

Supplementary Materials

Table S1. Vertebral BMD at baseline, end of therapy and 6-months post-therapy analyzed according to patient gender and age cutoff of 45 years.

Evaluated Parameters	Median (Range)	Females <45 Years vs. Males <45 Years		Males & Females ≥45 Years vs. Males <45 Years		Males & Females ≥45 Years vs. Females <45 Years	
	No. of pts 213	No. of pts 98 vs. 83	<i>p</i> -Value	No. of pts 32 vs. 83	<i>p</i> -Value	No. of pts: 32 vs. 98	<i>p</i> -Value
Age, years, median (range)	29 (18–59)	28 (18–45) vs. 27 (18–45)	0.488	54 (47–59) vs. 27 (18–45)	0.000	54 (47–59) vs. 28 (18–45)	0.000
Baseline BMD *, HU, median (range)	196.8 (30.5–320)	212.9 (30.5–320) vs. 200.4 (101.2–273.8)	0.073	138.9 (92–192.9) vs. 200.4 (101.2–273.8)	0.000	138.9 (92–192.9) vs. 212.9 (30.5–320)	0.000
EOT BMD **, HU, median (range)	164.9 (27.5–277.3)	170.6 (27.5–277.3) vs. 174.1 (74.5–267)	0.807	112.5 (64.3–172.5) vs. 174.1 (74.5–267)	0.000	112.5 (64.3–172.5) vs. 170.6 (27.5–277.3)	0.000
Δ between EOT and baseline BMD, %, median (range)	15.4 (0–54.6)	17.9 (0–42.1) vs. 13 (0–54.6)	0.107	17.1 (0–52.1) vs. 13 (0–54.6)	0.015	17.1 (0–52.1) vs. 17.9 (0–42.1)	0.192
	No. of pts 161	No. of pts 80 vs. 56	<i>p</i> -value	No. of pts 25 vs. 56	<i>p</i> -value	No. of pts 25 vs. 80	<i>p</i> -value
6 months post-EOT BMD *** HU, median (range)	169 (23.9–301)	181 (23.9–301) vs. 176.8 (102–275.7)	0.377	110 (69.3–168.7) vs. 176.8 (102–275.7)	0.000	110 (69.3–168.7) vs. 181 (23.9–301)	0.000
Δ between 6 months post-EOT and baseline BMD, %, median (range)	11.7 (0–49.8)	12.9 (0–37.9) vs. 8.6 (0–41.3)	0.194	23.7 (0–49.8) vs. 8.6 (0–41.3)	0.000	23.7 (0–49.8) vs. 12.9 (0–37.9)	0.000
	No. of pts 213	No. of pts 98 vs. 83	<i>p</i> -value	No. of pts 32 vs. 83	<i>p</i> -value	No. of pts: 32 vs. 98	<i>p</i> -value
Cumulative HE dose, mg, median (range)	6000 (1600–22,400)	6000 (2000–19,140) vs. 6000 (1600–22,400)	0.145	7325 (2000–20,040) vs. 6000 (1600–22,400)	0.802	7325 (2000–20,040) vs. 6000 (2000–19,140)	0.101
Cumulative HE dose per body surface, mg/m ² , median (range)	3468 (952–11,546)	3529 (1,170–10,950) vs. 3243 (952–11,546)	0.365	4152 (995–10,277) vs. 3243 (952–11,546)	0.958	4152 (995–10,277) vs. 3529 (1,170–10,950)	0.785

* HL staging PET/CT (non-IV contrast CT) scans were used to measure the baseline vertebral BMD at the L3 level. ** HL PET/CT (non-IV contrast CT) scans performed at the end of treatment were used to measure vertebral BMD at that time point. *** HL PET/CT (non-IV contrast CT) scans performed 6 months after the end of treatment were used to measure vertebral BMD at that time point. Mann-Whitney *p*-value; BMD: bone mineral density; no. of pts: number of patients; EOT: end-of-treatment; HU: Hounsfield units; Δ: difference; HE: hydrocortisone equivalent; y.o.: years old.

Table S2. BMD decrease of >15% between baseline and the end of treatment according to a cumulative hydrocortisone equivalent dose per body surface used in different treatment protocols: Bi-variate log regression analysis.

	HE Dose per Surface Area (mg/m ²)	No. of Patients	Patients with BMD Decrease of >15%		
			no. (%)	p-value	OR
Cumulative HE dose per surface area (mg/m²)	≤2100	24	5 (20.83)	0.000	1.00
	2100.1–3400	73	26 (35.62)	0.184	2.1 (0.7–6.3)
	>3400	116	71 (61.21)	0.001	6 (2.1–17.2)
Males ≤45 y.o.	≤2100	12	1 (8.33)	0.091	1.00
	2100.1–3400	34	13 (38.24)	0.082	6.81 (0.8–59.1)
	>3400	37	18 (48.65)	0.032	10.42 (1.2–89.1)
Males >45 y.o. and all females	≤2100	12	4 (33.33)	0.001	1.00
	2100.1–3400	39	13 (33.33)	1	1 (0.3–3.9)
	>3400	79	53 (67.09)	0.033	4.08 (1.1–14.8)
ABVD ×2–4	≤1800	8	1 (12.50)	0.472	1.00
	1800.1–2100	15	4 (26.67)	0.443	2.55 (0.2–27.7)
	<2100	25	3 (12.00)	0.97	0.96 (0.1–10.7)
ABVD ×6	≤2600	3	1 (33.33)	0.298	1.00
	2600.1–3399	45	22 (48.89)	0.607	1.91 (0.2–22.6)
	<3400	51	32 (62.75)	0.335	3.37 (0.3–39.7)
EB ×2 + ABVD ×4	≤5600	17	13 (76.47)		1.00
	>5600	21	16 (76.19)	0.984	0.99 (0.2–4.4)
EB ×4–6	≤8000	9	4 (44.44)		1.00
	>8000	19	6 (31.58)	0.509	0.58 (0.1–3)
EB ×2–6	≤5600	18	13 (72.22)	0.012	1.00
	5600–8000	28	19 (67.86)	0.754	0.81 (0.2–3)
	>8000	20	7 (35.00)	0.025	0.21 (0.1–0.8)

BMD: bone mineral density; HE: hydrocortisone equivalent; y.o.: years old; OR: odds ratio; ABVD: adriamycin, bleomycin, vinblastine, dacarbazine; EB: escalated BEACOPP, including bleomycin, etoposide, adriamycin, cyclophosphamide, oncovin, procarbazine, prednisone.