

**Evolution of bone mineral density in patients treated  
with high-dose topical corticosteroids for a bullous  
pemphigoid**  
Nolwenn Ropars

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ANNEE 2016



**THÈSE D'EXERCICE / UNIVERSITÉ DE RENNES 1  
FACULTÉ DE MEDECINE**

*sous le sceau de l'Université Européenne de Bretagne*

**THÈSE EN VUE DU  
DIPLOME D'ÉTAT DE DOCTEUR EN MEDECINE**

Présentée par

**Nolwenn ROPARS**

née le 25 janvier 1988 à Brest

---

**Evolution de la densité minérale  
osseuse chez des patients traités  
par dermocorticothérapie  
prolongée pour une pemphigoïde.**

**Evolution of bone mineral density  
in patients treated with high-dose  
topical corticosteroids for a  
bullous pemphigoid.**

**Thèse soutenue à RENNES  
le 26/04/2016**

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## **TABLE DES MATIERES**

|  |           |
|--|-----------|
| <b>ABSTRACT .....</b>  | <b>11</b> |
| <b>INTRODUCTION .....</b>  | <b>12</b> |
| <b>MATERIALS AND METHODS .....</b>   | <b>13</b> |
| <b>RESULTS .....</b>   | <b>15</b> |
| <b>DISCUSSION .....</b>  | <b>16</b> |
| <b>CONCLUSION.....</b>   | <b>18</b> |
| <b>REFERENCES BIBLIOGRAPHIQUES .....</b>   | <b>20</b> |
| <b>GLOSSAIRE.....</b>  | <b>24</b> |
| <br>   |           |
| FIGURE 1 FLOW CHART .....  | 25        |
| FIGURE 2 REPRESENTATION OF LUMBAR SPINE, FEMORAL NECK AND HIP BMD CHANGE,<br>BASELINE BMD, AND CUMULATIVE DOSE OF CLOBESTASOL PROPIONATE. .... | 26        |
| FIGURE 3 CORRELATION BETWEEN LUMBAR SPINE VARIATION (G/CM <sup>2</sup> ) AND DOSE OF<br>CLOBETASOL PROPIONATE (G/KG/DAY).....                  | 27        |
| TABLE 1 BASELINE CHARACTERISTICS .....   | 28        |
| TABLE 2 BASELINE BONE STATUS .....   | 29        |
| TABLE 3 CHARACTERISTICS OF PATIENTS WITH BMD CHANGE AND PATIENTS WITHOUT<br>BMD CHANGE.....  | 30        |

## **ABSTRACT**

**Introduction:** High dose topical corticosteroids may have same systemic side effects as systemic corticosteroids. Bone side effects are poorly known with topical corticosteroids. We studied evolution of Bone Mineral Density (BMD) in patients with Bullous Pemphigoid (BP) treated with high dose of clobetasol propionate in a retrospective monocentric cohort.

**Material and Methods:** BMD measurements and biological analysis were performed before and after topical corticosteroid treatment in patients with BP from January 2014 to June 2015. Tubes of clobetasol propionate were count every month. The objective was to describe changes in BMD and biological markers according to the dose of clobetasol propionate in patients with BP.

**Results:** 29 patients had BP, 22 patients had at least one assessment, and 9 patients had two assessments. 6 patients had a BMD variation  $> 0.03$  g/cm<sup>2</sup>. There was no correlation with dose of clobetasol propionate. There was no biological change before and after treatment. Limitations were missing data, small size of the sample, and number of patients excluded because high mortality of BP.

**Conclusion:** These results suggest larger studies to analyse links between high dose of topical corticosteroids and osteoporosis in patients with BP.

## **INTRODUCTION**

In France, first-line treatment for Bullous Pemphigoid (BP), an auto-immune bullous dermatosis, currently lies on prolonged use of high dose superpotent topical corticosteroid (1).

Use systemic corticosteroids was considered the mainstay treatment for BP patients (2,3), until a large French multicenter prospective randomized trial (4) showed that clobetasol propionate cream was more effective than systemic corticosteroids in disease control on day 21, and presented with a lower rate of severe systemic side effects. Another French multicenter randomized prospective trial (5) compared two regimens of topical corticosteroids and showed that a shorter treatment (4 months vs 12 months) using lower doses of clobetasol propionate (10-30 gram (g) vs 40 g per day) was as effective as the standard regimen with fewer life-threatening side effects. Consequently, clobetasol propionate cream has become the BP treatment of reference in France.

Systemic absorption following cutaneous application of corticosteroid cream ranges between 0.05 % and 0.3 % (6) and may cause systemic side effects. Cases of iatrogenic Cushing (7), adrenal suppression (8–13) or hyperglycemia (14–16), have been reported following cutaneous application caused by improper and prolonged usage of super potent topical corticosteroid. These side effects are well described with systemic glucocorticoids. Few cases of topical corticosteroids-related bone side effects (17–22) have been reported. Osteoporosis is one of the most frequent and clinically relevant side effect of long-term systemic glucocorticoid therapy (23) and not described with topical corticosteroid. Osteoporosis is a disease characterized by a reduce in bone strength, leading to an increased risk of fracture and related increases in morbidity and mortality (24). Bone strength is estimated by measuring bone mineral density (BMD). Cross-sectional studies have evidenced low values for BMD in patients with atopic dermatitis (25,26) and psoriasis (22,27). However, low BMD may be due to absorption of topical corticosteroids or to chronic inflammation.

The aim of the present study was to evaluate the change of BMD during high dose topical corticosteroids treatment in patients with BP.

## **MATERIALS AND METHODS**

We performed a retrospective monocentric review of newly diagnosed BP who attended the dermatological department in Rennes University Hospital from January 2014 to June 2015. For all BP patients, the diagnosis of active disease was established on the basis of the presence of blisters on the skin as well as the typical immunopathological criteria such as linear deposition of IgG and C3 at the basement membrane zone on direct immunofluorescence and circulating levels of anti BP180 and/or anti BP230 autoantibodies by ELISA.

Patients were treated with an initial dose of clobetasol propionate cream ranging from 20 to 40 g per day. The clobetasol propionate cream was tapered over 4 months according to the following protocol driven by SFD (Société Française de Dermatologie) guidelines: clobetasol propionate cream every day the first month, every other day the second month, twice a week the third month and once a week the fourth month. If there were less than ten blisters, the treatment was the same but with only 20 g per application. Osteoporosis prophylaxis was not routinely given.

In our Dermatology department, all newly BP underwent physical, biological examinations (complete blood cell counts, blood electrolyte, blood sugar, serum creatinine, thyroid stimulating hormone (TSH), parathyroid hormone (PTH), morning serum cortisol, electrophoresis, and markers of bone metabolism: serum calcium (adjusted with albumin), urinary calcium, serum phosphate, 25-hydroxyvitamin D (25-OHD), total alkaline phosphate, C-terminal telopeptid of type 1 collagen (CTx), N-terminal propeptide of type I procollagen (P1NP)) and a BMD measurement at the initial visit and after treatment (about 6 months later). Biological samples (blood electrolytes, blood sugar and creatinine) were performed every month.

Every month, at each follow up visit, the patients underwent physical examination and the number of new bullae that appeared daily was recorded, together with the number of empty tubes of clobetasol propionate that had been used. In this article, clobetasol propionate is expressed in grams: 10 g of clobetasol propionate correspond to one tube of topical corticosteroids containing 5 mg of clobetasol propionate.

BMD was measured in all patients at the lumbar spine, hip and femoral neck using Dual energy X-ray Absorptiometry (DXA)(Hologic QDR 4500 Bone Densitometer) in a single laboratory. The BMD are expressed in gram per square centimeter after which the Standard Derivation (SD) was calculated. Data was expressed as T-score (number of SDs from the mean value of the young adult of the same sex reference population). DXA was reported by one investigator who was aware of the patient's diagnosis but not of the frequency, amount or duration of clobetasol propionate used. We considered a meaningful BMD change above 0.03 g/cm<sup>2</sup> between both DXA at any site (28,29). Otherwise, bone density was considered stable. WHO Fracture Assessment Fracture tool (or Frax-tool) was calculated for all patients with necessary data according to recommendations (30) of the French Society of Rheumatology and the Groupe de Recherche et d'Information sur les Osteoporoses (we considered no familial history of osteoporosis).

Fracture risk factors were collected: history of osteoporosis with fracture, history of prolonged systemic corticosteroids, prolonged immobilization, current smoker, alcohol consumption, BMI < 19 kg/m<sup>2</sup>. Parental hip fracture, calcium intake, ages and treatment of menopause could not be evaluated in this study. We retrospectively collected data from the medical records.

We compared change of BMD and blood analysis before and after the treatment with clobetasol propionate. The objective of this retrospective cohort was to describe changes in BMD and biological markers according to the dose of topical corticosteroids.

The statistical analysis was done with SAS software (version 9.4). Continuous variables were expressed by mean and standard deviation and categorical variables were expressed by the number of patients and percentages. Comparisons between M0 and M6 were realized using Wilcoxon signed rank test.

## **RESULTS**

A total of 29 patients with BP attended the dermatological department of Rennes University Hospital between January 2014 and June 2015. Among the 29 patients, 22 had at least one BMD measurement and biological examination. Among them, 9 patients had 2 BMD measurements and biological examinations (flow chart **figure 1**).

**Table 1** shows clinical and biological baseline characteristics of patients. All patients had more than 70 years. Eighteen of them had at least one additional risk factor of fracture. The median BMI was  $26.7 \pm 6.0$  kg/m<sup>2</sup>. Thirteen patients were bedridden. Five patients had history of osteoporosis with fracture. Among these 5 patients, 1 had bisphosphonate treatment, 1 had calcium plus vitamin D treatment and 3 had vitamin D treatment alone. There was no patient with rheumatoid arthritis or with secondary osteoporosis. Frax-tool was calculated for patients without systemic corticosteroids, but could be calculated for only ten of the nineteen patients. For the other patients femoral necks BMD, weights or heights were missing. Among the ten patients, only two patients had an indication of osteoporosis treatment.

Baseline BMD measurements are presented in **table 2**.

Among the 22 patients, 11 patients had baseline < 10 bullae per day. Thirteen patients could not be evaluated and 9 patients were evaluated after treatment. Mean cumulative dose of clobetasol propionate was  $2070 \pm 922$  g. Five patients had an initial treatment with 30 g per day and 4 patients had 20 g per day. One patient (patient 1) was evaluating at 12 months. He was treated with a cumulate dose of 7220 g of clobetasol propionate. Six of the 9 patients with two assessments were in clinical remission at 6 months. Four patients still have clobetasol propionate treatment at 6 months. Three of these 4 patients had lower cortisol measurements after 6 months. Only patient 27 had a collapsed cortisol with no clinical symptom. He was treated with  $2270 \text{ g} \pm 929$  g of clobetasol propionate. There was no fracture during or after treatment.

Nine patients had initial and final evaluations. There was no significant biological variation before and after treatment especially in blood sugar, serum calcium, urinary calcium, serum phosphate, 25-OHD, alkaline phosphate, CTx and P1NP for the nine patients with two assessments. **Figure 2** presents schematically all variations for the 3 sites measurements together with the cumulative dose of clobetasol propionate. Among the 9 patients with both an initial and final BMD evaluations, 6 had a bone density loss and 3 were stable, without bone density loss. The mean bone loss at 6 months was  $- 5.0 \pm 6.4\%$  at the lumbar spine,  $- 4.8 \pm 4.5\%$  at the hip and  $- 4.6 \pm 7.5\%$  at the femoral neck. Clinical and biological characteristics of patients with or without bone density loss are compared in **table 3**. P1NP was higher with no significant difference between patients with and without bone loss. Calcium and 25-OHD were higher in patients with bone density loss compared to patients without. Paradoxically, the mean cumulative dose of clobetasol propionate per patient was lower in patients with bone density loss, compared to the patients without bone density loss, and no obvious correlation between clobetasol propionate dose and bone density variation was observed (**figure 3** for lumbar site measurements, and data not shown for other sites).



## **DISCUSSION**

In our study, among 9 BP patients treated with high dose of superpotent topical corticosteroids, 6 had BMD loss. No obvious correlation with cumulative or daily dose of clobetasol propionate was observed.

BMD decrease with systemic corticosteroid has been well described (31,32). Significant decrease is observed within the first six months (5 to 15%) then 2% per year in lumbar spine and femoral neck (33). This BMD decrease depends on the daily dose (34) and duration of corticosteroid therapy, rather than the cumulative dose. BMD decline is reversible when corticosteroid treatment is stopped (35–37). Current recommendations for prevention treatment of osteoporosis are to treat patients according Frax-tool and to treat all patients over 70 years having systemic corticosteroids for more than 3 months (38).

In immunobullous disease, change of BMD with systemic corticosteroids was – 0,6% in lumbar spine and + 1% in femoral neck at six months in a prospective study (39) on 14 patients supplemented with calcium and vitamin D. An association between pemphigus and osteoporosis reported independently of corticosteroid use has been reported (40). Immunobullous disease by itself might be associated with bone fractures (41), although the respective roles of corticosteroid and low vitamin D level are not easily disentangled.

Examples of low BMD have already been reported to be associated with atopic dermatitis (25,26) and psoriasis (27), with difficulties in assessing the respective responsibilities of corticosteroids and chronic inflammation. Cases of femoral head necrosis (17–21) and bone fractures (22) in patients with no other risk factor than topical corticosteroids have also been reported. The role of topical corticosteroid remains unclear (42–47). Systemic absorption is as low as 0.05% to 0.3% (6) have been shown to lead to systemic side effects such as cushing, adrenal suppression or hyperglycemia. BP treatment in France may represent a specific situation because of the singularity of the therapeutic scheme with high dose of superpotent corticosteroid during 4 months (1).

In our study, 6 of the 9 patients with both BMD measurements had a BMD loss but relations with cumulative or daily dose of topical corticosteroid were unclear. Only one of the six patients had a collapsed cortisol. Diminution of cortisol during treatment with topical corticosteroids was already reported (8–13) especially with a dose of clobetasol propionate over 50 g per week (8) and return to normal after stopping treatment if less than 50 g per week is applied (8,48).

In our study, patients with BP had multiple risk factor of fracture, in addition to age. There was no obvious relationship between BMD change and baseline BMD status, or risk factors for osteoporosis. Even if no significant variation were found between both groups, patients with higher dose of P1NP had a BMD change. There were more at risk of osteoporosis due to a high bone turnover, according to other study (49,50).

In our study a high mortality rate was observed. The relevance of implementing a systematic prevention of osteoporosis in BP patients is questionable because of the high mortality rate in older BP patients (51–53).

Our study has several limitations. First because of the retrospective nature of the study, data missing partly hampered the analysis. However, the amount of clobetasol propionate was precisely collected and was available for all the 9 patients with both BMD measurements. Second, our sample size was small, and made smaller by a high attrition rate in a population with a high mortality rate; the sample size was large enough, however, to evidence a decrease in BMD in 6 of the 9 patients, and we were able to describe the bone status in 22 patients with BP. Last, we had no information on the pre-treatment dynamics of bone loss in our patients, this piece of information would have been of great value to fully interpret the specific role of dermocorticosteroid in BMD decrease, by allowing a comparison between the periods before and during dermocorticosteroid therapy.

## **CONCLUSION**

Our results suggest that larger studies would be interesting to analyze the links between high dose of clobetasol propionate and osteoporosis in patients with bullous pemphigoid. It seems necessary to continue systematic evaluation of risk factor of osteoporosis for patients with bullous pemphigoid and to propose prevention on case-by-case basis.

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## FACULTE DE MEDECINE

NOM et Prénom : Ropars Nolwenn

### TITRE DE LA THESE d'EXERCICE

(Ce document sera à insérer dans les thèses définitives)

Titre :

**Evolution of bone mineral density in patients treated with high-dose topical corticosteroids for a bullous pemphigoid.**

**Evolution de la densité minérale osseuse chez des patients traités par dermocorticothérapie prolongée pour une pemphigoïde.**

Rennes, le 03/03/16

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Rennes, le

9/3/2016

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Le Président de l'Université  
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G. CATHELINEAU

## **REFERENCES**

1. Bernard P, Bedane C, Prost C, Ingen-Housz-Oro S, Joly P. Recommandations des centres de référence des maladies bulleuses auto-immunes pour le diagnostic et la prise en charge de la pemphigoïde bulleuse. *Ann Dermatol Vénérologie*. 2011 Mar;138(3):247–51.
2. Wood AJ, Fine J-D. Management of acquired bullous skin diseases. *N Engl J Med*. 1995;333(22):1475–84.
3. Korman NJ. Bullous pemphigoid. The latest in diagnosis, prognosis, and therapy. *Arch Dermatol*. 1998 Sep;134(9):1137–41.
4. Joly P, Roujeau J-C, Benichou J, Picard C, Dreno B, Delaporte E, et al. A comparison of oral and topical corticosteroids in patients with bullous pemphigoid. *N Engl J Med*. 2002 Jan 31;346(5):321–7.
5. Joly P, Roujeau J-C, Benichou J, Delaporte E, D'Incan M, Dreno B, et al. A comparison of two regimens of topical corticosteroids in the treatment of patients with bullous pemphigoid: a multicenter randomized study. *J Invest Dermatol*. 2009 Jul;129(7):1681–7.
6. Mizuchi A, Miyachi Y, Tamaki K, Kukita A. Percutaneous absorption of betamethasone 17-benzoate measured by radioimmunoassay. *J Invest Dermatol*. 1976 Aug;67(2):279–82.
7. Tempark T, Phatarakijrond V, Chatproedprai S, Watcharasindhu S, Supornsilchai V, Wananukul S. Exogenous Cushing's syndrome due to topical corticosteroid application: case report and review literature. *Endocrine*. 2010 Dec;38(3):328–34.
8. Carruthers JA, August PJ, Staughton RC. Observations on the systemic effect of topical clobetasol propionate (Dermovate). *Br Med J*. 1975;4(5990):203–4.
9. Munro DD. The effect of percutaneously absorbed steroids on hypothalamic-pituitary adrenal function after intensive use in in-patients\*. *Br J Dermatol*. 1976;94(s12):67–76.
10. Turpeinen M, Salo OP, Leisti S. Effect of percutaneous absorption of hydrocortisone on adrenocortical responsiveness in infants with severe skin disease. *Br J Dermatol*. 1986 Oct;115(4):475–84.
11. Weston WL, Fennessey PV, Morelli J, Schwab H, Mooney J, Samson C, et al. Comparison of hypothalamus-pituitary-adrenal axis suppression from superpotent topical steroids by standard endocrine function testing and gas chromatographic mass spectrometry. *J Invest Dermatol*. 1988 Apr;90(4):532–5.
12. Kerner M, Ishay A, Ziv M, Rozenman D, Luboshitzky R. Evaluation of the pituitary-adrenal axis function in patients on topical steroid therapy. *J Am Acad Dermatol*. 2011 Jul;65(1):215–6.
13. Böckle BC, Jara D, Nindl W, Aberer W, Sepp NT. Adrenal Insufficiency as a Result of Long-Term Misuse of Topical Corticosteroids. *Dermatology*. 2014;228(4):289–93.
14. Gomez EC, Frost P. Induction of glycosuria and hyperglycemia by topical corticosteroid therapy. *Arch Dermatol*. 1976 Nov;112(11):1559–62.
15. Sobngwi E, Lubin V, Ury P, Timsit F-J, Gautier J-F, Vexiau P. Adrenal insufficiency and diabetes mellitus secondary to the use of topical corticosteroids for cosmetic purpose. *Ann Endocrinol*. 2003 Jun;64(3):202–4.
16. van der Linden MW, Penning-van Beest FJ, Nijsten T, Herings RM. Topical Corticosteroids and the Risk of Diabetes Mellitus. *Drug Saf*. 2009;32(6):527–37.
17. El Maghraoui A, Tabache F, Bezza A, Ghafir D, Ohayon V, Archane MI. Femoral head osteonecrosis after topical corticosteroid therapy. *Clin Exp Rheumatol*. 2001 Apr;19(2):233.

18. Kubo T, Kojima A, Yamazoe S, Ueshima K, Yamamoto T, Hirasawa Y. Osteonecrosis of the femoral head that developed after long-term topical steroid application. *J Orthop Sci.* 2001;6(1):92–4.
19. Kane D, Barnes L, Fitzgerald O. Topical corticosteroid treatment: systemic side-effects. *Br J Dermatol.* 2003 Aug;149(2):417.
20. Kabata T, Shimanuki K, Shimanuki K, Tsuchiya H. Osteonecrosis of the femoral head and glaucoma caused by topical corticosteroid application. *Mod Rheumatol Jpn Rheum Assoc.* 2011 Dec;21(6):706–9.
21. Takahashi H, Tsuji H, Honma M, Ishida-Yamamoto A, Iizuka H. Femoral head osteonecrosis after long-term topical corticosteroid treatment in a psoriasis patient. *J Dermatol.* 2012 Oct;39(10):887–8.
22. Gönül M, Gönül E. A case of multiple bone fractures due to the use of topical corticosteroid therapy for psoriasis. *J Dermatol Treat.* 2014 Jun 20;1–2.
23. Henneicke H, Gasparini SJ, Brennan-Speranza TC, Zhou H, Seibel MJ. Glucocorticoids and bone: local effects and systemic implications. *Trends Endocrinol Metab.* 2014 Apr;25(4):197–211.
24. Bliuc D, Nguyen ND, Milch VE, Nguyen TV, Eisman JA, Center JR. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. *Jama.* 2009;301(5):513–21.
25. Aalto-Korte K, Turpeinen M. Bone mineral density in patients with atopic dermatitis. *Br J Dermatol.* 1997;136(2):172–5.
26. Haecck IM, Hamdy NAT, Timmer-de Mik L, Lentjes EGWM, Verhaar HJJ, Knol MJ, et al. Low bone mineral density in adult patients with moderate to severe atopic dermatitis. *Br J Dermatol.* 2009 Dec;161(6):1248–54.
27. Nymann P, Kollerup G, Jemec GB, Grossmann E. Decreased bone mineral density in patients with pustulosis palmaris et plantaris. *Dermatol Basel Switz.* 1996;192(4):307–11.
28. Ravaud P, Reny JL, Giraudeau B, Porcher R, Dougados M, Roux C. Individual smallest detectable difference in bone mineral density measurements. *J Bone Miner Res.* 1999;14(8):1449–56.
29. Baim S, Wilson CR, Lewiecki EM, Luckey MM, Downs RW, Lentle BC. Precision assessment and radiation safety for dual-energy X-ray absorptiometry: position paper of the International Society for Clinical Densitometry. *J Clin Densitom Off J Int Soc Clin Densitom.* 2005;8(4):371–8.
30. Briot K, Cortet B, Thomas T, Audran M, Blain H, Breuil V, et al. 2012 update of French guidelines for the pharmacological treatment of postmenopausal osteoporosis. *Joint Bone Spine.* 2012 May;79(3):304–13.
31. Laan RF, van Riel PL, van de Putte LB, van Erning LJ, van't Hof MA, Lemmens JA. Low-dose prednisone induces rapid reversible axial bone loss in patients with rheumatoid arthritis. A randomized, controlled study. *Ann Intern Med.* 1993 Nov 15;119(10):963–8.
32. McKenzie R, Reynolds JC, O'Fallon A, Dale J, Deloria M, Blackwelder W, et al. Decreased bone mineral density during low dose glucocorticoid administration in a randomized, placebo controlled trial. *J Rheumatol.* 2000 Sep;27(9):2222–6.
33. Lafage-Proust MH, Boudignon B, Thomas T. Glucocorticoid-induced osteoporosis: pathophysiological data and recent treatments. *Joint Bone Spine.* 2003;70(2):109–18.
34. van Staa TP, Leufkens HG, Abenhaim L, Zhang B, Cooper C. Oral corticosteroids and fracture risk: relationship to daily and cumulative doses. *Rheumatol Oxf Engl.* 2000 Dec;39(12):1383–9.

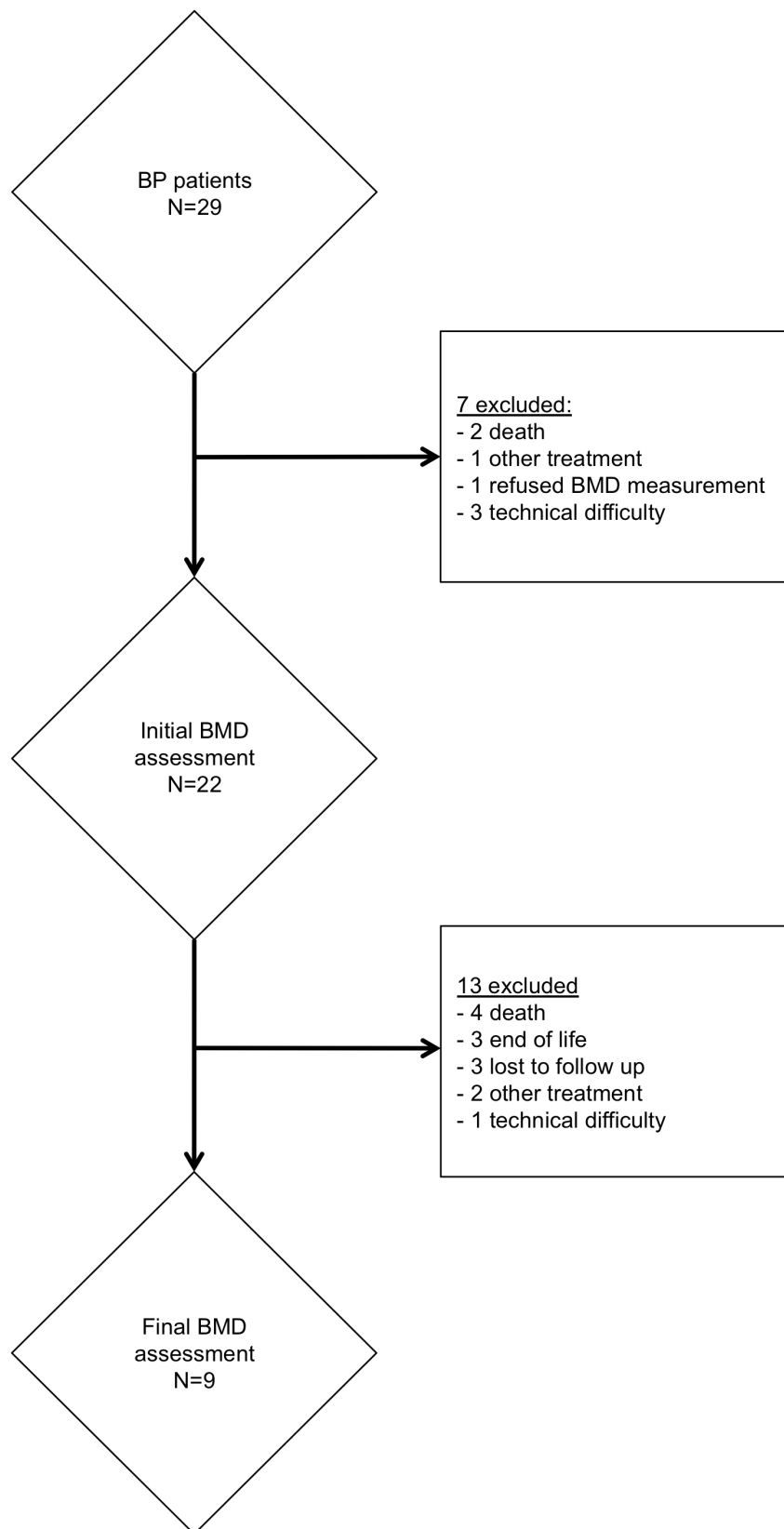
35. Staa T van, Staa T van, Staa T van, Leufkens HGM, Cooper C. The epidemiology of corticosteroid-induced osteoporosis: a meta-analysis. *Osteoporos Int*. 2002;13(10):777–87.
36. Rizzato G, Montemurro L. Reversibility of exogenous corticosteroid-induced bone loss. *Eur Respir J*. 1993;6(1):116–9.
37. Reid IR. Glucocorticoid osteoporosis—mechanisms and management. *Eur J Endocrinol*. 1997;137(3):209–17.
38. Briot K, Cortet B, Roux C, Fardet L, Abitbol V, Bacchetta J, et al. 2014 update of recommendations on the prevention and treatment of glucocorticoid-induced osteoporosis. *Joint Bone Spine*. 2014 Dec;81(6):493–501.
39. Tee S-I. Prevention of Glucocorticoid-Induced Osteoporosis in Immunobullous Diseases With Alendronate: A Randomized, Double-blind, Placebo-Controlled Study. *Arch Dermatol*. 2012 Mar 1;148(3):307.
40. Wohl Y, Dreiherr J, Cohen AD. Pemphigus and osteoporosis: a case-control study. *Arch Dermatol*. 2010;146(10):1126–31.
41. Marzano AV, Trevisan V, Eller-Vainicher C, Cairoli E, Marchese L, Morelli V, et al. Evidence for vitamin D deficiency and increased prevalence of fractures in autoimmune bullous skin diseases: Vitamin D and prevalence of fractures in bullous diseases. *Br J Dermatol*. 2012 Sep;167(3):688–91.
42. Vestergaard P, Olsen ML, Paaske Johnsen S, Rejnmark L, Toft Sørensen H, Mosekilde L. Corticosteroid use and risk of hip fracture: a population-based case-control study in Denmark. *J Intern Med*. 2003;254(5):486–93.
43. Vestergaard P, Rejnmark L, Mosekilde L. Fracture risk associated with systemic and topical corticosteroids. *J Intern Med*. 2005;257(4):374–84.
44. Van Velsen SGA, Knol MJ, van Eijk RLA, de Vroede MA, de Wit TC, Lam MGEH, et al. Bone mineral density in children with moderate to severe atopic dermatitis. *J Am Acad Dermatol*. 2010 Nov;63(5):824–31.
45. Van Velsen SGA, Haeck IM, Knol MJ, Lam MGEH, Bruijnzeel-Koomen CAFM. Two-year assessment of effect of topical corticosteroids on bone mineral density in adults with moderate to severe atopic dermatitis. *J Am Acad Dermatol*. 2012 Apr;66(4):691–3.
46. Mu Z, Zhang J. The effect of topical corticosteroids on bone mineral density in adults with atopic dermatitis. *J Am Acad Dermatol*. 2013 Jan;68(1):181–2.
47. Haeck I, van Velsen S, de Bruin-Weller M, Bruijnzeel-Koomen C. Bone Mineral Density in Patients with Atopic Dermatitis. In: Ring J, Darsow U, Behrendt H, editors. *Chemical Immunology and Allergy* [Internet]. Basel: KARGER; 2012 [cited 2016 Mar 28]. p. 96–9. Available from: <http://www.karger.com/doi/10.1159/000331893>
48. Van Velsen SGA, Haeck IM, Bruijnzeel-Koomen CAFM. Percutaneous absorption of potent topical corticosteroids in patients with severe atopic dermatitis. *J Am Acad Dermatol*. 2010 Nov;63(5):911–3.
49. Rogers A, Hannon RA, Eastell R. Biochemical markers as predictors of rates of bone loss after menopause. *J Bone Miner Res Off J Am Soc Bone Miner Res*. 2000 Jul;15(7):1398–404.
50. Gielen E, O'Neill T, Pye S, Adams J, Ward K, Wu F, et al. Bone turnover markers predict hip bone loss in elderly European men: results of the European Male Ageing Study (EMAS). *Osteoporos Int*. 2015 Feb;26(2):617–27.

51. Doffoel-Hantz V, Sparsa A, Marin B, Durox H, Bonnetblanc J-M, Bédane C. Profil évolutif des patients atteints de pemphigoïde bulleuse au cours de la première année de traitement. *Ann Dermatol Vénéréologie*. 2009 May;136(5):407–11.
52. Cortés B, Khelifa E, Clivaz L, Cazzaniga S, Saurat JH, Naldi L, et al. Mortality Rate in Bullous Pemphigoid: A Retrospective Monocentric Cohort Study. *Dermatology*. 2012;225(4):320–5.
53. Joly P, Baricault S, Sparsa A, Bernard P, Bédane C, Duvert-Lehembre S, et al. Incidence and mortality of bullous pemphigoid in France. *J Invest Dermatol*. 2012 Aug;132(8):1998–2004.

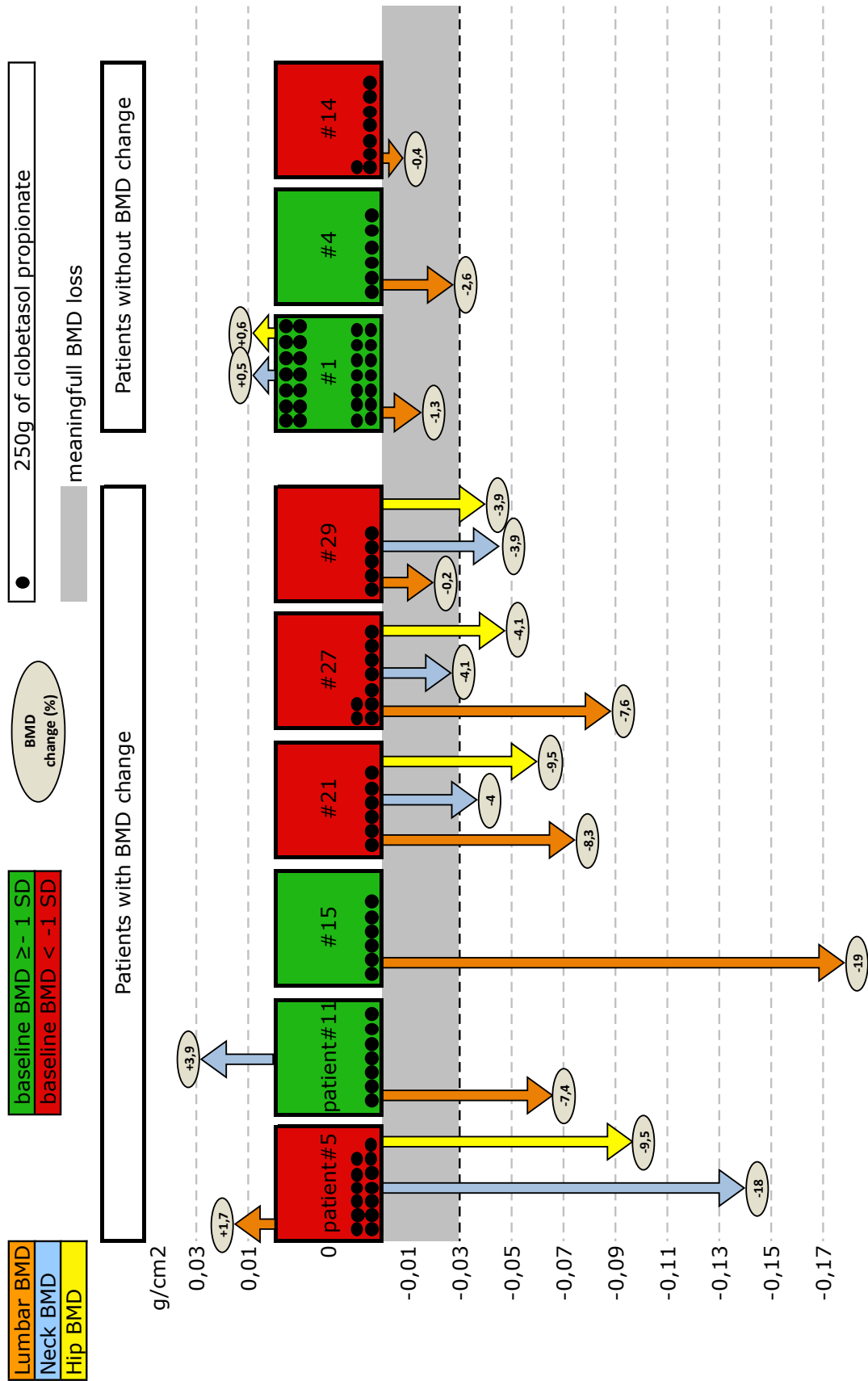


**GLOSSAIRE**

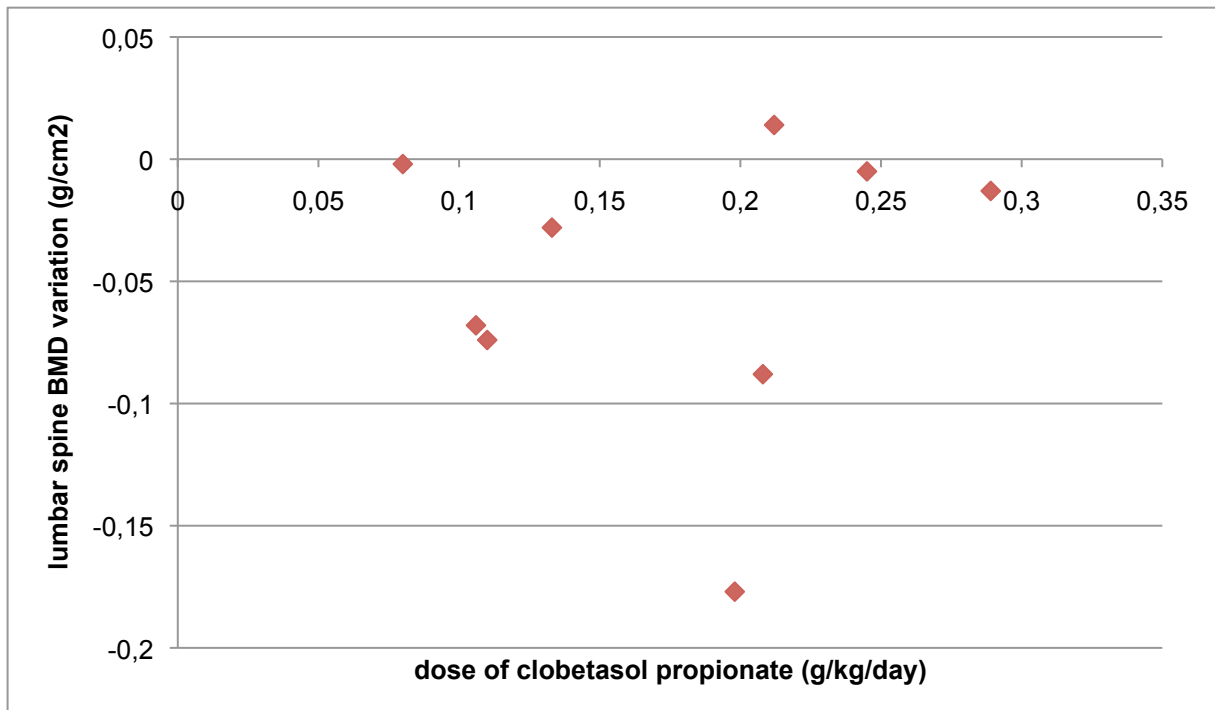
|        |   |
|--------|---|
| BMD    | Bone Mineral Density                        |
| BMI    | Body Mass Index                             |
| BP     | Bullous Pemphigoid                          |
| CTx    | C-terminal telopeptid of type I collagen    |
| DXA    | Dual energy X-ray Absorptiometry            |
| P1NP   | N-terminal propeptide of type I procollagen |
| PTH    | Parathyroid hormone                         |
| SD     | Standard Derivation                         |
| SFD    | Société Française de Dermatologie           |
| TSH    | Thyroid Stimulating Hormone                 |
| WHO    | World Health Organization                   |
| 25-OHD | 25-hydroxyvitamin D                         |

**Figure 1 Flow chart**

**Figure 2 Representation of lumbar spine, femoral neck and hip BMD change, baseline BMD, and cumulative dose of clobetasol propionate.**



**Figure 3 Correlation between lumbar spine variation (g/cm<sup>2</sup>) and dose of clobetasol propionate (g/kg/day)**



**Table 1 Baseline characteristics**

|  | Baseline characteristics<br>n=22 |       |        |
|--|----------------------------------|-------|--------|
|  | nb of<br>subjects                |       |        |
| <b>Clinical</b>                                |                                  |       |        |
| Age (years)                                    | 22                               | 86.1  | ± 7.2  |
| Sex (n)  | 22                               |       |        |
| Male n (%)                                     |                                  | 11    | (50)   |
| Female n (%)                                   |                                  | 11    | (50)   |
| Height (cm)                                    | 15                               | 162.4 | ± 7.7  |
| Weight (kg)                                    | 17                               | 65.6  | ± 14.2 |
| BMI (kg/m <sup>2</sup> )                       | 20                               | 26.7  | ± 6    |
| History of                                     |                                  |       |        |
| Oral corticosteroids n (%)                     | 22                               | 3     | (14)   |
| History of osteoporosis<br>with fracture n (%) | 22                               | 5     | (23)   |
| Current smoker n (%)                           | 22                               | 2     | (9)    |
| Alcohol consumer n (%)                         | 22                               | 0     | (0)    |
| Neurological disorder n (%)                    | 22                               | 13    | (59)   |
| <10 bullae n (%)                               | 22                               | 11    | (50)   |
| <b>Biological data</b>                         |                                  |       |        |
| Alkaline phosphate (U/l)                       | 22                               | 71.2  | ± 38.8 |
| Calcium (mmol/l)                               | 22                               | 2.27  | ± 0.15 |
| Urinary calcium (mmol/l)                       | 15                               | 1.95  | ± 1.9  |
| Phosphate (mmol/l)                             | 20                               | 2.4   | ± 6.2  |
| 25-OHD (ng/ml)                                 | 22                               | 15.2  | ± 8.5  |
| PTH (pg/ml)                                    | 19                               | 30.9  | ± 19.9 |
| TSH (μU/ml)                                    | 21                               | 2.2   | ± 1.6  |
| 8 am cortisol (ng/ml)                          | 21                               | 141   | ± 87   |
| CTx (pmol/l)                                   | 21                               | 4391  | ± 2176 |
| P1NP (ng/ml)                                   | 21                               | 58    | ± 57   |

**Table 2 Baseline bone status**

| <b>Baseline BMD</b>                | nb of subjects | <b>Baseline characteristics</b> |        |
|------------------------------------|----------------|---------------------------------|--------|
|                                    |                | <b>N=22</b>                     |        |
| Lumbar spine                       | 20             |                                 |        |
| BMD (g/cm <sup>2</sup> )           |                | 0.95                            | ± 0.22 |
| T score (SD)                       |                | - 0.93                          | ± 1.94 |
| Femoral neck                       | 17             |                                 |        |
| BMD (g/cm <sup>2</sup> )           |                | 0.66                            | ± 0.17 |
| T score (SD)                       |                | - 1.89                          | ± 1.29 |
| Hip                                | 20             |                                 |        |
| BMD (g/cm <sup>2</sup> )           |                | 0.82                            | ± 0.22 |
| T score (SD)                       |                | - 1.31                          | ± 1.43 |
| <b>Baseline repartition of BMD</b> |                |                                 |        |
| Lumbar spine                       | 20             |                                 |        |
| T score ≥ -1 n (%)                 |                | 10                              | (50)   |
| T score < -1 n (%)                 |                | 10                              | (50)   |
| Femoral neck                       | 17             |                                 |        |
| T score ≥ -1 n (%)                 |                | 5                               | (29)   |
| T score < -1 n (%)                 |                | 12                              | (71)   |
| Hip                                | 17             |                                 |        |
| T score ≥ -1 n (%)                 |                | 10                              | (59)   |
| T score < -1 n (%)                 |                | 7                               | (41)   |

**Table 3 Characteristics of patients with BMD change and patients without BMD change.**

|  | Patients with<br>BMD loss |        |         | Patients without<br>BMD loss |        |          |
|--|---------------------------|--------|---------|------------------------------|--------|----------|
|  | nb of<br>subjects         | N=6    |         | nb of<br>subjects            | N=3    |          |
| <b>Clinical</b>                                  |                           |        |         |                              |        |          |
| Age (years)                                      | 6                         | 84.3   | 7.4     | 3                            | 86.0   | ± 5.6    |
| Sex  | 6                         |        |         | 3                            |        |          |
| Male n (%)                                       |                           | 3      | (50)    |                              | 2      | (67)     |
| Female n (%)                                     |                           | 3      | (50)    |                              | 1      | (33)     |
| Height (cm)                                      | 5                         | 162.4  | ± 4.2   | 3                            | 164.7  | ± 6.8    |
| Weight (kg)                                      | 6                         | 64.7   | ± 13    | 3                            | 59.9   | ± 10.7   |
| BMI (kg/cm <sup>2</sup> )                        | 5                         | 26.3   | ± 5.5   | 3                            | 24.3   | ± 4.2    |
| History of                                       |                           |        |         |                              |        |          |
| Oral corticosteroids n (%)                       | 6                         | 0      |         | 3                            | 0      |          |
| History of osteoporosis n (%)                    | 6                         | 2      | (33)    | 3                            | 1      | (33)     |
| Current smoker n (%)                             | 6                         | 0      |         | 3                            | 0      |          |
| Alcohol consumer n (%)                           | 6                         | 0      |         | 3                            | 0      |          |
| Neurological disorder n (%)                      | 6                         | 3      | (50)    | 3                            | 3      | (100)    |
| History of osteoporosis<br>with fracture n (%)   | 6                         | 2      | (33)    | 3                            | 1      | (33)     |
| <10 bullae n (%)                                 | 6                         | 4      | (66.7)  | 3                            | 3      | (100)    |
| <b>Treatment</b>                                 |                           |        |         |                              |        |          |
| Cumulative dose<br>of topical corticosteroid (g) | 6                         | 2036.7 | ± 851.6 | 3                            | 3556.7 | ± 3292.2 |
| <b>Baseline biological data</b>                  |                           |        |         |                              |        |          |
| Alkaline phosphatase (UI/l)                      | 6                         | 72.7   | ± 56.2  | 3                            | 86.0   | ± 13.7   |
| Calcium (mmol/l)                                 | 6                         | 2.34   | ± 0.1   | 3                            | 2.09   | ± 0.29   |
| Urinary calcium (mmol/l)                         | 6                         | 1.76   | ± 1.3   | 3                            | 1.4    | ± 0.7    |
| Phosphate (mmol/l)                               | 6                         | 5.7    | ± 11.4  | 3                            | 1.2    | ± 0.1    |
| 25-OHD (ng/ml)                                   | 6                         | 22.5   | ± 8.8   | 3                            | 15.2   | ± 3.2    |
| PTH (pg/ml)                                      | 4                         | 42.8   | ± 29.1  | 2                            | 13.0   | ± 1.4    |
| TSH (μUI/ml)                                     | 6                         | 3.3    | ± 2.6   | 2                            | 1.3    | ± 0.1    |
| 8 am Cortisol (ng/ml)                            | 6                         | 205    | ± 46    | 2                            | 113    | ± 62     |
| CTx (pmol/l)                                     | 6                         | 4651   | ± 3476  | 3                            | 4490   | ± 2276   |
| P1NP (ng/ml)                                     | 6                         | 102    | ± 85    | 3                            | 29     | ± 18     |
| <b>Baseline BMD</b>                              |                           |        |         |                              |        |          |
| Lumbar BMD (g/cm <sup>2</sup> )                  | 6                         | 0.97   | ± 0.14  | 3                            | 0.94   | ± 0.17   |
| Femoral neck BMD (g/cm <sup>2</sup> )            | 5                         | 0.71   | ± 0.08  | 1                            | 0.8    |          |
| Hip BMD (g/cm <sup>2</sup> )                     | 5                         | 0.84   | ± 0.18  | 1                            | 0.97   |          |

U.F.R. DE MEDECINE DE RENNES

**ROPARS Nolwenn – Evolution de la densité minérale osseuse chez des patients traités par dermocorticothérapie prolongée pour une pemphigoïde.**

**Evolution of bone mineral density in patients treated with high-dose topical corticosteroids for a bullous pemphigoid.**

28 feuilles, 3 graphiques, 3 tableaux, 30 cm – Thèse : (Médecine); Rennes 1; 2016 ; N°

#### Résumé français

**Introduction** Les dermocorticoïdes (DC) utilisés à forte dose, peuvent avoir des effets secondaires systémiques (cushing, hyperglycémie) identiques à ceux observés avec la corticothérapie générale mais leurs effets secondaires osseux sont mal connus. Nous avons étudié l'évolution de la densité minérale osseuse (DMO) chez des patients traités par DC pour une pemphigoïde bulleuse (PB).

**Matériel & Méthodes** Une ostéodensitométrie et un bilan biologique étaient réalisés avant et après traitement par DC pour les patients suivis pour une PB au CHU de Rennes.

**Résultats** 29 patients ont eu une PB, 22 patients ont eu au moins une évaluation et 9 patients ont eu 2 évaluations. Nous avons observé une variation de la DMO supérieure à 0,03 g/cm<sup>2</sup> chez 6 des 9 patients. Il n'a pas été noté de corrélation avec la dose de DC.

**Conclusion** Ces résultats incitent à proposer des études de plus grande envergure pour l'analyse des liens entre DC et DMO chez les patients ayant une PB.

Rubrique de classement : Dermatologie - Thérapeutique

Mots-clés : Pemphigoïde Bulleuse ; Dermocorticothérapie ; Densité Minérale Osseuse

Mots-clés anglais MeSH : Bullous Pemphigoid; Topical Corticosteroids; Bone Mineral Density

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