UKINETS Bitesize Guidance for the use of zoledronic acid/denosumab* in patients with bone metastases from Neuroendocrine tumours (NETs)

PAGE 1 - SCREENING & INVESTIGATION ALGORITHM

<u>Diagnosis:</u> Isotope bone scan (detect skeletal pathology)
Functional imaging (Ga-68 PET/ Octreotide scan
Computerised tomography and magnetic resonance imaging (structural information on skeletal damage)

Bone metastases identified

Asymptomatic, incidentally detected

Further research is required to determine whether preventive therapy with zoledronic acid or the targeted receptor activator of nuclear factor-kB (RANK) ligand inhibitor denosumab may be of value for preventing development of skeletal-related events (SREs) in NETs

Use of zoledronic acid or denosumab in asymptomatic, incidental cases remains controversial and should be considered on a case-by-case basis after discussion with patient

Symptomatic

Multidisciplinary management integrating expertise in systemic treatments, radiotherapy, orthopaedic surgery, and supportive care is required for effective treatment of metastatic bone disease

Current standard of care for supportive care/pain management applies

Analgesic effect of bone-modifying agents (BMAs) [denosumab, zoledronic acid] are modest, and should not be used alone for bone pain

A BMA is recommended for patients with metastatic NET and evidence of bone destruction

One BMA is not recommended over another (mechanism of action, as well as potential benefit/harm should be considered)**

Treatment of hypercalcaemia should follow institutional guidelines

Orthopaedic surgery to be considered in appropriate cases

Radiotherapy is treatment of choice for palliation of localised bone pain

If evidence of metastatic spinal cord compression, follow institutional guidelines for management of same

All patients should have dental examination and preventive dentistry before using a BMA

BMAs for metastatic bone disease should continue indefinitely and throughout course of disease, if appropriate

Optimal frequency and duration of therapy is extrapolated from studies on other types of solid tumours

**Denosumab is slightly more effective in preventing skeletal morbidity (at least in other solid tumours), easier to adminster and avoids renal monitoring. However, needs to be given every month whereas zoledronic acid can be given 3 monthly, is 10x more expensive and difficult to discontinue due to rebound osteolysis.

Bone metastases occurred in 25% of all phaeochromocytomas and paragangliomas (25 out of 100), 20% of high grade neuroendocrine carcinomas (9 out of 46), 9% of carcinoid tumours (30 of 341), and 8% of pancreatic NETs (12 of 153).

A multi-institutional study in the US (2004-2008) [part of collaboration with the National Comprehensive Cancer Network (NCCN) Oncology Outcomes database] identified 82 patients out of 691 (12%) with a diagnosis of a neuroendocrine tumour (NET) who developed bone metastases.

Of the 82 patients with bone metastases, 59% were reported to be symptomatic at time of detection.

Among the patients who were asymptomatic at detection, 21% went on to develop a skeletal-related event.

Pain from bone metastases is a cause of impaired performance status and psychological distress among patients with cancer.

Bone metastases from NETs have unique features on radiological and nuclear imaging, and may be missed by conventional radiography.

Currently, there is no consensus regarding the management of bone metastases from NETs, and guidance has to be extrapolated from studies conducted in other solid tumours.

References

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