Randomized Trial Evaluating Radiation following Surgical Excision for "Good Risk" DCIS: 12-Year Report from NRG/RTOG 9804

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Disclosure for Dr. McCormick

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  - Memorial Sloan Kettering Cancer Center (BMc), NRG Oncology Statistics and Data Management Center/ACR (KW, JM), M D Anderson Cancer Center (HK, NS, ES), Odette Cancer Centre-Sunnybrook Health Sciences Centre (ER DV), Massachusetts General Hospital (BS), L Hotel-Dieu De Quebec (IG), Dartmouth-Hitchcock Medical Center (AH), Greenville CCOP Cancer Centers of The Carolinas (MO), Henry Ford Hospital (EW), Southeast Cancer Control Consortium, Inc. CCOP ((JA), University of Michigan Medical Center (LP), Sutter Medical Center Sacramento(accruals Radiological Associates of Sacramento) (AP), University of Hawaii Cancer Research Center (KS), Ohio State University (JW)
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Background

- RTOG 9804 was designed to address whether radiation therapy after breast-conserving surgery would decrease local failure (invasive, in situ) and need for mastectomy among a cohort of DCIS patients at low risk of recurrence

- Unlike previous prospective RCTs comparing whole breast radiation therapy with no RT for DCIS, RTOG 9804 included only “good risk” patients
  - Detected by mammogram, size ≤ 2.5 cm, final margins ≥ 3 mm, and low or intermediate nuclear grade

Schema

STRATIFY

Age
1. < 50
2 ≥ 50

Final Path Margins
1. Negative (re-excision)
2. 3-9 mm
3. ≥ 10 mm

Mammographic/Pathologic Size of Primary
1. ≤ 1 cm
2. > 1 cm to ≤ 2.5 cm

Nuclei Grade
1. Low
2. Intermediate

Tamoxifen Use
1. No
2. Yes

RANDOMIZE

Arm 1
Observation ± tamoxifen 20 mg per day for 5 years

Arm 2
Radiation therapy to the whole breast, ± tamoxifen 20 mg per day for 5 years

Endpoints

- Local failure
- Contralateral breast failure
- Salvage mastectomy

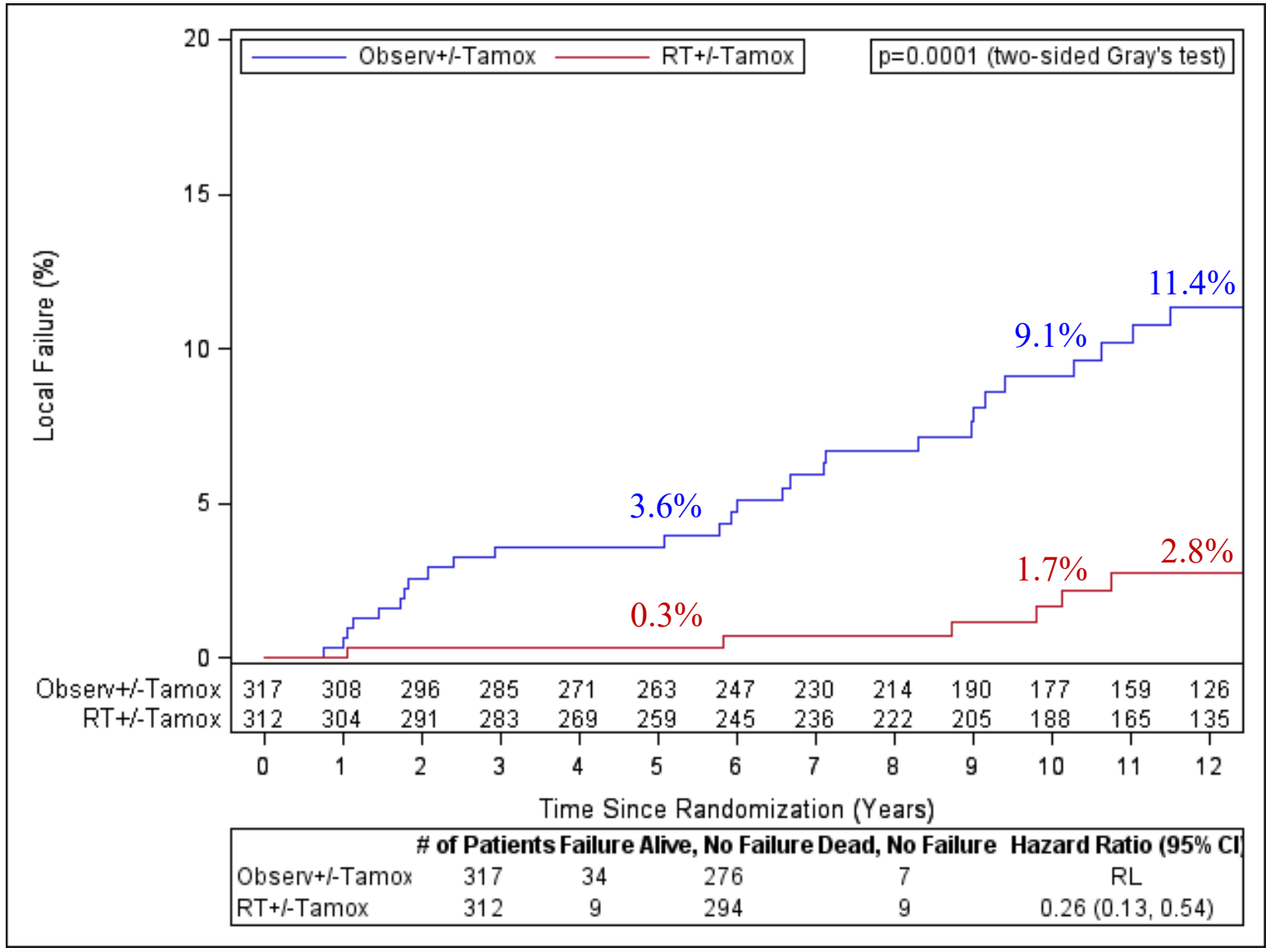
Median follow-up

- 12.4 years

Patient age and pathology

	Observation (n=317)	Radiation Therapy (n=312)
Age		
< 50	69 (21.8%)	60 (19.2%)
≥ 50	248 (78.2%)	252 (80.8%)
Final Microscopic Margins		
3mm - 9mm	111 (35.0%)	110 (35.3%)
≥ 10mm	50 (15.8%)	51 (16.3%)
Negative by negative re-excision	156 (49.2%)	151 (48.4%)
Mammographic Size of Primary Tumor		
≤ 1cm	229 (72.2%)	223 (71.5%)
> 1cm	88 (27.8%)	89 (28.5%)
Nuclei Grade		
NG1	141 (44.5%)	135 (43.3%)
NG2	176 (55.5%)	177 (56.7%)

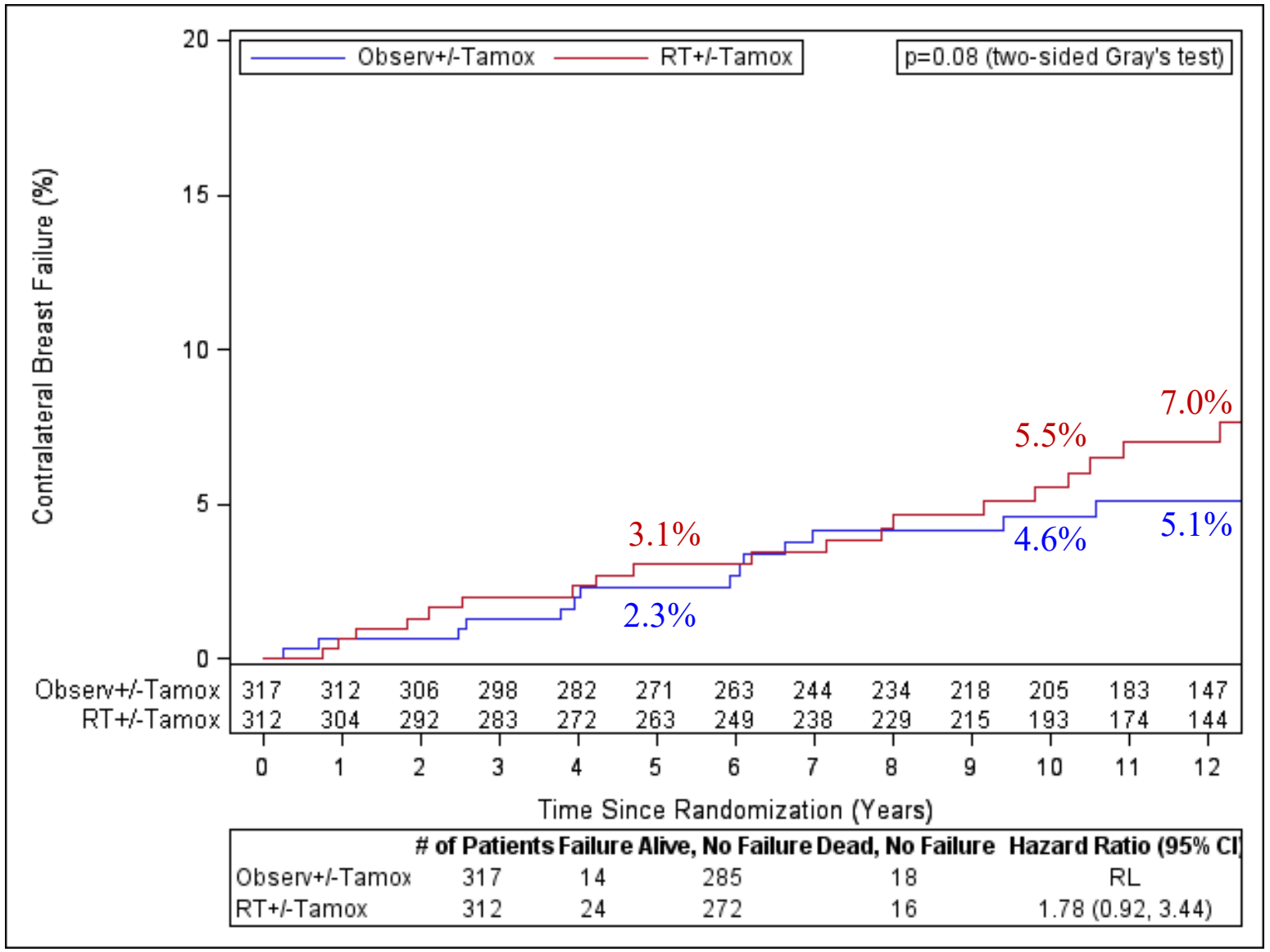
Local failure: Ipsilateral breast



Multivariable analysis: Local failure

Comparison	HR	p-value
Treatment: obs+tam vs RT+tam	0.25	0.0003
Age: <50 vs ≥50	0.93	0.84
Margins: neg vs 3-9mm	0.60	0.16
Margins: neg vs ≥10mm	0.37	0.098
Largest lesion: ≤0.5cm vs 0.6-1.0cm	1.14	0.72
Largest lesion: ≤0.5cm vs >1.0cm	1.81	0.16
Nuclei grade NG2 vs NG1	0.69	0.26
Tamoxifen received: no vs yes	0.50	0.024

Contra-lateral breast events



Mastectomy rates

Observation (n=317)	RT (n=312)
17 Mastectomies (5.4%)	**10 Mastectomies (3.2%)**
9 ipsilateral; 0 elective 8 bilateral; 2 elective	4 ipsilateral; 1 elective 6 bilateral; 1 elective

Adverse events/Toxicities

Acute Non-Hematological Toxicities

(Graded with CTC version 2.0)

Grade	Observation (n=317)	Radiation Therapy (n=312)
1	39 (12.3%)	107 (34.4%)
2	54 (17.0%)	124 (39.9%)
3	12 (3.8%)	11 (3.5%)
4	1 (0.3%)	2 (0.6%)
5	0 (0.0%)	0 (0.0%)

Late Radiation Therapy Toxicity

(Graded with RTOG/EORTC late toxicity criteria)

Grade	Radiation Therapy (n=307)
1	90 (29.3%)
2	15 (4.9%)
3	3 (1.0%)
4	1 (0.3%)
5	0 (0.0%)

Conclusions

- In this defined “good risk” DCIS population, the addition of whole breast radiation following breast conservation surgery significantly reduced the risk of any local recurrence and of invasive local recurrence.

- The larger-than-expected reduction has yielded meaningful results despite not meeting original targeted accrual.

- Findings should inform meaningful patient-doctor discussions about risks, benefits and the patient’s own degree of comfort, which varies greatly, with regards to local control with and without radiation therapy.