Thalidomide + Zoledroninezuur/Pamidroninezuur M1149

ONJ = osteonecrosis of the jaws

Onderbouwend	Stof	Effect	Code
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Overig: effect op nier	Stof	Effect
SPC Zometa, Pamipro	thalidomide + zoledroninezuur, pamidroninezuur	voorzichtig bij combinatie met thalidomide bij multipel myeloom vanwege verhoging van het risico op renale dysfunctie. Bijwerkingen: bij 1-10% stijging van de creatinine- en ureumconcentratie.
Spencer A. BMC Clin Pharmacol 2008;8:2.	thalidomide + zoledroninezuur	In myeloma patients receiving maintenance therapy, the combination of zoledronic acid and thalidomide appears to confer no additional renal safety risks over zoledronic acid alone. No significant differences by Wilcoxon rank-sum statistic were found in zoledronic acid pharmacokinetics or renal safety for up to 16 months in patients randomized to thalidomide or not. Regime: zoledroninezuur 4 mg iv elke 4 weken + prednisolon + thalidomide 100-200 mg/dag (n=12); zoledroninezuur + prednisolon zonder thalidomide (n=12); totaal 24 patienten met myeloma in a trial of maintenance therapy.
Jones SG. Br J Haematol 2002;119:576-7.	thalidomide + zoledroninezuur	toename creatinine en hypocalciemie na switch van pamidro-ninezuur naar zoledroninezuur bij 2 myeloom patiënten die tevens thalidomide gebruikten. Nadere studie nodig of dosisaanpassing zoledroninezuur nodig is bij myeloompatiënten met verminderde nierfunctie.
Werkgroep Geneesmiddelen bij verminderde nierfunctie	zoledroninezuur	bij verminderde nierfunctie is dosisverlaging noodzakelijk

Overig: effect op ONJ	Stof	Effect
Aragon-Ching JB. Cancer Invest 2009;27:221-6.	thalidomide + bisfosfonaten	The incidence of ONJ in patients who have been treated with bisphosphonates for non-malignant conditions had been around 0.8%. Although the incidence is variable among prostate cancer patients, it had been reported to occur around 6.5%. We reviewed the medical and dental records of 11 patients (metastatic prostate cancer) who developed ONJ out of 60 participants enrolled in a phase II clinical trial of bevacizumab, thalidomide, docetaxel, and prednisone (ATTP) for the treatment of mCRPC. Auteurs: another theory for the development of ONJ is the inhibition of capillary angiogenesis. ZA has been shown to exhibit anti-angiogenic properties in in vitro studies. We hypothesize that coupled with known anti-angiogenic therapies such as bevacizumab and thalidomide, the effects of ZA on avascularization may be enhanced, accounting for the high rate of ONJ in our patients.

Pozzi S. Leuk Lymphoma 2007;48:56-64.	thalidomide + zoledroninezuur pamidroninezuur	Over a period of 28 months, we observed 5 cases of ONJ in cancer patients treated with bisphosphonates (BP) at our institution. Retrospective analyse: we identified 35 cases during the period 2002-05. The median time from cancer diagnosis to the clinical onset of ONJ was 70 months. The time for the onset of ONJ was significantly shorter for patients treated with zoledronic acid alone than for those treated with pamidronate followed by zoledronic acid. Our analysis strongly suggested an association between the use of BP and the occurrence of ONJ, although we were unable to identify any definite risk factors with a retrospective study. The most frequently ONJ-associated clinical characteristics were chemotherapy treatment, steroid treatment, advanced age, female sex, anemia, parodonthopaties/dental procedures and thalidomide (in the case of MM patients).
Tosi P. Blood 2006;108:3951-2.	thalidomide + zoledroninezuur	Retrospectively review: 259 consecutive patients with symptomatic MM who were enrolled in a clinical trial. All patients received 4 months of primary therapy with thalidomide 200 mg/d combined with high-dose dexamethasone followed by double autologous transplantation with melphalan 200 mg/m^2. Thalidomide and dexamethasone were continued until the second autologous transplantation. I.v. zoledronic acid 4 mg every 28 days was administered throughout the whole treatment period and continued thereafter. Only patients receiving zoledronic acid for longer than 4 months were included in the present analysis. ONJ after 24 months of zoledronic acid exposure was 6.6%, a value comparable with those found in other analyses. This observation might suggest that neither antiangiogenic activity of thalidomide, nor impaired bone remodeling related to dexamethasone, nor severe immunosuppression induced by high-dose melphalan was an important additional risk factor for the development of ONJ.
Zervas K. Br J Haematol 2006;134:620-3.	thalidomide + zoledroninezuur	The incidence, characteristics and risk factors for the development of ONJ were evaluated among 303 myeloma patients. Only patients who received bisphosphonates developed ONJ (28/254; 11%). Zoledronic acid produced 9.5-fold greater risk for developing ONJ than pamidronate alone and 4.5-fold greater risk than subsequent use of pamidronate + zoledronic acid. Use of thalidomide and number of bisphosphonate infusions also increased the risk for ONJ by 2.4-fold, and 4.9-fold respectively. ONJ developed earlier among patients receiving zoledronic acid. Our data indicates that administration of zoledronic acid for more than 2 years or in combination with thalidomide requires caution in myeloma.

Opmerkingen
Stockley: 'no interaction is established'. Gegevens uit Spencer 2008 suggereren dat het risico op nierproblemen door zoledroninezuur+thalidomide niet groter is dan alleen zoledroninezuur. Mechanisme: onduidelijk.

SPC Fosamax, Bonefos, Didrokit, Actonel, Bonviva: thalidomide niet genoemd.

PubMed: niks op alle bisfosfonaten + thalidomide, behalve therapeutische combinatie.

Risicogroep	

	Interactie	**Actie**	**Datum**
Beslissing WG OncolA	Nee	Nee	28 november 2012