

The Recurrence Score® Result Has Demonstrated Clinical Validity in Numerous Landmark Studies

- Validated results from well designed randomized cooperative group clinical trials in homogenous patient populations

Prognostic for distant recurrence and predictive for treatment benefit

Oncotype DX® Clinical Validation: NSABP B-14

- Objective:** Prospectively validate the Recurrence Score® result as a predictor of distant recurrence in node-negative, ER+ patients

```

    graph TD
      R[Randomized] --> P[Placebo—not eligible]
      R --> T1[Tamoxifen—eligible]
      Reg[Registered] --> T2[Tamoxifen—eligible]
      T1 --- T2
  
```

- Multicenter study with prespecified 21-gene assay, algorithm, endpoints, analysis plan

Park S, et al. N Engl J Med. 2004;351:2817-2826. 10

Oncotype DX® Clinical Validation: NSABP B-20

- Objective:** Prospectively determine the relationship between Recurrence Score® result and chemotherapy benefit in node-negative, ER+ patients

```

    graph TD
      R[Randomized] --> TMF[Tam + MF]
      R --> TCMF[Tam + CMF]
      R --> T[Tam]
      TMF --- TCMF
      TCMF --- T
  
```

- Multicenter study with prespecified 21-gene assay, algorithm, endpoints, analysis plan

Park S, et al. J Clin Oncol. 2006;24:3726-3734. 15

Trans ATAC Study Overview

ATAC study population (N = 9366)

- Tamoxifen
- Anastrozole
- Tamoxifen + Anastrozole (combination arm not examined)

Primary Analysis: To determine whether Oncotype DX® as say significantly adds to a proportional hazards model for time to distant recurrence (age, tumor size, grade, treatment) in node-negative, HR+, patients with no adjuvant chemotherapy

- Secondary analyses:**
 - Determine whether the relationship between continuous Recurrence Score® result and time to distant recurrence differs by nodal status or treatment arm
 - Determine the relationship of predefined Recurrence Score groups with time to distant recurrence by nodal status and treatment arm
 - Evaluate whether Recurrence Score result adds to the Adjuvant! Online estimate of risk

Coverletti H, et al. J Clin Oncol. 2010;28:111-120-133A. 31

SWOG 8814:Oncotype DX® Clinical Validation in Node-Positive Patients

SWOG 8814

Postmenopausal, node-positive, ER-positive breast cancer
N = 1477

- Tamoxifen × 5 yrs n = 361
- CAF × 6 + tamoxifen n = 550
- CAF × 6 → tamoxifen n = 566

SUB ANALYSIS

Patients with samples (n = 666)

RT-PCR obtained (n = 601)

- Tamoxifen alone (n = 148)
- CAF + T (n = 243)
- CAF → T (n = 219)

Sample for primary analysis
+148 + 219 = 367 (40% of parent trial)

Superior disease-free survival and overall survival over 10 years

Albain KS, et al. Lancet Oncol. 2010;11:59-65. 35