

Bone protection in Lymphoma

Background

Published data indicate an increased risk of osteoporosis and fracture in patients who have received steroid containing combination chemotherapy for lymphoma. A retrospective analysis of 729 UK patients receiving full dose or attenuated R-CHOP for diffuse large B-cell lymphoma > 70 years identified a cumulative fracture risk of 11.4% at 18 months¹.

Independent risk factors for fracture included rheumatoid arthritis, bone involvement by high grade lymphoma and the use of pre-phase steroids before chemotherapy: patients with one or more of these risk factors had an 18-month risk of fracture of 12.7 – 26.7%.

Bisphosphonates are of established benefit in reducing fracture risk post-menopausal osteoporosis². Intravenous zoledronic acid has been demonstrated to be safe and to reduce loss of bone density in patients receiving steroid containing chemotherapy for lymphoma³. Evidence also indicates compliance with infrequent parenteral bisphosphonates is better than regular oral bisphosphonates⁴. The licenced dose of zoledronic acid for treatment of osteoporosis is 5 mg once a year and therefore a single 5 mg dose has been chosen for prevention of glucocorticoid induced osteoporosis. This use is not licenced but has been approved in OUH by the MMTC.

Prednisolone containing regimens for lymphoma

This supportive care document applies to patients receiving the following regimens.

CHOP14 / R-CHOP 14
 CHOP21 / R-CHOP 21
 O-CVP
 R-CP
 R-CVP
 R-mini-CHOP

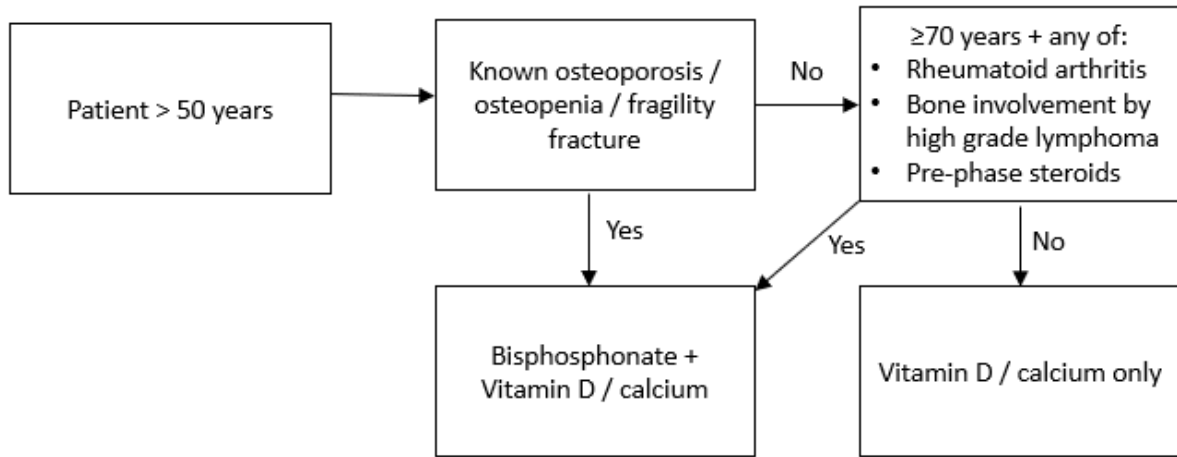
Bone protection

All patients > 50 years who are not currently hypercalcaemic should be offered ADCAL-D3 2 tablets daily to concomitant medications from cycle 1 day 1 to the end of treatment. Patients who are deficient in vitamin D should receive a loading course of 7 weeks of 40000 IU cholecalciferol once a week.

Consider Zoledronic acid 5 mg IV single dose with cycle 1 (or cycle 2 if a dental assessment is required and not yet completed) for the following patients with risk of fracture > 10% at 18 months, unless already established on a bisphosphonate or denosumab in primary care:

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Figure 1: bone protection for patients receiving steroid containing chemotherapy for lymphoma



Where patients are prescribed a single dose of zoledronic acid for prevention of glucocorticoid induced osteoporosis this should be clearly communicated to the GP in the clinic correspondence. Those diagnosed with established osteoporosis should be considered for primary care bone protection from one year after the zoledronic acid.

Safety

Renal impairment: Zoledronic acid 5 mg is contra-indicated if CrCl < 35 ml / min (unlike in the myeloma indication where the threshold is CrCl < 30 ml/min)

Dentition: All patients who have not recently seen a dentist should be evaluated by a dentist, before starting bisphosphonates if there is any clinical concern about dentition. Patients must be warned of the risk of osteonecrosis of the jaw and the need to make their dentist aware they have received bisphosphonates prior to dental work.

References

1. Booth, Stephen, et al., *Fractures are common within 18 months following first-line R-CHOP in older patients with diffuse large B-cell lymphoma*. Blood Advances, 2020. **4**(18): p. 4337-4346.
2. EMC. *Zoledronic acid 5 mg solution for infusion. Summary of Product Characteristics*. [cited 2020 06 August]; Available from: <https://www.medicines.org.uk/EMC/medicine/14062/SPC/Zometa+4mg+5ml+Concentrate+for+Solution+for+Infusion/>.
3. Westin, Jason R., et al., *Zoledronic acid for prevention of bone loss in patients receiving primary therapy for lymphomas: a prospective, randomized controlled phase III trial*. Clinical lymphoma, myeloma & leukemia, 2013. **13**(2): p. 99-105.
4. Fobelo Lozano, M. J. and S. Sánchez-Fidalgo, *Adherence and preference of intravenous zoledronic acid for osteoporosis versus other bisphosphonates*. Eur J Hosp Pharm, 2019. **26**(1): p. 4-9.

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