

Esperienza torinese di radioterapia adiuvante ipofrazionata con boost concomitante in un gruppo di 939 pazienti trattate con chirurgia conservativa per carcinoma mammario

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Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10 801 women in 17 randomised trials

Lancet 2011; 378: 1707-16

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)*

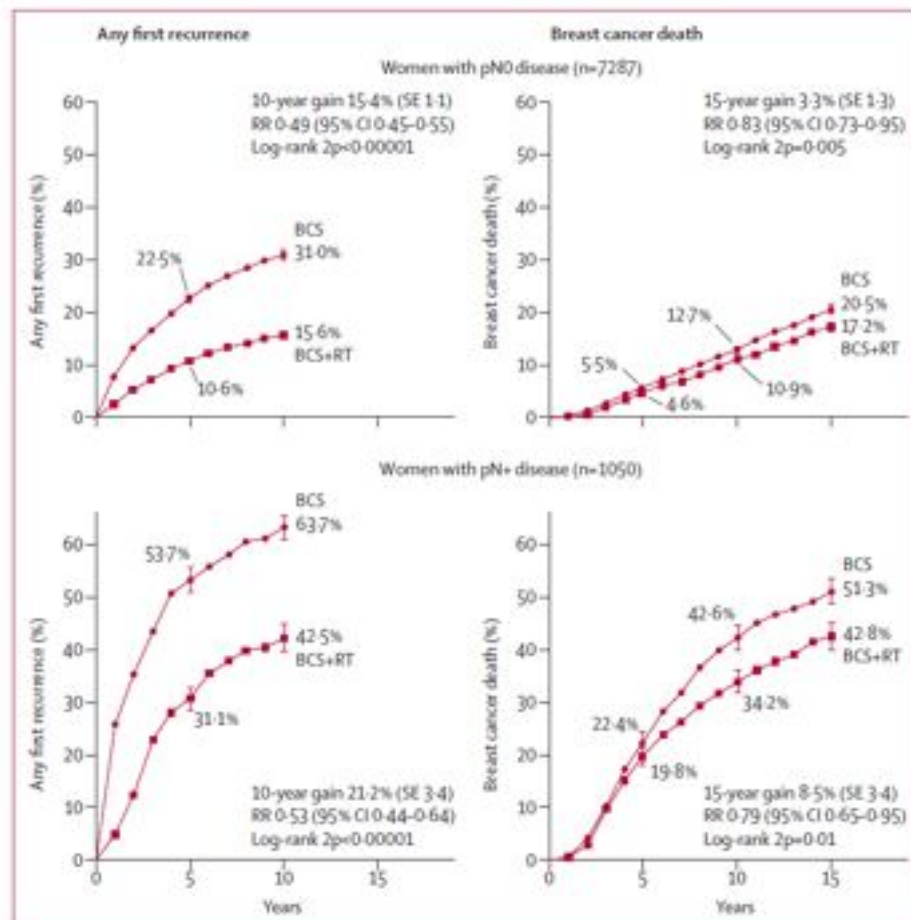


Figure 2: Effect of radiotherapy (RT) after breast-conserving surgery (BCS) on 10-year risk of any (locoregional or distant) first recurrence and on 15-year risk of breast cancer death in women with pathologically verified nodal status

N₀ pts:

- 10-yr LF reduction: 15,4%
- 15-yr OS increase: 3,3%

N₊ pts:

- 10-yr LF reduction: 21,2%
- 15-yr OS increase: 8.5%

Impact of radiation boost

JOURNAL OF CLINICAL ONCOLOGY

Role of a 10-Gy boost in the conservative treatment of early breast cancer: results of a randomized clinical trial in Lyon, France.

JCO March 1997 vol. 15 no. 3
963-968

P Romestaing, Y Lehingue, C Carrie, R Coquard, X Montbarbon, J M Ardiet,
N Mamelle and J P Gérard

- ✓ Boost provided benefit in terms of local failure (3.6% vs 4.5% at 5 yrs; $p < 0.05$)

The addition of a boost dose on the primary tumour bed after lumpectomy in breast conserving treatment for breast cancer. A summary of the results of EORTC 22881-10882 “boost versus no boost” trial

CANCER
RADIOTHÉRAPIE

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A. Fourquet^f, J.J. Jager^g, W. Hoogenraad^h, R.-P. Müllerⁱ, J.-B. Dubois^j, M. Bolla^k,
M. Van Der Hulst^a, C.C. Wárlám-Rodenhuis^l, M. Pierart^b, J.-C. Horiot^m

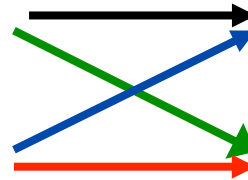
- ✓ Boost provided a benefit in terms of local failure (6.2% vs 10.2% at 10 yrs; $p < 0.0001$), especially in younger pts (< 40 yrs)

Boost Schedules

Whole breast irradiation

Boost

Standard fractionation



Standard fractionation

Hypofractionation

Hypofractionation

- Monoinstitutional experiences
- Ontario, RMH, START A and START B trials
- Phase III trial of IMRT vs standard treatment

Boost Strategies

Comparative study

Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 4, pp. 1018–1023, 2007

CLINICAL INVESTIGATION

Breast

THREE-DIMENSIONAL CONFORMAL SIMULTANEOUSLY INTEGRATED BOOST TECHNIQUE FOR BREAST-CONSERVING RADIOTHERAPY

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ERIK W. KOREVAAR, Ph.D., MIRANDA HOLLANDER, B.A., AND JOHANNES A. LANGENDIJK, M.D., Ph.D.

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✓ **WBRT + sequential boost (50 Gy/25 fr + 16 Gy 8 fr) vs concomitant boost (WBRT: 50.68 Gy/28 fr; 1.81 Gy daily; TB: 64.4 Gy/28 fr; 2.3 Gy daily)**

- **Mean volume $\geq 107\%$ breast dose reduced by 20%**
- **Mean volume outside TB receiving $> 95\%$ of the boost dose reduced by 54.4%**
- **MHD and MLD reduced by 10%**

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Patient and tumour characteristics

Total of patients	939
Age	
>50	884 (94.1%)
<50	55 (5.9%)
T size	
T1	671 (71.4%)
T2	176 (18.8%)
T3	8 (0.9%)
Tis	84 (8.9%)
N status	
N0	671 (71.6%)
N1	233 (24.8%)
N2	29 (3.1%)
N3	6 (0.5%)
Histology	
DCI	618 (65.8%)
LCI	103 (11%)
DCIS	84 (8.9%)
Other	55 (5.8%)
DCI-LCI	79 (8.5%)
Grading	
G1	213 (22.7%)
G2	507 (54%)
G3	219 (23.3%)
Margin status	
R0	801 (85.3%)
close	73 (7.8%)
R1	65 (6.9%)
Ki-67	
<20%	609 (64.8%)
>20%	246 (26.2%)
HER-2	
negative	797 (84.9%)
positive	86 (9.2%)
uncertain	56 (5.9%)
Biological subtype	
Luminal A	438 (46.6%)
Luminal B	325 (34.6%)
HER-2 like	35 (3.7%)
Triple negative	57 (5.1%)
Adjuvant therapy	
HT	728 (77.5%)
CT	370 (39.5%)

Gennaio 2004 -Dicembre 2008

939 pz: pTis, pT1-pT3a pN0-pN3a

Età mediana 61.7 anni (range 31-86)

FU mediano 66.9 mesi
(22.5-100)

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Dose prescription

PTV ^{whole breast}	45 Gy/2.25 Gy/20 fractions
PTV ^{boost}	5-6 Gy/0.25-0.30 Gy/20 fractions
PTV ^{SVC}	50 Gy/2 Gy/25 fractions

Radiation Techniques

- 3D-CRT – SIB → Tangential breast beams with MLC + one or more boost beams with no-tangential beams directions
- Field in field segments to improve HI and CI
- PTVs coverage: 95% isodose to 98% volume
- PTV volumes receiving $\geq 107\%$ less than 2%

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Radiobiological aspects

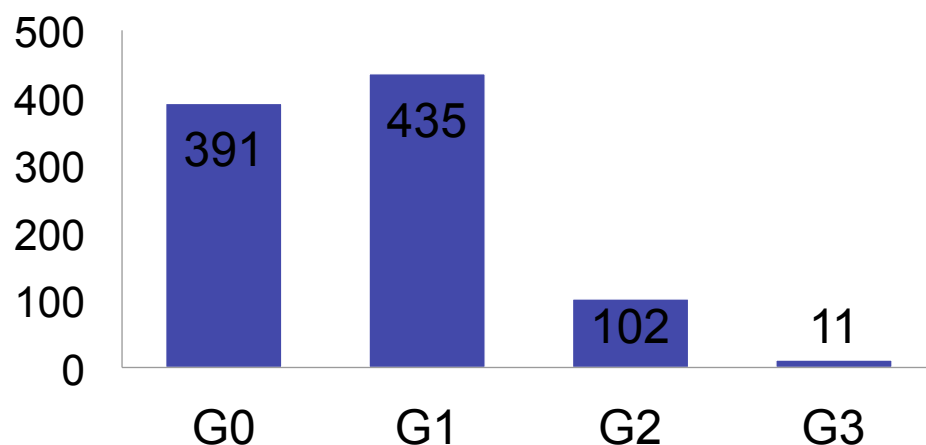
Tissue	α/β ratio	Standard - EQD₂	Hypo - EQD₂
Breast tumor control	4	90	81
Early-responding tissue	10	72	62.5
Late-responding tissue	3	100	91.5

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Results

Tossicità acuta (cutanea)

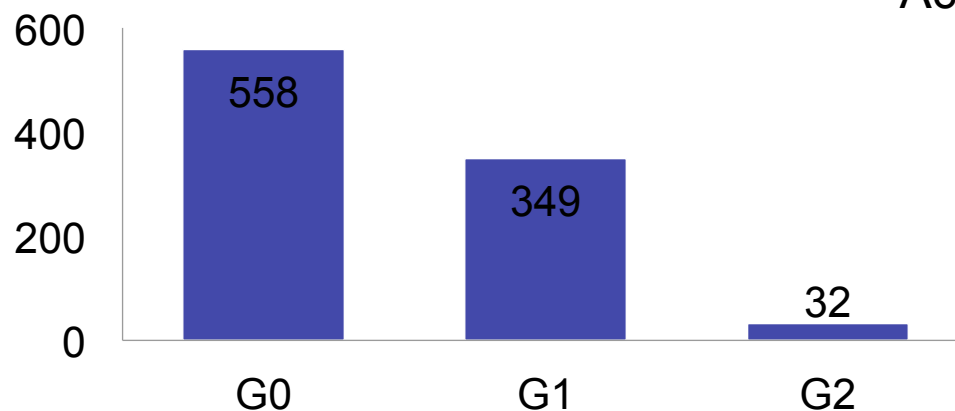
According with RTOG scale



G0: 41.6%
G1: 46.3%
G2: 10.9%
G3: 1.2%

Tossicità tardiva (fibrosi)

According with LENT-SOMA scale

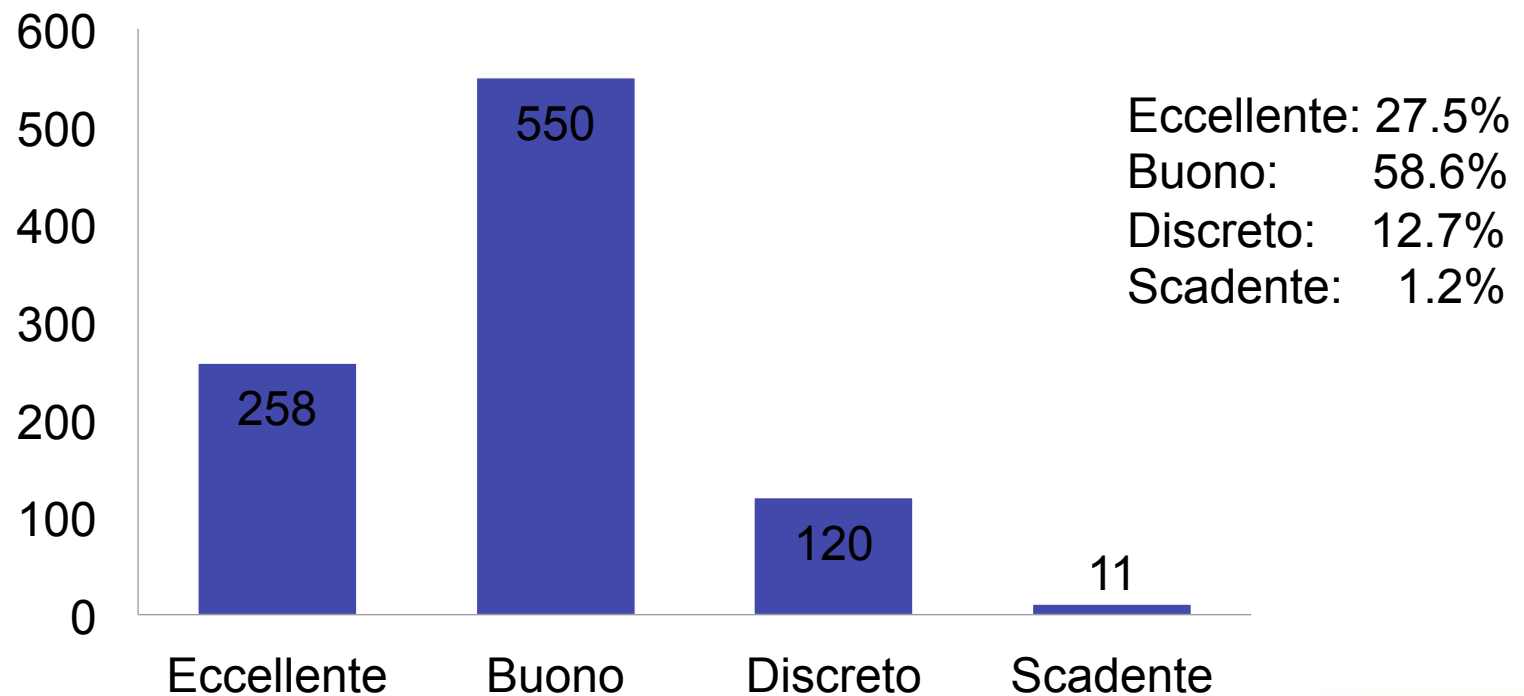


G0: 59.4%
G1: 37.2%
G2: 3.4%

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Results

Cosmesi

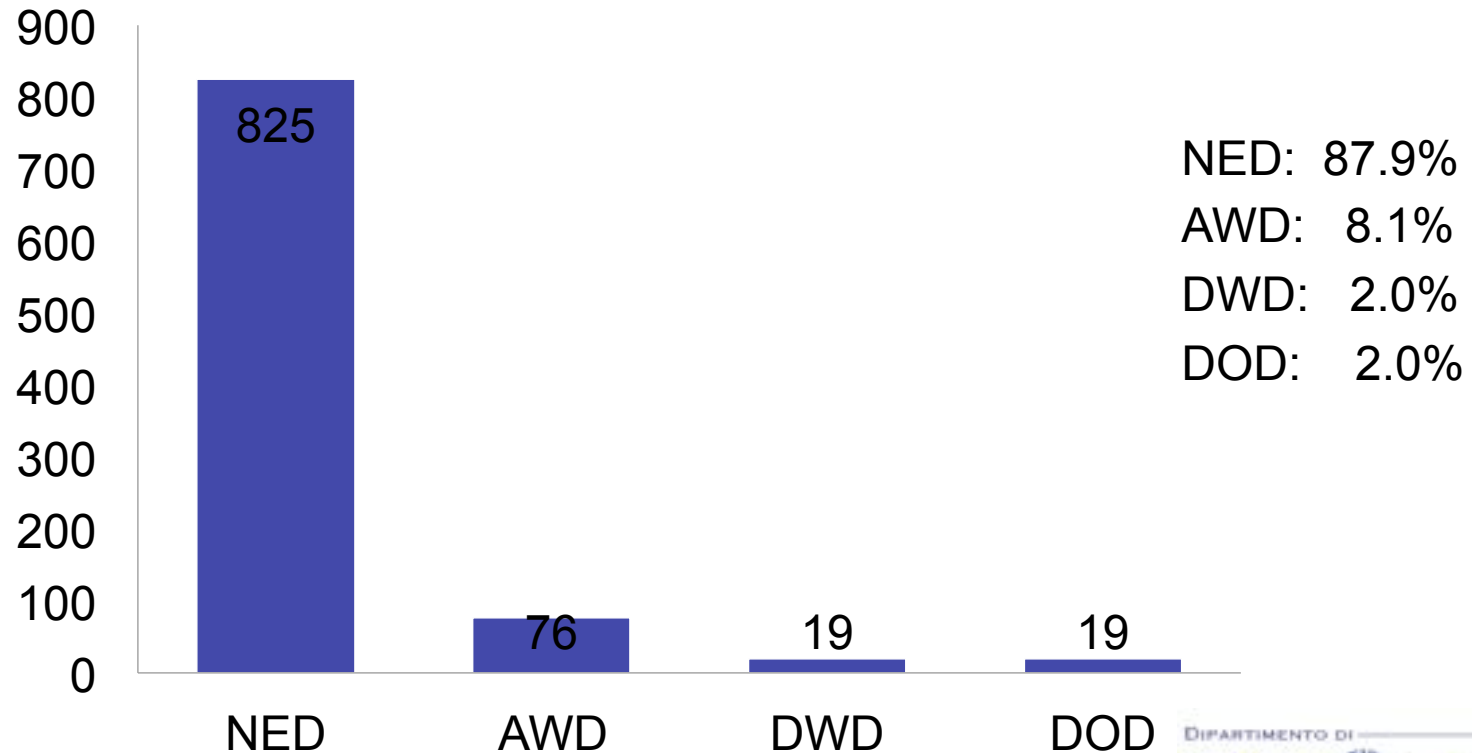


According with HARVARD scale

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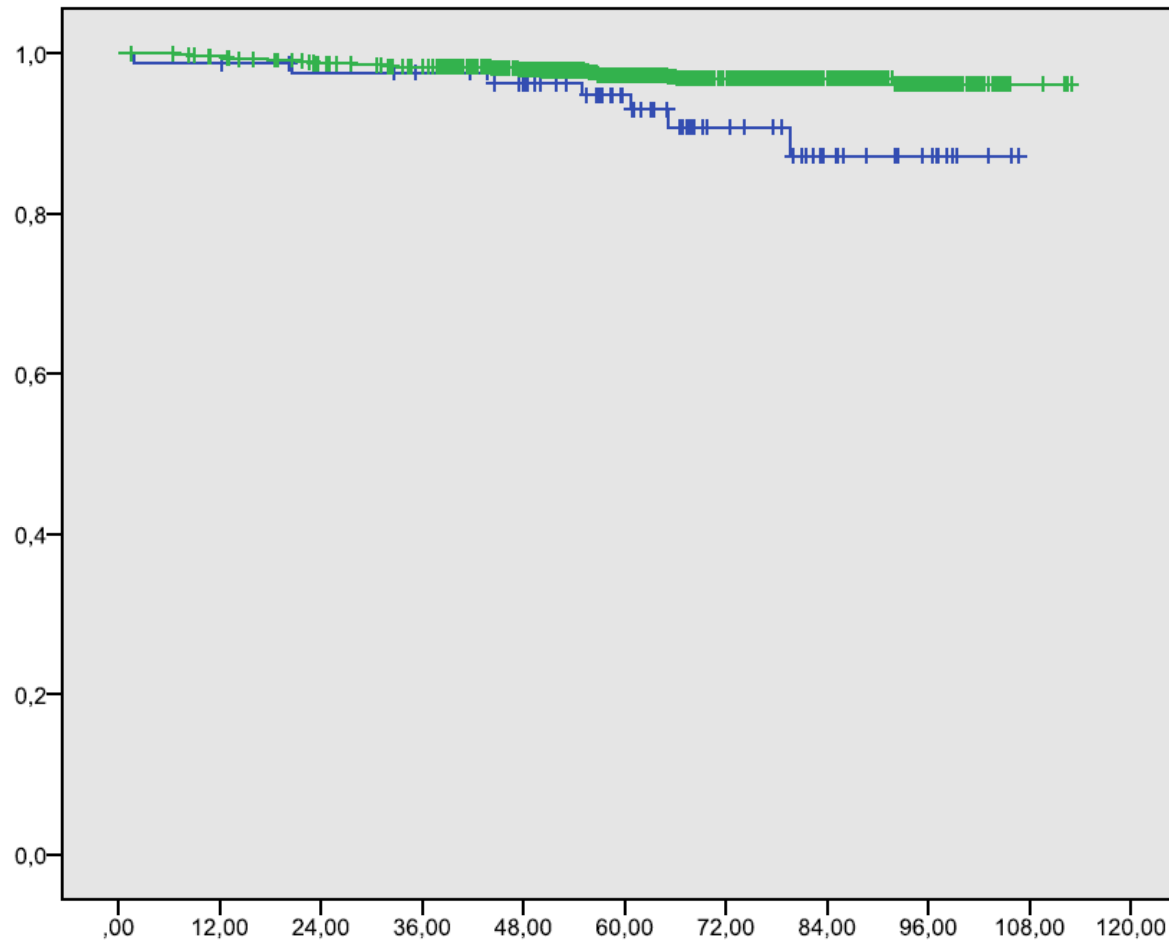
Results

Pattern of failure



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Local Control



Invasive carcinoma

97.3% @ 5 yrs

96.8% @ 7 yrs

DCIS

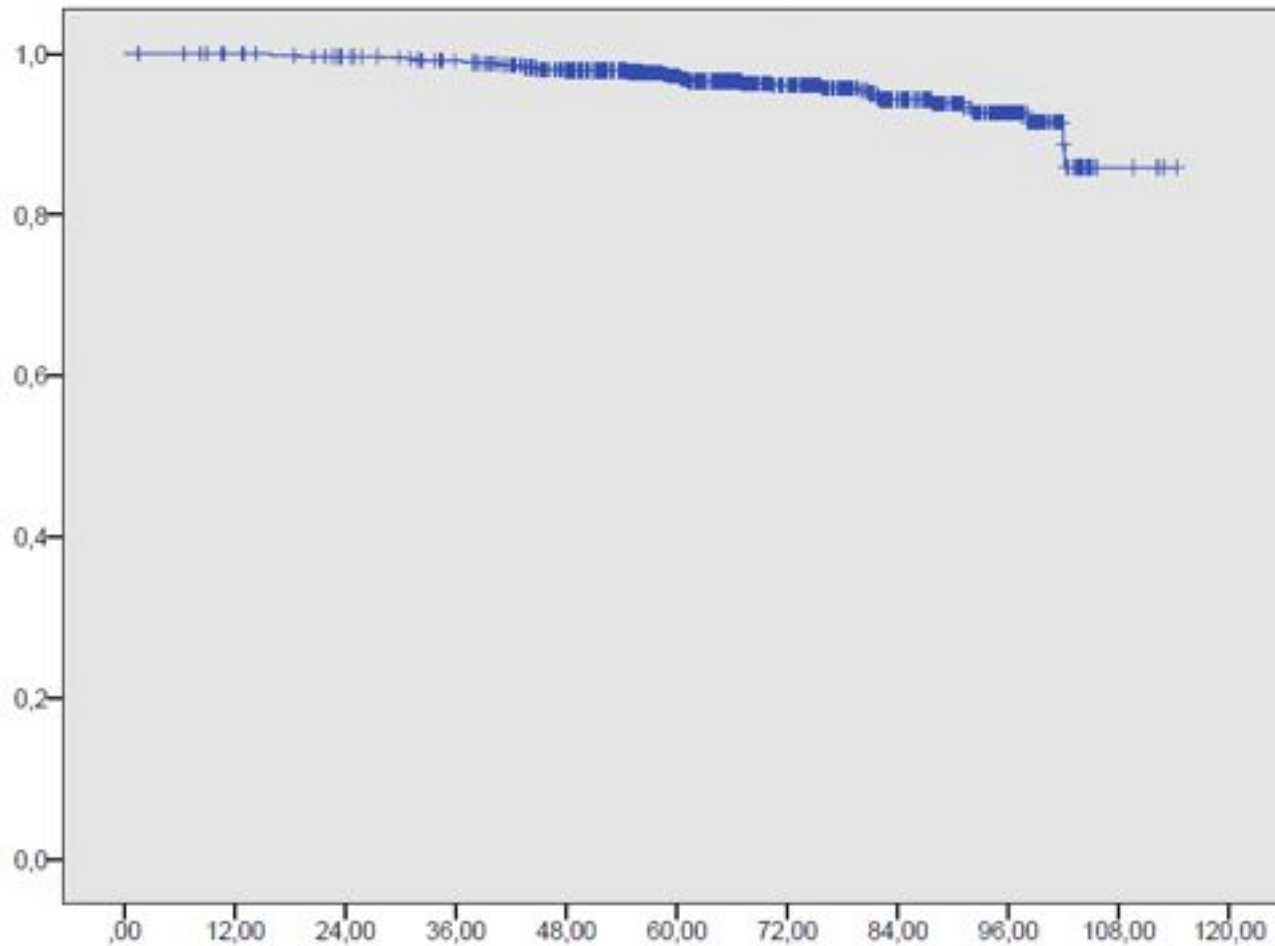
95.3% @ 5 yrs

88.7% @ 7 yrs

Months

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Overall Survival



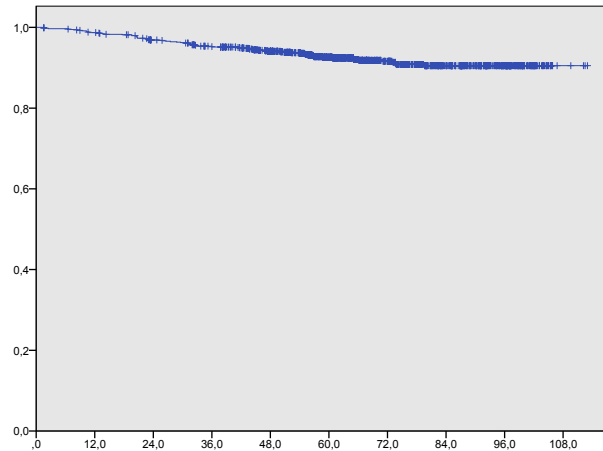
98.5% @ 5 yrs

94.8% @ 7 yrs

Months

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Disease Free Survival

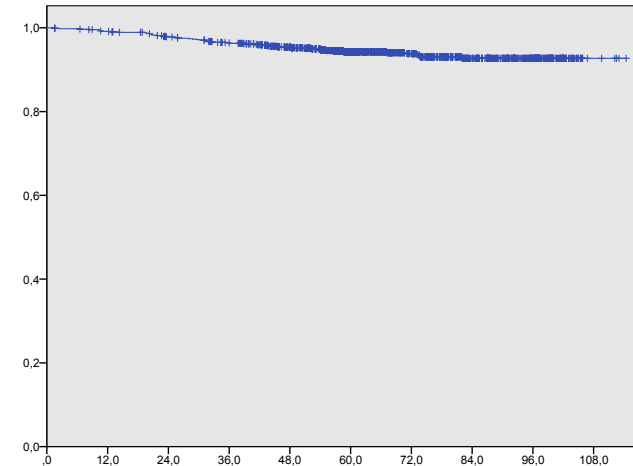


Months

92.6% @ 5 yrs

90.5% @ 7 yrs

Metastasis Free Survival



Months

94.3% @ 5 yrs

92.7% @ 7 yrs

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Univariate Analysis

Variables	LC		DFS	
	%	p value	%	p value
T (≤ 2 vs > 2 cm)	3.1% vs 4.4%	0.4	6% vs 15.8%	<0.001
N (N0-1 vs N2-N3)	0% vs 3.1%	0.15	6.8% vs 31.4%	<0.001
G (G3 vs G1-G2)	5% vs 2.8%	0.16	14.6% vs 5.8%	<0.001
ER (+ vs -)	2.8% vs 7%	0.04	6.9% vs 13.8%	0.016
PgR (+ vs -)	2.9% vs 5.7%	0.08	6.9% vs 11.3%	0.053
Triple Neg (No vs Yes)	3.1% vs 7.1%	0.16	7.1% vs 15.8%	0.033

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Multivariate Analysis

- **None** of the variables confirmed a predictive value on **LC** at the multivariate analyses
- **T > 2 cm** (OR 2.29, CI 1.29 – 4.04), **N > 2** (OR 3.44, CI 1.38 – 8.58) and **G3** (OR 2.31, CI 1.28 – 4.17) were related to worse **DFS** also at the multivariate analyses.

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Conclusions

- Toxicity profile and cosmetic outcomes are comparable to standard fractionation
- Good results in terms of LC, DFS, OS
- In univariate analysis: T1, N0-1, low grade, less aggressive biological profile are associated with a better **DFS**
- In multivariate analysis: T1, N0-1, low grade are associated with a better **DFS**



...GRAZIE!