Two Years of Anti-Androgen Treatment Increases Other-Cause Mortality in Men Receiving Early Salvage Radiotherapy:

*A Secondary Analysis of the NRG Oncology/RTOG 9601 Randomized Phase III Trial*

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Disclosures for Dr. Spratt

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**Background**

**NRG Oncology/RTOG 96-01**

- **Recurrent PCa (PSA 0.2-4.0)**
- AND
- pT3 or pT2 with (+) margin

**Entry PSA (1.5 ng/mL)**
- Post-Surgery Nadir PSA
- Prior ADT
- Margin status

**Salvage RT**
- Placebo (2 years)
- Bicalutamide (2 years)

**Sample size:** 760 patients

**Median follow up:** 13 years

**Primary endpoint:** Overall Survival

- Persistently elevated PSA post-RP of >0.1 ng/mL
- Undetectable PSA
- Late salvage RT (PSA >0.5 ng/mL)
- Early salvage RT (PSA ≤0.5 ng/mL)

Sample size: 760 patients
Median follow up: 13 years
Primary endpoint: Overall Survival
Methods

Secondary analysis of NRG Oncology/RTOG 9601 approval through the NCI

Developed a priori statistical plan to determine differential benefit and harm of antiandrogen treatment in men by entry PSA via statistical interaction tests

Early Salvage RT PSA subgroups:

- Pre-specified protocol stratum: 0.2-1.5 ng/mL
- Median PSA on RTOG 9601: 0.2-0.6 ng/mL
- Median PSA of GETUG-16 & SPPORT: 0.2-0.3 ng/mL

Endpoints Assessed:
- Overall Survival
- Other-Cause Mortality
- Distant Metastasis

Toxicity Assessment:
- Grade 3-5 Cardiac Events
- Grade 3-5 Neurologic Events

Results

85% of trial was in the PSA 0.2-1.5 stratum

PSA 0.2-1.5 ng/mL stratum

12 year estimates:
Placebo: 76% (71-81)
Bicalutamide: 77% (72-82)

P=0.36

<table>
<thead>
<tr>
<th>Stratum</th>
<th>Number at Risk</th>
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<tbody>
<tr>
<td>Placebo</td>
<td>313 302 272 243 177 21</td>
</tr>
<tr>
<td>Bicalutamide</td>
<td>329 315 288 251 190 25</td>
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</tbody>
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HR (95%)

| 1.78 (0.88, 3.57) |
| 0.94 (0.59, 1.5) |
| 0.61 (0.39, 0.94) |
| 0.45 (0.25, 0.81) |
| 0.95 (0.39, 2.34) |
| 0.65 (0.36, 1.17) |
| 0.69 (0.43, 1.12) |
| 0.36 (0.15, 0.84) |

Interaction p value

| 0.02 |
| 0.03 |
Results

Other-Cause Mortality
PSA 0.2-0.6 ng/mL

12 year estimates:
- Placebo: 10% (5-14)
- Bicalutamide: 19% (13-25)

HR 1.94 (1.17-3.20)
P=0.009

Odds Ratio for Grade 3-5 Event

Overall Cohort
- Cardiac
- Cardiac plus Neurologic

PSA ≤1.5 stratum
- Cardiac
- Cardiac plus Neurologic

PSA ≤0.6 subgroup
- Cardiac
- Cardiac plus Neurologic
Conclusions

• Current guidelines recommend all men be offered hormone therapy when receiving salvage radiotherapy.

• Our data demonstrate that men with lower PSAs are more harmed than helped by long-term hormone therapy.

• We have now 3 randomized trials with over 2400 men total that do not demonstrate that short or long-term hormone therapy improves overall survival in men receiving early salvage radiotherapy at low PSAs.

• PSA prior to salvage radiotherapy predicts who will benefit most from hormone therapy.
  
  • *Guidelines should change to reflect this finding.*