

BCCA Protocol Summary for Therapy of Myelodysplastic Syndrome using Lenalidomide

Protocol Code	<i>ULKMDSL</i>
Tumour Group	<i>Leukemia/BMT</i>
Contact Physician	<i>Dr. Tom Nevill</i>
Contact Pharmacist	<i>Judith Nyrose</i>

ELIGIBILITY:

- Transfusion-dependent anemia due to low or intermediate-1 risk myelodysplastic syndrome (MDS) associated with a deletion 5q cytogenetic abnormality with or without other cytogenetic abnormalities.
- A BCCA “Compassionate Access Program” request with appropriate clinical information for each patient must be approved prior to treatment

EXCLUSIONS:

- Contraindicated in patients who are hypersensitive to lenalidomide or to thalidomide.
- Lenalidomide is structurally similar to thalidomide, a known teratogen, and is contraindicated in pregnant women and women at risk of becoming pregnant.
- Contraindicated in breast feeding women.
- If ANC less than 0.5, Platelets less than $30 \times 10^9/L$ (if Platelets 30-50, consider giving platelet transfusion and if increments to greater than 50, start Lenalidomide)

TESTS:

- Baseline:
 - Bone Marrow aspiration and cytogenetic testing.
 - CBC and Differential, platelets, serum creatinine.
 - If premenopausal female: lab based pregnancy test x 2 prior to initiation of treatment. Test #1 – 7-14 days prior, Test #2 – 24 hour prior
 - TSH
- Weekly x 1 month: CBC and differential, platelets, serum creatinine; if premenopausal female, pregnancy test.
- Monthly after 1st month therapy: CBC and Differential, platelets, serum creatinine, pregnancy test
- 3-monthly after 1st month therapy: TSH
- 4 weeks after discontinuing lenalidomide – pregnancy test
- regular clinical assessments and grading of rash, diarrhea, fatigue and respiratory symptoms

PREMEDICATIONS:

- Consider therapeutic anticoagulation with low molecular weight heparin (LMWH) in patients with previous deep vein thrombosis and/or pulmonary embolism; maintain platelets greater than $50 \times 10^9/L$ while on therapeutic LMWH (see Precautions)

TREATMENT:

Drug	Dose*	BCCA Administration Guideline
Lenalidomide	10 mg once daily for 21 days (d 1-21)	PO

- Repeat every 28days until loss of response (progression of MDS or need for RBC transfusion)
- Discontinue if no response after 4 cycles.
 - * Select dose carefully and closely monitor renal function in the elderly due to the potential for decreased renal function. The incidence of serious and non-serious adverse events is significantly higher in patients greater than 65 years (constipation, confusion, dyspnea, atrial fibrillation).

DOSE MODIFICATIONS:

1. Hematological:

Thrombocytopenia

Initial dose*	Platelet ($\times 10^9/L$)		Dose*
	Baseline	within 4 wks**	
10 mg/d	greater than or equal to 100	less than 50	Hold until platelet greater than or equal to 50, then resume at 5 mg/d
	less than 100	less than 30 <u>or</u> less than 50% of baseline	Hold for greater than or equal to 1 wk until platelet greater than 30 <u>and</u> greater than 50% of baseline, then resume at 5 mg/d
	Baseline	after 4 wks	
	greater than or equal to 100	less than 30-50 despite platelet transfusion	Hold until platelet greater than 30 and without clinical bleeding, then resume at 5 mg/d
5 mg/d	Baseline	after 4 wks	
	greater than or equal to 100	less than 30-50 despite platelet transfusion	Hold until platelet greater than 30 and without clinical bleeding, then resume at 5 mg every other day

* dosing for 21 days (d 1-21) of each 28-day cycle

** physician will be responsible to check and advise patient on dose adjustment based on weekly platelets

Neutropenia

Initial dose*	ANC (x10 ⁹ /L)		Dose*
10 mg/d	Baseline	within 4 wks**	
	greater than or equal to 1.0	less than 0.75	Hold until ANC greater than or equal to 1.0, then resume at 5 mg/d
	less than 1.0	less than 0.5	Hold until ANC greater than or equal to 0.5, then resume at 5 mg/d
	Baseline	after 4 wks	
	less than or equal to 1.0	less than 0.5	Hold for greater than or equal to 1 wk until ANC greater than or equal to 0.75, then resume at 5 mg/d
5 mg/d	Baseline	after 4 wks	
	less than or equal to 1.0	less than 0.5	Hold for greater than or equal to 1 wk until ANC greater than or equal to 0.75, then resume at 5 mg/d every other day

* dosing for 21 days (d 1-21) of each 28-day cycle

** physician will be responsible to check and advise patient on dose adjustment based on weekly ANC

2. Renal dysfunction:

Creatinine clearance (mL/min)	Dose*
greater than or equal to 50	10 mg/d
30-49	5 mg/d
less than 30, not requiring dialysis	5 mg every other day
less than 30, dialysis dependent	5 mg three times weekly (administer after dialysis)

* dosing for 21 days (d 1-21) of each 28-day cycle

3. **Hepatic dysfunction:** Not specifically studied in patients with hepatic dysfunction. Patients with severe hepatic failure should be monitored closely and consideration given to dose modification.

PRECAUTIONS:

- Neutropenia (grade 3-4):** occurs in 62% of patients. Fever or other evidence of infection must be assessed promptly and treated aggressively. Refer to BCCA Febrile Neutropenia Guidelines.
- Thrombocytopenia (grade 3-4):** occurs in 53% of patients. Monitor for signs of bleeding.

3. **Thromboembolism:** occurs in 3-5% of MDS patients receiving lenalidomide as a single agent but is more frequent in myeloma patients when lenalidomide is used in combination therapy with dexamethasone. Use of lenalidomide and Erythropoietin together in MDS patients is not recommended. Also see Premedications for use of LMWH.
4. **Cardiac Toxicity:** Edema, weight gain (24%), cardiac failure (3%), Hypertension (7%), chest pain (6%)
5. **Hypersensitivity:** Rarely, hypersensitivity pneumonitis-like syndrome has been reported with lenalidomide use. In the case of unexpected respiratory symptoms such as dyspnea on exertion, crackles on physical examination, radiological bilateral ground-glass opacities and non-resolving pneumonia, lenalidomide should be discontinued until further investigation excludes hypersensitivity pneumonitis-like syndrome.
6. **Interactions:** lenalidomide increases digoxin concentration. It also increases the risk of bleeding in patients taking anticoagulants, NSAIDS, platelet inhibitors, thrombolytic agents, etc.

Call Dr. Tom Nevill or tumour group delegate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 1 Oct 2008

Date revised: 1 Oct 2010 (thyroid function tests clarified)

References¹⁻³:

1. List A, Kurtin S, Roe DJ, et al. Efficacy of lenalidomide in myelodysplastic syndromes. *N Engl J Med* 2005;352(6):549-57.
2. List A, Dewald G, Bennett J, et al. Lenalidomide in the myelodysplastic syndrome with chromosome 5q deletion. *N Engl J Med* 2006;355(14):1456-65.
3. List AF, Dewald GW, Bennett JM, et al. Long-term clinical benefit of lenalidomide (Revlimid) treatment in patients with myelodysplastic syndrome and chromosome deletion 5q. *ASH Annual Meeting Abstracts* 2006;108(11):251-.