UCONN HEALTH

Volume 2, Issue 6; October 31, 2016

Oncology Pharmacy Newsletter

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.

My patient reacted, and won't complete this dose. What do I do with the rest of the chemo?

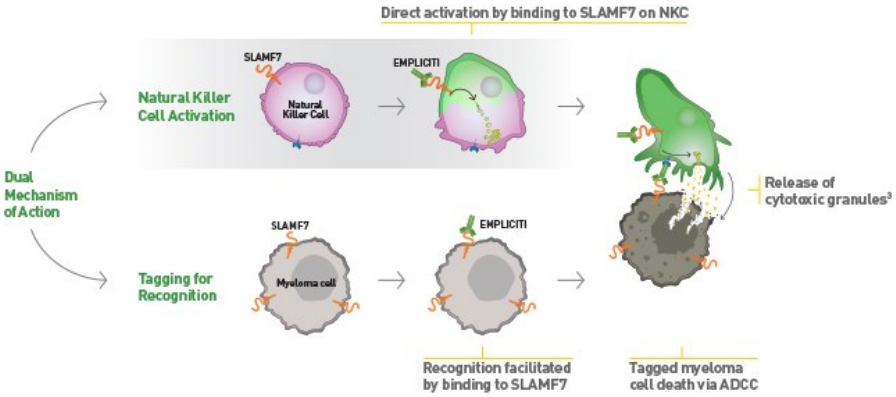
You may have noticed new requirements in our waste disposal process.

Partially used chemotherapy doses are considered bulk waste. These must be enclosed in a sealed zip lock plastic bag and be disposed of in black hazard labeled bins. There are black bins in the Infusion Center's medication room and on the patient units.

If you have to disconnect a bag containing chemotherapy from a patient who has had an infusion reaction and will not be continuing the dose, and have questions, please contact Pharmacy for assistance.

Empliciti® — elotuzumab

Empliciti® (elotuzumab) is a new agent in the anti-myeloma armamentarium that targets a novel pathway, SLAMF7. Signaling Lymphocyte Activation Molecule Family 7 (SLAMF7) is present on both myeloma cells and natural killer cells. It causes direct cytotoxicity to myeloma cells and activates natural killer cells. SLAMF7 is not found on normal tissue cells, allowing for a selective targeting of myeloma cells.



http://www.emplicitihcp.com/mechanism-of-action

Elotuzumab was granted accelerated approval following the results of the ELOQUENT-2 trial, which compared a regimen containing elotuzumab, lenalidomide and dexamethasone, to lenalidomide and dexamethasone (REV-DEX) in over 600 patients. Patients were treated until progression or unacceptable side effects. The study arm demonstrated improvements in progression-free survival (1 year PFS 68% vs. 57% , 2 year PFS 41% vs. 27%) and overall response rate (ORR 79% vs. 66%). Median progression-free survival was 19.4 months in the elotuzumab treated patients as compared to 14.9 months. Side effect profiles of the two regimens were similar, but the addition of elotuzumab to the regimen adds the possibility of infusion reactions.

Elotuzumab is currently indicated as part of a combination regimen with lenalidomide (Revlamid®) and dexamethasone (REV-DEX) in patients who have had 1-3 previous chemotherapeutic regimen for their recurrent or refractory multiple myeloma. It is dosed based on weight, with 10mg/kg administered on days 1, 8, 15, and 22 for the first two 28 day cycles. Subsequent cycles can proceed until disease progression or intolerable side effects, but elotuzumab is only given on days 1 and 15 during cycle 3 and beyond.

There are currently no dose modifications for renal impairment. Hepatic impairment has not been studied, but the manufacturer recommends holding elotuzumab should hepatic impairment (≥ grade 3) occur during treatment. Treatment may be resumed when the LFTs return to baseline.

Elotuzumab requires premedication with IV **and** PO dexamethasone, IV or PO diphenhydramine 25-50mg, ranitidine 50mg IV or 150mg PO, and acetaminophen 650-975mg PO given 45-90 minutes prior to starting the infusion. As this agent is given with REV-DEX, the dexamethasone performs dual functions, anti-tumor and anti-emetic. In fact, the dexamethasone requirement fluctuates depending on the cycle and day (see chart below).

Dosing of dexamethasone:

Cycle Day	Day 1	Day 8	Day 15	Day 22
Cycle 1 and 2 Oral Dexamethasone	28 mg given 3-24 hours pre-elotuzumab	28 mg given 3-24 hours pre-elotuzumab	28 mg given 3-24 hours pre-elotuzumab	28 mg given 3-24 hours pre-elotuzumab
Cycle 1 and 2 IV Dexamethasone	8 mg given 45-90 minutes pre-elotuzumab	8 mg given 45-90 minutes pre-elotuzumab	8 mg given 45-90 minutes pre-elotuzumab	8 mg given 45-90 minutes pre-elotuzumab
Cycle 3 and on Oral Dexamethasone	28 mg given 3-24 hours pre-elotuzumab	40 mg	28 mg given 3-24 hours pre-elotuzumab	40 mg
Cycle 3 and on IV Dexamethasone	8 mg given 3-24 hours pre-elotuzumab	none	8 mg given 3-24 hours pre-elotuzumab	none

Preparation of Elotuzumab:

Vial size	SWFI to reconstitute	Concentration	Withdrawable amount	Final concentration	Stability in final preparation	Filter and light protection
300 mg	13 ml*	25 mg/ml	12 ml	1-6mg/ml. Most doses will be in 250ml NS. Doses >1500mg will be in 500ml NS.	Maximum 8 hr room temp. Up to 24 hrs refrigerated. Complete infusion within 24 hours of mixing.	0.2-1.2µm inline filter and protect from light during infusion.
400 mg	17 ml*	25 mg/ml	16 ml			

*inject SWFI slowly down side of vial. Back pressure may be felt. Rotate vial while upright to dissolve. Do not shake. Dissolution should take <10min.

Elotuzumab Infusion Titration:

Infusion	Initial rate	Titration if no reaction:	Titration if no reaction:	Max rate:
First: Cycle 1, Day 1	0.5 ml/min x 30 minutes	Increase to 1 ml/min x 30 min	Increase to 2 ml/min until complete	2 ml/min
Second: Cycle 1, Day 8	If no reaction cycle 1, day 1: 1 ml/min x 30 min	Complete at 2 ml/min		
All other infusions	If no reactions during first 2 infusions, 2 ml/min			
In pts with no reactions Cycle 5 #	2 ml/min	3 ml/min		3 ml/min
In pts with no reactions Cycle 6 #	3 ml/min	4 ml/min		4 ml/min
In pts with no reactions Cycle 7#	4 ml/min	5 ml/min		5 ml/min

Hold for reactions ≥ grade 2. Restart infusion when symptoms resolve to grade ≤1. If patient has experienced a reaction, monitor vital signs every 30 minutes for 2 hours following completion of infusion prior to discharge.

Evolving recommendations.

As elotuzumab is not indicated as a single agent, discrete adverse reaction data is not readily available. Many adverse reactions in the two study arms of ELOQUENT-2 were comparable in incidence. Reactions reported in most commonly in patients taking elotuzumab in combination with lenalidomide and dexamethasone include (Any grade %/Grade 3-4 %) :

Lymphocytopenia (99%/77%), anemia (96%/19%), thrombocytopenia (84%/19%), neutropenia (82%/34%), infections (81%/28%), fatigue (47%/8%), pyrexia (37%/3%), peripheral edema (26%/1%),diarrhea (47%/5%), constipation (36%/1%), muscle spasms (30%/<1%), back pain (28%/5%), cougn (31%/ <1%), insomnia (23%/ 2%).

In addition, 7-9% of patients developed a second primary malignancy. Infusion reactions occurred in 5-10% of patients, most often with the first dose, and most were grade 1-2 with fever, chills, hypertension, hypotension, bradycardia. Antidrug antibodies have been reported.

Similar to several other agents (daratumumab, ofatumumab and siltuximab) IgG kappa assays used to determine degree of response to therapy can be falsely elevated by elotuzumab. It may therefore be difficult to accurately assess for complete response.

Elotuzumab is currently being studied in combination with bortezomib and dexamethasone in a phase 2 trial. Preliminary results demonstrate prolonged PFS with minimal additional toxicity. Elotuzumab is not currently approved for off study use in this regimen.

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Questions or comments?

Please contact:

Susan Glassman ***glassman@uchc.edu***

Chris Niemann ***niemann@ uchc.edu***