Oncology Pharmacy Newsletter

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The Oncology Pharmacy Newsletter is publication dedicated to providing useful information for the staff treating patients who come to the Oncology Outpatient Pavilion.

We welcome questions and requests for topics.

References available upon request.

Since you asked....

Do we keep track of cumulative anthracycline doses?

Yes, the Pharmacists track the cumulative anthracycline dose administered here at UConn Health. There is a record kept in the pharmacy patient file that accounts for the "doxorubicin equivalents" administered. If you have a patient who has received anthracyclines at another center or in the distant past, please bring it to our attention. A sample of the tracking sheet is found on the last page of this edition of the newsletter.

Temsirolimus in Endometrial Carcinoma

Several recent Phase II studies have demonstrated activity and periods of progression free survival in previously treated patients with endometrial cancer receiving temsirolimus (Torisel®).

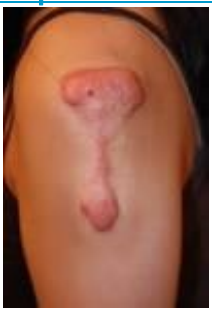
Oza, et al. looked at both chemotherapy naïve and previously treated patients treated with 25mg temsirolimus weekly. The chemotherapy naïve patients had a better response rate with 82% having measurable responses or stable disease, and 52% of previously treated had response or periods of stable disease.

Fleming, et al. investigated the use of temsirolimus 25mg weekly in advanced or recurrent endometrial carcinoma alone, or in combination with megestrol acetate and tamoxifen, hoping to overcome resistance to hormonal therapy. The study was stopped early due to an increase in PEs and DVTs in the combination therapy, but no improvement in responses.

Alvarez, et al. looked at the combination of weekly temsirolimus 25mg and bevacizumab 10mg/kg every 14 days in metastatic or recurrent endometrial carcinoma to see if the combination of mTOR inhibitor and prevention of angiogenesis would improve progression free survival. Clinical response was seen in 24.5% of patients, and 46.9% achieved a 6 month or more progression free survival. Treatment was discontinued in 38.8% of patients due to toxicities and 3 patients died due to treatment. Toxicities included those expected from either temsirolimus or bevacizumab.

Refer to the next page for references.

Bleomycin Treatment of Keloids and Hypertrophic Scars



Spontaneously or following surgery, injury , or vaccination, abnormal hypertrophic scarring may occur. Although hypertrophic scars may improve over time, keloids tend to expand. These lesions are associated with itching, and their appearance my be troublesome to patients. Treatment may include corticosteroids, cryotherapy and/or intra-lesional bleomycin.

Espana, et al., describe a method of treatment of keloids and hypertrophic scars that achieved good resolution of the scarring. The lesion is infiltrated with 2% mepivicaine. A 1.5 IU/ml solution of bleomycin is administered intra-lesionally by dripping the solution over the surface of the scar, then the scar is repeatedly punctured with a 25 gauge needle to allow the bleomycin to penetrate the scar. This process can be repeated at 1—4 month intervals for maximal improvement of the scar.

in this small set of patients, all patients experienced elimination of pruritis, and significant improvement of lesions. Some patients have some residual pigmentation, but no other side effects were reported.

Espana, et al., Dermatol Surg 27:1: January 2001, pages 23-27

Torisel ® (temsirolimus)

Toricel is an mTOR inhibitor approved for the treatment of advanced renal cell cancer. It causes cell cycle arrest and prevents angiogenesis, leading to decrease in tumor size. There is also evidence supporting its use in Mantle Cell lymphoma and endometrial cancer. See the previous page for information on its use in endometrial cancer.

Patients should be pretreated with an antihistamine such as diphenhydramine to prevent infusion reactions which are seen in 1% of patients. If an infusion reaction occurs, hold the infusion and monitor the patient for 30-60 minutes. When symptoms resolve the infusion may be restarted at a slower rate. Additional premedication may be needed, such as famotidine to further decrease the likelihood of reaction.

Major side effects include immunosuppression, decreased hemoglobin (89%), low ANC (53%) or platelet counts (40%), which may require delays and dose reductions to 20mg or 15mg weekly.

Other major side effects include bowel perforation/GI bleed, hyperglycemia (89%) or metabolic acidosis, edema (35%), hyperlipidemia (87%), hypophosphatemia (49%),interstitial lung disease, intracranial bleeding, especially if brain metastasis exists, and renal failure (serum creatinine increases in 57% of patients), which may require dialysis. Patients may need adjustments in insulin dose or addition of insulin, or anti-cholesterol agents due to these side effects. Doses may also need to be held or reduced for neurologic toxicity or pulmonary toxicity.

Side effects also include acne vulgaris, rash (47%), nausea (37%), stomatitis, constipation, diarrhea, back pain, arthralgia, asthenia (51%), insomnia, xeroderma, nail changes, epistaxis, rhinorrhea, lack of appetite, dysgeusia, or weight loss.

Concurrent use with ACE inhibitors may increase chances of angioedema. Concurrent use with warfarin may increase the risk of intracranial bleeding. Drug interactions which may require temsirolimus dose reduction to 12.5mg weekly include itraconazole, voriconazole, and similar, clarithromycin, and protease inhibitors (HIV meds). Drug interactions that may require temsirolimus dose increase up to 50mg weekly include carbamazepine, phenytoin, phenobarbital, and rifampin, rifabutin, and Saint John's wort. Please consult the Pharmacist if you have a patient on multiple other medications, and they will be happy to review the medication interactions for you.

Impaired wound healing may occur, so caution should be used if the patient has had a recent surgery. Patients should be instructed to report difficulty with wound healing.

Laboratory monitoring should include CBC with diff, Chem 10 and LFTs with bilirubin.

Doses should be reduced if there is mild hepatic impairment defined as bilirubin > 1-1.5 x ULN or AST >ULN with Biirubin < ULN to 15mg once a week. Do not give temsirolimus in patients with moderate or severe hepatic dysfunction, or with bilirubin >1.5 x ULN. Dose modifications are not needed for renal dysfunction, dosing in dialysis patients has not been evaluated.

Temsirolimus is mixed in 250ml NS in a non-DHEP/non-PVC bag and infused over 30-60 minutes through a0.22micron inline filter. The admixed drug must be infused within 6 hours.

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http://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/909301#pai
Oza et al., Journal of Clinical Oncology, Volume 29, Number 24, August 20, 2011, pages 3278-85
Fleming et al., Gynecologic Oncology, Volume 132, Issue 3, March 2014, Pages 585–592
Alvarez, et al., Gynecologic Oncology 129 (2013) 22-27
NCCN.org, Kidney Cancer Chemotherapy Order Template, Temsirolimus, KDN10, 3/19/2015
Micromedex Online, Temsirolimus.

ANTHRACYCLINE LIFETIME CUMULATIVE DOSE Pt Name:_____

T0_____ DOB:____/____/_____

Anthracyclines may cause cardiotoxicity. Increased incidence and severity are associated with higher lifetime exposure. Current recommendations suggest limiting lifetime exposure to 450-500mg/m2 of Doxorubicin isotoxic equivalents. At the MD's discretion, this dose can be exceeded if recent cardiac evaluation is good. The following conversion factors are an estimate only. Liposomal products convey a significantly lower risk of cardiotoxicity, but are currently evaluated as the active chemical. Cumulative maximum doses have not been established for liposomal preparations.

Doxorubicin x 1 Daunorubicin x 0.833 Epirubicin x 0.67 Idarubicin x 5 Mitoxantrone x 4

Previous Anthracycline drug/total dose:_____

Baseline Cardiac testing preformed:_____

Other Risk Factors: [ ] Trastuzumab [ ]Pertuzumab [ ]Ado-trastuzumab [ ]Other_____

Date	**Drug**	**Dose in mg/m2**	**Factor**	**Equivalent Dose**	**Cumulative dose**