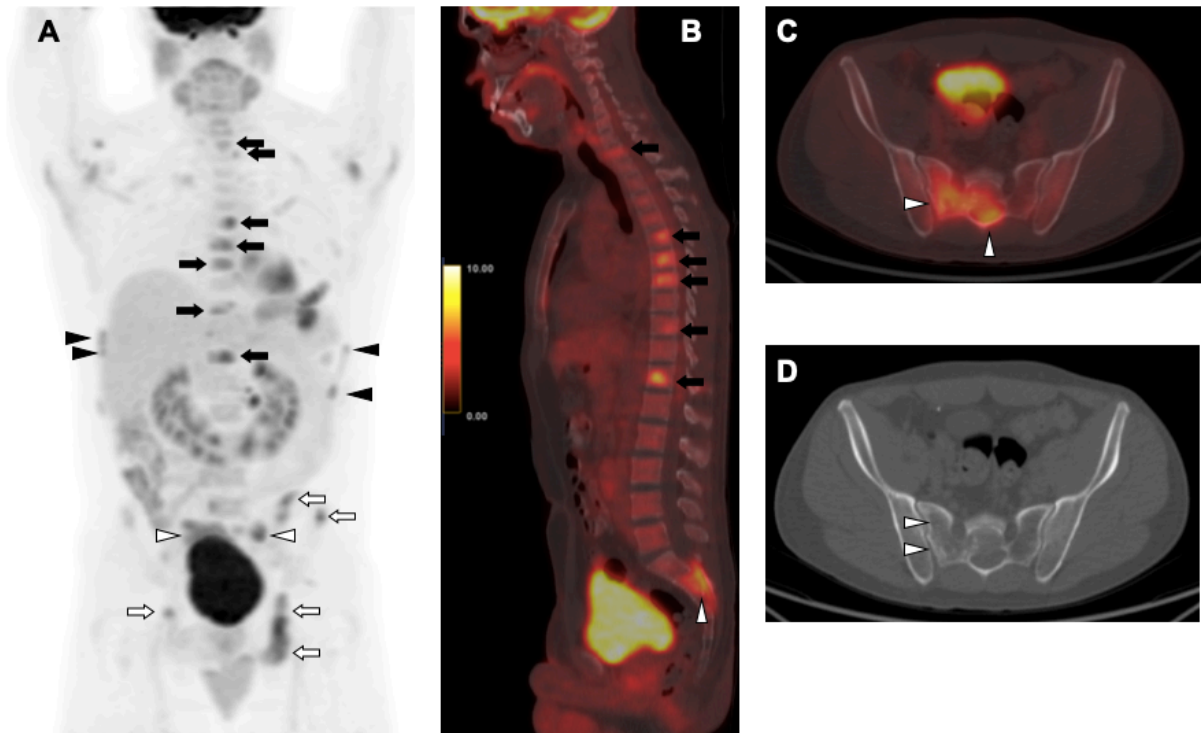
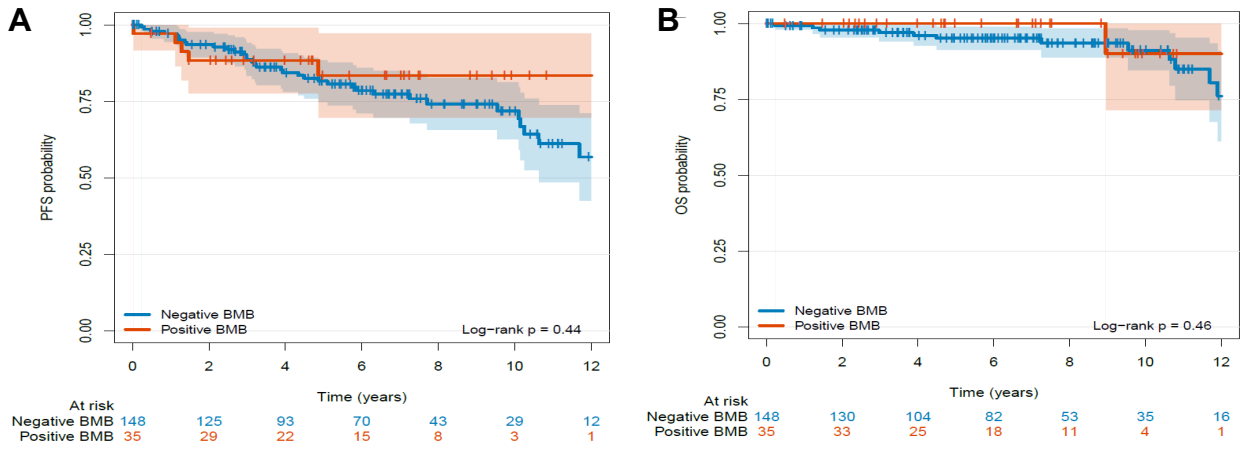


SUPPLEMENTAL DATA



Supplemental Figure 1. 45-year-old male diagnosed with follicular lymphoma involving bone marrow. FDG PET-CT (A; MIP) showed intensely increased FDG uptake at several vertebral bodies (arrows, B, C; Fused PET-CT images), multiple ribs (black arrowheads), pelvic bones (white arrows) and bilateral scapula (white arrowheads, D; CT axial). Patient underwent targeted biopsy of a PET/CT detected lesion (right sacrum), which confirmed bone marrow involvement (BMI), whereas routine iliac crest biopsy did not show BMI.



Supplemental Figure 2. Kaplan-Meier analysis (A: PFS, B: OS) for patients without evidence for BMI by PET. Color bands indicate 95% CI. There was no association between BMI by BMB alone and patient outcome ($p = 0.44$ and 0.46 , respectively).

Supplemental Table 1. Clinical characteristics of patients upstaged to stage IV when additionally considering BMB findings

PET stage	Number of lymph node/ lesions	The longest diameter of largest involved node/ lesion (cm)	FLIPI score	Initial treatment regime	Progression -free survival (years)	Prognosis	Detected by BMB
Stage I							
Patient 1	1	3.6	Intermediate	R-CHOP	9.9	Alive	BMB
Patient 2	1	1.2	Intermediate	Rituximab	8.8	Alive	BMB
Patient 3	1	2.8	Low	Observation	4.7	Alive	BMB (< 5%)
Patient 4	None	Not available	Intermediate	Methotrexate	2.9	Alive	Flow cytometry
Stage II							
Patient 5	4	7.8	Intermediate	R-CHOP	5.7	Alive	Flow cytometry
Patient 6	6	2.4	Low	Rituximab	4.6	Alive	BMB (15%)

Supplemental Table 2. Role of PET for detecting BMI in FL. Summary of previous and current study findings.

Ref	N	PET-positive criteria	CT criteria for BMI detection by PET	BMB and PET result (N)	Comments	Prognosis
(24)	68	Either focal or diffuse	Not reported	BMB+/PET+, 16 BMB+/PET-, 0 BMB-/PET+, 17 BMB-/PET-, 35	-Visual analysis: PPV 43% -Tested various SUV metrics (e.g. SUVmean > 2.7: sens 68%, PPV 100%)	-Median FU 46 mos -BM SUVmean > 2.7 associated with a lower treatment free probability
(25)	48 (Baseline PET)	Either focal or diffuse	Not specified	BMB+/PET+, 13 BMB+/PET-, 11 BMB-/PET+, 20 BMB-/PET-, 4	-Visual analysis -PET sens 46%	Not reported
(20)	57	Either focal or diffuse	Exclude findings whose FDG uptake is explained by CT findings or clinical histology (e.g. GCFS)	BMB+/PET+, 16 BMB+/PET-, 8 BMB-/PET+, 5 BMB-/PET-, 28	-Visual analysis Also included N=106 with other lymphoma entities -Most pts in whom PET failed to detect BMI were already in advanced stage	Not reported
(23)	41	Either focal or diffuse	"Bone involvement also assessed on concurrent contrast CT"	BMB+/PET+, 5 BMB+/PET-, 11 BMB-/PET+, 2 BMB-/PET-, 23	-Small sample -CT criteria not entirely clear Tested various SUV metrics (e.g., SUVav* > 2.0: sens 58%, spec 96%)	Not available
(26)	142	Not reported	Not reported	BMB+/PET+, 24 BMB+/PET-, 46 BMB-/PET+, 10 BMB-/PET-, 62	-Visual analysis: PET sens 34.3%, PPV 70.6%	Not available
Current study	261	-Focal uptake (alone or in combination with diffuse) -Diffuse uptake <i>per se</i> NOT considered sufficient	Only considered focal uptake NOT explained by any concurrent CT abnormality (<i>such as benign bone lesion, fractures</i>)	BMB+/PET+, 46 BMB+/PET-, 35 BMB-/PET+, 32 BMB-/PET-, 148	-Visual analysis	-Median FU 6.0 yrs -BMI+ by PET is an independent predictor of PFS and OS in multivariate analysis

Only focal uptake pattern was considered positive at PET/CT, * Focally and diffuse uptake pattern were considered positive at PET/CT; BMB, bone marrow biopsy; NR, not reported; PPV, positive predictive value; NPV, negative predictive value.