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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.

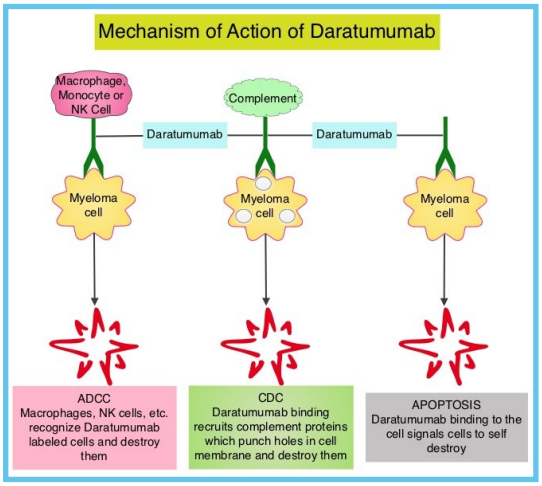
You're doing a great job!

Pharmacy recently undertook a chart audit to see how well we were doing with monitoring blood pressure and urine protein levels prior to administration of bevacizumab.

ONE HUNDRED PERCENT of the patients who received bevacizumab during the period between January 1, 2016 and June 30, 2016 had both their blood pressure and urinary protein results documented in their clinic charts. Although there was some variability in where this information was found, it was uniformly available.

Patients who initially had high pressures, also uniformly had follow up pressures in the acceptable range documented prior to receiving bevacizumab.

Darzalex® daratumumab



Darzalex® (Daratumumab) is a new offering in the battle against multiple myeloma. Daratumumab is a human IgG1 kappa CD38 specific monoclonal antibody which targets the CD38 antigen expressed by myeloma cells and induces cell death by several different mechanisms including complement-dependent cytotoxicity, antibody-dependent cell-mediated cytotoxicity, antibody-dependent cellular phagocytosis, and induction of apoptosis.[1] It is indicated in relapsed or refractory myeloma in patients who have had 3 or more previous treatments and can be used in patients who have undergone a stem cell transplant.

The SIRIUS study is the largest study using daratumumab in patients with previously treated, refractory multiple myeloma. Patients had an overall response rate of 29%, a median duration of response of 7.4 months, and a median progression-free survival of 3.7 months. Median overall survival was 17.5 months. Some of the responses had not progressed by 12 months.[1]

The usual dose of daratumumab is 16mg/kg weekly for 8 weeks. If no progression of disease and no intolerable side effects, dosing is modified to every 2 weeks for weeks 9-24, and to every 4 weeks beyond that. Patients may continue treatment until disease progression or unacceptable side effects. There are no dosing adjustments for renal or hepatic dysfunction at this time.

Daratumumab requires premedication 60 minutes before starting the infusion with methylprednisolone 125mg IV, acetaminophen 975mg PO and diphenhydramine 25mg PO or IV, and there should be subsequent doses of oral methylprednisolone 20mg on days 2 and 3 to decrease the likelihood of a delayed infusion

reaction. Methylprednisolone doses may be reduced to 60mg after 2 doses without reaction. Patients with a history COPD of may be at increased risk for delayed reaction and should have inhaled B agonists and steroids for the first 4 weeks. Premedication with traditional anti-emetics is generally not necessary. Valacyclovir prophylaxis, or equivalent, should be administered starting 1 week before the first treatment, and continuing for 3 months following the last dose, to prevent herpes zoster outbreaks.

Daratumumub is mixed in 1000ml NS for the first dose and should not be shaken. It is infused in a titrate-as-tolerated fashion starting at 50ml/hr for one hour. If no infusion reaction occurs, the infusion rate may be increased by 50ml/hr every hour until the maximum infusion rate of 200ml/hr is reached. The entire dose must be infused with 15 hours.

Subsequent daratumumab doses are mixed in 500ml (twice the concentration) and may be infused more rapidly if the patient tolerates. The second dose is infused at 50ml/hr to start and the rate may be increased only if there were no reactions during the first 3 hours of the initial infusion, and the patient is tolerating the current infusion. The third and subsequent infusions may start at 100ml/hr if the second infusion was well tolerated and there were no reactions to previous infusions running at 100ml/hr. In all of these scenarios if the patient is tolerating the current infusion rate, the rate may be titrated up by 50ml/hr to a maximum of 200ml/hr to complete the infusion.

Patients must be closely monitored during all infusions, and if any infusion reaction occurs, the dose should be interrupted until symptoms improve. The infusion should be restarted at 1/2 the hourly rate that was infusing when the reaction occurred. As up to 50% of patients may have a reaction during their first infusion, rescue medications for infusion reactions must be readily available. Reactions most usually occur while daratumumab is infusing or up to 4 hours after completion, but may occur as much as 48 hours after completion of a dose. Dose escalations may be attempted after one hour of tolerating a restarted, reduced rate infusion.

Infusion reactions discussed above may be severe, although the majority are grade 1-2, and may occur in almost half of patients treated. Other frequently reported adverse reactions include bone marrow suppression (8% required G-CSF support), fatigue, joint pain, headache, constipation, diarrhea, anorexia, nausea, back pain, pyrexia, pharyngitis, cough or upper respiratory tract infection. Pneumonia, general decline in health, and fevers have also been reported.

False positive Coombs testing may occur for up to 6 months following cessation of daratumumab, but blood typing and ABO tests are not affected. The manufacturer recommends typing and screening patients prior to starting daratumumab. Testing done to determine the level of response in patients with IgG Kappa myeloma protein producing disease is also impacted by daratumumab, as it is a human IgG kappa monoclonal antibody and may produce falsely elevated readings.

[1]Lional et al, The Lancet, Volume 387, Issue 10027, 9–15 April 2016, Pages 1551–1560

http://www.darzalex.com/shared/product/darzalex/darzalex-prescribing-information.pdf accessed 9/29/15

http://online.lexi.com/lco/action/doc/retrieve/docid/patch_f/5928764 accessed 10/2/16

http://www.oncoprescribe.com/newsletter.php?top=460