As morbidity and mortality from graft dysfunction and failure after kidney transplantation have declined, transplant-related malignancies have become one of the most significant sources of posttransplant complications. Currently, cancer is a major factor limiting the life expectancy of kidney transplant patients, and cancer management is now a crucial component of their medical care. This paper discusses the incidence of cancer and its most common types after renal transplantation, the etiology of posttransplant malignancy, and prevention and management of cancer in the renal transplant recipient. Clinicians providing care for renal transplant recipients should be familiar with the types of malignancies for which the renal transplant recipient is at risk, keep immunosuppressive therapy to the minimum level that maintains good graft function, judiciously choose immunotherapies based on the most current and rigorous evidence, engage in cancer prevention efforts throughout the transplant course, practice vigilant cancer surveillance after transplantation, and aggressively treat cancers that do arise.

the incidence of cancer reflects the intersection of several factors including changing trends in the use of immunosuppressive therapy, which can indirectly and directly contribute to oncogenesis; improved graft and patient survival, which lengthens the period of time for observing de novo cancers; and increasing age of the average transplant recipient.

Information on the incidence of cancer in renal transplant patients originates primarily from registries, including the Israel Penn International Transplant Tumor Registry (also known as the Cincinnati Transplant Tumor Registry), the Collaborative Transplant Study, and the Australian and New Zealand Transplant Registry.\(^7\),\(^9\)\(^\text{–}\)\(^\text{11}\) In the Israel Penn International Transplant Tumor Registry, the only global registry of transplant-associated malignancies, the risk of cancer is 3 to 4 times higher in renal transplant recipients than the general population.\(^2\),\(^3\) As of 2000, the registry had data on 9032 kidney transplant recipients who developed 9688 types of cancer. The main cancer types in renal transplant recipients were lymphomas and lymphoproliferations (posttransplant lymphoproliferative disorder [PTLD]) and cancers of the skin and lips followed by cancers of the vulva and perineum, in situ carcinomas of the cervix, Kaposi’s sarcoma, hepatocellular carcinomas, and renal carcinomas. PTLDs were distinguished by involvement of extranodal sites, particularly the brain.

Similar results have been found in other registries. In the Australian and New Zealand Transplant Registry, which included data from 13077 renal transplants performed in Australia and New Zealand from 1980 to 2003, renal transplant recipients were at least 3 times more likely than the general population to develop cancer (Table).\(^8\) The cumulative risk of developing at least 1 malignancy (except nonmelanoma skin cancer) increased with time and was approximately 30% by 20 years after transplant (Figure 1).\(^5\) Specific cancers for which renal transplant recipients were at particularly high risk included Kaposi’s sarcoma, genitourinary cancers, and lymphomas (Table).\(^8\)

Contributions to registries are often voluntary, some types of tumors are excluded, and only first cancer cases are included.\(^1\) Therefore, registry data may underestimate cancer risk because of underreporting and incomplete data on reported malignancies. Studies that have attempted to overcome these limitations generally demonstrate a higher incidence of cancer than the registry studies. For example, in an analysis of Medicare billing claims of 35765 kidney transplant recipients from 1995 to 2001, the 3-year cumulative incidence of cancer was 15%.\(^12\) In an observational cohort study to assess cancer rates in 2419 renal transplant recipients treated at the Transplantation Center Munich from 1978 to 2005, the cumulative incidence of cancer in renal transplant patients over 25 years of follow-up was 49.3% compared with 21% for healthy sex- and age-matched controls.\(^7\)

The most common cancers in renal transplant recipients were nonmelanoma skin cancers (20.5%) followed by kidney cancers (12%) and cancers of the pharynx, larynx, or oral cavity (8.2%). Compared with age- and sex-matched controls, renal transplant recipients were 4.3 times more likely to develop any cancer, 52.7 times more likely to develop skin cancer, 17.6 times more likely to develop kidney cancer, 12.9 times more likely to develop pharyngeal or laryngeal cancer, and 142.3 times more likely to develop cancer involving the central nervous system. Risk factors for cancer development included being male, being older, having preformed antibodies before transplantation, and longer time on immunosuppression. Although cancer risk did not significantly differ as a function of type of maintenance immunosuppressive therapy, mammalian target of rapamycin (mTOR) inhibitor-based regimens were associated with numerically lower rates of malignancy than other regimens.

**Figure 1. Cumulative Risk of at Least 1 Cancer While Graft Continues to Function After Transplantation**

*Excluding nonmelanoma skin cancer. Patients cease to be at risk at the time of graft failure, death, or last known follow-up. The expected incidence is calculated for a general population of the same age and sex distribution. Reprinted with permission from Chapman and Webster. Cancer Report: ANZDATA Registry 2004 Report. Adelaide, Australia: Australia and New Zealand Dialysis and Transplant Registry; 2004.\(^8\)
The standardized incidence ratio is the ratio of the observed number of tumors to the expected number in transplant recipients compared with age- and sex-matched controls in the same geographical area. Based on observation of 13,077 patients in Australia and New Zealand from 1980–2003 for 110,395 person-years of observation. CI = confidence interval. Data from Chapman and Webster.8

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Observed Frequency</th>
<th>Expected Frequency</th>
<th>Standardized Incidence Ratio*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All registerable cancers</td>
<td>1545</td>
<td>495.08</td>
<td>3.12</td>
<td>2.97, 3.28</td>
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<tr>
<td>Head, neck, lip</td>
<td>63</td>
<td>22.77</td>
<td>2.77</td>
<td>2.16, 3.54</td>
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<td>4.73</td>
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<td>1.49</td>
<td>2.01</td>
<td>0.65, 6.23</td>
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<td>Colorectal</td>
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<td>72.76</td>
<td>1.94</td>
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<td>3.21</td>
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<td>Pancreas</td>
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<td>9.3</td>
<td>1.72</td>
<td>1.05, 2.81</td>
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<td>Nasal cavity</td>
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<td>2.25, 13.0</td>
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<td>5.54</td>
<td>1.99</td>
<td>1.11, 3.95</td>
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<tr>
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<td>2.01</td>
<td>1.66, 2.42</td>
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<td>0.57</td>
<td>10.6</td>
<td>4.76, 23.6</td>
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<tr>
<td>Bone, articular cartilage</td>
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<td>1.01</td>
<td>4.99</td>
<td>2.06, 11.87</td>
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<tr>
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<td>Mesothelemoma</td>
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<td>0.51, 3.59</td>
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<td>Kaposi's sarcoma</td>
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<td>26.44</td>
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<td>Connective, other soft tissue</td>
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<td>Breast</td>
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<td>1.01, 1.54</td>
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<td>0.9</td>
<td>45.6</td>
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<td>36.02</td>
<td>20.46, 63.43</td>
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<tr>
<td>Cervix uteri</td>
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<td>6.9</td>
<td>6.6</td>
<td>4.94, 8.81</td>
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<tr>
<td>Corpus uteri</td>
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<td>9.73</td>
<td>1.85</td>
<td>1.16, 2.93</td>
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<tr>
<td>Ovary</td>
<td>8</td>
<td>7.56</td>
<td>1.06</td>
<td>0.53, 2.12</td>
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<tr>
<td>Other female genital organs</td>
<td>0</td>
<td>0.32</td>
<td>0</td>
<td>---, ---</td>
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<tr>
<td>Penis, other male genital organs</td>
<td>11</td>
<td>0.62</td>
<td>17.81</td>
<td>9.86, 32.16</td>
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<td>Prostate</td>
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<td>54.72</td>
<td>0.97</td>
<td>0.74, 1.27</td>
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<tr>
<td>Testis</td>
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<td>4.36</td>
<td>0</td>
<td>---, ---</td>
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<td>Kidney, ureter, urethra</td>
<td>125</td>
<td>14.73</td>
<td>8.49</td>
<td>7.12, 10.12</td>
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<tr>
<td>Bladder</td>
<td>82</td>
<td>15.97</td>
<td>5.14</td>
<td>4.14, 6.38</td>
</tr>
<tr>
<td>Eye</td>
<td>4</td>
<td>1.5</td>
<td>2.67</td>
<td>1.71, 3.72</td>
</tr>
<tr>
<td>Brain, central nervous system</td>
<td>16</td>
<td>9.59</td>
<td>1.67</td>
<td>1.02, 2.72</td>
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<tr>
<td>Thyroid</td>
<td>27</td>
<td>5.96</td>
<td>4.53</td>
<td>3.11, 6.61</td>
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<tr>
<td>Other endocrine glands</td>
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<td>0.43</td>
<td>9.37</td>
<td>3.52, 24.97</td>
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<tr>
<td>Unknown primary site</td>
<td>70</td>
<td>16.74</td>
<td>4.18</td>
<td>3.31, 5.28</td>
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<tr>
<td>All lymphomas</td>
<td>231</td>
<td>22.74</td>
<td>10.16</td>
<td>8.93, 11.55</td>
</tr>
<tr>
<td>Immunoproliferative neoplasms</td>
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<td>10.23</td>
<td>3.3, 31.73</td>
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<tr>
<td>Multiple myeloma</td>
<td>15</td>
<td>5.62</td>
<td>2.67</td>
<td>1.61, 4.42</td>
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<tr>
<td>Leukemia</td>
<td>32</td>
<td>12.28</td>
<td>2.61</td>
<td>1.84, 3.69</td>
</tr>
</tbody>
</table>

*The standardized incidence ratio is the ratio of the observed number of tumors to the expected number in transplant recipients compared with age- and sex-matched controls in the same geographical area.

Based on observation of 13,077 patients in Australia and New Zealand from 1980–2003 for 110,395 person-years of observation. CI = confidence interval. Data from Chapman and Webster.8
Etiology of Posttransplant Malignancy

The causes of posttransplant malignancy are multifactorial and include the following:

• **Chronic disease.** A contribution of chronic disease to posttransplant malignancy is suggested by the finding that the risk of native kidney renal cell carcinoma in kidney transplant recipients is directly related to the duration of end-stage renal disease. In a study of 260 renal transplant recipients, the incidence of posttransplant renal cell carcinoma in patients with end-stage renal disease undergoing transplantation was 4.2%.

• **Chronic immunosuppressive therapy.** A role of chronic immunosuppression in posttransplant malignancy is suggested by the observation of an elevated incidence of cancer in most medical disorders associated with immunosuppression. In renal transplant recipients, the risk of malignancy is directly related to the intensity of immunosuppression. For example, in a prospective, open-label, randomized assessment of the effect of 2 cyclosporine maintenance regimens on cancer incidence, 231 kidney transplant recipients received maintenance cyclosporine yielding trough blood concentrations either between 75 and 125 ng/mL (n = 116) or between 150 and 250 ng/mL (n = 115). At 66 months of follow-up, the incidence of cancer was significantly higher in the group that received the higher cyclosporine dose (32% vs 20%, P < .034).

• **Oncogenic viruses.** Immunosuppression increases the risk of infection with pro-oncogenic viruses. Acquisition of specific viruses has been linked to the development of cancer in renal transplant recipients. For example, Epstein-Barr virus infection is associated with PTLD; human herpesvirus 8 is associated with Kaposi's sarcoma; human papilloma viruses are associated with cervical cancer; penile cancer, nonmelanoma skin cancer, and Bowen's disease; and hepatitis B and C are associated with hepatocellular carcinoma.

Immunosuppressive Agents and Posttransplant Malignancy

There is little question that the incidence of cancer increases with increasing time on immunosuppression and with dose of immunosuppressive therapy. The association between cumulative exposure to immunosuppressive therapy and cancer risk has been observed with most immunosuppressive agents studied for prolonged periods of time. This finding has led to the suggestion that the development of cancer is linked to the immunosuppressed state per se rather than to a specific immunosuppressive agent or combination of agents. Although immunosuppression, regardless of its cause, is in fact linked to cancer development, growing evidence suggests that immunosuppressive agents may have unique oncogenic profiles. On the basis of data available to date, some immunosuppressive agents appear to have direct oncogenic properties (eg, causing DNA damage, interfering with DNA repair, and upregulating cytokines and other proteins that promote tumor progression) whereas others appear to be less oncogenic or even to have antiproliferative properties.

The main immunosuppressive agents used today in renal transplant recipients include induction therapy using anti-T cell antibodies (depleting and nondepleting), corticosteroids, the calcineurin inhibitors cyclosporine and tacrolimus, the antimetabolite azathioprine, the inosine monophosphate dehydrogenase inhibitor mycophenolate mofetil, and the mTOR inhibitors sirolimus and everolimus. Conclusions about the relative carcinogenic potential of each individual immunosuppressive agent should be drawn cautiously. Most randomized, controlled clinical trials have insufficient sample sizes and length of follow-up to detect differences in cancer incidence among immunosuppressive therapies. Registries often lack important contextualizing information, such as drug doses, and the outcomes of those lost to follow-up. Assessing the relative carcinogenic potential of immunosuppressive agents also is complicated by the different eras of introduction of the various immunosuppressive agents with respect to advances in prevention, diagnosis, and treatment of posttransplant malignancies. Furthermore, in clinical studies, the potential direct carcinogenicity of...
specific immunosuppressive drugs is difficult to assess independently of carcinogenicity secondary to immunosuppression.

Some antibody induction therapies, particularly lymphocyte-depleting antibodies, have been associated with an increased risk of posttransplant malignancy.16 In a study of 38,519 kidney transplant recipients, the incidence of PTLD was 0.85% in 2713 patients treated with the monoclonal antibody muromonab-CD3, 0.81% in 4343 patients treated with polyclonal antilymphocyte antibodies, 0.5% in 7800 patients treated with a non-depleting interleukin (IL)-2 receptor antibody, and 0.51% in 23,663 patients with no induction therapy.17 The risk of PTLD was 72% higher in patients treated with depleting antibodies compared with those with no induction therapy ($P = .005$). The risk of cancer with depleting antibodies may be higher than that associated with nondepleting regimens. In an observational cohort study to assess cancer rates in 2419 renal transplant recipients treated at the Transplantation Center Munich from 1978 to 2005, induction therapy using IL-2 receptor antagonists significantly reduced the tumor risk of transplant recipients compared with those given depleting antibodies.18

Data from the Collaborative Transplant Study database show that the risk of graft loss associated with induction agents and that of non-Hodgkin lymphoma are dissociable, a finding that counters the common perception that the graft-enhancing and lymphoma-inducing properties of antilymphocyte induction agents are closely linked.19 Among 112,122 patients receiving a kidney transplant from 1985 to 2004, the inducing agents associated with the highest rates of graft survival (ie, rabbit antithymocyte globulin or IL-2RA), were not necessarily associated with the highest rates of lymphoma (ie, horse antithymocyte globulin, muromonab-CD3, or rabbit antithymocyte globulin; Figure 2).20

Considered in aggregate, the data show that monoclonal and polyclonal depleting antibodies increase cancer risk.

Corticosteroids are a standard component of many immunosuppressive regimens and are almost always used with other immunosuppressants. The relative contribution of corticosteroids to malignancy is therefore difficult to assess in observational studies. Because corticosteroids have been shown to have pro-oncogenic action in vitro and to decrease tumor immunosurveillance, they are regarded as carcinogenic.1 Corticosteroids are associated with an elevated risk of malignancy in patients receiving them for reasons other than immunosuppression, thus supporting this possibility.

Among 59,043 individuals with prescriptions for corticosteroids in the population-based North Jutland Prescription Database and the Danish Cancer Registry, the risks of squamous cell carcinomas and basal cell carcinomas of the skin were increased relative to expected values over an 8-year observation period.21 The risks were particularly elevated in those with at least 15 prescriptions for corticosteroids, among whom the standardized incidence ratios for squamous cell carcinomas and basal cell carcinomas were 2.45 and 1.52, respectively. During the past few years, steroid avoidance and steroid withdrawal protocols have been more widely employed, but reliable information on cancer risk has not yet emerged.

![Figure 2. Cumulative Incidence of NHL After Renal Transplantation *](image-url)
The calcineurin inhibitors cyclosporine and tacrolimus have been associated with the development of malignancies in renal transplant recipients and nontransplanted patients.\textsuperscript{22-25} The prospective, open-label, randomized demonstration (described earlier) that the incidence of cancer was significantly higher in a group of patients who received higher cyclosporine doses than in a group receiving lower doses (32\% vs 20\%, \(P<.034\)) is consistent with a pro-oncogenic effect of cyclosporine.\textsuperscript{15} Whether the pro-oncogenic effects of tacrolimus differ from those of cyclosporine has not been definitively established. In a meta-analysis of 30 clinical trials (\(n=4102\)) of tacrolimus versus cyclosporine as primary immunosuppression for kidney transplant recipients, no difference was observed between the drugs in the incidence of malignancy at 1 year.\textsuperscript{26} Possible mechanisms of calcineurin inhibitor oncogenicity as demonstrated in preclinical studies include impairment in ability to repair DNA damage and stimulation of production of pro-oncogenic cytokines, such as transforming growth factor \(\beta\), vascular endothelial growth factor (VEGF), and their receptors.\textsuperscript{27-29}

Like the calcineurin inhibitors, azathioprine has been associated with the development of malignancies in renal transplant recipients and nontransplanted patients.\textsuperscript{30-33} Possible mechanisms of azathioprine oncogenicity as demonstrated in preclinical studies include impairment in ability to repair DNA damage and elicitation of codon misreads.\textsuperscript{34}

Both in vitro and in vivo, mycophenolate mofetil has antiproliferative activity against leukemias and lymphomas.\textsuperscript{35,36} Whether these effects are realized in a reduction in risk of malignancy is not clear. In the North American Pediatric Renal Transplant Cooperative Study of 6720 pediatric renal transplant recipients, the use of mycophenolate mofetil on day 30 as a component of initial immunosuppression was not a significant risk factor for PTLD.\textsuperscript{38} The incidence of PTLD for those taking mycophenolate mofetil on day 30 was 0.78\% compared with 1.78\% in the sample as a whole. Some evidence suggests that mycophenolate mofetil compared with other immunosuppressive regimens may be associated with reduced risk of some cancers whereas other studies suggest no difference between mycophenolate mofetil and other agents. Results of studies on the relationship between mycophenolate mofetil treatment and PTLD are inconsistent.\textsuperscript{3} In a large study of PTLD in 38 519 kidney transplant recipients, mycophenolate mofetil maintenance immunosuppression was associated with significantly lower risk of PTLD and graft loss compared with azathioprine.\textsuperscript{39} In a meta-analysis of 20 clinical trials (\(n=6387\)) of mycophenolate mofetil versus azathioprine in renal transplantation, the incidence of skin malignancy did not differ between the drugs.\textsuperscript{40} Overall, the data suggest that mycophenolate mofetil is not associated with increased risk of malignancy, but more systematic study is warranted.

The mTOR inhibitors sirolimus and everolimus inhibit replication of cancer cells and tumor angiogenesis, often accompanied by a decrease in tumor expression of VEGF and its receptors.\textsuperscript{36,37} The preclinical anti-oncogenic and antitumor effects of mTOR inhibitors are reviewed extensively later on.\textsuperscript{38-41} The mTOR inhibitors are being investigated in clinical trials as anticancer agents.\textsuperscript{42} For example, the mTOR inhibitor temsirolimus compared with interferon (IFN) \(\alpha\) improved survival among patients with metastatic renal cell carcinoma in a randomized phase III trial of 623 patients. Patients who received temsirolimus alone had longer overall survival (hazard ratio for death, 0.73) and longer progression-free survival (\(P<.001\)) than did patients who received IFN alone. Median overall survival time was 10.9 months in the temsirolimus group and 7.3 months in the IFN group. Combination therapy with temsirolimus and IFN did not improve survival relative to administration of IFN alone.

Data in renal transplant recipients suggest that the mTOR inhibitors may be associated with a lower incidence of malignancies than other immunosuppressive agents. In a review of the incidence of skin cancer in 5 clinical trials of sirolimus for renal transplant recipients, patients receiving sirolimus as base therapy had no malignancies at 2 years compared with a 5\% incidence in patients receiving cyclosporine.\textsuperscript{44} Five-year outcomes have been reported for 1 of the studies included in the review—a comparison of effects of sirolimus plus continuous cyclosporine (\(n=215\)) with sirolimus plus cyclosporine that was eliminated while sirolimus was continued in concentration-controlled doses (\(n=215\)).\textsuperscript{45} The incidence of malignancy was significantly lower in patients receiving sirolimus with elimination of cyclosporine than patients in whom cyclosporine was not eliminated (Figure 3).\textsuperscript{46}

mTOR inhibitors were associated with a lower incidence of de novo malignancies than calcineurin inhibitors in a multivariate analysis of posttransplant malignancies in 33 249 kidney transplant recipients.\textsuperscript{47} To
have comparable follow-up among treatment groups, data were censored at 963 days. The incidence of any de novo posttransplant malignancy was 0.6% with an mTOR inhibitor alone, 0.6% with an mTOR inhibitor plus a calcineurin inhibitor, and 1.81% with a calcineurin inhibitor alone. The incidence of any de novo solid tumor was 0% with an mTOR inhibitor alone, 0.47% with an mTOR inhibitor plus a calcineurin inhibitor, and 1% with a calcineurin inhibitor alone.

Besides possibly reducing the risk of de novo cancer, mTOR inhibitors may be useful in immunosuppressant minimization regimens employed in the treatment of established cancer. In several studies, conversion from calcineurin inhibitors to mTOR inhibitors was associated with regression of Kaposi’s sarcoma.49-51

Additional research is necessary to better define the role of immunosuppressive therapies in cancer after renal transplantation. Some of the evidence reviewed in this article suggests that immunosuppressive therapies may differ in oncogenic potential. In particular, chronic T-cell suppression associated with chronic indolent infection with oncogenic viruses creates an environment of increased cancer risk. However, the data are often conflicting, and drug effects often cannot clearly be differentiated from the multiple other potential contributors to posttransplant malignancies.

**MANAGEMENT OF MALIGNANCY IN THE RENAL TRANSPLANT RECIPIENT**

**PREVENTION**

Several of the risk factors for malignancy in the renal transplant patient are modifiable and are foci of preventive efforts.1,2,6:

- First and foremost, transplant recipients should stop tobacco smoking.
- Because the risk of cancer is strongly linked to the intensity of immunosuppression, minimization of immunosuppression could reduce the risk of malignancy. Overimmunosuppression, particularly with depleting antibody-based therapies, should be avoided. Furthermore, use of multiple agents could allow reduction in dose or elimination of agents that appear to have direct oncogenic effects. The dilemma arising from such strategies is creating a balance between the potential benefits of immunosuppression minimization and the possibility of organ rejection from under-immunosuppression.
- Because the posttransplantation risk of certain cancers is linked to infection with viruses, prevention and control of viral infections are crucial, particularly in patients who develop a primary viral infection and in chronic carriers with Epstein-Barr, herpes, papilloma, or hepatitis viruses. Measures to prevent and control posttransplantation infections include careful screening of recipients and donors for infectious disease, prophylactic antimicrobial therapy, meticulous postoperative care, judicious use of immunosuppression, efficient use of laboratory and other diagnostic tests for specific diagnosis, and treatment targeted at causative pathogens.
- To reduce skin cancer risk, sun exposure should be minimized with sun block and clothing, and premalignant lesions, such as warts and actinic keratoses, should be treated early. Administration of low-dose retinoids could be useful in treating premalignant lesions and, perhaps, reducing skin cancer risk. However, in some high sun exposure climates, childhood sun exposure may be a difficult obstacle to overcome. The potential for pretransplant vaccination to prevent human papilloma virus is a fertile area for research.
SURVEILLANCE

Thorough cancer screening in the renal transplant recipient includes yearly examination for fecal occult blood, abdominal ultrasonography to detect kidney tumors (especially in those with acquired renal cystic disease), chest X ray, gynecologic examinations, mammography, dermatologic examinations, and digital rectal examination with assessment of prostate-specific antigen. In patients at high risk of malignancy by virtue of having a prior cancer, a strong family history, or a predisposing condition (e.g., prior cytoxan use), more aggressive surveillance, including voided urine cytology, cystoscopy, colposcopy, and colonoscopy, should be employed.6

TREATMENT OF A MALIGNANCY

Once malignancy has been identified in the renal transplant recipient, it should be aggressively managed. Most cancers in renal transplant recipients are treated using the same surgical, radiotherapeutic, and chemotherapeutic treatments administered to non-transplant patients.2 Because intensity of immunosuppressive therapy is associated with the rate of disease progression, minimization of immunosuppression (≥50% reduction initially), particularly calcineurin inhibitors and azathioprine, could improve prognosis.16 The management of immunosuppression in patients with de novo cancers has not been well studied.5 Reduction of immunosuppression is recommended in patients with Kaposi’s sarcoma or PTLDs, but the degree to which reduction of immunosuppression is beneficial in solid tumors is controversial. Conversion to an mTOR inhibitor therapy may be helpful. The antineoplastic effects of the mTOR inhibitor drugs may be particularly useful in renal cell carcinomas,16 and several trials are under way.

Many polyclonal PTLDs are associated with Epstein-Barr virus infections and respond to a reduction in immunosuppression alone. Active Epstein-Barr virus infections should be aggressively treated with nucleoside inhibitors. Monoclonal lymphoproliferations, those that are extrarenal, require combination chemotherapy, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and steroids). More recently, the anti-CD20 monoclonal antibody rituximab has been added to the protocol. The resolution of Kaposi’s sarcoma by conversion from cyclosporine or tacrolimus to sirolimus has been reported.49-51 Most solid tumors should be treated as they would be in nonimmunosuppressed patients.1

CONCLUSIONS

With advances in transplant surgery and medicine, cancer has become a leading cause of late mortality in renal transplant recipients, and its incidence is increasing. Some of the risk factors for transplantation-associated cancer are modifiable. Clinicians providing care for renal transplant recipients should be familiar with the types of malignancies for which the renal transplant recipient is at risk, keep immunosuppressive therapy to the minimum level that maintains good graft function, judiciously choose immunotherapies based on the most current and rigorous evidence, engage in cancer prevention efforts throughout the transplant course, practice vigilant cancer surveillance after transplantation, and aggressively treat cancers that do arise.

REFERENCES