

BCCA Protocol Summary for Therapy of Bone Metastases in Breast Cancer using Oral Clodronate

Protocol Code

BRAVCLOD

Tumour Group

Breast

Contact Physician

Dr. Susan Ellard

ELIGIBILITY:

- breast cancer with bone metastases
- A “Class II Drug Registration Form” must be submitted at the time of initiation of treatment.

EXCLUSIONS:

- severe renal dysfunction (serum creatinine greater than 440 micromol/L)
- severe inflammation of the gastrointestinal tract

TESTS:

- Completion of necessary dental work is recommended prior to starting clodronate
- Additional test: serum creatinine every 3rd treatment.
- If clinically indicated: serum calcium* and albumin (or ionized calcium)
*corrected calcium (mmol/L) = total calcium (mmol/L) + (0.02 x [40 – albumin in g/L])

PREMEDICATIONS:

- None

TREATMENT:

Drug	Dose	BCCA Administration Guideline
Clodronate	1600 mg once daily**	PO on an empty stomach (at least 1 h before or 2 h after eating)

**800 mg once daily to start, increased slowly over 1-3 weeks to minimise the risk of gastrointestinal intolerance

Continue to a maximum continuous exposure of 2-3 years (see precautions) or intolerance or obvious rapid deterioration in performance status.

- If unable to tolerate oral clodronate, pamidronate or parenteral clodronate may be used (a new “Class II Drug Registration Form” must be submitted at the time of initiation of treatment)

Drug	Dose	BCCA Administration Guideline
Pamidronate	90 mg	IV in 250 mL NS over 1 hour
OR		
Clodronate	1500 mg	IV in 500 mL NS over 3-4 hours

Repeat once monthly

Continue to a maximum continuous exposure of 2-3 years (see precautions) or intolerance or obvious rapid deterioration in performance status.

DOSE MODIFICATIONS:

1. Gastrointestinal intolerance (e.g., nausea, vomiting, diarrhea)

- divide dose (e.g., bid or qid)
- if not resolved by dividing dose, reduce dose until tolerated
- temporary interruption in treatment may be beneficial

2. Renal dysfunction:

- **Clodronate** has not been studied in patients with serum creatinine greater than 220 micromol/L; dose reduction may be required.
- There is limited experience with **pamidronate** in patients with serum creatinine greater than 440 micromol/L; caution is required.

PRECAUTIONS:

1. **Oral bioavailability** is only 1-3% and is reduced to zero in the presence of food, milk, antacids or minerals (including calcium). Instruct patients to take clodronate on an empty stomach (at least 1 hour before or 2 hours after eating or taking other medications including supplements).
2. **Symptomatic hypocalcemia** (e.g., muscle spasms, irritability) may occur with oral clodronate (1% incidence) and pamidronate and may require calcium supplement. Avoid concomitant use of other calcium lowering agents such as corticosteroids and loop diuretics.
3. Pamidronate and clodronate should NEVER be given as a bolus since severe local reactions and thrombophlebitis may result from high concentrations.
4. After the use of bisphosphonates, there is a persistent risk of jaw osteonecrosis. Patients in whom bisphosphonates are 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.
5. **Duration of treatment:** The BCCA Breast Systemic Tumour Group recommends a maximum continuous exposure of patients to bisphosphonates of 2-3 years, due to

increasing incidence of atypical femoral fractures with prolonged use. However, patients may be treated for longer if additional clinical benefit is likely in the judgement of their treating oncologist.

Call Dr. Susan Ellard or tumour group delegate at (250) 712-3900 or 1-888-563-7773 with any problems or questions regarding this treatment program.

Date activated: 01 May 1999

Date revised: 01 Jan 2012 (duration of treatment clarified)

References:

1. Badros A, et al. J Clin Oncol 2006;24:945-52.
2. Schilcher J, et al. N Engl J Med 2011 ;364 :1728-378.
3. Van Poznak CH, et al. J Clin Oncol 2011;29(4): 1221-1227.