



TREATMENT OF BONE METASTASIS WITH METRONOMIC ZOMETA INCREASES

07-10-10

PROGRESSION FREE SURVIVAL FOR BREAST CANCER PATIENTS.

Zoledronic Acid or **zoledronate** (marketed by [Novartis](#) under the trade names **Zometa**, **Zomera**, **Aclasta** and **Reclast**) is a [bisphosphonate](#). Zometa is used to prevent [skeletal fractures](#) in patients with [cancers](#) such as breast cancer, [multiple myeloma](#) and [prostate cancer](#), as well as for treating [osteoporosis](#). It can also be used to treat [hypercalcemia](#) of malignancy and can be helpful for treating pain from bone metastases. It is 100–1000 times more potent than other bisphosphonates such as pamidronate, alendronic acid, risedronate, clodronate, or etidronate.

An annual dose of Zometa may also prevent recurring fractures in patients with a previous hip fracture. The normal dosage for treatment of bone metastasis has been 4 mg once a month.

[A Chinese study](#) from [September 2010](#) by Zhao et al showed improvement in biomarker changes and a significantly increased progression free survival when Zometa was given in a weekly dose of 1 mg, instead of a monthly dose of 4 mg. Compared to the patients receiving conventional dose, the metronomic patients had a significantly greater reduction in serum levels of the angiogenesis(cancer blood vessel formation) biomarkers VEGF and N-telopeptide of type I collagen (Ntx).

The most commonly used breast cancer biomarker, Serum CA 15-3 level stabilized over time in the metronomic arm, but increased in the conventional arm.

The median follow-up time was 21.8 months (range 12.8–33.8 months). Patients in the metronomic arm had a median Progression Free Survival (PFS) of 7.5 months (95% CI, 5.3–9.6 months),

whereas patients in the conventional arm had a median of PFS of 2.8 months (95% CI, 0–5.8 months; $P = 0.127$).

Patients pretreated with 2 or fewer chemotherapy regimens, with ER-positive tumors, with serum VEGF of less than 500 pg/ml after 3 months of intervention, or with baseline serum NTx of less than 18 nM BCE also had significantly longer PFS.

Zometa was well tolerated with minimal severe toxicities. The most frequent all-grade adverse event for all patients as randomized and

as recorded during the first month after administration of Zometa was fever (40%, 24/60).

The main explanation for these revolutionary new data is that VEGF after an initial reduction in connection with a single dose of Zometa may return to the usual baseline levels within a few days. Therefore, an optimized anti-VEGF approach associated with Zometa will be best obtained using a pharmacokinetic-guided dosing strategy, i.e., weekly Zometa, since its half-life is 169 h (i.e., just over 7 days) . The metronomic dosage of Zometa will make better use of its anti-angiogenic properties, thus preventing new blood vessel formation to the cancer tumor.

Immediately after getting to know these new data, we have decided to recommend the patients at Humlegaarden receiving Zometa for treatment of bone metastases to use the metronomic dosing schedule with 1 mg per week instead of the conventional schedule with 4 mg per month.