BCCA Protocol Summary for Treatment of Prostate Cancer Bone Metastases using Denosumab (XGEVA®)

Protocol Code	*SCDMAB*
Tumour Group	*Supportive Care*
Contact Physician	*Dr. Kim Chi*

ELIGIBILITY

- Metastatic prostate cancer to bone
- Evidence of castration resistance (progressive disease despite testosterone less than 1.7 nmol/L)
- Denosumab is covered by BC Pharmacare Plan P (a "Palliative Drug Benefit" application form must be submitted prior to initiation of treatment). As a supportive care medication, denosumab is not covered by the BC Cancer Agency but may be reimbursed by private insurance plans.

TESTS:

- Oral examination, any concerns (e.g. poor oral hygiene, recent oral surgery/tooth extractions, mobile teeth, dental caries, ulcers) should be referred for dental examination and treatment withheld until resolved. Completion of necessary dental work and full healing is recommended prior to starting denosumab. Oral examination should be performed prior to each subsequent denosumab administration.
- Serum calcium and albumin or ionized calcium (Corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 – albumin in g/L])). Calcium must be within normal range prior to initiating denosumab. Calcium repeated at least monthly prior to each subsequent denosumab administration.
- Magnesium, phosphate, creatinine at baseline and as clinically indicated.

CONCOMITTANT PRE-MEDICATIONS (MANDATORY MINIMUM):

- Calcium: minimum 500 mg daily, recommend 1000 mg daily
- Vitamin D: minimum 400 units daily, recommend 800 units daily

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Denosumab	120 mg (1.7 mL single use vial)	subcutaneously into upper thigh or abdomen with a 27 gauge needle

- Repeat every 4 weeks

DOSE MODIFICATIONS:

Hypocalcemia	Management
Asymptomatic grade 1 hypocalcemia (corrected calcium < LLN –2.0 mmol/L, ionized calcium < LLN – 1.0 mmol/L)	▪ Increase calcium supplementation to 2000 to 3000 mg daily and proceed with denosumab dosing. ▪ Check calcium level every 2 weeks until normal.
Asymptomatic grade 2 hypocalcemia (corrected calcium < 2.0 – 1.75 mmol/L, ionized calcium < 1.0 – 0.9 mmol/L)	▪ Increase calcium supplementation to 2000 to 3000 mg daily and proceed with denosumab dosing. ▪ Check calcium level every 2 weeks until normal. If not normalized before next denosumab dose, hold denosumab until normalized.
Symptomatic hypocalcemia (e.g. parasthesias, tetany, muscle spasms, irritability) or CTCAE grade 3 (corrected calcium < 1.75 mmol/L, ionized calcium < 0.9 mmol/L)	▪ Treat with intravenous calcium supplementation and hold denosumab until resolved to normal.

PRECAUTIONS:

1. Patients can develop severe, symptomatic hypocalcemia with fatal cases being described. Regular calcium monitoring is required.
2. Denosumab has not be tested in patients with creatinine clearance less than 30 mL/min and is not recommended in such patients.
3. After the use of denosumab, there is a risk of jaw osteonecrosis. Patients in whom denosumabis planned should have prophylactic assessment and management by a dentist and all later dental work should be undertaken cautiously by dental specialists experienced in the recognition and management of jaw osteonecrosis. The incidence of osteonecrosis after 1-2 years of denosumab therapy is 1-2% and increases with longer therapy.
4. Duration of treatment: the BCCA GU Systemic Tumour Group recommends treatment for as long as patient is deemed having benefit and an ECOG performance status of ≤2.

Call Dr. Kim Chi or GU Tumour Group designate at (604) 877-6000 or 1-800-663-3333 with any problems or questions regarding this treatment program.

Date activated: 1 May 2014

Date revised:

REFERENCES

Fizazi K, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomized, double-blind study. Lancet. 2011;377(9768):813-22.