

BCCA Protocol Summary for Therapy of Multiple Myeloma Using Thalidomide

Protocol Code	<i>UMYTHALID</i>
Tumour Group	<i>Lymphoma</i>
Contact Physician	<i>Dr. Kevin Song</i>

ELIGIBILITY:

- Multiple Myeloma unresponsive to standard treatments with melphalan, prednisone, pamidronate, bortezomib and dexamethasone and not a candidate for lenalidomide.
- A “Compassionate Access Program” form must be submitted and approved.
- Registration of the prescribing physician and patient in the RevAid Program (1-888-738-2431 or www.RevAid.ca)
- For BCCA-funded thalidomide: Dispensed from BC Cancer Agency Pharmacy
- For non-BCCA-funded thalidomide: Contact the RevAid Program (above) for drug access and funding options

EXCLUSIONS:

- Thalidomide often causes somnolence, constipation or peripheral neuropathy. It should be avoided in patients already symptomatic from one of those problems regardless of cause.

TESTS:

- Baseline: (required before first treatment) CBC and diff, platelets, creatinine, calcium and serum protein electrophoresis, if premenopausal female: negative pregnancy test (blood) or evidence of hysterectomy/tubal ligation
- Baseline (required, but results do not have to be available to proceed with first treatment) HBsAg, HBcoreAntibody
- Every 28 days: if female of childbearing potential: pregnancy test (blood)
- **Every 28 days (required, but results do not have to be available to proceed with treatment):** CBC and diff, platelets, creatinine, calcium and serum protein electrophoresis
- **Every three months (required, but results do not have to be available to proceed with treatment):** T3, T4, TSH

PREMEDICATIONS:

None

TREATMENT:

Cycles 1 - 4

Drug	Dose	BCCA Administration Guideline
Thalidomide	The standard starting dose is 200 mg daily. The dose should then be adjusted to the maximum that can be tolerated on a regular basis. The final dose may vary from 50 mg to 800 mg per day depending on patient tolerance.	PO, once daily at bedtime. If necessary, the total daily dose can be divided into as many as 4 doses to improve patient tolerance.
Dexamethasone (optional)	40 mg once daily on days 1-4, 9-12, 17-20	PO, in the morning may be preferred

- Repeat every 28 days for 4 cycles

Cycles 5 and subsequent cycles

Drug	Dose	BCCA Administration Guideline
Thalidomide	The dose should then be adjusted to the maximum that can be tolerated on a regular basis. The final dose may vary from 50 mg to 800 mg per day depending on patient tolerance.	PO, once daily at bedtime. If necessary, the total daily dose can be divided into as many as 4 doses to improve patient tolerance.
Dexamethasone (optional)	40 mg once daily on days 1-4	PO, in the morning may be preferred

- Repeat every 28 days until progression of the myeloma or unacceptable toxicity

OTHER OPTIONS FOR STEROID DOSING (OPTIONAL)

Option A: Oral dexamethasone 20mg daily on days 1-4, 9-12, 17-20 x 4 cycles; then 20 mg daily on days 1-4 only for subsequent cycles. The dose should be adjusted based upon toxicity and patient tolerance.
Option B: Oral dexamethasone 40mg weekly on days 1, 8, 15 and 22 for all cycles. The dose should be adjusted based upon toxicity and patient tolerance.
Option C: Prednisone may be substituted for patient or physician preference, in a variety of regimens based upon toxicity and patient tolerance.
Option D: No dexamethasone. Dexamethasone may need to be avoided in certain patients who are intolerant or have difficulty with side-effects. It is expected that the response will be inferior using thalidomide alone. Dexamethasone may be added for non-response.

- Repeat every 28 days until progression of the myeloma or unacceptable toxicity

DOSE MODIFICATIONS:

Somnolence, constipation or peripheral neuropathy may respond to dose reduction.

PRECAUTIONS:

1. **Teratogenicity:** If thalidomide is taken during pregnancy, it causes severe birth defects or death to the fetus. Thalidomide 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 can cause birth defects. The critical period occurs between 20 and 40 days of gestation. The defects seen have included amelia, phocomelia, hypoplasia of the bones and absence of bones, anotia, microtia, facial palsy, anophthalmos, microphthalmos, congenital heart defects, and gastrointestinal and renal anomalies.
2. **Peripheral Neuropathy:** Permanent peripheral neuropathy may occur. Clinical symptoms may include symmetrical sensorimotor neuropathy, painful paresthesia in the hands and feet, distal hypoesthesia, proximal weakness in the lower limbs, slight postural tremor, leg cramps, absent ankle jerks and redness of the palms. Thalidomide should be discontinued or substantially reduced in dose if signs and symptoms of peripheral neuropathy occur.
3. **Constipation:** Patients should be warned that constipation is common and difficult to manage. Thalidomide should be given very cautiously to patients already taking narcotic analgesics. Patients should follow the same anti-constipation measures used by those taking large doses or narcotic analgesics to prevent constipation.
4. **Somnolence:** Patients should be warned that thalidomide causes somnolence and that they should avoid driving unless fully alert. They should not drive at all if also taking narcotics or alcohol.
5. **Hepatitis B Reactivation:** All lymphoma patients should be tested for both HBsAg and HBcoreAb. If either test is positive, such patients should be treated with Lamivudine 100 mg/day orally, for the entire duration of chemotherapy and for six months afterwards. 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.
6. **Venous thrombosis/embolism:** Thalidomide 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.
7. **Hypothyroidism:** the use of thalidomide may result in hypothyroidism. Thyroid function tests should be repeated every 3 months. Treatment with thyroid replacement should be considered even for subclinical hypothyroidism. Thalidomide can be continued if hypothyroidism can be easily managed.

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)

Date activated: 01 Jun 2001

Date revised: 01 July 2011 (Revised thalidomide access, included thyroid testing)

References:

Singla S, Mehta J, Desikan R, et al. Antitumor activity of thalidomide in refractory multiple myeloma. *N Engl J Med* 1999;341(21):1565-71.