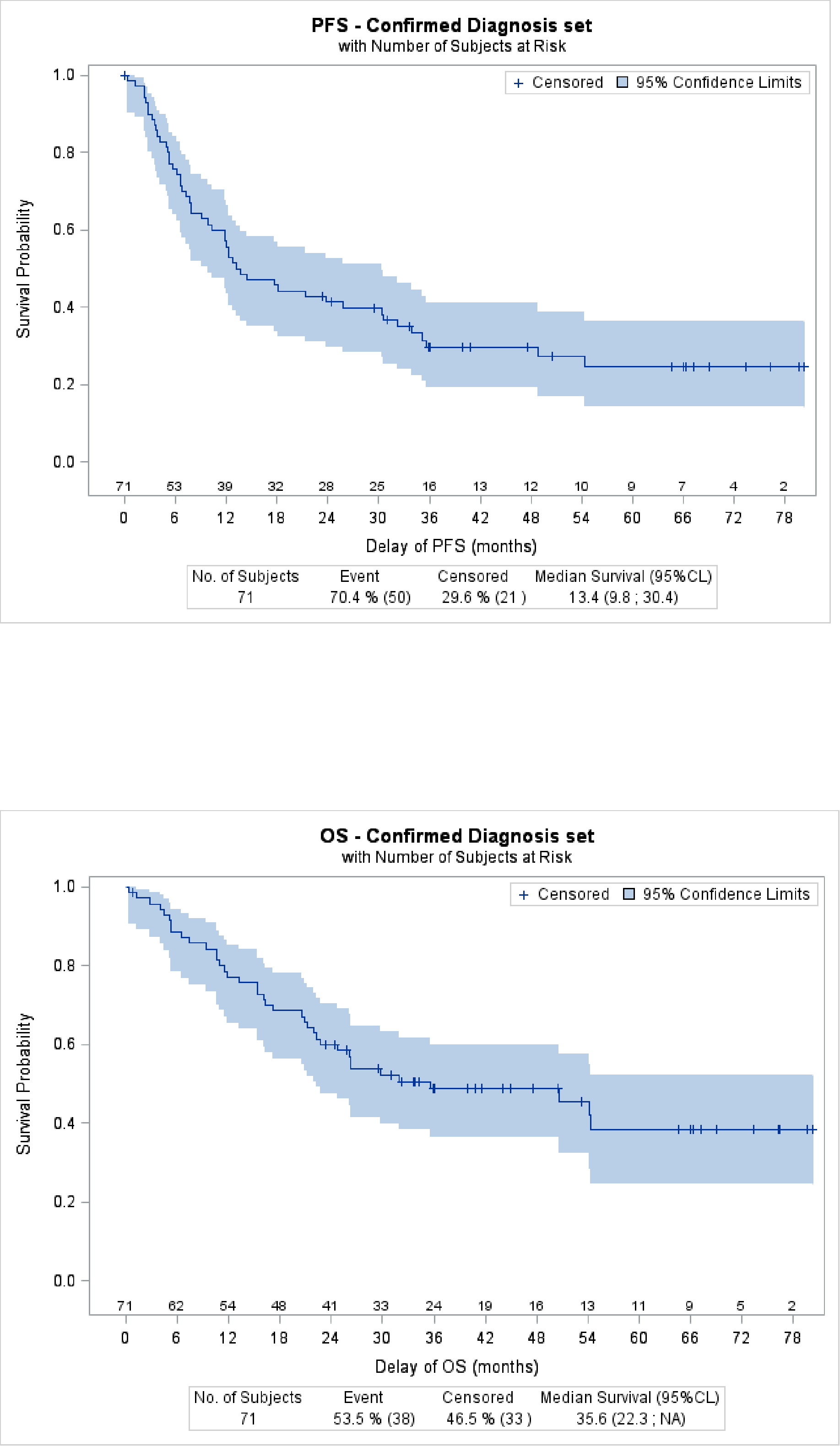
Supplemental Figures and Tables

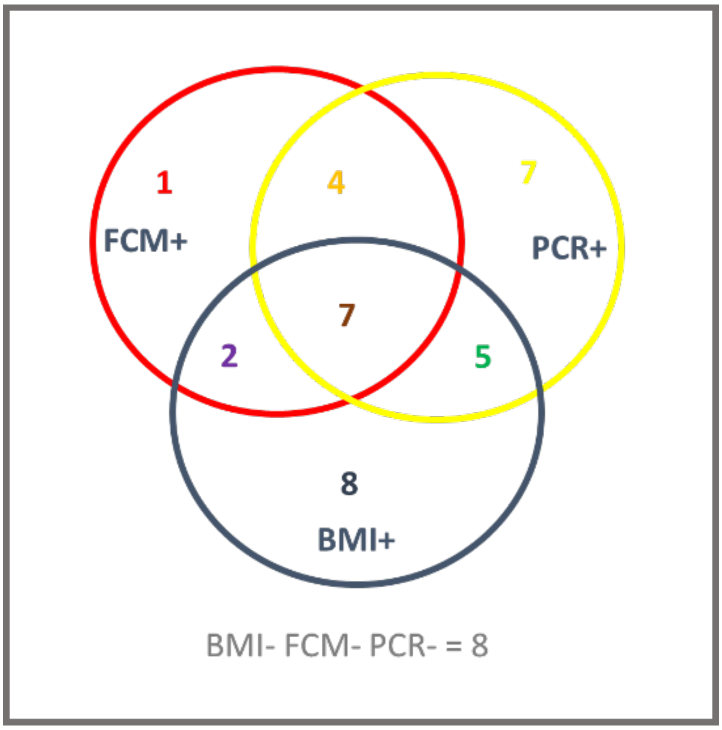
Supplemental Figure 1: Kaplan Meier curve representing A) PFS and B) OS of the 71 patients with a confirmed AITL.



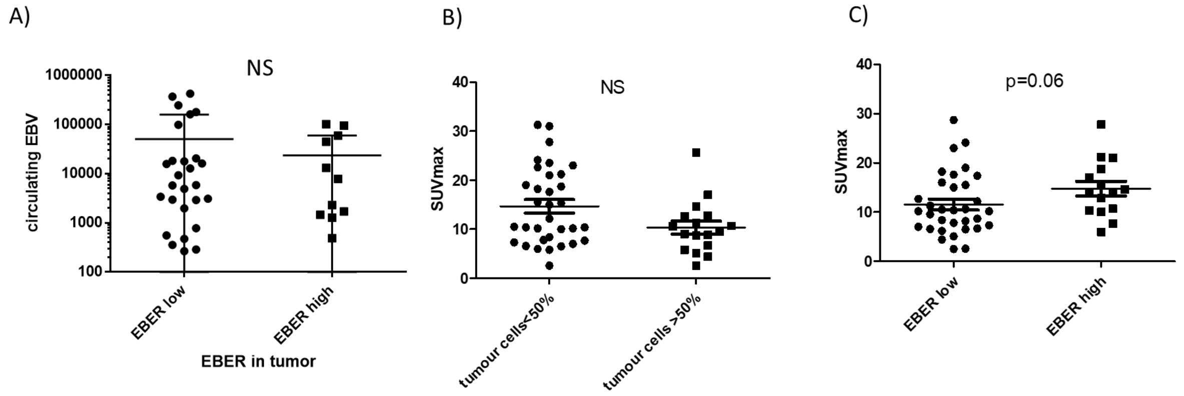
No. of Subjects	Event	Censored	Median Survival (95%CL)
71	70.4 % (50)	29.6 % (21)	13.4 (9.8 ; 30.4)

No. of Subjects	Event	Censored	Median Survival (95%CL)
71	53.5 % (38)	46.5 % (33)	35.6 (22.3 ; NA)

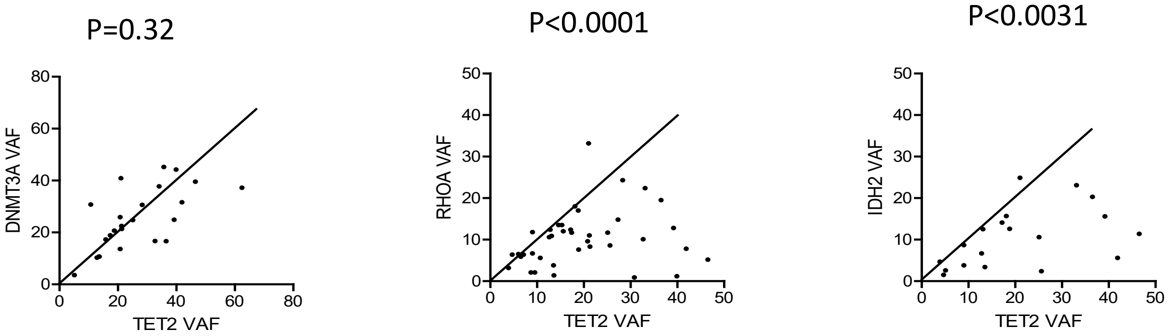
Supplemental figure 2: Coexistence of Bone marrow involvement assessed by bone marrow trephine (BMI+) and blood involvement assessed by flow cytometry (FCM) or PCR-DGGE. 8 patients (gray) was BMI, FCM and PCR negative. 8 patients (blue) had a BMI (demonstrated in bone marrow biopsy), but no detectable circulating population by PCR or FCM. 7 patients (yellow) had a clonal circulating population assessed by PCR, but no circulating population detectable by FCM or BMI. One patient (red) had a detectable circulating population detectable by FCM, but not by PCR or BMI. 5 patients (green) were BMI+ and PCR+, with a negative FCM. 2 patients (purple) were BMI+ and FCM+ but had no detectable clonal circulating population in PCR. Four patients (orange) were FCM+ and PCR+, with no evidence of BMI on bone marrow biopsy. Seven patients had BMI and positive FCM and PCR.



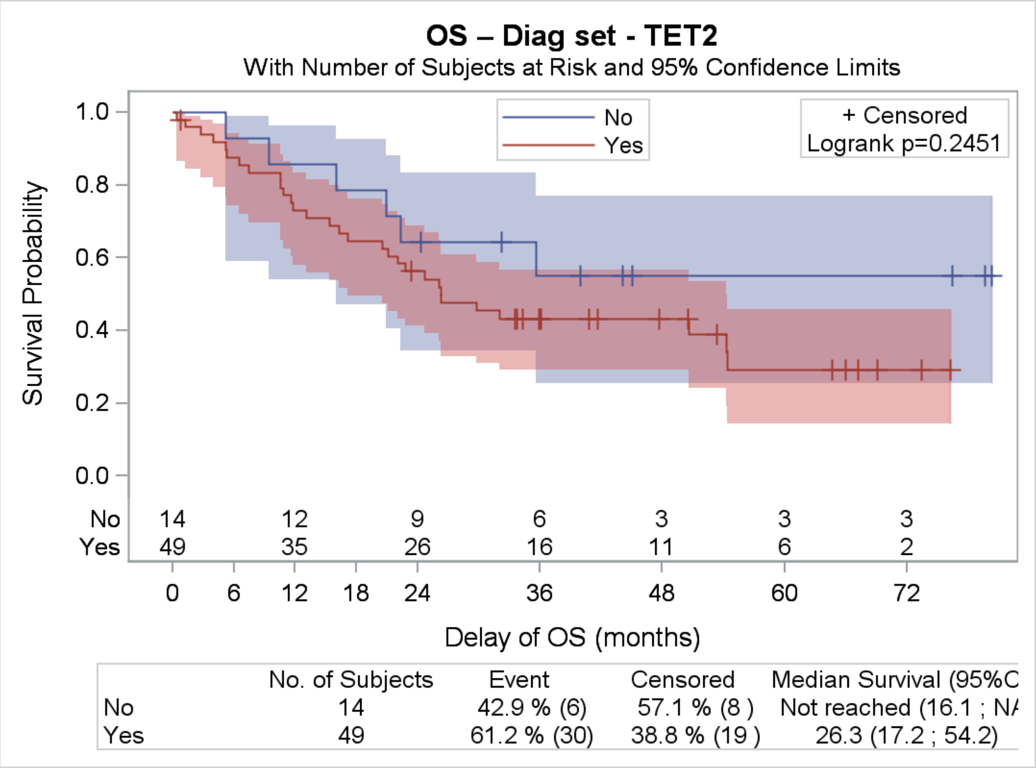
Supplemental Figure 3: Correlation between the number of copies of EBV genome in blood and expression of EBV RNA (EBER) in tumour, and between SUVmax and % of neoplastic T cells, estimated by morphology and immunochemistry (< or > 50%) and presence of EBV positive B blast within the tumour microenvironment. EBV low means EBV score 0 or 1, and EBV high, EBV score 2 or 3 with score 0: absence of large EBV-positive cells; score 1: up to 5 large EBV positive cells per high power field (hpf), score 2: 5 to 50 per hpf and score 3 : > 50 per hpf , or sheets or aggregates of large EBV-positive cells. Comparison was made using a Mann Whitney test.



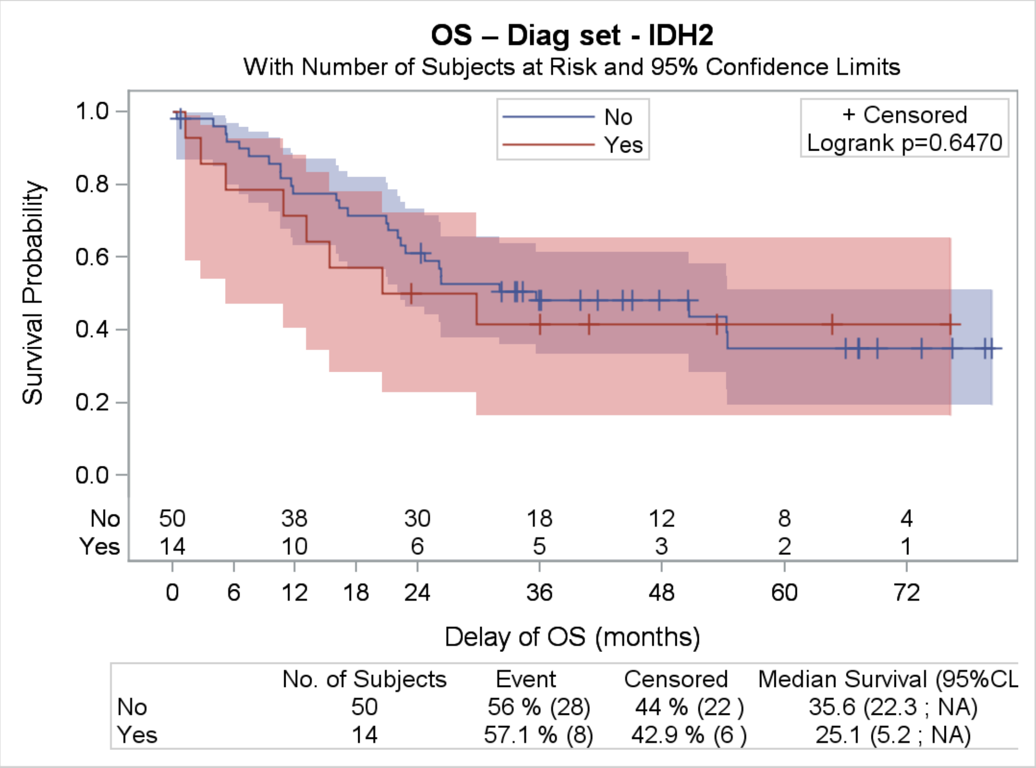
Supplemental figure 4: Comparison of variant allele frequency (VAF). Wilcoxon rank sum test.



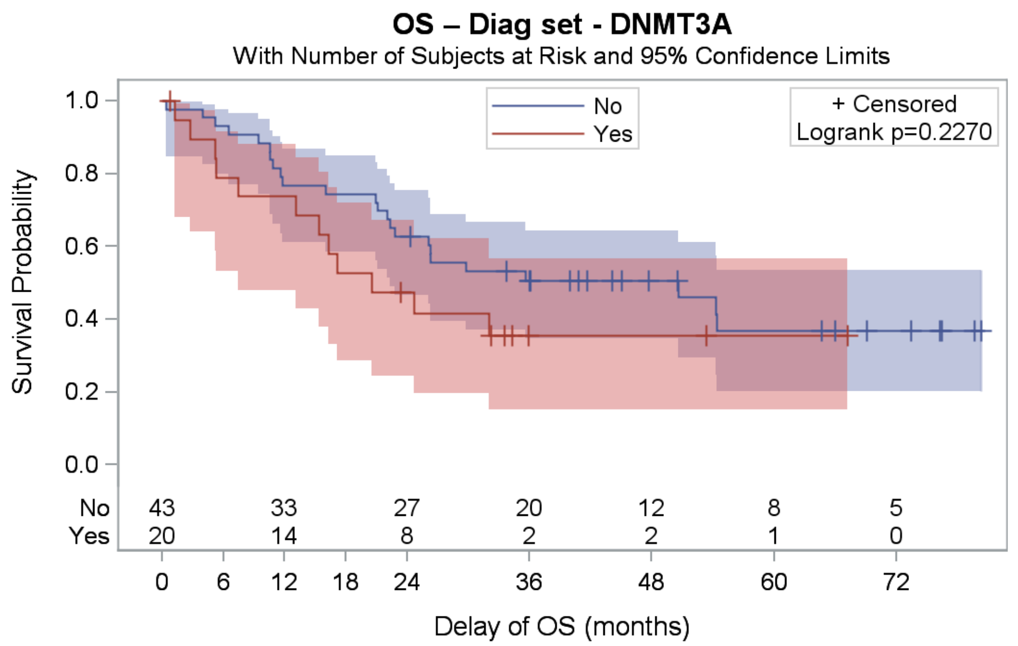
Supplemental Figure 5: Overall survival Kaplan Meier curves depending on the presence of TET2, IDH2, DNMT3A, TET2+IDH2+DNMT3A and RHOA mutation



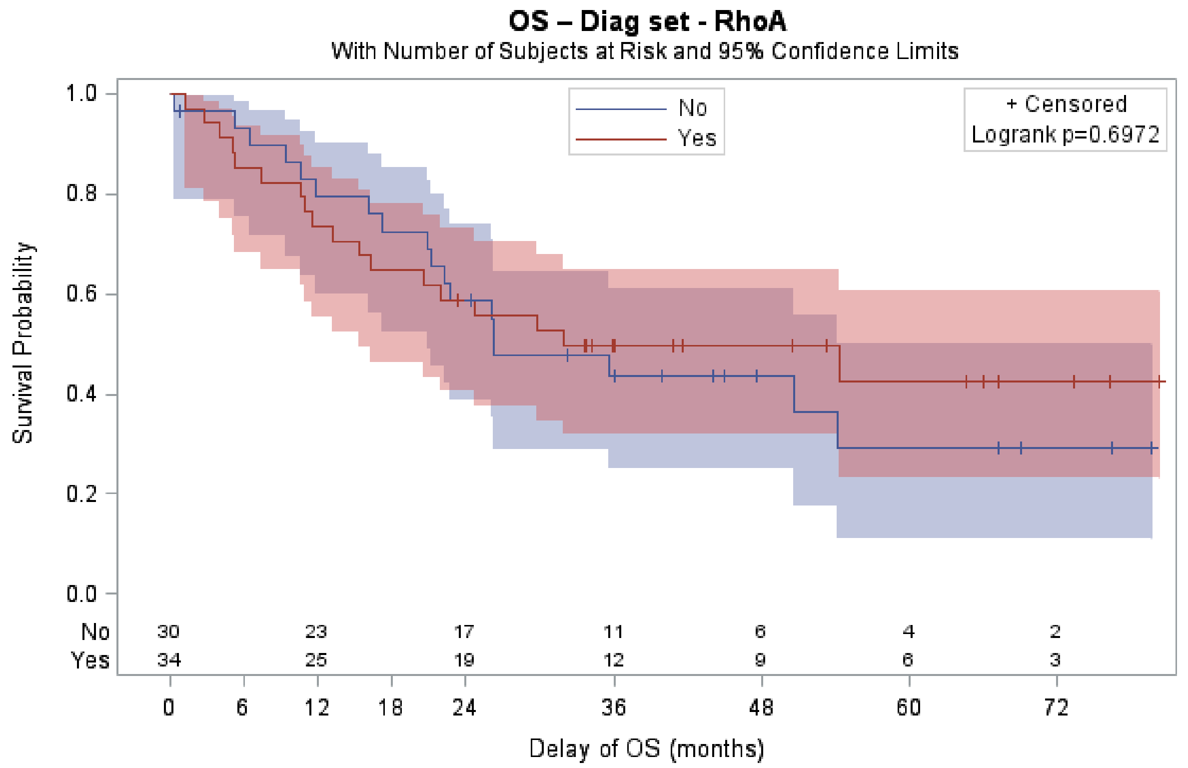
	No. of Subjects	Event	Censored	Median Survival (95%C
No	14	42.9 % (6)	57.1 % (8)	Not reached (16.1 ; N
Yes	49	61.2 % (30)	38.8 % (19)	26.3 (17.2 ; 54.2)



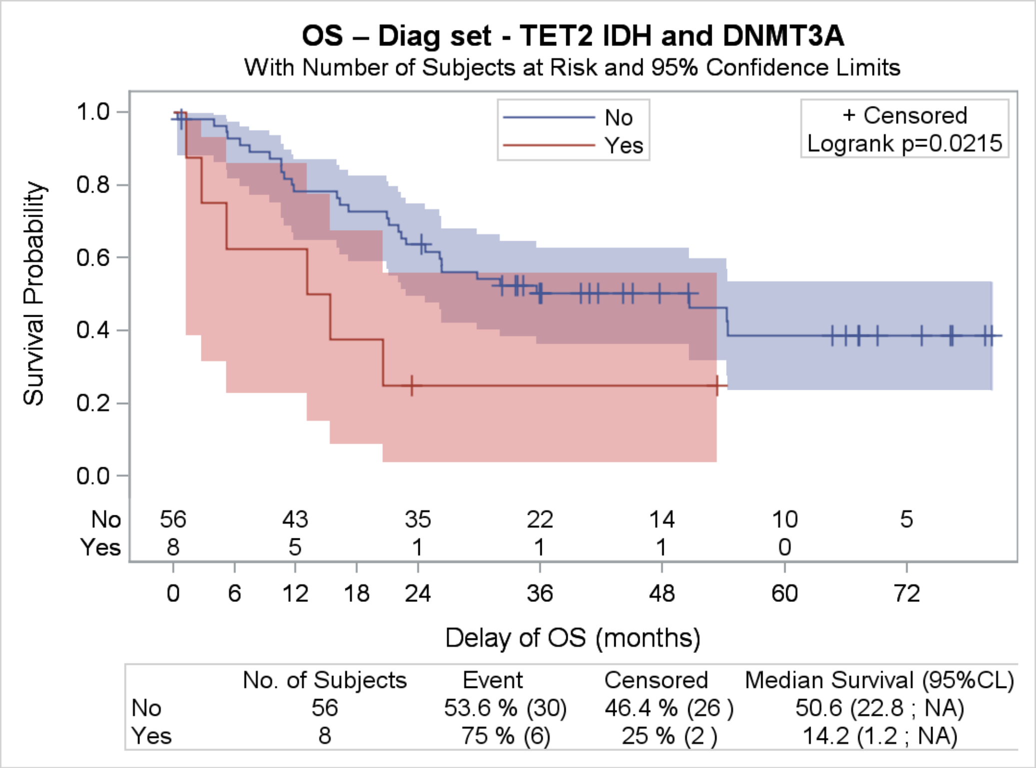
	No. of Subjects	Event	Censored	Median Survival (95%CL
No	50	56 % (28)	44 % (22)	35.6 (22.3 ; NA)
Yes	14	57.1 % (8)	42.9 % (6)	25.1 (5.2 ; NA)



	No. of Subjects	Event	Censored	Median Survival (95%C
No	43	55.8 % (24)	44.2 % (19)	50.6 (22.3 ; NA)
Yes	20	60 % (12)	40 % (8)	20.6 (7.4 ; NA)

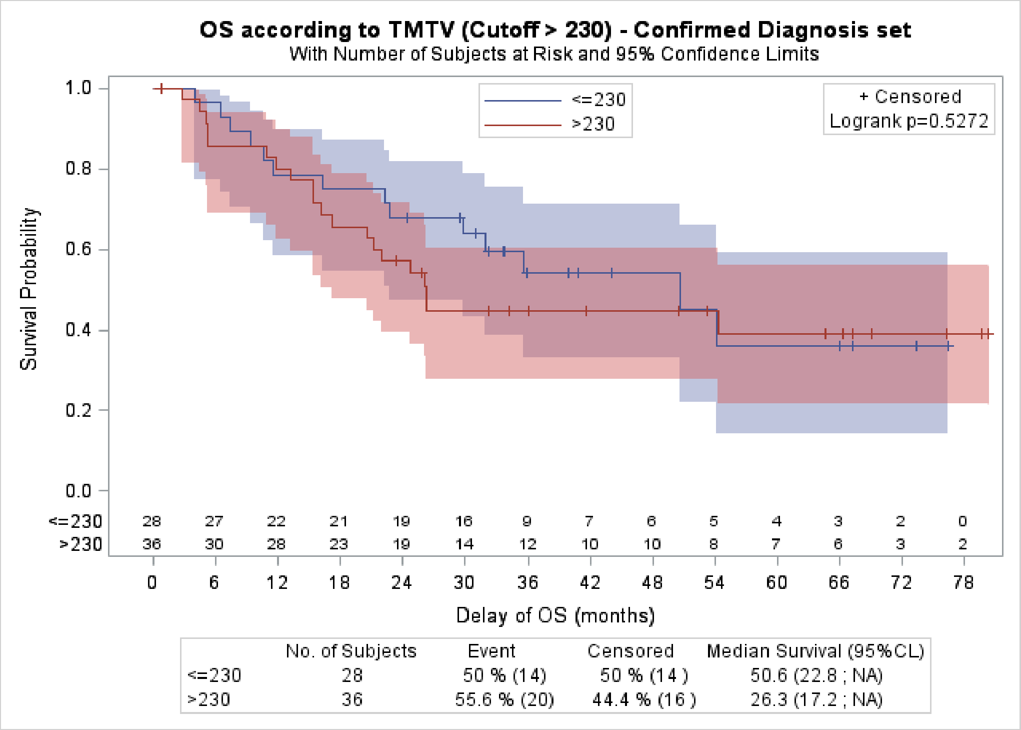


	No. of Subjects	Event	Censored	Median Survival (95%CL)
No	30	60 % (18)	40 % (12)	26.3 (20.9 ; 54.2)
Yes	34	52.9 % (18)	47.1 % (16)	32 (15.3 ; NA)

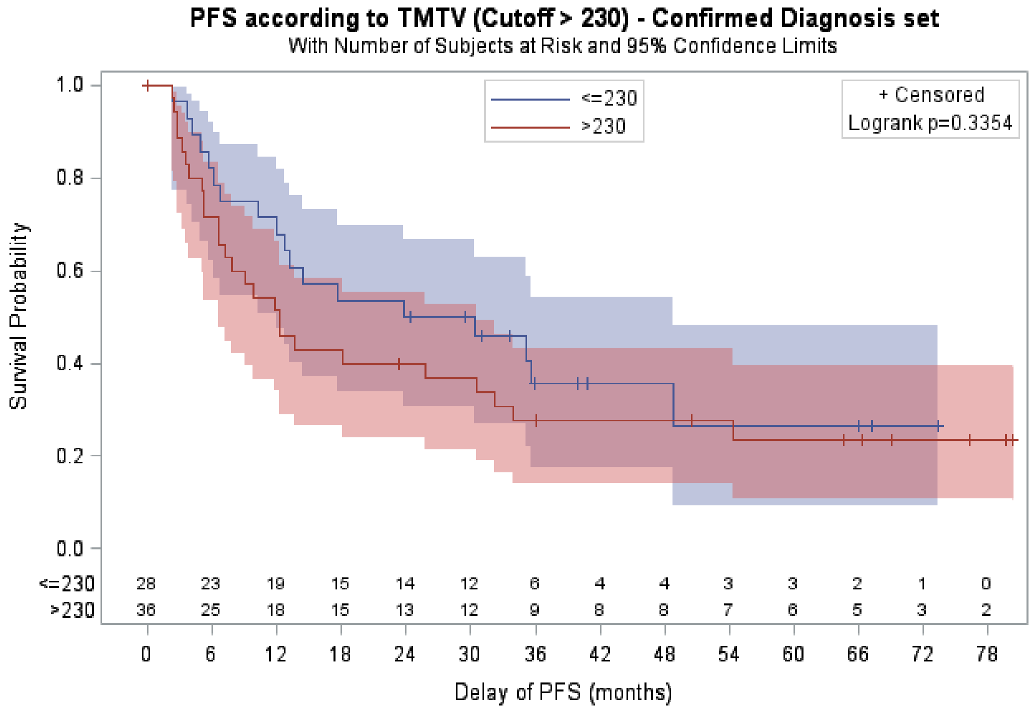


	No. of Subjects	Event	Censored	Median Survival (95%CL)
No	56	53.6 % (30)	46.4 % (26)	50.6 (22.8 ; NA)
Yes	8	75 % (6)	25 % (2)	14.2 (1.2 ; NA)

Figure S6: OS and PFS depending on the TMTV, with a threshold at 230cm^3, or in dichotomizing the cohort at the median



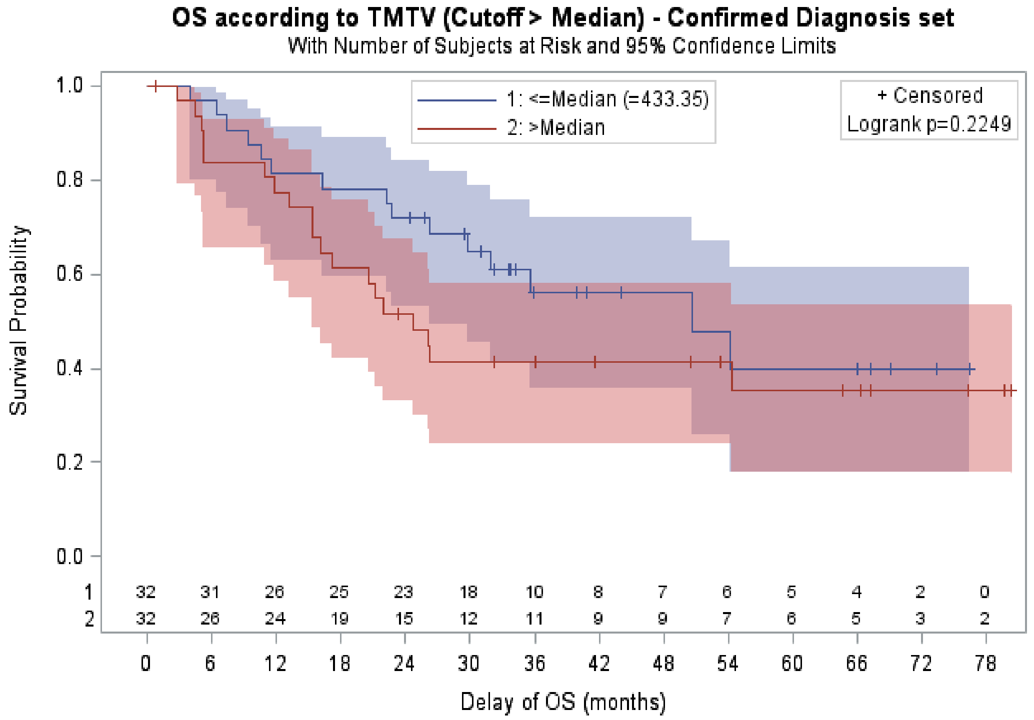
	No. of Subjects	Event	Censored	Median Survival (95%CL)
<=230	28	50 % (14)	50 % (14)	50.6 (22.8 ; NA)
>230	36	55.6 % (20)	44.4 % (16)	26.3 (17.2 ; NA)



PFS according to TMTV (Cutoff > 230) - Confirmed Diagnosis set

With Number of Subjects at Risk and 95% Confidence Limits

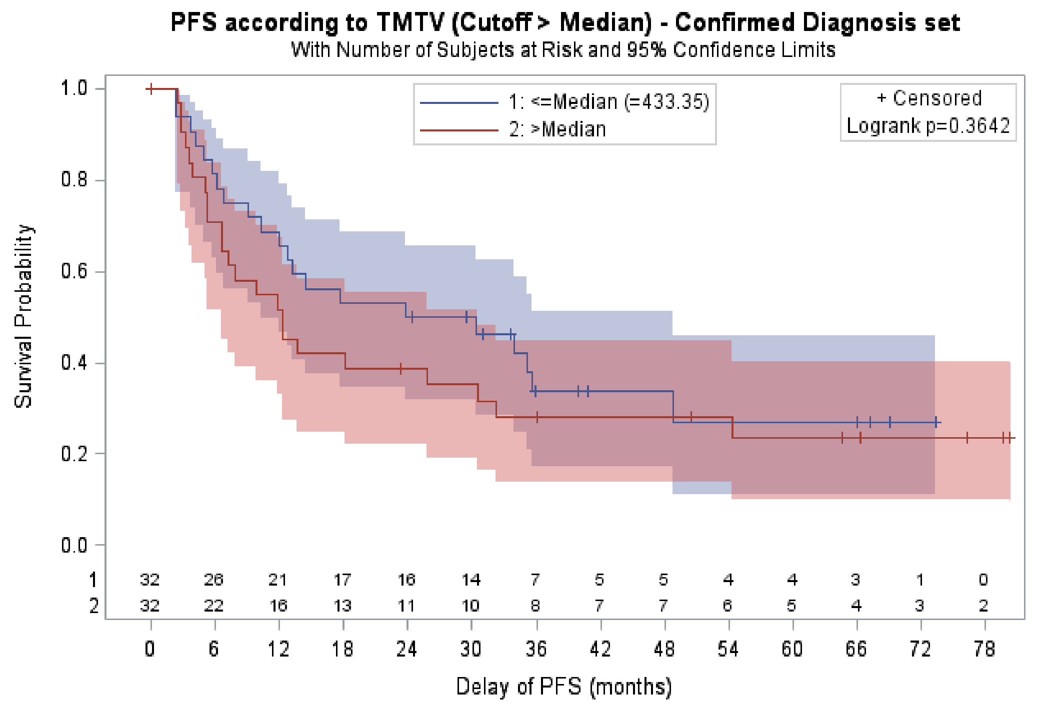
	No. of Subjects	Event	Censored	Median Survival (95%CL)
<=230	28	64.3 % (18)	35.7 % (10)	27.1 (12 ; 48.9)
>230	36	72.2 % (26)	27.8 % (10)	12.3 (6.6 ; 30.6)



OS according to TMTV (Cutoff > Median) - Confirmed Diagnosis set

With Number of Subjects at Risk and 95% Confidence Limits

	No. of Subjects	Event	Censored	Median Survival (95%CL)
<=Median (=433.35)	32	46.9 % (15)	53.1 % (17)	50.6 (26.3 ; NA)
>Median	32	59.4 % (19)	40.6 % (13)	24.7 (15.4 ; NA)



	No. of Subjects	Event	Censored	Median Survival (95%CL)
<=Median (=433.35)	32	65.6 % (21)	34.4 % (11)	27.1 (10.3 ; 48.9)
>Median	32	71.9 % (23)	28.1 % (9)	12.3 (6.6 ; 30.6)

Supplemental table 1: Correlation between the detection of the mutations in TET2, RHOA, DNMT3A and IDH2 and clinical and pathological factors. Bold characters represent significant values.

	Odds ratio[95%CI]			
	TET2 mut	*RHOA* mut	*DNMT3A* mut	*IDH2* mut
Age>65 years	**6.2** **[1.4 ;30]**	1.5 [0.4 ;6.6]	4.3 [0.7; 80.6]	2.4 [0.4; 48]
IPI (3-5)	**6.7** **[1.9 ;25.9]**	2.2 [0.7;7.6]	4.1 [0.99; 28.1]	1.3 [0.3;6.5]
PIT (3-4)	3.1 [0.7 ; 21.9]	3.6 [1;14]	2.3 [0.7; 7.6]	3.2 [0.9;12.0]
BMI	0.5 [0.1-1.9]	**0.3 [0.1-0.8]**	0.6 [0.2-1.8]	**0.05 [0.003-0.3]**
Strong ICOS expression	**4.2** **[1.0; 19.2]**	**3.7** **[1.1; 14.5]**	1.5 [0.4;6.7]	1.5 [0.4; 8.2]
FDC expansion	1.8 [0.5; 6.6]	7.7 **[2.3 ;31.3]**	2.1 [0.6;8.7]	**11.32** **[2.19;I]**
Clear cells	5.7 [0.9; 111]	3.3 [0.8;14.3]	2.6 [0.6;11.1]	24 **[4.5;195]**

Supplemental Table 2: impact of the mutational landscape on response rate and survival

Mutated vs unmutated	**CMR** **Odds ratio [IC95%]**	**PFS** **Hazard ratio [IC95%]**	**OS** **Hazard ratio [IC95%]**
TET2	0.633 (0.188-2.122)	1.3080 (.649-2.639)	1.673 (0.696-4.021)
DNMT3A	0.349 (0.099-1.079)	**1.924 (1.033-3.583)**	1.535 (0.762-3.092)
IDH2	1.500 (0.449-5.030)	0.947 (0.457-1.962)	1.201 (0.547-2.638)
RHOA	1.535 (0.567-4.258)	0.843 (0.472-1.506)	0.878 (0.456-1.689)
TET2+IDH2+DNMT3A	0.800 (0.152-3.588)	2.120 (0.935-4.809)	**2.737 (1.119-6.694)**