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Changes in treatment recommendation for patients with ductal carcinoma in situ using a 7-gene predictive biosignature: Analysis of the PREDICT Study

Pat W Whitworth, MD[1], Steven C Shivers, PhD[2], Chirag Shah, MD[3], Rakesh Patel, MD[4], Karuna Mittal, PhD[2], Troy Bremer, PhD[2], Charles E Cox, MD[5]

[1]University of Tennessee, Knoxville, TN, USA; [2]PreludeDx, Laguna Hills, CA, USA; [3]Cleveland Clinic, Cleveland, OH, USA;
[4]Good Samaritan Hospital, Los Gatos, CA, USA; [5]University of South Florida Morsani College of Medicine, Tampa, FL, USA

Background

- The role of adjuvant radiotherapy (RT) following breast conserving surgery (BCS) for women with ductal carcinoma in situ (DCIS) remains controversial.
- Although definitive trials provide Level 1 evidence supporting the use of RT in reducing the risk of local recurrence, the same randomized trials demonstrate that approximately 70-80% of DCIS patients do not have a local recurrence at 10 years after BCS alone.
- The DCISionRT® Test (PreludeDx™, Laguna Hills, CA) is a 7-gene predictive biosignature that uses tumor biology in conjunction with clinicopathologic factors.
- The test provides a validated score (DS) for women receiving BCS that assesses 10-year risk of DCIS recurrence and development of invasive breast cancer with and without adjuvant RT.
- We established a registry to evaluate the decision impact of the 7-gene predictive biosignature on DCIS treatment recommendations.

Methods

- The PREDICT study is a prospective, multi-institutional registry for patients who received DCISionRT testing as part of their routine care.
- The registry includes females 26 and older who are diagnosed with DCIS and are candidates for BCS and eligible for RT or systemic therapy.
- Treating physicians completed treatment recommendation forms before and after receiving test reports to capture surgical, radiation and hormonal treatment (HT) recommendations and patient preferences.
- The primary endpoint is to identify the proportion of patients where testing led to a change in RT recommendation.
- Additional analyses include changes in recommendations in patient subgroups based on clinicopathologic factors or clinician specialty.

Results

- Analysis was performed in 2,304 patients treated at 63 clinical sites.
- The median age of patients was 62 years old (18% < 50 years old), nuclear grade was high in 33%, and tumor size was 2.5 cm or greater in 11%.
- Test results were DS Low Risk (DS ≤ 3) for 63% of women and 37% were DS Elevated Risk (DS > 3).
- Overall, RT recommendation (yes/no) was changed for 38% of women after the 7-gene biosignature testing and HT recommendation was changed for 11%.
- There was a net decrease in RT recommendation from 71% pre-assay to 53% post-assay (p<0.001), where RT recommendations decreased 53% in DS Low Risk patients but increased 25% in DS Elevated Risk patients.
- Surgeons were more likely to change their RT recommendation (47%) than radiation oncologists (35%).
- When test results indicated DS Elevated Risk, both surgeons (79%) and radiation oncologists (88%) were likely to recommended RT, but when the results were DS Low risk, surgeons were more likely than radiation oncologists to recommend omitting RT (82% vs. 60%, respectively).
- Compared to traditional clinicopathologic features, the factor most strongly associated with RT recommendation was the biosignature result with other factors of importance being patient preference, tumor size and grade.

- DCISionRT changed RT recommendations in 38% of women overall (n=2304)
- **40%** of women initially recommended RT were **NOT** recommended RT after DCISionRT
- **34%** of women initially **NOT** recommended RT were recommended RT after DCISionRT

TABLE 1. Impact of the 7-gene predictive biosignature on adjuvant radiation recommended overall and by clinicopathologic factors

Clinical Factor	N	RT Recommended: Pre-test (%)	RT Recommended: Post-test (%)	RT Recommended: Net change (%)	Pre- to post-test change in RT recommended: Yes to no (%)	Pre- to post-test change in RT recommended: No to yes (%)	Total change in RT recommended: Overall change (%)	Total change in RT recommended: Overall change (95% CI)	p-Value
Overall	2304	71	53	-18	40	34	38	36, 40	<0.001
Age, years									
≤ 50	422	80	47	-33	45	15	39	35, 44	<0.001
> 50	1886	69	54	-15	38	37	38	36, 40	<0.001
Nuclear Grade									
1 or 2	1553	64	48	-16	45	34	41	39, 44	<0.001
3	755	86	64	-22	27	31	34	**29, 35**	<0.001
Tumor Size									
≤ 2.5 cm	1534	65	48	-17	43	31	39	37, 41	<0.001
> 2.5 cm	218	90	71	-20	26	38	27	22, 33	<0.001
RTOG 9804-like Criteria*									
'Good Risk'	1125	61	44	-17	49	33	43	40, 46	<0.001
Not 'Good Risk'	1183	81	62	-19	33	37	34	31, 36	<0.001

*RTOG 9804-like criteria (nuclear grade 1 or 2, non-palpable, screening detected, negative margins)

Figure 1. RT Recommendation Pre- and Post DCISionRT Test Results

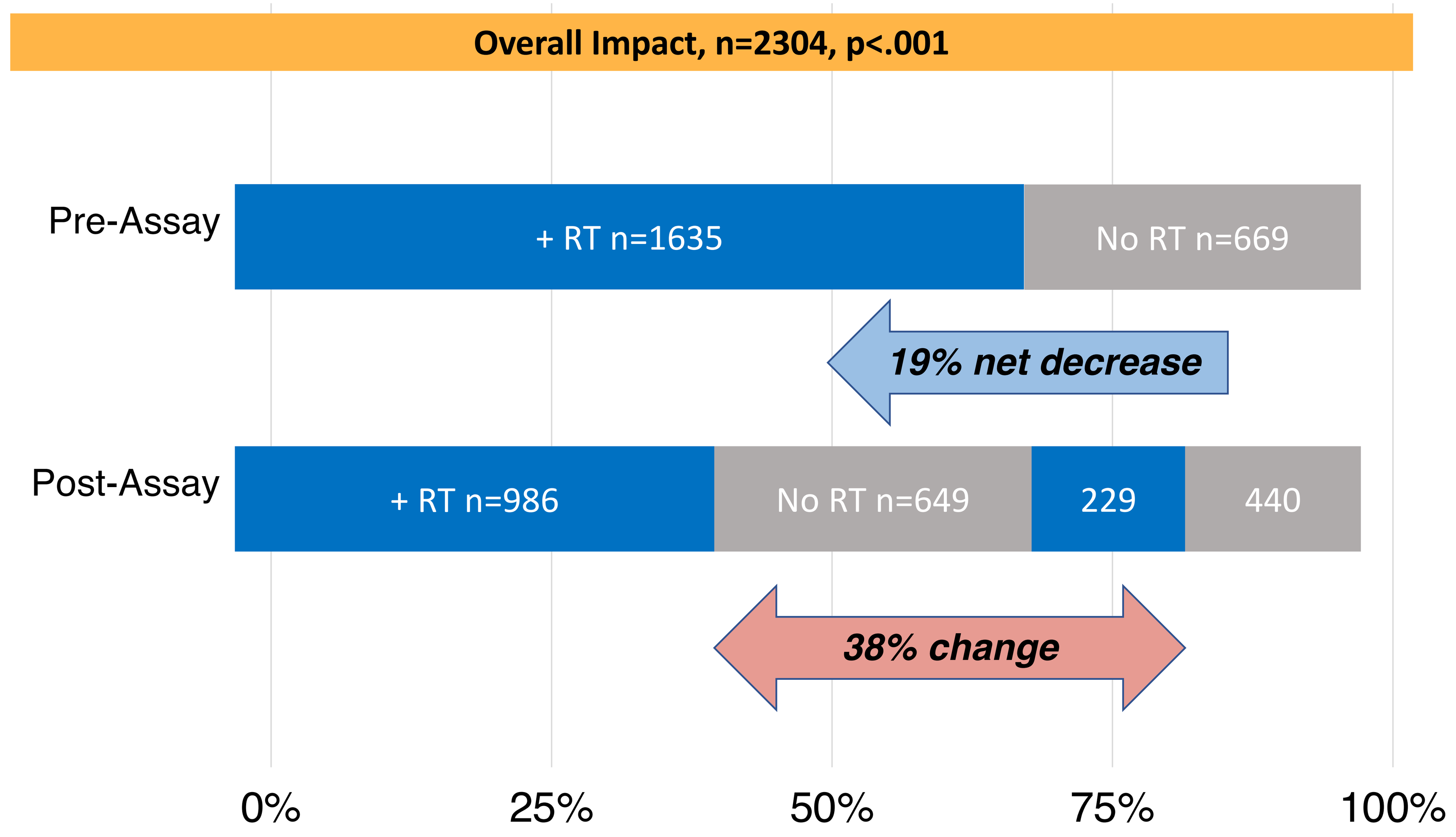
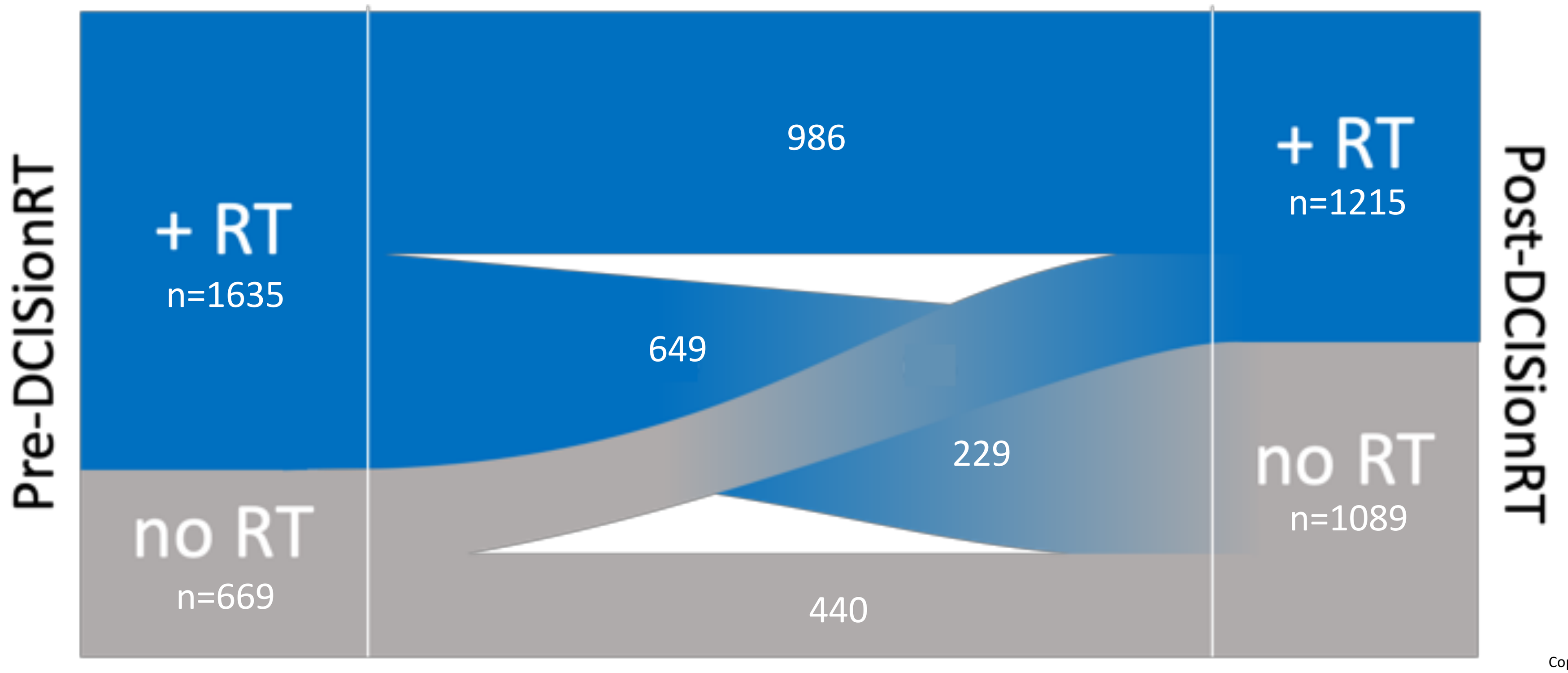


Figure 2. DCISionRT Decision Impact on RT Recommendation



Conclusions

- This analysis demonstrates significant changes in recommendations to add or omit RT based on the 7-gene predictive biosignature in 2,304 patients.
- The integration of DCISionRT into clinical decision processes has substantial impact on recommendations aimed at optimal management to prevent over- or under-treatment.