BC Cancer Protocol Summary for Therapy of Multiple Myeloma Using Pomalidomide with Dexamethasone

Protocol Code	***UMYPOMDEX***
Tumour Group	***Lymphoma, Leukemia/BMT***
Contact Physician	***Dr. Kevin Song***
Contact Pharmacist	***Louisa Pang***

ELIGIBILITY:

- For the treatment of multiple myeloma in patients for whom both bortezomib and lenalidomide have failed and who have received at least 2 prior treatment regimens and have demonstrated disease progression on the last regimen
- Patients who have failed lenalidomide but are contraindicated or intolerant to bortezomib
- Bortezomib failure includes patients with prior response to bortezomib but ineligible for bortezomib re-treatment at relapse
- A BC Cancer "Compassionate Access Program" request with appropriate clinical information for each patient must be approved prior to treatment
- May be used in combination with cyclophosphamide, or predniSONE (in place of dexamethasone)
- Registration of the prescribing physician and patient with the RevAid Program (www.RevAid.ca)

EXCLUSIONS:

- Pregnant or lactating women
- Platelet count less than 50 x 10^9/L may be considered a relative contraindication.
- Absolute neutrophil count (ANC) less than 1.0 x 10^9/L may be considered a relative contraindication; consider giving filgrastim (not funded by the BC Cancer)
- Known hypersensitivity to pomalidomide or lenalidomide or thalidomide

TESTS:

- Baseline (required before first treatment): CBC & diff, platelets, creatinine, LFTs (bilirubin, ALT). If female of child-bearing potential (FCBP): Confirm negative pregnancy test results via a quantitative beta-hCG blood test obtained 7 to 14 days and 24 hours prior to initial prescription.
- Baseline (required, but results do not have to be available to proceed with first treatment): serum protein electrophoresis ***and/or*** serum free light chain levels, HBsAg, HBcoreAb, TSH, calcium
- Weekly for the first 8 weeks then may reduce frequency to every 4 weeks: CBC and diff, platelets

- Every 4 weeks (required before treatment): CBC and diff, platelets, creatinine
- Every 4 weeks (required, but results do not have to be available to proceed with treatment): serum protein electrophoresis ***and/or*** serum free light chain levels, calcium
- Every three months (required, but results do not have to be available to proceed with treatment): TSH
- If female of childbearing potential: Every week for 4 weeks during cycle 1: quantitative beta-hCG blood test
- If clinically indicated: bilirubin, ALT, see Precautions #2

PREMEDICATIONS:

None

SUPPORTIVE MEDICATIONS:

- If HBsAg or HBcoreAb positive, start lamiVUDine 100 mg PO daily for the duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive
- Oral proton-pump inhibitor or H_2 antagonist for the duration of treatment with dexamethasone or prednisone may be considered
- ASA (enteric coated), warfarin, direct oral anticoagulant (DOAC) PO or low molecular weight heparin (LMWH) SC daily continuing for the duration of treatment with pomalidomide

TREATMENT:

Drug	Dose	BC Cancer Administration Guideline
pomalidomide	4 mg once daily for 21 days (d 1-21)	PO, in the evening may be preferred
dexamethasone	*40 mg on days 1, 8. 15 and 22	PO, in the morning may be preferred

* Dose may vary dependent on tolerability and co-morbidities

- Patients over 75 years of age: consider using dexamethasone 20 mg
- predniSONE may be substituted for patient or physician preference, in a variety of regimens based upon toxicity and patient tolerance. (e.g. prednisone 10 – 100 mg PO once weekly)
- Repeat every 28 until progression of the myeloma or unacceptable toxicity.

POMALIDOMIDE DOSE MODIFICATIONS:

NB: Use one of the 1 mg, 2 mg, 3 mg or 4 mg capsules for dosing. Currently there is no evidence to support the use of other dosing regimens (i.e., there is no clinical reason or research available to support the use of a combination of pomalidomide capsules for dosing, however the use of such dosing does have significant budgetary implications).

Hematological:

Neutropenia

<table>
<tr><th>Initial dose*</th><th>ANC (x10^9/L) on Day 1 of Cycle</th><th colspan="2">Dose*</th></tr>
<tr><td rowspan="2">4 mg</td><td>less than 1 and greater than or equal to 0.5</td><td rowspan="8">Hold until ANC greater than or equal to 1†,</td><td>then restart at the same dose</td></tr>
<tr><td>less than 0.5</td><td>then restart; consider resuming at 3 mg dosing</td></tr>
<tr><td rowspan="2">3 mg</td><td>less than 1 and greater than or equal to 0.5</td><td>then restart at the same dose</td></tr>
<tr><td>less than 0.5</td><td>then restart; consider resuming at 2 mg dose</td></tr>
<tr><td rowspan="2">2 mg</td><td>less than 1 and greater than or equal to 0.5</td><td>then restart at the same dose</td></tr>
<tr><td>less than 0.5</td><td>then restart; consider resuming at 1 mg dose</td></tr>
<tr><td rowspan="2">1mg</td><td>less than 1 and greater than or equal to 0.5</td><td>then restart at the same dose</td></tr>
<tr><td>less than 0.5</td><td>Consider stopping treatment, otherwise hold until ANC greater than or equal to 1†;</td><td>then restart at the same dose</td></tr>
</table>

*dosing for 21 days (d 1-21) of each 28-day cycle
† follow hematology weekly

For the first 8 weeks, CBC will be monitored weekly by physician and physician will be responsible to check and advise patient on dose adjustment based on ANC. Dose modifications for the weekly CBC monitoring will follow the dose modifications for Day 1 of Cycle in the above table.

May use filgrastim if clinically indicated and filgrastim is available (Currently not funded by the BC Cancer)

For females of child-bearing potential on weekly pregnancy test during cycle 1, physician will be responsible for checking results

Thrombocytopenia

Initial dose*	Platelets (x10^9/L) Day 1 of Cycle	Dose*	
4 mg	less than 50 and greater than or equal to 25	Hold until platelets greater than or equal to 50†, and no evidence of hemostatic failure (i.e., bleeding or petechiae),	then restart at the same dose
	less than 25		then restart; consider resuming at 3 mg dose
3 mg	less than 50 and greater than or equal to 25		then restart at the same dose
	less than 25		then restart; consider resuming at 2 mg dose
2 mg	less than 50 and greater than or equal to 25		then restart at the same dose
	less than 25		then restart; consider resuming at 1 mg dose
1 mg	less than 50 and greater than or equal to 25		then restart at the same dose
	less than 25		then restart at the same dose

* dosing for 21 days (d 1-21) of each 28-day cycle
† follow hematology weekly

For the first 8 weeks, CBC will be monitored weekly by physician and physician will be responsible to check and advise patient on dose adjustment based on platelet. Dose modifications for the weekly CBC monitoring will follow the dose modifications for Day 1 of Cycle in the above table.

1. **Hepatic Impairment:**

Hepatic impairment	Pomalidomide Dose
Mild or moderate (Child-Pugh Class A or B)	3 mg
Severe (Child-Pugh Class C)	2 mg

Pomalidomide is metabolized in the liver

2. **Renal Impairment:**

Estimated GFR (eGFR) or Creatinine clearance (mL/min)	Pomalidomide Dose
Less than 30 including dialysis dependence	3 mg* *For patients on hemodialysis, on hemodialysis days, take pomalidomide following hemodialysis

Pomalidomide and its metabolites are excreted by the kidneys

PRECAUTIONS:

1. **Teratogenicity**: If pomalidomide is taken during pregnancy, it may cause severe birth defects or death to the fetus. Pomalidomide should never be used by females who are pregnant or who could become pregnant while taking the drug. Even a single dose taken by a pregnant woman may cause birth defects.
2. **Venous thrombosis/embolism:** Pomalidomide with dexamethasone is known to increase the risk for thromboembolic disease. **ASA 81 mg** oral daily should be considered in all patients. For those with higher risk of thrombo-embolic disease, full anti-coagulation should be considered.
3. **Hepatitis B Reactivation**: All myeloma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with Lamivudine 100 mg PO daily, for the entire duration of chemotherapy and continue for one year from treatment completion for patients who are HBsAg positive and for six months for patients who are HBcoreAb positive. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring,

management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to halting chemotherapy.

4. **Need for irradiated blood products:** Patients receiving an autotransplant require irradiated blood products from 7 days prior to collection to 3 months post transplant (6 months if total body irradiation conditioning) to eliminate the risk of potentially life-threatening transfusion-related graft-versus-host-disease. All other myeloma patients do not require irradiated blood products

Call Dr. Kevin Song (Leukemia/BMT) or Dr Laurie Sehn (Lymphoma) or tumour group delegate with any problems or questions regarding this treatment program. (Leukemia/BMT at (604) 875-4863 or after hours (604) 875-4111; Lymphoma at (604) 877-6000 or 1-800-663-3333)

References:

1. San Miguel J, Weisel K, Moreau P, et al. Pomalidomide plus low-dose dexamethasone versus high-dose dexamethasone alone for patients with relapsed and refractory multiple myeloma (MM-003): a randomized, open-label, phase 3 trial. Lancet Oncol 2013;14(21):1055-66.
2. Richardson PG, Siegal DS, Vij R, et al. Pomalidomide alone or in combination with low-dose dexamethasone in relapsed and refractory multiple myeloma: a randomized phase 2 study. Blood 2014;123(12):1826-32.
3. Pomalidomide Product Monograph, April 7, 2017. Celgene Inc.