Statin Use and Risk of Prostate Cancer Recurrence in Men Treated With Radiation Therapy

Ruchika Gutt, Nathan Tonlaar, Rangesh Kunnavakkam, Theodore Karrison, Ralph R. Weichselbaum, and Stanley L. Liauw

See accompanying editorial on page 2651

ABSTRACT

Purpose
There has been growing interest in the potential anticancer activity of statins based on preclinical evidence of their antiproliferative, proapoptotic, and radiosensitizing properties. The primary objective of this study was to determine whether statin use is associated with improved clinical outcomes in patients treated with radiotherapy (RT) for prostate cancer.

Patients and Methods
In total, 691 men with prostate adenocarcinoma treated with curative-intent RT between 1988 and 2006 were retrospectively analyzed. Of those, 189 patients (27%) were using statins, either during initial consultation or during follow-up. Lipid panels were collected (n = 298) a median of 5 months before RT start. Median follow-up was 50 months after RT.

Results
Statin use was associated with improved freedom from biochemical failure (FFBF; P < .001), freedom from salvage androgen deprivation therapy (FFADT; P = .0011), and relapse-free survival (RFS; P < .001). Improved FFBF for statin users was seen in low-, intermediate-, and high-risk groups (P = .0401, P = .0331, and P = .0034, respectively). The improvement in FFBF with statin use was independent of ADT use or radiation dose. On multivariable analysis, statin use was associated with improved FFBF (P < .001) along with pretreatment prostate-specific antigen ≤ 8.4 (P < .001), stage less than T2b (P = .0111), and Gleason score < 7 (P = .0098). On univariate analysis, pretreatment total cholesterol < 187 (89% vs 80%; P = .0494) and low-density lipoprotein (LDL) < 110 (96% vs 85%; P = .0462) were associated with improved 4-year FFBF.

Conclusion
Statin use was associated with a significant improvement in FFBF, FFADT, and RFS in this cohort of men treated with RT for prostate cancer. The favorable effect of statins may be mediated by direct effect or via the LDL-lowering effect of these medications.

J Clin Oncol 28:2653-2659. © 2010 by American Society of Clinical Oncology

INTRODUCTION

The management of prostate cancer is a significant health care challenge. Many treatment options exist, but the morbidity and cost of treatment are not trivial. Although risk classification schemes and nomograms attempt to identify men most likely to benefit from treatment, it remains difficult to balance the risks of disease progression against competing risks of mortality. This has resulted in controversy over prostate-specific antigen (PSA) screening and possible overtreatment leading to decreased quality of life and a drain on health care dollars. It is therefore of interest to conduct research regarding cancer prevention, identification of men who will benefit most from treatment, and effective therapy that limits treatment-related morbidity at reasonable cost.

Statin use has also been associated with improved freedom from biochemical failure in prostate cancer patients. However, there is limited evidence on the effect of statin use before radiotherapy on disease outcome. The purpose of this study was to determine whether statin use is associated with improved freedom from biochemical failure (FFBF), freedom from salvage androgen deprivation therapy (FFADT), and relapse-free survival (RFS) after radiotherapy for prostate cancer.
outcomes in patients undergoing radiation therapy (RT) and/or chemotherapy for rectal cancer,\textsuperscript{27} hepatocellular carcinoma,\textsuperscript{28} and bladder cancer.\textsuperscript{29}

We sought to determine the impact of statin therapy on clinical outcomes in a cohort of men treated with curative-intent RT for prostate cancer. A favorable interaction between statin use and RT on clinical outcome could have implications toward creating a low-cost, low-morbidity treatment option for men with prostate cancer. In this study, we compared the rates of biochemical control and relapse-free survival (RFS) for men undergoing RT for prostate cancer who were using a statin against the rates for men not using a statin. In addition, we sought to determine whether statin dosage, pretreatment cholesterol levels, and low-density lipoprotein (LDL) levels were associated with the magnitude of effect.

### PATIENTS AND METHODS

#### Patient Population

Between 1988 and 2006, 691 patients were treated at the University of Chicago Pritzker School of Medicine with curative-intent RT for nonmetastatic prostate adenocarcinoma. All men had known medication use at initial consultation. Patients were treated with external-beam RT and/or brachytherapy seed implants; patients with prior prostatectomy were excluded. The median age was 69 years. The majority of patients had clinical stage T1-2a disease (81%) and a median Gleason score (GS) of 6, with a median PSA of 8.4. A mediant of eight biopsy cores were taken with a median of three positive cores. Only seven patients (1%) had radiographic or pathologic lymph node—positive disease. Patients were stratified as low risk (T1-2a, PSA ≤10, GS ≤6), intermediate risk (either T2b and PSA 10-20 or GS 7), or high risk (≥T2c and PSA >20 or GS 8-10), based on National Comprehensive Cancer Network criteria.\textsuperscript{30} Medication use was documented in all patients at initial visit and follow-up. One hundred eighty-nine patients (27%) received statin therapy during RT (n = 150) or during follow-up (n = 39).

#### Data Collection

Physicians at the University of Chicago reviewed available medical records with approval from the institutional review board. Patients were clinically staged according to the American Joint Commission on Cancer staging system. Typical work-up included a digital rectal examination, PSA, and transrectal ultrasound with biopsies. Clinical stage was defined strictly on digital rectal exam only. Patients underwent computed tomography—based imaging or bone scans as indicated, based on risk factors. Information was collected regarding baseline demographic, disease, and treatment characteristics.

For the group of patients receiving statin therapy, a physician recorded information on the type of statin used and statin dose. The patient population used six different types of statins: atorvastatin, lovastatin, fluvastatin, pravastatin, simvastatin, and rosuvastatin. Statin doses were adjusted by normalizing to simvastatin equivalents.\textsuperscript{24,31} Patients were thereby classified as taking a high-, low-, or medium-dose statin, based on whether their dose was < 10 mg or ≥ 10 mg simvastatin equivalents. Pretreatment lipid panel data were recorded when available (n = 293). Lipid panels were drawn a median of 5 months before RT start date. Total cholesterol values were available for 184 patients who were not taking statins and 109 patients who were taking statins. The median pretreatment total cholesterol was 192 (range, 92 to 292) in patients not taking statins and 186 (range, 104 to 315) in patients taking statins. LDL values were available for 75 patients not taking statins and 94 patients taking statins. The median pretreatment LDL was 111 (range, 56 to 252) in patients not taking statins and 107 (range, 34 to 196) in patients taking statins.

#### Treatment

All patients were treated with curative-intent RT consisting of external-beam RT in 584 men (84%), brachytherapy seed implants in 61 men (9%), or a combination of both in 46 men (7%). Ninety-three percent of patients received RT to the prostate and seminal vesicles only. Patients treated with external-beam RT received treatment once daily, 5 d/wk. Forty-one percent were treated using intensity-modulated RT.\textsuperscript{32} The median radiation dose was 72 Gy with a median treatment time of 51 days. Patients treated with brachytherapy seed implants alone received 144 Gy. Two hundred eighty-six patients received androgen deprivation therapy during RT (n = 150) or during follow-up (n = 39).

### Table 1.

Patient Characteristics (n = 691)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Statin (n = 189)</th>
<th>No Statin (n = 502)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>Median 69</td>
<td>Range 42-83</td>
</tr>
<tr>
<td></td>
<td>Range 68</td>
<td>Range 44-83</td>
</tr>
<tr>
<td>Race</td>
<td>White 88</td>
<td>African American 90</td>
</tr>
<tr>
<td></td>
<td>Other/Unknown 6</td>
<td>Other/Unknown 6</td>
</tr>
<tr>
<td>Pre-RT PSA level, ng/mL</td>
<td>Median 7.2</td>
<td>Range 1.3-154.6</td>
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<tr>
<td>PSA level, ng/mL (n = 686)</td>
<td>Median 105</td>
<td>Range 45-76.4</td>
</tr>
<tr>
<td>Risk category (n = 684)</td>
<td>Low 74</td>
<td>Intermediate 73</td>
</tr>
<tr>
<td></td>
<td>High 41</td>
<td>Range 34-49</td>
</tr>
<tr>
<td>Gleason score</td>
<td>2-6 105</td>
<td>7 65</td>
</tr>
<tr>
<td></td>
<td>8-10 19</td>
<td>8-10 19</td>
</tr>
<tr>
<td>Androgen deprivation therapy</td>
<td>Median duration, months 4</td>
<td>Range 12-80</td>
</tr>
<tr>
<td>Duration of therapy, months (n = 258)</td>
<td>≤ 6 72</td>
<td>≤ 12 80</td>
</tr>
<tr>
<td></td>
<td>Range 104-315</td>
<td>Range 56-252</td>
</tr>
<tr>
<td>Pretreatment total cholesterol (n = 293)</td>
<td>Median 186</td>
<td>Range 104-315</td>
</tr>
<tr>
<td>Pretreatment LDL (n = 169)</td>
<td>Median 107</td>
<td>Range 34-196</td>
</tr>
<tr>
<td>Intensity-modulated RT (n = 691)</td>
<td>Median 112</td>
<td>Range 45-76.4</td>
</tr>
<tr>
<td>Brachytherapy boost</td>
<td>Median 31</td>
<td>Range 0.6-145</td>
</tr>
</tbody>
</table>

Abbreviations: RT, radiotherapy; PSA, prostate-specific antigen; LDL, low-density lipoprotein.

\[<\text{Table 1. Patient Characteristics (n = 691)}\]
(41%) received androgen deprivation therapy (ADT) in the neoadjuvant, concurrent, or adjuvant setting with RT, consisting of a gonadotropin-releasing hormone with or without a concurrent antiandrogen. The median duration of ADT was 4 months. Of 258 patients with records of ADT duration available, 226 (87%) received ≤ 6 months of ADT.

**Assessment of Response**

The primary end point was freedom from biochemical failure (FFBF) defined using the Phoenix definition (PSA nadir + 2 ng/mL). Other end points included RFS, which was inclusive of biochemical failure; distant metastasis; salvage ADT; death from any cause; freedom from androgen deprivation therapy; freedom from distant metastases; cause-specific (death from prostate cancer) survival; and overall survival. With all end points except RFS, patients who did not meet the specified end point of interest (eg, FFBF) but had any other event (eg, death) were censored at the time of last follow-up pertaining to that end point. The median follow-up time was 50 months from the completion of RT to the last measured PSA.

**Statistics**

Differences in categoric variables between groups were tested using χ² analysis. Continuous variables were compared using two-sample t tests. Kaplan-Meier curves for FFBF were generated, and survival comparisons were made with the log-rank test. Univariate analysis was performed according to risk category, radiation dose, use of statins, use of ADT, and lipid levels. Multivariable analysis was performed using a Cox proportional hazards model to determine prognostic factors for FFBF and RFS. The effects of statin use and other covariates in terms of the cumulative incidence function, treating deaths from causes other than prostate cancer as a competing risk, were estimated using the methods described in Fine and Gray.24 Explanatory variables were included in the multivariable model if they were found to be associated with outcome (P < .01) on univariate analysis.

**RESULTS**

**Overall Group**

Analysis of the entire cohort (N = 691) revealed an FFBF of 83% and an RFS of 73% at 4 years. By risk category, 4-year FFBF was 92% for low-risk patients, 87% for intermediate-risk patients, and 67% for high-risk patients (P < .001). Four-year RFS was 83% for low-risk patients, 77% for intermediate-risk patients, and 56% for high-risk patients (P < .001).

The group of patients taking statins had more favorable pretreatment characteristics (Table 1). Patients taking statins had significantly lower median pretreatment PSA (7.2 vs 8.7 ng/mL; P = .0166) and more T1-2a disease (88% vs 79%; P = .0208). Higher percentages in the statin group were treated with intensity-modulated RT (59% vs 34%; P < .001) and ADT (47% vs 39%; P = .0913). Median radiation dose was higher in the statin group (74 vs 72 Gy; P = .0231).

Factors associated with improved FFBF on univariate analysis included statin use (P < .001), risk group (P < .001), total cholesterol < 187 (P = .0494), and LDL < 110 (P = .0462; Table 2). Statin use (P < .001) and risk group (P < .001) were also associated with improved RFS. On multivariable analysis, factors associated with improved FFBF were statin use (P = .002) and log PSA (P < .001; Table 3). Factors associated with RFS on multivariable analysis included log PSA (P < .001), dose > 74 Gy or brachytherapy (P < .001), statin use (P = .005), and GS < 7 (P = .04). There was a trend toward improved RFS with use of hormone therapy (P = .06).

**Analysis of Patients Receiving Statins**

A total of 189 patients (27%) received statin therapy during or after RT. Statin users had significantly better FFBF (P < .001; Fig 1), RFS (P < .001; Fig 2), and freedom from androgen deprivation therapy (98% vs 93% at 4 years; P = .0011). Statin use was associated with improved FFBF in low-risk (95% vs 91%; P = .0401), intermediate-risk (94% vs 84%; P = .0331), and high-risk groups (85% vs 61%; P = .0034). There was no difference in overall survival (94% vs 90%; P = .1235), cause-specific survival (99% vs 97%; P = .1535), and freedom from distant metastases (98% vs 96%;

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**Table 2. Univariate Analysis for Factors Associated With Improved FFBF and RFS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>4-Year FFBF (%)</th>
<th>P</th>
<th>4-Year RFS (%)</th>
<th>P</th>
</tr>
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<tbody>
<tr>
<td>Risk group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>92</td>
<td>&lt; .001</td>
<td>84</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Medium</td>
<td>87</td>
<td>.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>67</td>
<td>.56</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Statin use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>93</td>
<td>&lt; .001</td>
<td>84</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>No</td>
<td>80</td>
<td>.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timing of statin use</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Before RT</td>
<td>.94</td>
<td>.3260</td>
<td>.85</td>
<td>.9774</td>
</tr>
<tr>
<td>After RT</td>
<td>89</td>
<td>.84</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; Median of 187 mg/dL</td>
<td>89</td>
<td>.0494</td>
<td>.75</td>
<td>.4549</td>
</tr>
<tr>
<td>≥ Median of 187 mg/dL</td>
<td>79</td>
<td>.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; Median of 110 mg/dL</td>
<td>96</td>
<td>.0462</td>
<td>.82</td>
<td>.8606</td>
</tr>
<tr>
<td>≥ Median of 110 mg/dL</td>
<td>84</td>
<td>.81</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: FFBF, freedom from biochemical failure; RFS, relapse-free survival; RT, radiotherapy; LDL, low-density lipoprotein.

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**Table 3. Multivariable Analysis for Factors Associated With Improved FFBF and RFS**

<table>
<thead>
<tr>
<th>Variable</th>
<th>FFBF</th>
<th>RFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statin use</td>
<td>HR</td>
<td>95% CI</td>
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<tr>
<td></td>
<td></td>
<td>P</td>
</tr>
<tr>
<td>Yes</td>
<td>0.43</td>
<td>0.25 to 0.73</td>
</tr>
<tr>
<td>No</td>
<td>0.71</td>
<td>0.47 to 1.08</td>
</tr>
<tr>
<td>Stage &lt; T2b</td>
<td>0.72</td>
<td>0.5 to 1.04</td>
</tr>
<tr>
<td>Gleason score &lt; 7</td>
<td>1.7</td>
<td>1.4 to 2.05</td>
</tr>
<tr>
<td>Log PSA</td>
<td>1.0</td>
<td>0.48 to 1.1</td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>0.73</td>
<td>0.52 to 1.1</td>
</tr>
</tbody>
</table>

Abbreviations: FFBF, freedom from biochemical failure; RFS, relapse-free survival; HR, hazard ratio; PSA, prostate-specific antigen.
Patients benefited from statin therapy independent of treatment characteristics such as ADT use or radiation dose. In the subset of patients treated with ADT, FFBF was 93% for statin users compared with 77% for nonusers (P = .0040). In the subset not receiving ADT, a significant benefit was also seen (93% vs 82%; P = .0011). The effect of statin therapy was seen regardless of radiation dose, but a larger benefit was seen in men treated with lower radiation doses. In men treated with < 74 Gy, FFBF was 93% for statin users compared with 75% for nonusers (P = .0025). In those treated with > 74 Gy or seed implants, FFBF was 92% in statin users and 85% in nonusers (P = .0167).

The type of statin used was known for all 189 patients, and there was no relationship between the type of statin and FFBF by log-rank analysis (P = .1190). This analysis was limited by patient numbers because the majority of patients were taking either atorvastatin (n = 96) or simvastatin (n = 49). There was no significant difference in FFBF (P = .9375) or RFS (P = .5367) for statin dose < 40 mg compared with > 40 mg simvastatin equivalents.

Lipid panel data were collected when available, including values for total cholesterol, LDL, high-density lipoprotein, and triglycerides. All men with missing data were excluded from this analysis. There was no correlation between pretreatment high-density lipoprotein and triglycerides and any outcomes. There was, however, an association between lower total cholesterol and LDL pretreatment values with improved FFBF. Patients were stratified on the basis of whether their pretreatment total cholesterol and LDL values were lower or higher than the median value (187 and 110, respectively). Those with lower total cholesterol, stratified by the median, had improved FFBF at 4 years (89% vs 80%; P = .0494). Lower LDL was also associated with improved FFBF (96% vs 85%; P = .0462). Of note, there were no significant differences in pretreatment PSA, T-stage, or GS distributions between the low- and high-cholesterol groups or between the low- and high-LDL groups. The prognostic effect of LDL level was greatest in men not treated with concurrent ADT, with improved FFBF for men with LDL < 110 (100% vs 88%; P = .0119). Patients were divided into four groups depending on statin use and LDL level: (1) statin, LDL greater than or equal to the median; (2) statin, LDL less than the median; (3) no statin, LDL greater than or equal to the median; and (4) no statin, LDL less than the median. Men taking a statin with LDL less than median had the highest FFBF, while men not taking a statin with LDL greater than or equal to the median had the lowest FFBF (98% vs 78%; P = .0918). In the subset of men with LDL information available and not taking statins, LDL was associated with FFBF at 4 years, although this difference was not statistically significant (96% LDL less than median vs 78% LDL greater than or equal to median; P = .1552). A separate multivariable analysis including only statin use and LDL in the model was performed against FFBF. In this analysis, lower LDL was associated with improved FFBF (P = .0473), while statin use was not (P = .1394; Table 4).

Statin use has steadily increased over the past two decades, and it is estimated that 24 million Americans are using these medications. Patients benefit from statin therapy independent of treatment characteristics such as ADT use or radiation dose. In the subset of patients treated with ADT, FFBF was 93% for statin users compared with 77% for nonusers (P = .0040). In the subset not receiving ADT, a significant benefit was also seen (93% vs 82%; P = .0011). The effect of statin therapy was seen regardless of radiation dose, but a larger benefit was seen in men treated with lower radiation doses. In men treated with < 74 Gy, FFBF was 93% for statin users compared with 75% for nonusers (P = .0025). In those treated with > 74 Gy or seed implants, FFBF was 92% in statin users and 85% in nonusers (P = .0167).

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Statin use has steadily increased over the past two decades, and it is estimated that 24 million Americans are using these medications. Given the favorable effect of statins on vascular health,17 statin use is expected to increase worldwide. The potential role of statins in carcinogenesis and cancer therapy has been investigated in several studies,
Statins and Risk of Prostate Cancer Recurrence

Our study showed that statin use improved FFBF and RFS in prostate cancer patients treated with RT. This effect was seen across all risk categories and RT dose ranges and was independent of ADT use. There was an association between lower LDL levels and improved FFBF. Because statin use lowers LDL levels, it is difficult to determine whether improved outcomes are truly related to lower LDL or whether low LDL and improved FFBF are both by-products of statin use. Interestingly, low LDL was more predictive of improved FFBF in men not receiving ADT (P = .0306) than in men receiving ADT (P = .7920). This finding raises the question of whether LDL may represent the activity of, or interact with, the hormonal axis in lieu of more traditional forms of hormonal therapy. Cholesterol is a precursor for androgen formation, and it is conceivable that by lowering cholesterol levels, statins may lower levels of intraprostatic androgens. Hamilton et al postulated that depletion of intraprostatic androgens could, in turn, result in PSA decline. In our study, statin use was associated with lower PSA and clinical stage at diagnosis. Additionally, LDL levels may be modifying intraprostatic hormonal levels, resulting in a differential effect of RT.

Statins inhibit 3-hydroxy-3-methyl-glutaryl coenzyme A (HMG-CoA) reductase, the rate-limiting enzyme in cholesterol biosynthesis, to lower LDL cholesterol and triglyceride levels. Multiple studies have shown that lipogenic enzymes contribute to cancer pathogenesis and that increased cholesterol content in prostatic tissue correlates with malignancy. The relationship between statins and carcinogenesis is undefined, but there are several possible explanations. Reducing cholesterol bioavailability inhibits the prosurvival effects of epidermal growth factor receptor activation. Cholesterol disruption has been shown to inhibit AKT1 activity and stimulate apoptosis in prostate cells. While the effects of statins on prostate biology may be mediated by cholesterol, it is also possible that statins have non-cholesterol–mediated effects. For instance, statin use results in depletion of mevalonate. Mevalonate is a precursor of farnesyl pyrophosphate and geranylgeranyl pyrophosphate, both of which are important for function of intracellular survival signals such as Rho and Ras.

Clinical data regarding the use of statin therapy in the setting of prostate cancer treatment are limited. Another study of 871 men presented in abstract form, indicated an improvement in PSA RFS for men taking statins treated with RT. However, in a similar analysis of 968 men, Soto et al found that statin use was associated with PFS on univariate but not on multivariable analysis. The statin users tended to have better disease characteristics such as lower pretreatment PSA and T stage, leading to fewer high-risk patients taking statins. As a result, the beneficial effect of statins may have been confounded with less advanced tumors at presentation. Differences in patient population, RT techniques, or follow-up time may have contributed to the discrepancy in results among these studies. It is possible that patients undergoing more aggressive radiation treatments derive less benefit from statin use. In contrast to the study by Soto et al, patients in our study were treated with lower radiation doses and less frequently received whole pelvis RT. Similarly, Moyad et al did not report a benefit to statin use in patients treated with brachytherapy, which could be related to the relatively high radiation doses delivered with brachytherapy.

Conclusions from this data set are limited by the retrospective nature of analysis. The study cohort is heterogeneous, without control over RT techniques or duration of statin therapy, dose, or timing over the period of follow-up. Subset and multivariable analyses attempted to control for this heterogeneity, and the results indicate that the benefit seen for men taking a statin is not only the result of differences in stage or grade at presentation. However, residual confounding or confounding due to other factors not controlled for cannot be ruled out, and a randomized study would be necessary to test this hypothesis. Our study suggests an association between lower LDL levels and improved FFBF, but numbers are relatively limited in this subset, and this association should be explored in future studies. Finally, although the median follow-up is sufficient to analyze end points including FFBF and RFS, the follow-up needs to mature further to draw conclusions regarding end points such as cause-specific or overall mortality.

Despite the limitations, the implications of this study are important. Statins have been shown to have in vitro anticancer activity and synergetic effects with radiation in various cell lines, by means of cell cycle arrest and apoptosis. Our own preliminary preclinical experiments in prostate cancer xenografts demonstrates a clear radiosensitizing effect of simvastatin on cell growth (unpublished data). If confirmed as potent radiation sensitizers or if they have anticancer effects otherwise, statins could allow for less use of ADT as well as radiation dose de-escalation. These modifications could in turn lead to decreased treatment costs and decreased treatment morbidities. Further study is essential, especially regarding the mechanism of action, to explore the possibility that statin therapy may improve clinical outcomes, treatment costs, and treatment morbidity in men treated with RT for prostate cancer.

Table 4. Multivariable Analysis for Factors Associated With Improved FFBF in Patients With Pretreatment LDL Available (n = 169)

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statin use</td>
<td>0.51</td>
<td>0.20 to 1.24</td>
<td>1.394</td>
</tr>
<tr>
<td>LDL &lt; median</td>
<td>0.38</td>
<td>0.12 to 0.99</td>
<td>0.0473</td>
</tr>
</tbody>
</table>

Abbreviations: FFBF, freedom from biochemical failure; LDL, low-density lipoprotein; HR, hazard ratio.

Although all authors completed the disclosure declaration, the following author(s) indicated a financial or other interest that is relevant to the subject matter under consideration in this article. Certain relationships marked with a "U" are those for which no compensation was received; those relationships marked with a "C" were compensated. For a detailed description of the disclosure categories, or for more information about ASCO’s conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

Employment or Leadership Position: None
Consultant or Advisory Role: Ralph R. Weichselbaum, GenVec (C)
Stock Ownership: None
Honoraria: None
Research Funding: None
Expert Testimony: None
Other Remuneration: None

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Manuscript writing: Ruchika Gutt, Theodore Karrison, Ralph R. Weichselbaum, Stanley L. Liauw

Final approval of manuscript: Ruchika Gutt, Nathan Tonlaar, Rangesh Kunnakavakkam, Theodore Karrison, Ralph R. Weichselbaum, Stanley L. Liauw
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