

SUPPLEMENTARY MATERIALS

Supplementary Tables

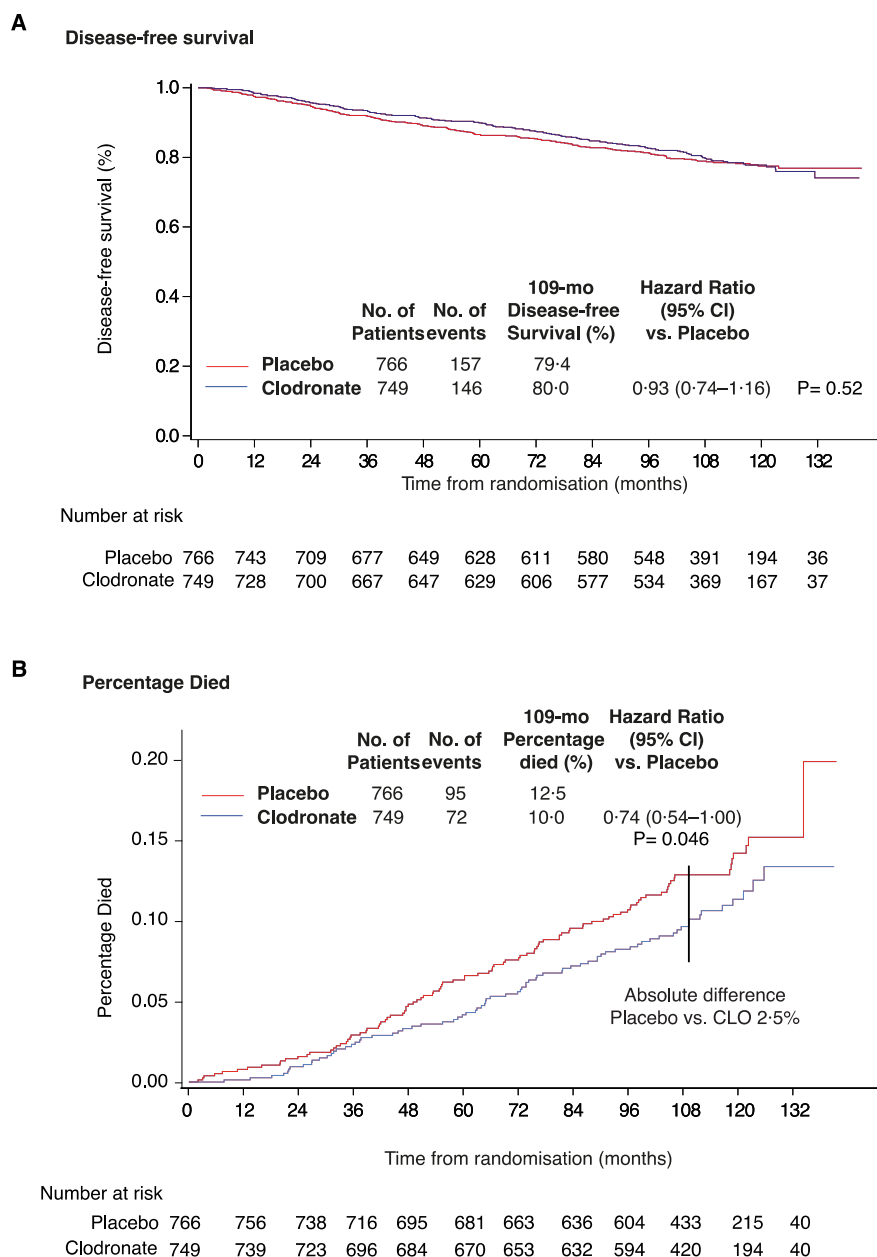
Supplementary Table 1. Outcomes HR of the trial endpoints according to patients' subgroups and follow-up time

Endpoints		5 years	7 years	median FU=109m
All B-34 N=3311	OS	HR= 0.81 (0.61, 1.09) p= 0.15	HR= 0.86 (0.68, 1.10) p= 0.22	HR= 0.90 (0.74, 1.10) p= 0.29
	DFS	HR= 0.85 (0.70, 1.03) p= 0.10	HR= 0.92 (0.78, 1.09) p= 0.34	HR= 0.97 (0.83, 1.12) p= 0.65
	RFI	HR= 0.81 (0.64, 1.02) p= 0.07	HR= 0.89 (0.72, 1.09) p= 0.26	HR= 0.92 (0.76, 1.11) p= 0.38
	Bone mets	HR= 0.83 (0.56, 1.24) p= 0.36	HR= 0.77 (0.54, 1.10) p= 0.15	HR= 0.82 (0.59, 1.12) p= 0.21
	Non_Bone mets	HR= 0.67 (0.48, 0.93) p= 0.01	HR= 0.74 (0.55, 1.00) p= 0.04	HR= 0.72 (0.55, 0.96) p= 0.02
MAF Samples N=2419	OS	HR= 0.74 (0.53, 1.04) p= 0.08	HR= 0.83 (0.63, 1.09) p= 0.17	HR= 0.83 (0.66, 1.04) p= 0.10
	DFS	HR= 0.81 (0.65, 1.02) p= 0.07	HR= 0.89 (0.73, 1.08) p= 0.24	HR= 0.96 (0.81, 1.14) p= 0.63
	RFI	HR= 0.79 (0.59, 1.04) p= 0.09	HR= 0.89 (0.69, 1.14) p= 0.34	HR= 0.92 (0.73, 1.15) p= 0.45
	Bone Mets	HR= 0.85 (0.54, 1.36) p= 0.49	HR= 0.78 (0.52, 1.18) p= 0.24	HR= 0.79 (0.55, 1.15) p= 0.22
	Non_Bone mets	HR= 0.73 (0.50, 1.08) p= 0.11	HR= 0.82 (0.58, 1.15) p= 0.25	HR= 0.80 (0.58, 1.10) p= 0.16

Supplementary Table 2. Endpoint events in patient subgroups

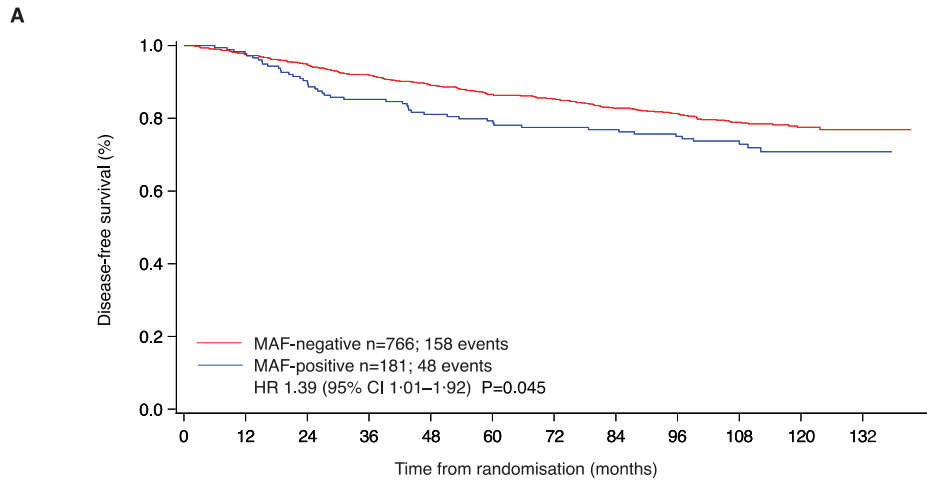
Events	FULL B-34 (n= 3311)			MAF evaluable (n=1883)			MAF Negative (n=1515)			MAF Positive (n=368)		
	Placebo (n=1656)	Clodronate (n=1655)	Total	Placebo (n=947)	Clodronate (n=936)	Total	Placebo (n=766)	Clodronate (n=749)	Total	Placebo (n=181)	Clodronate (n=187)	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
DFS	355 (21.4)	347 (21.0)	702 (21.2)	206 (21.8)	200 (21.4)	406 (21.6)	158 (20.6)	150 (20.0)	308 (20.3)	48 (26.5)	50 (26.7)	98 (6.5)
OS	204 (12.3)	184 (11.1)	388 (11.7)	133 (14.0)	108 (11.5)	241 (12.8)	98 (12.8)	75 (10.0)	173 (11.4)	35 (19.3)	33 (17.6)	68 (4.5)
RFI	221 (13.3)	206 (12.4)	427 (12.9)	123 (13.0)	113 (12.1)	236 (12.5)	74 (9.7)	67 (8.9)	141 (9.3)	36 (19.9)	28 (15.0)	64 (4.2)
Bone Mets	85 (5.1)	70 (4.2)	155 (4.7)	51 (5.4)	37 (4.0)	88 (4.7)	34 (4.4)	31 (4.1)	65 (4.3)	16 (8.8)	6 (3.2)	22 (1.5)
Non-Bone Mets	115 (6.9)	84 (5.1)	199 (6.0)	73 (7.7)	55 (5.9)	128 (6.8)	52 (6.8)	42 (5.6)	94 (6.2)	21 (11.6)	13 (7.0)	34 (2.2)

Supplementary Figures



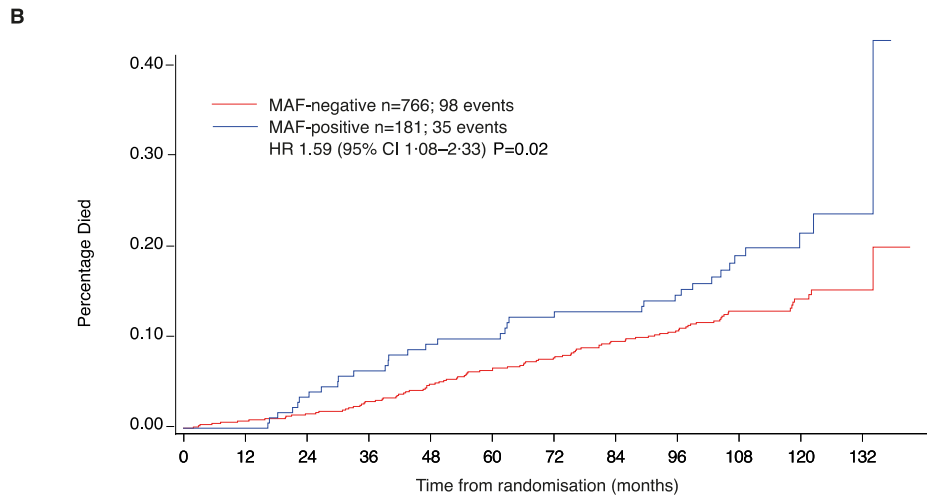
Supplementary Figure 1. Adjuvant clodronate outcomes according to MAF stratification A)

Disease-free survival and B) Percentage died by treatment group in *MAF*-non-amplified patients at complete follow-up from Cox multivariable model adjusted for differences in age; nodal status; presence of ER/PgR; histological grade; and pathological tumor size. HR=hazard ratio, CI=Confidence Interval.



Number at risk
(number censored)

MAF-negative	766	743	709	677	649	628	611	580	548	391	194	36
MAF-positive	181	174	157	145	137	133	129	127	118	83	36	6



Number at risk
(number censored)

MAF-negative	766	756	738	716	695	681	663	636	604	433	215	40
MAF-positive	181	178	169	160	154	152	147	145	136	97	48	8

Supplementary Figure 2. MAF amplification prognostic capacity. A) Disease-free survival and B) Percentage died by *MAF* status in placebo treated patients Output at complete follow up from Cox multivariable model. HR=hazard ratio, CI=Confidence Interval