Temsrirolimus is a targeted therapy that inhibits mammalian target of rapamycin (mTOR), a central regulator of tumor cell responses to growth stimuli. Temsirolimus has a broad anticancer activity profile that impacts tumor cell growth, proliferation, and survival through its specific inhibition of mTOR. In a randomized phase III trial that enrolled previously untreated patients with advanced renal cell carcinoma (RCC) and poor prognostic features, temsirolimus significantly prolonged overall survival compared with interferon-α, a standard therapy (p = 0.008). Because of the results, temsirolimus was approved by the U.S. Food and Drug Administration for treatment and is considered a first-line treatment for patients with advanced RCC with poor prognostic features. Temsirolimus is administered at a flat weekly IV dose of 25 mg given over 30–60 minutes. Gastrointestinal disorders (stomatitis, anorexia, nausea, diarrhea, and vomiting), rash, fatigue, edema, infections, and dyspnea, as well as hematologic and metabolic laboratory abnormalities occur in patients receiving temsirolimus. Metabolic side effects include hyperglycemia, hypercholesterolemia, hypertriglyceridemia, and hypophosphatemia. Most adverse reactions associated with temsirolimus can be managed medically or addressed by supportive measures. Nurses can improve patient outcomes through early recognition of side effects and prompt interventions.

At a Glance

- Temsirolimus is an anticancer agent that inhibits mammalian target of rapamycin, a central regulator of tumor growth and angiogenesis.
- Temsirolimus is the first targeted therapy to show survival benefits in patients with renal cell carcinoma and can be considered first-line treatment for advanced renal cell carcinoma with poor prognostic features.
- Oncology nurses have varied and important roles in optimizing patient outcomes with temsirolimus therapy, such as patient education, safe administration, and the recognition and management of side effects.
Mechanism of Action

mTOR is now recognized as a unique and important target for cancer therapeutics. mTOR is a kinase enzyme inside the cell that collects and interprets the numerous and varied growth and survival signals received by tumor cells (Bjornsti & Houghton, 2004; Rubio-Viqueira & Hidalgo, 2006) (see Figure 1). When the kinase activity of mTOR is activated, its downstream effectors, the mRNA translation regulatory factors ribosomal protein S6 kinase and eukaryote initiation factor 4E-binding protein-1, are phosphorylated (Fingar et al., 2004; Hara et al., 1997), increasing the synthesis of cell cycle proteins such as cyclin D and hypoxia-inducible factor-1α (HIF-1α), the latter of which stimulates VEGF production (Forsythe et al., 1996; Grewel, Gansauge, Schmid, Adler, & Seufferlein, 1999; Hudson et al., 2002). The activation status of mTOR kinase determines whether the tumor cell produces key proteins needed for proliferation, growth, survival, and angiogenesis (Brown et al., 1994; Cardenas, Cutler, Lorenz, Di Como, & Heitman, 1999; DelBufalo et al., 2006; Forsythe et al., 2004; Wan, Shen, Mendoza, Khanna, & Helman, 2006; Yu et al., 2001).

mTOR is activated in tumor cells by various mechanisms known to be important for malignant transformation and progression, including growth factor surface receptor tyrosine kinases, oncogenes, and loss of tumor suppressor genes (Conde et al., 2006; Dancey, 2006; Podsypanina et al., 2001). In addition to its role in cell proliferation, mTOR is particularly important in the biology of RCC owing to its function in regulating HIF-1α levels (Cho, Signoretti, Regan, Mier, & Atkins, 2007; Pantuck, Zeng, Beldegrun, & Figlin, 2003). Mutation or loss of the von Hippel Lindau tumor-suppressor gene is common in RCC and is manifested by reduced degradation of HIF-1α (Ohh et al., 2000; Patel, Chadalavada, Chaganti, & Motzer, 2006; Thomas et al., 2006). In RCC tumors, activated mTOR further exacerbates accumulation of HIF-1α by increasing synthesis of this transcription factor and its angiogenic target gene products.

Temsirolimus is a specific inhibitor of mTOR and interferes with the synthesis of proteins that regulate proliferation, growth, and survival as studied in many tumor models (DelBufalo et al., 2006; Gera et al., 2004; Wan, Shen, Mendoza, Khanna, & Helman, 2006; Yu et al., 2001).
al., 2006; Wan et al., 2006; Wislez et al., 2005; Yu et al., 2001). Treatment with temsirolimus leads to cell cycle arrest in the G₁ phase (DelBufalo et al.; Gibbons et al., 1999; Wan et al., Wislez et al.). Temsirolimus also inhibits tumor angiogenesis by reducing synthesis of VEGF (DelBufalo et al.; Guba et al., 2002; Wan et al.). Therefore, unlike targeted therapies that inhibit multiple targets and chemotherapy agents that are generally cytotoxic, the broad antitumor activities of temsirolimus result from highly specific inhibition of a central and multifunctional target, mTOR.

Clinical Experience

A phase I study of patients with advanced refractory RCC demonstrated that temsirolimus is safe and well tolerated over a range of doses from 75–220 mg/m² when administered weekly as a 30-minute IV infusion (Raymond et al., 2004). Based on the results, a phase II study of 111 patients with advanced refractory RCC was initiated (Atkins et al., 2004). Patients had extensive disease and were heavily pretreated. Eighty-three percent had two or more sites of metastases, and 51% had received at least two prior treatment regimens. Three different dose levels of temsirolimus were tested in this study: 25 mg, 75 mg, and 250 mg. The overall response rate for all dose levels was 7.2%, with one complete response and seven partial responses. Responses were defined using standard bidimensional measurements in accordance with World Health Organization guidelines. Twenty-six percent of patients reported minor responses (25% or greater decrease and 50% or less decrease in the size of all measurable lesions), and 17% experienced stable disease for six months or longer. In addition, temsirolimus showed encouraging survival parameters, with a median time to progression of 5.8 months and median overall survival of 15 months. No significant differences in outcome were noted between the temsirolimus dose levels studied.

A retrospective analysis of data from the phase II study revealed that the activity of temsirolimus may have been impacted by the presence of poor prognostic factors (Atkins et al., 2004). Prognostic classification systems for patients with RCC vary, but some characteristics are commonly associated with poor outcomes. A study by the Memorial Sloan-Kettering Cancer Center identified five factors indicative of poor prognosis in RCC: low Karnofsky performance status (less than 80%), high lactate dehydrogenase levels (more than 1.5 times the upper limit of normal), low serum hemoglobin levels, high corrected serum calcium levels (more than 10 mg/dl), and time from initial diagnosis to start of interferon-α treatment of less than one year (Motzer, Bacik, Mariani, et al., 2002; Motzer, Bacik, Murphy, et al., 2002).

An international phase III study investigated temsirolimus as first-line therapy for patients with advanced RCC and three or more of six specific poor prognostic features comprising the five Memorial Sloan-Kettering Cancer Center poor risk factors plus metastases in multiple organs (Hudes et al., 2007). The study randomized 626 patients to receive 25 mg temsirolimus IV weekly, interferon-α escalating to 18 million units three times per week, or the combination of temsirolimus 15 mg IV weekly plus interferon-α escalating to 6 million units three times per week. Median overall survival improved significantly in the temsirolimus monotherapy arm (10.9 months) compared with interferon-α arm (7.5 months) (hazard ratio for death = 0.73; p = 0.008). Median overall survival in the combination group was 8.4 months and did not differ significantly from interferon-α (hazard ratio for death = 0.96; p = 0.70). Single-agent temsirolimus also significantly increased median progression-free survival by 5.5 months compared with 3.1 months with interferon-α (p < 0.001). Although the combination of temsirolimus plus interferon-α did not translate to a significant overall survival benefit, progression-free survival was significantly increased to 4.7 months versus interferon-α (p = 0.007). An overall survival benefit in the combination arm (p = 0.70) was possibly the result of increased toxicity of the combination regimen or the lower dosage of temsirolimus used. The pivotal study was the first to show an overall survival advantage with single-agent temsirolimus compared with interferon-α in patients with previously untreated advanced RCC.

Quality-Adjusted Survival

Because all patients enrolled in the temsirolimus versus interferon-α trial had advanced RCC and at least three poor prognostic features, their quality of life had to be assessed. Quality-adjusted survival was compared across treatment groups using the quality-adjusted time without symptoms of disease or toxicity of treatment (Q-TWiST) approach (Crowley & Ankerst, 2006). The standard Q-TWiST method assumes that patients progress through a series of health states that differ in quality of life. For the temsirolimus study, Q-TWiST was estimated by partitioning overall survival into three distinct health states: time with serious toxicity, time with disease progression, and time without symptoms and toxicity (Parasuraman et al., 2007). The analysis revealed that patients with advanced RCC treated with single-agent temsirolimus had 38% greater Q-TWiST than those treated with interferon-α (temsirolimus = 6.5 months versus interferon-α = 4.7 months; p = 0.00048) (Parasuraman et al.).

Adverse Reactions

Treatment with temsirolimus has been generally well tolerated in clinical settings by patients with advanced RCC. The most frequent side effects in the phase III study were maculopapular rash, mucositis, fatigue, and nausea, occurring in 76%, 70%, 50%, and 43% of patients, respectively (Atkins et al., 2004). Grade 3 or 4 adverse reactions were mainly related to laboratory abnormalities, including hyperglycemia in 17%, hypophosphatemia in 13%, anemia in 9%, and hypertriglyceridemia in 6% of patients.

The adverse events associated with single-agent temsirolimus in the phase III RCC trial (Hudes et al., 2007) were consistent with those observed in previous temsirolimus studies (see Table 1). Temsirolimus is associated with mild to moderate rash (often maculopapular) but not with hand/foot skin reaction, which can occur in patients treated with sunitinib and sorafenib (Escudier et al., 2006; Motzer et al., 2007). Grade 3 or 4 adverse events were experienced by 67% of patients in the temsirolimus arm versus 87% of patients in the interferon-α arm (p = 0.02). The most frequent serious adverse events were anemia, fatigue, hyperglycemia, dyspnea, and infection. Allergic or hypersensitivity reactions occurred in 9% of patients. Rare but potentially fatal adverse events included pneumonitis (interstitial lung disease) (Bellmunt, Szczylik, Feingold, Strahs,
& Berkenblit, in press), bowel perforation, renal failure, and intracerebral bleeding (Wyeth Pharmaceuticals, Inc., 2007). Dose reduction was required in 39% of interferon-α patients and 23% of temsirolimus patients (Hudes et al.). Reasons for discontinuation of temsirolimus treatment included disease progression (74%), adverse events (7%), symptomatic deterioration (7%), patient request (4%), and death (3%).

### Nursing Implications

#### Dosing and Administration

Oncology nurses play an important role in the dosing and administration of temsirolimus and monitoring for infusion-related reactions. The recommended dose of temsirolimus is 25 mg IV infused over 30–60 minutes once per week (Wyeth Pharmaceuticals, Inc., 2007). Weekly treatment may continue until disease progression or until patients experience intolerable side effects. Antihistamine pretreatment is recommended to prevent an allergic reaction. The temsirolimus 25 mg/ml vial contents must be diluted with the accompanying diluent before being further diluted with 250 ml of 0.9% sodium chloride injection. The drug is stable for six hours after it is fully diluted. Infusion pump is the preferred method of administration, and the materials should be composed of glass, polyolefin, or polyethylene to avoid excessive loss of drug and to decrease the rate of di-(2-ethylhexyl) phthalate (DEHP) extraction. Tubing should consist of non-DEHP, non-polyvinyl chloride tubing using an inline filter with a pore size no greater than 5 microns.

#### Hypersensitivity Reactions

Although infusion reactions can occur while temsirolimus is being administered, most hypersensitivity reactions occurring on the same day as temsirolimus administration were not severe (Bellmunt et al., in press). In the phase III randomized study, 4.8% of patients treated with temsirolimus alone had allergic reactions on the same day as treatment (Hudes et al., 2007). The events, which may have been reactions to infusion, included dyspnea (11%), headache (6%), chills (6%), fever (5%), wheezing (1%), flu-like syndrome (0.5%), and respiratory failure in one patient. In the phase I dose escalation study of temsirolimus and interferon-α, serious (grade 3 or 4) acute hypersensitivity reactions were observed in 12 patients (17%) and included dyspnea, syncope, and headache.

To maximize safe administration of temsirolimus, several prophylactic measures should be taken prior to drug delivery (see Figure 2). Complete blood counts with differential and other tests should be conducted and reviewed within 72 hours before drug administration. Vital signs, including pulse, blood pressure, and body temperature, should be obtained for all patients to establish a baseline from which to diagnose infusion-related fever and hypotension (Thomas, 2005). Premedication with an antihistamine, such as diphenhydramine 25–50 mg IV, should occur 30 minutes before the start of each temsirolimus infusion to minimize the chance of an infusion reaction (Atkins et al., 2004). Caution should be used when administering temsirolimus if a patient cannot receive antihistamines because of a known hypersensitivity or other medical reason.

Temsirolimus administration should be stopped if a hypersensitivity reaction develops during infusion despite premedication. Depending on the severity of the reaction, the patient should be observed for a minimum of 30–60 minutes (Hudes et al., 2007). Infusion of temsirolimus may resume with the physician’s approval. A histamine H2-receptor antagonist (IV famotidine 20 mg or ranitidine 50 mg) should be administered about 30 minutes before restarting the infusion. The temsirolimus infusion may be slowed to 60 minutes.

If a severe hypersensitivity reaction occurs, temsirolimus infusion should be stopped immediately and not reattempted (Thomas, 2005). To restore normal cardiac and respiratory function, medical therapy, including fluids, epinephrine, corticosteroids, diphenhydramine, bronchodilators, and oxygen, should be administered. The patient should be closely monitored until the hypersensitivity reaction resolves.

#### Interactions and Special Populations

At the recommended dose (25 mg IV once weekly), the mean half-life of temsirolimus is approximately 13 hours, whereas that of its metabolite, sirolimus, is 50 hours (Atkins et al., 2004).

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>ALL GRADES (%)</th>
<th>GRADE 3 OR 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenia</td>
<td>51</td>
<td>11</td>
</tr>
<tr>
<td>Rash</td>
<td>47</td>
<td>5</td>
</tr>
<tr>
<td>Mucositis or stomatitis</td>
<td>41</td>
<td>3</td>
</tr>
<tr>
<td>Nausea</td>
<td>37</td>
<td>2</td>
</tr>
<tr>
<td>Edema</td>
<td>35</td>
<td>3</td>
</tr>
<tr>
<td>Anorexia</td>
<td>32</td>
<td>3</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>28</td>
<td>9</td>
</tr>
<tr>
<td>Pain</td>
<td>28</td>
<td>5</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>Cough</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>21</td>
<td>4</td>
</tr>
<tr>
<td>Infections</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Constipation</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>Back pain</td>
<td>20</td>
<td>3</td>
</tr>
<tr>
<td>Dygeusia</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>Hematologic abnormality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin decreased</td>
<td>94</td>
<td>20</td>
</tr>
<tr>
<td>Lymphocytes decreased</td>
<td>53</td>
<td>16</td>
</tr>
<tr>
<td>Platelets decreased</td>
<td>40</td>
<td>1</td>
</tr>
<tr>
<td>Leukocytes decreased</td>
<td>32</td>
<td>1</td>
</tr>
<tr>
<td>Laboratory abnormalities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triglycerides increased</td>
<td>83</td>
<td>44</td>
</tr>
<tr>
<td>Glucose increased</td>
<td>89</td>
<td>16</td>
</tr>
<tr>
<td>Total cholesterol increased</td>
<td>87</td>
<td>2</td>
</tr>
<tr>
<td>Alkaline phosphate increased</td>
<td>68</td>
<td>3</td>
</tr>
<tr>
<td>Creatinine increased</td>
<td>57</td>
<td>3</td>
</tr>
<tr>
<td>Phosphorus decreased</td>
<td>49</td>
<td>18</td>
</tr>
<tr>
<td>Aspartate transaminase increased</td>
<td>38</td>
<td>2</td>
</tr>
<tr>
<td>Potassium decreased</td>
<td>21</td>
<td>5</td>
</tr>
</tbody>
</table>

* National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0

Note. Based on information from Wyeth Pharmaceuticals, Inc., 2007.
Sirolimus quickly appears after temsirolimus infusion and has a peak concentration of about 10% of the parent drug (Atkins et al.). Temsirolimus is eliminated in the feces with no apparent drug accumulation from multiple dosing (Raymond et al., 2004).

Drugs or foods that inhibit, induce, or are metabolized by the CYP3A4/CYP3A5 enzymes may affect blood levels of temsirolimus (see Table 2). For example, P450 enzyme-inducing antiepileptic drugs (EIAEDs), such as phenytoin, carbamazepine, and phenobarbital, accelerate the metabolism of temsirolimus (Chang et al., 2004). In a phase I pharmacokinetic study, patients with recurrent malignant gliomas taking EIAEDs were able to tolerate 38% higher doses of temsirolimus compared with patients not on EIAEDs. Similar results were obtained in another phase I pharmacokinetic study of patients with inoperable and/or recurrent malignant gliomas or brain metastases from solid tumors treated with temsirolimus in the presence or absence of EIAEDs (Boni, Leister, Burns, Cincotta, & Moore, 2007). Other agents known to be cytochrome P450 inhibitors or otherwise identified as agents that may affect blood levels of temsirolimus should be avoided because they may result in altered levels of temsirolimus.

Limited data are currently available on the use of temsirolimus in special populations. No dose adjustments for body surface area, age, gender, or patients with renal impairment have been made in clinical trials to date (Raymond et al., 2004; Wyeth Pharmaceuticals, Inc., 2007). No data are currently available regarding the influence of hepatic dysfunction on temsirolimus disposition.

**Patient Monitoring and Intervention**

Nurses play a critical role in the success of temsirolimus therapy. Through early recognition of side effects, nurses can offer prompt supportive care measures that may ensure patient safety and improve outcomes. Common side effects of temsirolimus therapy include fatigue, stomatitis, and rash (Hudes et al., 2007). Although the toxicities are usually mild, they can lead to dose delays or reductions.

Fatigue was one of the most common adverse events cited as the reason for dose delays, dose reductions, and discontinuation of single-agent temsirolimus in the phase III randomized study (Raymond et al., 2004). Rash and stomatitis led to dose delay in 4% and 2% of patients, respectively. Successful treatment of stomatitis with topical therapies has been shown in patients with high-risk RCC and may prevent such treatment disruptions. Skin should be moisturized with fragrance-free moisturizer to prevent rash; topical or short-course oral glucocorticoids may be used if the patient does not respond to more conservative measures (Griffin, Amand, & Demetri, 2005), although caution should be exercised given the potential for immunosuppression with prolonged oral steroid use.
Hematologic and laboratory abnormalities such as anemia, hypertriglyceridemia, and hyperglycemia also have been commonly observed with temsirolimus therapy. Prompt management with transfusion, lipid-lowering agents, and glucose-lowering agents (e.g., insulin, oral hypoglycemic agents) can resolve toxicities in many cases.

Nurses should be aware that, although rare, pneumonitis has occurred in patients treated with temsirolimus. Some patients who have developed pneumonitis were asymptomatic and the pneumonitis was only detected by computed tomography or chest x-ray. Patients with a cough, dyspnea, or fever should have a chest x-ray performed, although high-resolution computed tomography scans are more sensitive. Pneumonitis often is described as having a ground-glass opacity on chest radiographs. Pneumonitis may require dose interruption and treatment with corticosteroids or antibiotics, although some patients may continue treatment without intervention.

In the phase III temsirolimus trial, dose reduction was not recommended in the event of grade 0–2 toxicities unless grade 2 toxicity was persistent and troublesome to the patient despite medical management (Hudes et al., 2007). In the case of grade 3 or 4 toxicity, treatment was held until recovery. If recovery occurred within three weeks, the dose was reduced to the next lowest level (e.g., 20 mg, 15 mg, 10 mg) and held there for the remainder of the treatment period. Patients requiring more than three dose reductions were withdrawn from the study. In practice, once toxicities have resolved to grade 2 or less, temsirolimus may be restarted with the dose reduced by 5 mg per week to a dose no lower than 15 mg per week (Wyeth Pharmaceuticals, Inc., 2007).

Active patient monitoring is necessary for optimal outcomes with temsirolimus treatment. Clinical laboratory assessments should be performed frequently and include complete blood counts, fasting glucose and lipid levels, and renal and hepatic function tests (see Table 3). Patients should be monitored for hypokalemia and hypophosphatemia. Patients also must be monitored closely for hypersensitivity reactions while receiving temsirolimus infusions. No observation period is required after treatment.

### Patient Education

Nurses often are the primary healthcare contact for patients, who rely on them for information about all aspects of their disease and treatment. Nurses are called on to address not only medical issues but the social, psychological, and financial aspects of living with cancer.

Oncology nurses can optimize treatment outcomes by educating patients about the benefits and risks of temsirolimus treatment. The Oncology Nursing Society’s (2007) guide for patients receiving targeted therapies for RCC overviews potential side effects that may occur with temsirolimus, sunitinib, and sorafenib and provides suggestions for managing common side effects. Nurses can provide encouragement by explaining that temsirolimus has been shown to prolong the time to progression of the disease and to prolong survival in patients with advanced RCC (Hudes et al., 2007). Before receiving temsirolimus, patients should be informed of the possibility of serious allergic reactions, including anaphylaxis despite premedication with antihistamines, and should know to immediately report any facial swelling or difficulty breathing.

Patients receiving temsirolimus may experience increased blood glucose levels, elevated triglycerides, and elevated cholesterol levels, which may result in the need for insulin, hypoglycemic agents, or lipid-lowering agents (Wyeth Pharmaceuticals, Inc., 2007). Excessive thirst or frequent urination may be a sign of increased blood glucose levels and should be reported to healthcare professionals. Patients may be more susceptible to infections while being treated with temsirolimus. Abnormal wound healing also is possible if patients have had surgery during or within a few weeks of therapy.

Patients should be instructed about the possible development of interstitial lung disease—a chronic inflammation of the lungs that rarely results in death—and directed to report any new or worsening respiratory symptoms to the healthcare team. Patients should be warned about the possibility of bowel perforation and should report any new or worsening abdominal pain or blood in their stools. Renal failure also is a possibility and patients with brain

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### Table 2. Medications That Alter the Plasma Concentration of Temsirolimus

<table>
<thead>
<tr>
<th>EFFECT ON CYP3A4</th>
<th>DRUGS</th>
<th>CLINICAL CONSEQUENCES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibitors</td>
<td>Clarithromycin, erythromycin, itraconazole, and ketoconazole; also grapefruit juice</td>
<td>May increase plasma temsirolimus concentrations</td>
</tr>
<tr>
<td>Inducers</td>
<td>Carbamazepine, dexamethasone, fosphenytoin, oxcarbazepine, phenobarbital, phenytoin, primadone, and rifampicin; also St. John’s wort</td>
<td>May decrease plasma temsirolimus concentrations</td>
</tr>
<tr>
<td>Substrates</td>
<td>Cyclosporine, dihydropyridine calcium channel blockers, pimozide, simvastatin and other hydroxymethylglutaryl coenzyme A reductase inhibitors, triazolobenzodiazepines, and warfarin</td>
<td>May alter plasma temsirolimus concentrations</td>
</tr>
</tbody>
</table>

---

### Table 3. Suggested Temsirolimus Monitoring of Hematologic and Clinical Laboratory Parameters

<table>
<thead>
<tr>
<th>LABORATORY ASSESSMENT</th>
<th>FREQUENCY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood count with differential</td>
<td>Weekly</td>
</tr>
<tr>
<td>Fasting lipid panel</td>
<td>Biweekly</td>
</tr>
<tr>
<td>Fasting chemistry or electrolytes</td>
<td>Biweekly</td>
</tr>
<tr>
<td>Coagulation test for patients taking anticoagulants</td>
<td>Biweekly</td>
</tr>
</tbody>
</table>

*May be performed more or less frequently, as clinically indicated.*
metastases or patients receiving anticoagulants should be informed of the increased risk of developing intracerebral bleeding.

Because temsirolimus may have immunomodulatory activity, vaccinations may be less effective in patients treated with temsirolimus. In addition, the use of live vaccines and close contact with those who have received live vaccines should be avoided. Examples of live vaccines are measles, mumps, rubella, oral polio, BCG, yellow fever, varicella, and TY21a typhoid vaccines.

Temsirolimus has been linked to fetal harm. Women of childbearing age should avoid becoming pregnant during treatment and for three months after ending treatment. Men with partners who may become pregnant should use reliable contraception while on temsirolimus and for three months after the final dose.

Because some foods and drugs can interfere with the breakdown or metabolism of temsirolimus, patients should notify the healthcare team if they are taking any of the following medications: protease inhibitors, antiepileptic medications (including carbamazepine, phenytoin, and barbiturates), St. John’s wort, rifampicin, rifabutin, nefazodone, selective serotonin reuptake inhibitors (used to treat depression), and antibiotics or antifungal agents (used to treat infections) (NCCN Kidney Cancer Panel, 2007).

The use of IV agents facilitates adherence, frequent interaction with the healthcare team, and reimbursement, which benefits patients and healthcare professionals. Nurses can ensure treatment adherence by setting up a schedule for patients to receive temsirolimus on the same day each week. Some patients may ask nurses to provide assistance with reimbursement requests.

**Conclusions**

Temsirolimus is an important addition to the targeted therapies approved for RCC. This novel inhibitor of mTOR delays RCC progression and prolongs survival compared with interferon-α, a standard therapy, and has substantially better tolerability. Based on the survival benefits demonstrated in the pivotal phase III study (Hudes et al., 2007), temsirolimus can be considered a first-line treatment for patients with advanced RCC with poor prognostic features. Nurses should inform patients of the benefits and the potential side effects of temsirolimus, explain how adverse reactions may manifest, and advise patients on when to call the nurse or doctor. Through their central role in patient education, IV drug administration, and adverse event management, nurses will promote optimal clinical outcomes for patients with advanced RCC who are receiving temsirolimus.

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