Personal Statement- Tara Beaumont Clinical Nurse specialist- metastatic breast cancer @ Breast Cancer Care

Bone is the most common site of metastatic spread for breast cancer; around 80% of all patients' diagnosed with metastatic breast cancer will have bone metastases. A significant concern regarding metastatic breast cancer in the bone is a skeletal related event or complication of bone metastasis including; hypercalcaemia, pathological fracture, bone pain and spinal cord compression. Randomised trials in advanced breast cancer have shown that a major skeletal related event occurs for the patient, on average, every 3–4 months (1). This may result in a poor quality of life, including reduced mobility and life expectancy with the average life expectancy from diagnosis of bone metastases at around two years, with approximately only 20% of patients surviving five years (1, 2, 3,4,10). Additionally it has been shown that prognosis is considered to reduce with an increasing number of skeletal related events experienced by a patient (11).

For patients' with metastatic breast cancer the importance of quality of life can not be underestimated and it is imperative it is taken into full account in this appraisal. This population group want access to treatments that will give them an improved quality of life to spend more quality time with their friends and families (3), as well as maintain other commitments such as work, volunteering and travel. Therefore, the focus of the economic analysis should be placed on patient quality of life due to advanced/metastatic breast cancer being a life limiting condition (3,6).

Currently in the UK Bisphosphonates are the established 'gold standard' for treatment of bone metastases for people with advanced breast cancer (1). Denosumab has been studied in clinical trials as a treatment for adults with metastatic breast cancer in the bone, comparing it against a placebo as well as bisphosphonates (4,9). Denosumab is a fully human monoclonal antibody. It targets the receptor activator of nuclear factor kappa B ligand known as RANKL .

The phase III study of denosumab vs zolendronic acid, results showed a;

17% risk reduction in time to first on-study skeletal related event with denosumab vs zoledronic acid. There was significant risk reduction in time to first on-study skeletal related event seen in patients' with and without a previous skeletal related event and denosumab was favored across all skeletal related event types. Although, there was no significant difference in median time to disease progression or median overall survival. In terms of side-effects, there were less acute phase reactions with denosumab, and less renal dysfunction. There is slightly more incidence of osteonecrosis of the jaw (8%), but this was still rare and associated with risk factors around oral health. One other point to note with denosumab was a slight increase in hypocalcaemia and so regular blood tests are indicated (8). Improved quality of life and pain control have been demonstrated with denosumab over zoledronic acid (3,4).

Administration of denosumab is via subcutaneous injection as opposed to intravenous delivery (a common administration route for bisphosphonates). There may be a possibility of administering denosumab via the GP, thus saving the patient the added financial costs of travelling to a hospital, increasing convenience for them, and reducing acute sector costs.

Many patients that are prescribed oral bisphosphonates tolerate these drugs well. However, some patients find oral medication difficult, and would prefer more regular contact with healthcare professionals than is the normal standard when taking oral bisphosphonates. Monthly subcutaneous injections offer regular contact with a healthcare professional in which to discuss ongoing health needs.

References

1.Brown J.E., Coleman R.E. (2002) 'The present and future role of bisphosphonates in the management of patients with breast cancer' in Breast Cancer Research, 4(1):24-9

2. Stopeck A.T.,Lipton A., Body J.J., et al. (2010) 'Denosumab compared with zolendronic Acid for the treatment of bone metastases in patients with advanced breast cancer: A randomized double blind study' in Journal of Clinical Oncology 28(35):5132-9

. .

3. Fallowfield L., Patrick D., Body J., et al. (2010) 'Effects of Denosumab versus zolendronic acid on health-related quality of life in metastatic breast cancer: Results from a randomized phase III trial' in Journal of Clinical Oncology 28(15)

4. Stopeck A., Fallowfield L., Patrick D., et al. (2010) 'Effects of Denosumab versus zolendronic acid on pain in patients with metastatic breast cancer: results from a phase III clinical trial' in Journal of Clinical Oncology 28(15)

5. Schwarz E., Ritchlin C., (2007) 'Clinical development of anti- RANKL therapy' in Arthritis Res Ther. 9 (suppl1)

6. Coleman, R. E., (1997) 'Skeletal complications of malignancy' in Cancer 80: 1588-94.

7. Lipton A. (2006) 'Biochemical bone markers in breast cancer' in Cancer Treat Rev 32: 20-22 (suppl 1)

8. Lipton, A. et al. (2007) 'Randomized active-controlled Phase II study of Densoumab efficacy and safety in patients with breast cancer-related bone metastases' in Journal of Clinical Oncology 25(28): 4431-37.

9. 'A Randomized, Double-Blind, Multicenter Study of Denosumab Compared With Zoledronic Acid (Zometa®) in the Treatment of Bone Metastases in Subjects With Advanced Breast Cancer' NCT00321464.

10. Paterson A H G (2006) The use of bisphosphonates in the management of advanced breast cancer in (Ed) Booth S *Advanced Breast Cancer* Oxford University. Press Oxford Chapter 8 91-102

11. Coleman RE (2004) Bisphosphonates: clinical experience *Oncologist*. 9 (suppl.4) 14-27