All authors declare no conflict of interest

DEPARTMENT OF ONCOLOGY
UNIVERSITY OF TURIN

“Hypofractionation with no boost after breast conservation in early-stage breast cancer patients”

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Introduction

In early-stage breast cancer, adjuvant RT after breast-conserving surgery reduce LR with a detectable benefit in terms of breast cancer-related mortality

HF represents a convenient option for patients and decreases treatment costs

Reduction in OTT through acceleration may also enhance tumor control probability

Long-term results of randomized phase III trials comparing standard fractionation and HF showed no difference in LC and OS with a milder toxicity profile for the shorter schedules without impairment of cosmesis

Materials and Methods

From 2005, we considered the systematic implementation of HF after BCS

At first, we employed a schedule consisting of 46 Gy in 20 fr/ 4 weeks (2005–2013)

After mature results of UK trials, we used 40 Gy in 15 fr over 3 weeks (2014–2015) as recommended by NICE guidelines in 2009

Most of the patients were treated with HF without any further boost dose to the lumpectomy cavity, mainly due to age or favorable tumor characteristics

Materials and Methods

493 women treated between August 2005 and August 2015

Inclusion criteria:

diagnoses of invasive breast cancer
T1–T2 pathologic tumor stage
primary lesion < 3 cm in maximum diameter
N0–N1 pathologic nodal stage
Negative surgical margins

Exclusion criteria:

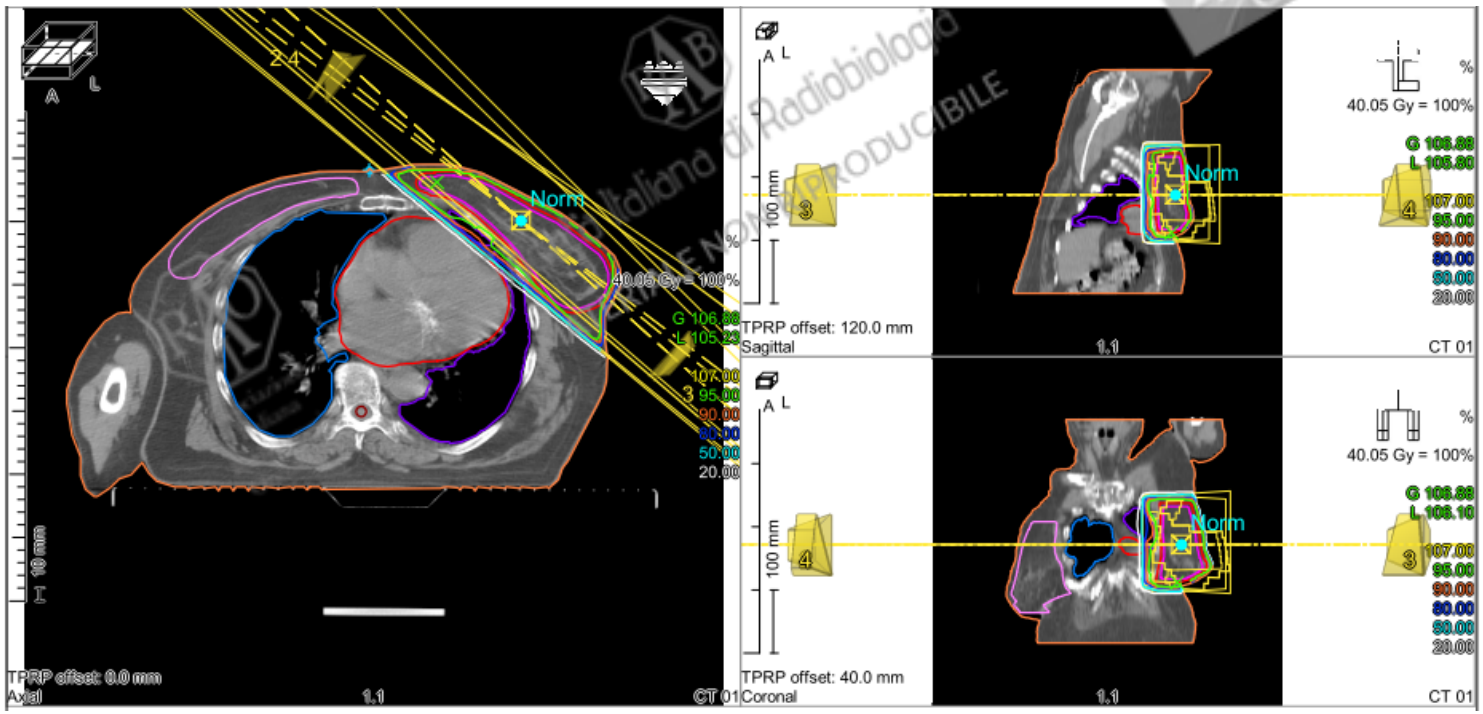
patients aged <40
positive surgical margins
eventual prior thoracic radiation
pregnancy

No patients received irradiation to nodal volumes

Materials and Methods

Planning CT was performed in supine position on a breast board with one arm raised on the same side as the treated breast and an isocenter was found

Beam arrangement consisted of 2–4 tangential fields covering the whole breast, according to patient's anatomy; 'field in field' technique was employed, when needed, to decrease dose heterogeneity



Materials and Methods

Radiation was usually delivered immediately after BCS (<3 months), for those submitted to CT, an interval of 4–6 weeks after the end of systemic treatment was introduced

Follow-up consisted of clinical examination every 6 months and an annual mammogram, up to 10 years after treatment completion

Acute toxicity was scored according to RTOG/EORTC toxicity scale
The maximal detected late toxicity was scored according to the Common Terminology Criteria for Adverse Events, version 3.0
Cosmesis was evaluated according to the Harvard criteria

Results

Patient and tumor characteristics	*N* (%)
Age (yrs)	
Mean	64
Range	41–86
Laterality	
Left-sided	254 (52)
Right-sided	229 (46)
Histology	
Ductal carcinoma	350 (70)
Lobular carcinoma	63 (12)
Tubular carcinoma	26 (5)
Other	64 (13)
Tumor size (mm)	
Mean	13
Range	1–30
Pathological tumor stage	
pT1a	35 (7)
pT1b	158 (32)
pT1c	258 (51)
pT2	52 (10)
Pathological nodal stage	
pN0	397 (79)
pN1	84 (17)
pNx	2 (4)

N number; *yrs* years

Patient and tumor characteristics	*N* (%)
Grading	
G1	224 (45)
G2	232 (46)
G3	47 (9)
Estrogen receptor	
Positive	475 (94)
Negative	28 (6)
Progesterone receptor	
Positive	383 (76)
Negative	120 (24)
c-erbB2	
Amplification	32 (6)
No amplification	471 (94)
Ki-67 (%)	
≤20	402 (80)
>20	101 (20)
≤14	309 (61)
>14	194 (39)
Biological type	
Luminal A	369 (73)
Luminal B	83 (17)
HER2-like	32 (6)
Triple negative	19 (4)

N number; *yrs* years

Results

Treatment characteristics	*N* (%)
Radiotherapy schedule	
46 Gy/20 fractions	378 (75)
40.05 Gy/15 fractions	125 (25)
Chemotherapy	
Yes	75 (15)
No	418 (85)
Type of chemotherapy (75 pts)	
FEC	13 (18)
AC	37 (49)
TC	22 (29)
Other	3 (4)
Hormonal therapy	
Yes	466 (95)
No	27 (5)
Type of hormonal therapy (466 pts)	
Tamoxifen	146 (31)
Aromatase inhibitor	320 (69)
Trastuzumab	
Yes	27 (5)
No	466 (95)
Axillary treatment	
SLNB	417 (83)
ALND	65 (13)
None	21 (4)

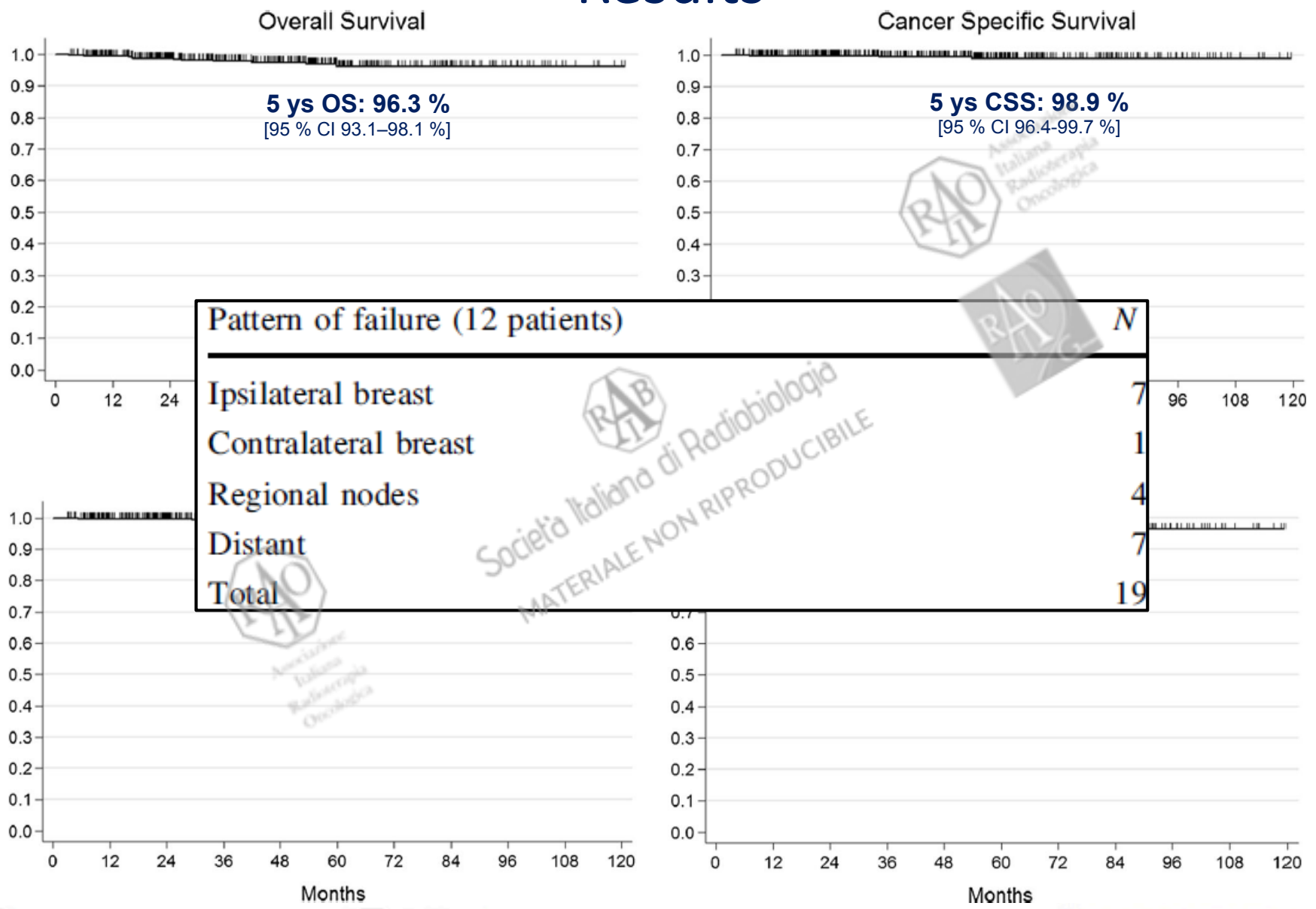
All patients underwent BCS

Exclusive SLNB was performed in 83 % of patients, while 13 % received axillary dissection

Adjuvant hormonal therapy was administered in 95 % of patients, while 15 % received adjuvant CT

Median follow-up was 57 months (range 6–124)

Results



Pattern of failure (12 patients)	N
Ipsilateral breast	7
Contralateral breast	1
Regional nodes	4
Distant	7
Total	19

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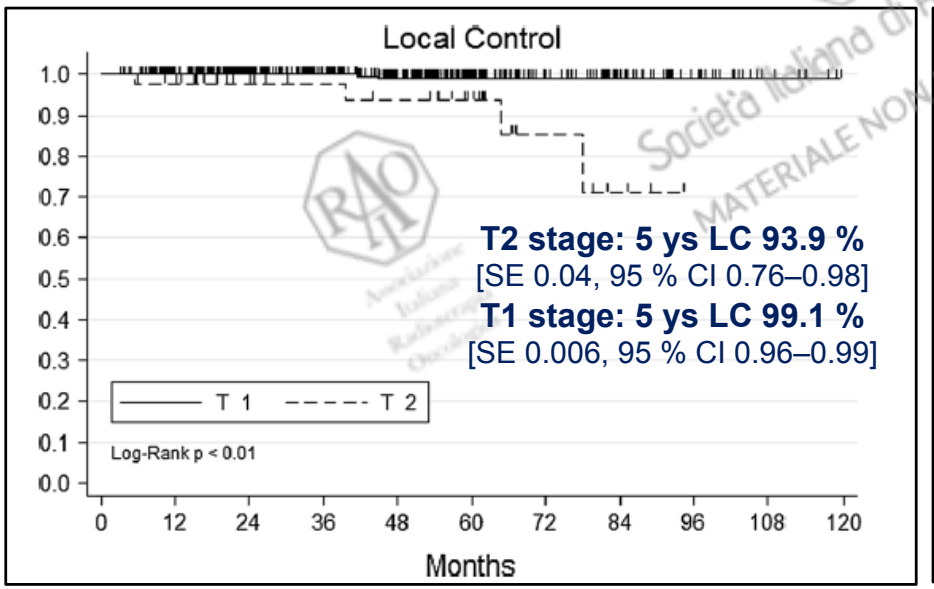
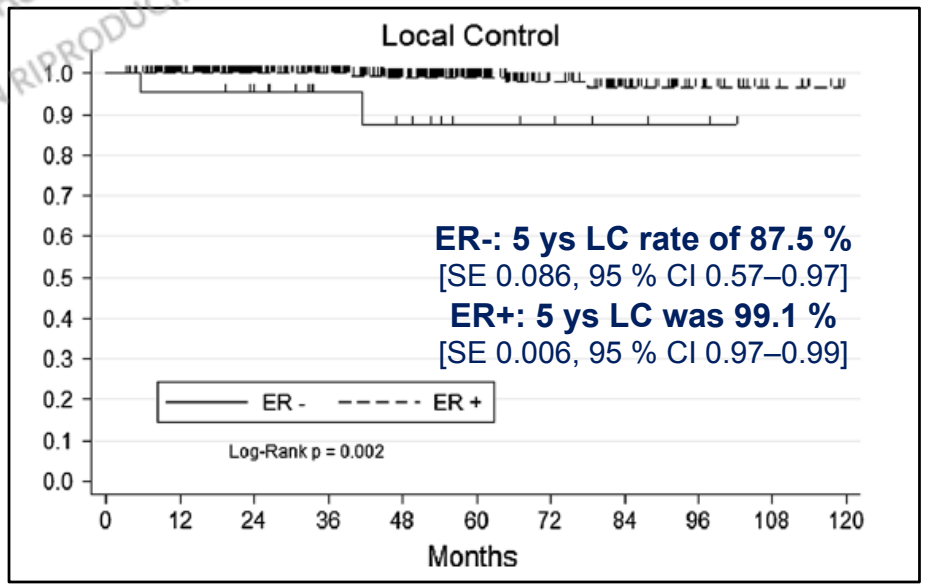
Results

Variable	HR	SE	z	95 % CI	p
Age	0.97	0.119	−0.20	0.767–1.242	0.844
Tumor stage (pT2 vs. pT1)	27.71	41.001	2.25	1.525–503.6	**0.025**
Nodal stage (pN1 vs. pN0)	13.09	21.146	1.59	0.552–310.4	0.111
Grading (G3 vs. G1–G2)	6.92	9.089	1.47	0.527–90.8	0.141
Ki-67 (>14 vs. ≤14 %)	1.06	0.041	1.60	0.986–1.148	0.109
Hormonal status (pos vs. neg)	0.922	0.034	−2.18	0.858–0.991	**0.029**
Hormonal therapy (yes vs. no)	196.5	607.1	1.71	0.460–8384	0.087
Chemotherapy (yes vs. no)	0.16	0.314	−0.93	0.003–7.707	0.353
Triple negative (no vs. yes)	0.02	0.078	−1.31	0.001–5.764	0.190



T2 stage: 5 ys LC 93.9 %
[SE 0.04, 95 % CI 0.76–0.98]
T1 stage: 5 ys LC 99.1 %
[SE 0.006, 95 % CI 0.96–0.99]



ER-: 5 ys LC rate of 87.5 %
[SE 0.086, 95 % CI 0.57–0.97]
ER+: 5 ys LC was 99.1 %
[SE 0.006, 95 % CI 0.97–0.99]

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Toxicity

Table 5 Toxicity profile and cosmesis

	N	(%)
Skin toxicity		
Acute		
G0	305	62
G1	162	32
G2	24	4
G3	12	2
Late (all grades)		
Fibrosis	11	2
Telangiectasia	5	1
Hyperpigmentation	12	2
Cosmesis		
Excellent	46	9
Good	431	86
Fair	20	4
Poor	6	1

One case of G2 pulmonary fibrosis was reported, no cardiac toxicities

Previous CT had a significant correlation with G2 late skin toxicity (OR 6.88, 95 % CI 1.74–27.2, p = 0.006) and fair to poor cosmetic outcomes (OR 2.6, 95 % CI 1.12–6.02, p = 0.025)

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Discussion

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Joanne S Haviland, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane Dobbs, Penelope Hopwood, Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith M Bliss*, John R Yarnold*, on behalf of the START Trialists' Group

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D., Jim A. Julian, Ph.D., Robert MacKenzie, M.D., Sameer Parpia, M.Sc., Wendy Shelley, M.D., Laval Grimard, M.D., Julie Bowen, M.D., Himu Lukka, M.D., Francisco Perera, M.D., Anthony Fyles, M.D., Ken Schneider, M.D., Sunil Gulavita, M.D., and Carolyn Freeman, M.D.

START A:41.6 Gy or 39 Gy/13 fr
5 ys Relapse rate 3.5%

START B: 40 Gy / 15 fr
44% received BOOST
5 ys Relapse rate 2%

Canadian Trial: 42.5 Gy/16 fr NO BOOST
5 ys Relapse rate 2.8%

Our rate of local relapse below 2 % at 5 years, seems to be in accordance with the preponderant low-risk profile of our patients

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Discussion

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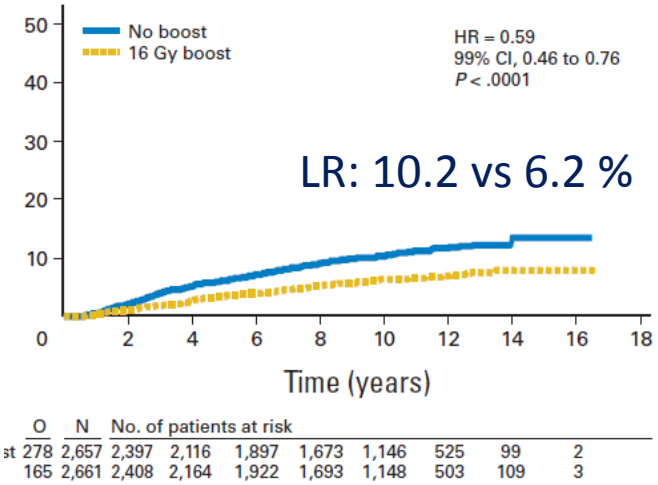
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Impact of a Higher Radiation Dose on Local Control and Survival in Breast-Conserving Therapy of Early Breast Cancer: 10-Year Results of the Randomized Boost Versus No Boost EORTC 22881-10882 Trial

Harry Bartelink, Jean-Claude Horiot, Philip M. Poortmans, Henk Struikmans, Walter Van den Bogaert, Alain Fourquet, Jos J. Jager, Willem J. Hoogenraad, S. Bing Oei, Carla C. Wárlám-Rodenhuis, Marianne Pierart, and Laurence Collette



LR: 10.2 vs 6.2 %

Risk factors for LR without boost: young age <50 ys and G3 invasive ductal carcinoma

Nomogram generated based on data coming from EORTC 'boost versus no boost trial' included tumor diameter among risk factors for ipsilateral in-breast recurrence, HR 1.13 for every 10 mm increase in tumor size

On our analysis, tumor stage and hormonal status had a significant impact on LC

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Conclusion

Hypofractionated RT with no boost delivered, is a safe and effective option for a population of low-risk breast cancer patients with excellent 5-year LC, mild toxicity profile and promising cosmetic outcome

A subgroup of patients with larger tumors and/or with no estrogen receptor expression may potentially benefit from treatment intensification with a boost dose to the lumpectomy cavity