Bone Protection in Patients with Lymphoma

Protocol

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Applies to	Adults requiring prednisolone-containing therapy for lymphoma (R-CHOP, R-CVP or similar)	**Exclusions**	Paediatrics

CONTENTS

1.0 Background and rationale

Many patients with lymphoma have very good response to prednisolone-containing chemotherapy. There is a good chance of cure and therefore a focus on late effects of therapy and survivorship, to ensure the best long-term health.

There is a known increased risk of osteoporotic fracture, including vertebral and hip fractures, in patients during prednisolone-containing chemotherapy, and for 1-2 years thereafter.[1,2] Additive risk factors include previous fracture, known osteopenia, rheumatoid arthritis, bone involvement by high-grade lymphoma and the use of a steroid pre-phase before chemotherapy.[1] Additional risk factors for osteoporortic fracture are increasing age, female gender, family history (parent with osteoporotic hip fracture), current smoking, low body-mass index and daily alcohol consumption of 3 or more units.[1,3]

There is evidence for reduction in fracture risk in people with osteoporosis, using vitamin D plus calcium supplementation and bisphosphonates. Small studies have shown reduction in loss of bone mineral density for lymphoma patients on chemotherapy taking zoledronic acid[4] or alendronic acid,[5] compared with calcium and vitamin D alone. There is, as yet, no randomised trial evidence of a reduction in fracture risk.

Evidence indicates compliance with infrequent parenteral bisphosphonates is better than regular oral bisphosphonates.[6] The licenced dose of zoledronic acid for treatment of osteoporosis is 5 mg once a year[7] and therefore a single 5 mg dose has been chosen for prevention of glucocorticoid induced osteoporosis.

2.0 Patient selection

This document applies to patients receiving a significant amount of steroids with their chemotherapy for lymphoma:

CHOP / CVP, with or without rituximab or obinutuzumab
Including mini-CHOP

Low risk	Medium risk	High risk
Patients <50 with no relevant history	Patients aged 50-69 without additional risk factors	All patients aged >69 Patients aged 50-69 + any of: • Rheumatoid arthritis • Bone involvement with high grade lymphoma • Pre-phase steroids • Strong family history osteoporosis • Low BMI < 19kg/m^2 • Known osteoporosis/ osteopenia/ fragility fracture
Offer vitamin D replacement if level <35 nmol/l; consider loading dose	Offer 2 tablets ADCAL-D3 daily whilst on treatment (if not hypercalcaemic)	Offer 2 tablets ADCAL-D3 daily whilst on treatment (if not hypercalcaemic) AND Consider single dose zoledronic acid 5mg with cycle 1 or 2

3.0 Zoledronic acid safe prescribing

Osteonecrosis of the jaw: Zoledronic acid should be avoided if there is active dental infection, or recent dental extraction not yet fully healed. However, the risk of osteonecrosis is generally lower for a single dose of IV bisphosphonate compared with long-term, regular treatment. If there are no overt dental problems, delaying the dose for a formal dental assessment is not required. Consider delay for dental assessment if some concerns.

Check vitamin D and calcium before the single dose of zoledronic acid:

If vitamin D <35 nmol/l, start vitamin D replacement (with calcium if not hypercalcaemic), and delay zoledronic acid to allow at least 2 weeks' replacement. Vitamin D level does not need to be repeated.

If Calcium <2.2, replace with oral Adcal D3, and ensure ≥ 2.2 before zoledronic acid is given

Limits for go ahead:

Vitamin D	Within 4 months, ensure replaced if previously low, no need to repeat
Calcium	Within 28 days, repeat if low to ensure adequately replaced

Consent

Formal, written consent is not required for a single dose of zometa. It should be discussed with the patient.

4.0 References

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4. Westin JR, Thompson MA, Cataldo V, et al. Zoledronic acid for prevention of bone loss in patients receiving primary therapy for lymphomas: a prospective, randomized controlled phase III trial. Clin Lymphoma Myeloma Leuk 2013; 13(2):99-105
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6. Fobelo Lozano MJ and Sánchez-Fidalgo. Adherence and preference of intravenous zoledronic acid for osteoporosis versus other bisphosphonates. European Journal Hospital Pharmacy 2019;26:4-9
7. Zoledronic acid | Drugs | BNF | NICE