

## Aggravated bone density decline following symptomatic osteonecrosis in children with acute lymphoblastic leukemia

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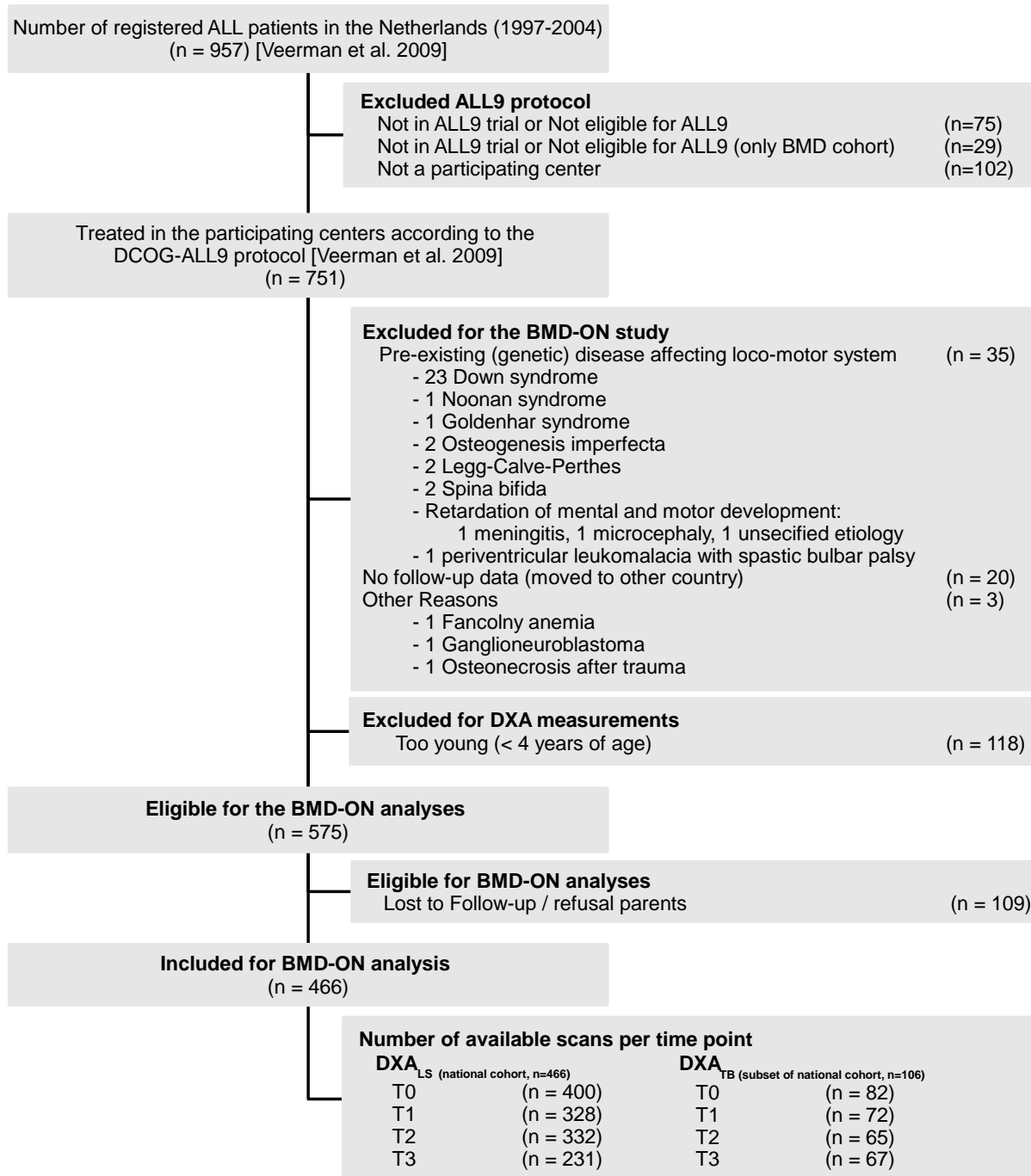
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**Supplemental figure 1: CONSORT diagram of patient inclusion**

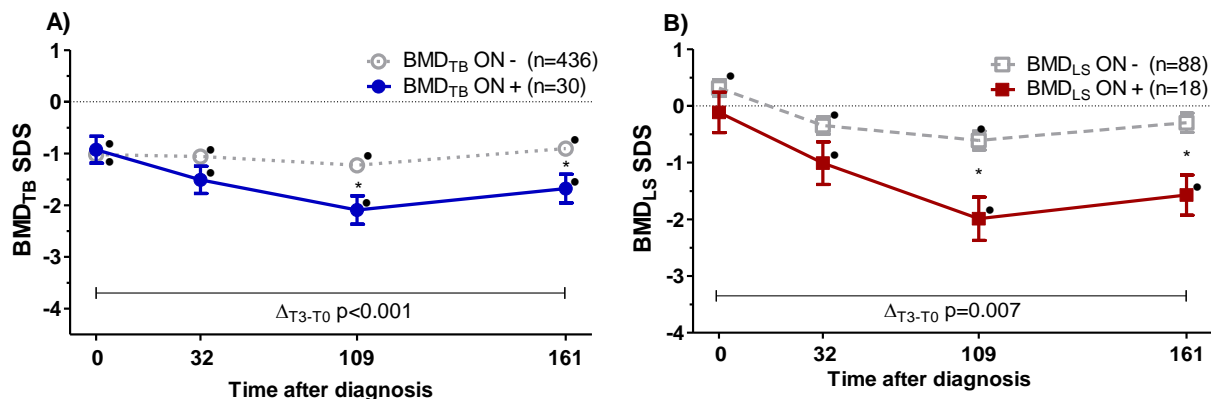


Abbreviations: ALL = acute lymphoblastic leukemia; DCOG = Dutch Childhood Oncology Group;

FU = follow-up; HR = high risk; SCT = stem-cell transplantation; yr. = year; BMI = Body Mass Index;

DXA = Dual X-Ray Absorptiometry; <sub>TB</sub> = total body; <sub>LS</sub> = lumber spine; ON = osteonecrosis ; n = number.

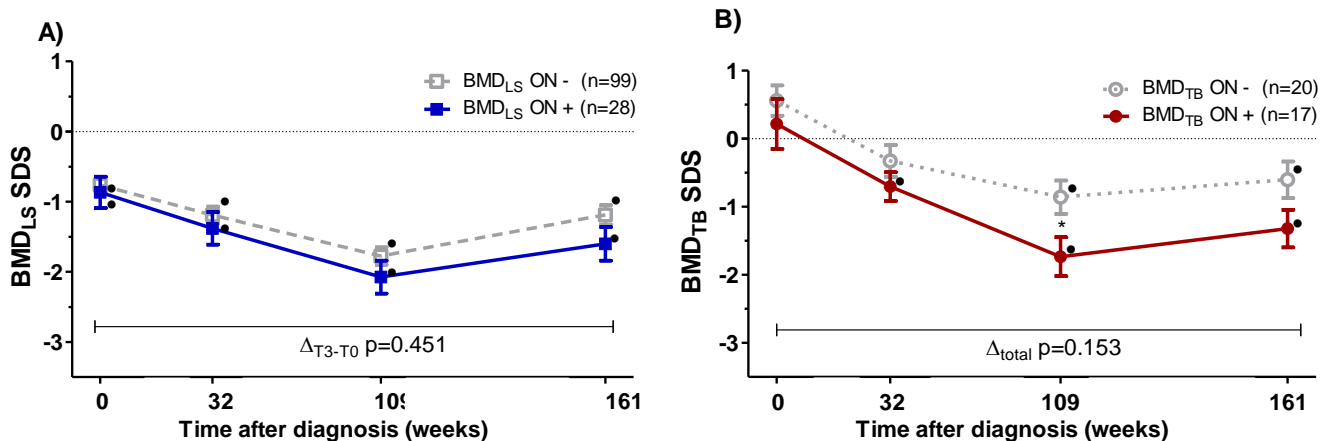
**Supplemental figure 2: Comparison of BMD<sub>SDS</sub> change in pediatric ALL patients (4-18 years of age) with and without ON adjusted for age at diagnosis and risk group.**



BMD change of the lumbar spine (2A) and total body (2B) in pediatric ALL patients (4-18 years of age) with and without ON. The dots represent the estimated mean from the mixed linear model and the whiskers represent the standard error of the mean BMD.

Abbreviations: T0 = at diagnosis; T1 = start maintenance therapy (32 weeks); T2 = at cessation therapy (109 weeks); T3 = 1 year after cessation of therapy (161 weeks); BMD<sub>LB</sub> = bone mineral density of the lumbar spine; BMD<sub>TB</sub> = bone mineral density of total body;  $\Delta_{T3-T0}$  = "interaction group time \* ON" ; p = p-value ; \* difference p<0.05.

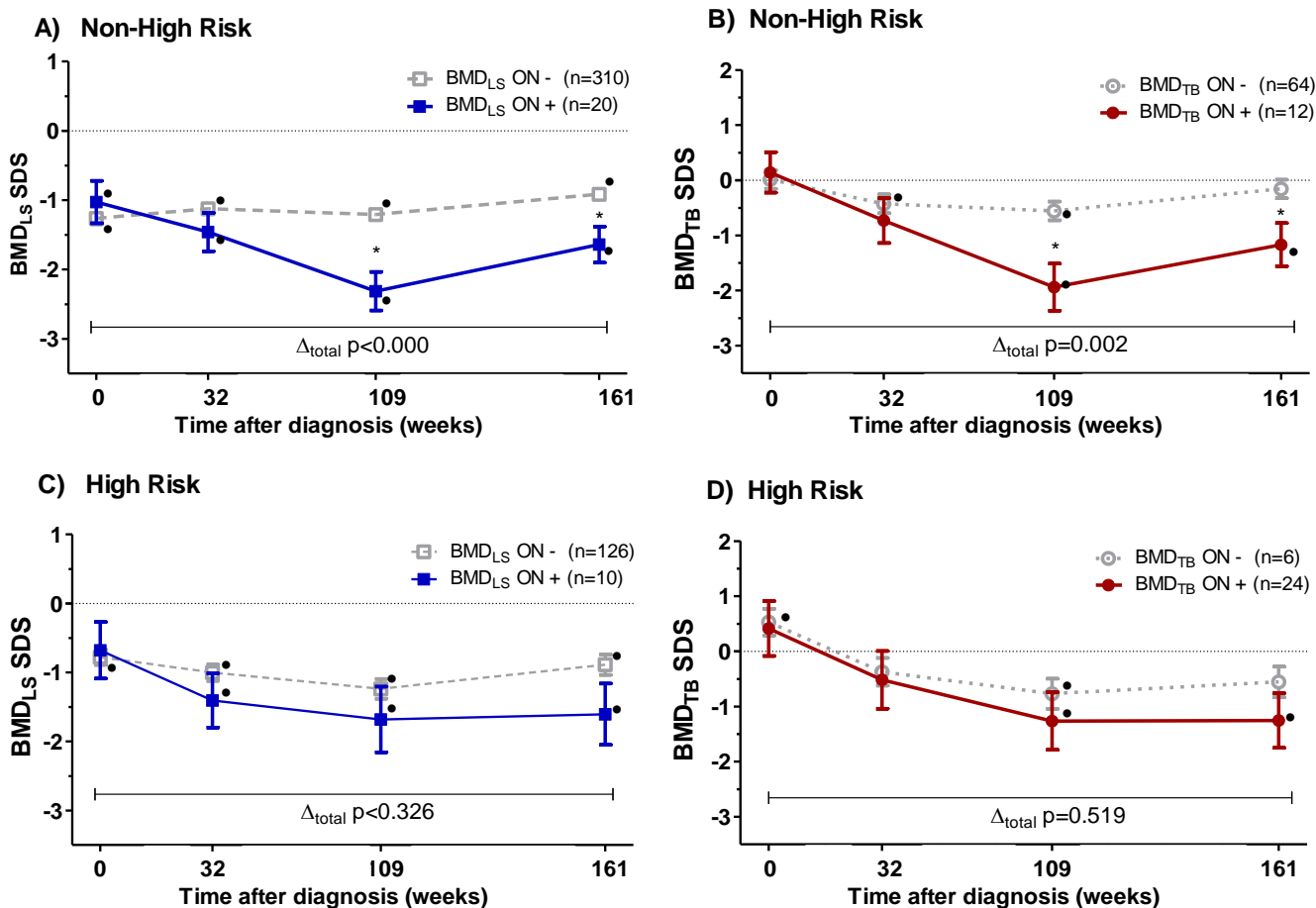
**Supplemental figure 3: Comparison of  $BMD_{SDS}$  change in pediatric ALL patients (10-18 years of age) with and without ON.**



BMD change of the lumbar spine (3A) and total body (3B) in pediatric ALL patients (10-18 years of age) with and without ON. The dots represent the estimated mean from the mixed linear model and the whiskers represent the standard error of the mean BMD.

Abbreviations: T0 = at diagnosis; T1 = start maintenance therapy (32 weeks); T2 = at cessation therapy (109 weeks); T3 = 1 year after cessation of therapy (161 weeks);  $BMD_{LB}$  = bone mineral density of the lumbar spine;  $BMD_{TB}$  = bone mineral density of total body;  $\Delta_{T3-T0}$  = "interaction group time \* ON" ; p = p-value ; \* difference  $p < 0.05$ .

**Supplemental figure 4: Comparison of  $BMD_{SDS}$  change in pediatric ALL patients (4-18 years of age) with and without ON stratified according to risk protocol.**



BMD change of the lumbar spine (4A/C) and total body (4B/D) stratified according to risk protocol in pediatric ALL patients (4-18 years of age) with and without ON. The dots represent the estimated mean from the mixed linear model and the whiskers represent the standard error of the mean BMD.

Abbreviations: T0 = at diagnosis; T1 = start maintenance therapy (32 weeks); T2 = at cessation therapy (109 weeks); T3 = 1 year after cessation of therapy (161 weeks);  $BMD_{LB}$  = bone mineral density of the lumbar spine;  $BMD_{TB}$  = bone mineral density of total body;  $\Delta_{T3-T0}$  = "interaction group time \* ON" ; p = p-value ; \* difference  $p < 0.05$ .