Background
No data on bone biomarkers and BMD changes in subjects treated with atazanavir/ritonavir (ATV/r) monotherapy are available.

This is a substudy of the MODA4 trial with the aim to evaluate the association between bone biomarkers and changes in BMD over 96 weeks in patients treated with ATV/r monotherapy vs ATV/r+2NRTIs.

Methods
MODA4 (NCT01511809) is a multicentre, randomized, open-label, non-inferiority trial. Patients on ATV/r/300/100mg+2NRTIs since 48 weeks, virologically suppressed since 24 weeks, were randomized to ATV/r monotherapy or to maintain ATV/r+2NRTIs. This sub-study included patients treated with either ATV/r triple therapy or monotherapy (with no re-initiation due to virological failure) who reached week 96 or prematurely discontinued with available BMD determinations and plasma samples at baseline, week 48 and week 96. Participants underwent standardized DXA scan and tested bone biomarkers (osteocalcin, vitamin D, RANKL, osteoprotegerin, CTX-II).

BMD, T-score and Z-score were measured at lumbar spine (L1-L4) and total proximal femur, low BMD for chronological age (LBA), osteopenia and osteoporosis defined according to the International Society for Clinical Densitometry² and WHO criteria³, respectively. Bone biomarkers were evaluated as continuous variables or categorical variables, stratified according to their median value.

Results as median (interquartile range, IQR). Chi-square/Fisher exact test or Mann-Whitney test were used to compare groups. Linear regression was applied to evaluate the predictors [age, gender, body mass index (BMI), smoking, HCV baseline CD4+, study-arm, vitamin D or calcium supplementation, BL values of osteocalcin, RANKL, vitamin D osteoprotegerin, CTX-II] of 48- and 96-week percent changes in vertebral and total proximal femur BMD.

Among the 103 patients enrolled in the MODA4 trial, 69 subjects had available BMD data [29 patients on ATV/r monotherapy, 40 patients on ATV/r+2NRTIs (RTIs)] as reported in Figure 1. Baseline characteristics according to study arm is reported in Table 1.

Median (IQR) percent changes in lumbar spine and femoral neck and total proximal femur BMD according to study arm is reported in Table 2. Patients treated with ATV/r monotherapy or ATV/r+2NRTIs had a similar incidence of vertebral or femoral LBA/osteopenia [ATV/r: 3 (10.3%); ATV/r+2NRTIs: 6 (15.0%); p=0.724]. No incident osteoporosis observed in both arms during follow-up.

Among patients treated with ATV/r monotherapy, higher baseline values of RANKL (32 pg/mL) were associated with lower 48-week percent changes in L1-L4 BMD and in total proximal femur BMD (Figure 3); this effect tended to be observed also among patients on ATV/r+2NRTIs, although it was not statistically significant. All the other bone biomarkers were not associated with % changes in BMD at week 48 or week 96 in both arms.

At multivariate analysis (Table 2), ATV/r monotherapy was associated with an increase in the 48- and 96-week % change in total proximal femur BMD [β=1.14 (0.83); p=0.025; W96: β=1.16 (1.01), p=0.012] as compared to ATV/r+2NRTIs. Femoral BMD increased among subjects on ATV/r monotherapy rather than on ATV/r+2NRTIs or among patients with low BL RANKL (<32 vs >32 pg/mL) at week 48 [β=1.24 (0.92); p=0.001] and at week 96 [β=1.23 (1.12), p=0.003].

Discussion
We are thankful to all patients who participated to the study.

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RANKL predicts 96-week BMD changes in ATV/r monotherapy: a MODA4 trial sub-study

Figure 1. Patients distribution

Figure 2. 96-week univariate percent changes in lumbar spine and total proximal femur BMD according to study arm

Figure 3. Median percent changes in lumbar spine and total proximal femur BMD according to study arm and baseline values of RANKL

Table 1 – Baseline characteristics of study participants

Table 2 – Multivariate regression analysis: adjusted means of % change in BMD at week 48 and week 96 by site-specific DXA

References

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