
10Gy/5x or 16Gy/8x.

WBRT or chest wall RT ONLY Nodal RT was not given.

<u>Primary endpoint</u>: ipsilateral breast tumor relapse Design: non-inferiority; randomised; phase 3



FAST-Forward trial

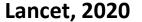


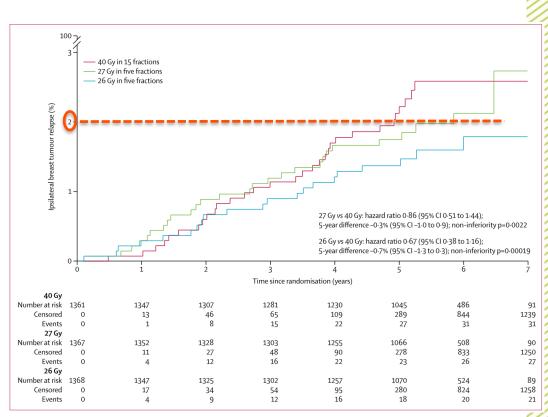
RESULTS:

4096 patients recruited Median follow-up: 71.5 months

Primary endpoint at 5 years: no differences between 3 arms in ipsilateral local failure (non-inferior)

Ipsilateral breast relapse: 2,1%







FAST-Forward trial



Secondary endpoints:

- Normal tissue effects (clinician-assessed; patient-assessed and photographic):
 - 26 Gy in 5 fractions <u>non-inferior</u> to 40 Gy in 15 fractions
 - 27 Gy in 5 fractions <u>inferior</u> to 40 Gy in 15 fractions
- No differences between treatment arms in:
 - Locoregional relapse
 - Distant relapse
 - Any breast cancer-related event
 - Overall survival
 - Second primary
 - Contralateral breast
 - Non-breast second primary
 - Cardiac death



FAST-Forward trial



FAST-Forward results:

WBRT/PMRT: 26 Gy/5x [1 week] non-inferior to 40 Gy/15x [3 weeks] regarding local control & cosmesis DCIS not included in trial [median follow-up of 71,5 months]

Early 2020:

Accelerated implementation in daily practice in view of **COVID-19 pandemic**

United Kingdom, November 2020:

- 26 Gy/5x [1 week] became standard of care for WBRT, PMRT, and PBI (partial breast RT)
- For invasive cancers and DCIS
- Not approved yet in case of nodal RT (results of nodal substudy are awaited)

WBRT = whole breast radiation therapy PMRT = post-mastectomy radiation therapy (chest wall irradiation)





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Conclusion (1/2)



Low-risk breast cancer in patients > 65 years

Recent trial data

PRIME-2: Can RT be omitted?

- At 10 years: WBRT + ET reduces local failure rate (9,8%→0,9%) in comparison to ET alone
- Low ER: 18,8% failure at 10 years if no RT
- No OS benefit

FAST-Forward: 5 fractions vs 15 fractions WBRT

- 5-fractions WBRT non-inferior to 15-fractions WBRT
- 26 Gy/5x non-inferior to 40 Gy/15x regarding normal tissue effects
- 6 years follow-up

Message for clinical practice

High ER:

- Life expectancy estimated < 5 years: consider RT omission
- Life expectancy estimated > 5 years: do not omit RT.
- Give WBRT in 5 fractions (26Gy/5x)
- Consider partial breast irradiation

Low ER or refusal/contra-indication for ET:

- Do not omit RT
- Give RT in 5 fractions (26Gy/5x)

<u>Non-low risk breast cancer</u>: do not omit RT (grade III, LVI, margins<1mm, size>3cm, N+)



Conclusion (2/2)



WBRT for non-low risk DCIS

Recent trial data

BIG 3-07/TROG 07.01: role of tumor bed boost?

- Addition of a tumor bed boost reduces local failure at 5 years: 7% → 3%; at the expense of an increase in skin/soft tissue fibrosis
- > 80% of patients in this trial were > 50 years
- WBRT in 25 fractions is equivalent to WBRT in 16 fractions

FAST-Forward: 5 fractions vs 15 fractions WBRT

- 5-fractions WBRT non-inferior to 15-fractions WBRT
- DCIS were not included in FAST-Forward
- UK consensus: 5 fractions WBRT is standard of care for DCIS (as from November 2020)

Message for clinical practice

- Consider a tumor bed boost for non-low risk DCIS, also for patients > 50 years
- WBRT dose:
 - 15 or 16 fractions preferable to 25 fractions
 - Consider 5 fractions WBRT (26Gy/5x)