Consensus Panel 1: Guidelines for Bone Disease

IMW 2011

Use of BPs in MGUS

- Guidelines for the use of bisphosphonates in MGUS are not yet clear except for patients with osteoporosis.
- Dexa's should be considered for patients with MGUS or SMM because of the reported increase in skeletal related events in these patients.
- If the Dexa shows osteoporosis (T score<2) consider treating in a similar manner as patients with osteoporosis.

BPs in SMM

- For low and intermediate risk SMM, if osteoporosis is identified by Dexa, consider treating with bisphosphonates as for osteoporosis.
- For high risk SMM and if one can not differentiate between MM-related versus age-related bone loss, providers should consider using dosing and schedule of bisphosphonates as for symptomatic myeloma, especially in patients with abnormal MRIs.

Plasmacytoma

- If solitary plasmacytoma-no BP therapy is indicated.
- If osteoporosis is present then treat as osteoporosis.
- If multiple plasmacytomas-treat like MM

MM without lytic bone lesions

- It is still unclear if bisphosphonates should be used in patients without bone lesions.
- The MRC IX trial demonstrated benefit of zoledronate in patients without bone disease.
- MM with diffuse osteopenia and active myeloma - use bisphosphonates as recommended by the ASCO guidelines for myeloma bone disease.

BP's in patients with MM and bone lesions

- IV bisphosphonates are preferred based on MRC IX trial which showed the superiority of zoledronate over an oral bisphosphonate.
- The Nordic trial compared 30 mg versus 90 mg of pamidronate IV in 500 newly diagnosed MM patients and found these doses to be equivalent. Low dose treatment with zoledronate has not been shown to be effective in MM.

Frequency and Duration of BPs

- No data yet available to warrant changing q 3-4 week schedule for IV BPs.
- There is no randomized prospective data on using bisphosphonates beyond two years. Consideration for discontinuing bisphosphonates after 2 years should be based on an assessment of risk and benefit by the treating physician.

Monitoring Toxicity of BPs

- It is clear that dental screening prior to starting bisphosphonates and maintaining good dental hygiene while on bisphosphonates decreases the incidence of ONJ.
- The current practice is to stop bisphosphonates for 90 days before and after invasive dental procedures (tooth extraction, dental implants and surgery to the jaw). Other dental procedures do not require holding BPs. There are no randomized prospective data demonstrating that holding bisphosphonates for three months impacts the development of ONJ.

Monitoring toxicity of BPs

- Providers should ask patients about dental procedures every month when the creatinine is checked.
- Creatinine should be checked prior to each administration of IV BP.
- The risk for development of atypical femoral fractures that has been reported in patients with osteoporosis on very long term oral bisphosphonates is extremely low and the association has not been confirmed.
- Metatarsal fractures in 6 patients on long term BPs have been reported recently.

Anti-myeloma effects of BPs

- There is emerging data that bisphosphonates have anti-myeloma activity both in vitro and in patient studies.
- Their use as a single agent for their anti-myeloma activity is not indicated.

Use of Vitamin D and Calcium

- 60% of Myeloma patients are Vit D deficient or insufficient.
- It is very important that patients be calcium and vitamin D sufficient.
- Calcium supplementation should be used with caution in patients with renal insufficiency.

Use of New Agents

- There are a variety of new agents in development to block osteoclastic bone resorption or stimulate bone formation- Denosumab, an Activin A receptor antagonist, anti-DKK-1 etc. Current data on these agents are not adequate to recommend their routine use.

Surgery for MM Bone Disease

- The CAFÉ study has shown that kyphoplasty is an effective and safe treatment that reduces pain and improves function.
- The role of vertebroplasty for myeloma patients is less clear. Case series have reported benefits of vertebroplasty. Two randomized trials have failed to show a benefit of vertebroplasty compared to sham operation for patients with osteoporotic fractures. No similar randomized data is available for myeloma.

Radiotherapy

- Radiotherapy for local disease control and palliation should be used judiciously and sparingly depending on patient's presentation, need for urgent response, and prior treatment history and response.
- It should be limited as much as possible to spare the patient's marrow function.
- Current novel agents work rapidly and should decrease the need for palliative XRT.