Rapport d'analyses statistiques

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1 Objectives

The primary objective of the study was to assess the survival, the risk of relapse and GVHD of patients who underwent allogenic sterm-cell transplantation (alloSCT) for aggressive T-cell lymphomas. The second objective was to determine the variables associated with these outcomes.

2 Methods

A retrospective analysis was conducted.A descriptive analysis of the variables recorded was perfomed. Different endpoints were defined : death, relapse, Event-free survival(EFS), Progression free Survival (PFC). Relapse was only considered in patients who had a complete remission after allo SCT.

Survival curves were estimated using Kaplan-Meier product-limit estimator. Competing risk survival analysis methods were applied to estimate the cumulative incidence (CIF) of developing events over time from alloSCT. These methods allow for the fact that a patient may experience an event which is different from that of interest. These events are known as competing risk events, and may preclude the onset of the event of interest, or may modify the probability of the onset of that event.In particular, a transplanted patient may die before a relapse occurs.

Factors associated with overall sur-vival were analyzed using Cox proportional hazards models. The proportional hazards assumption was checked by examination of Schoenfeld residuals. For the different endpoints, univariable analyses were first carried out, then a multivariable analysis was used where all factors with P-value < 0.15 in the univariable analyses were considered. Factors where then sequentially removed from the adjusted model with a P-value cut- at 0.05. Survival is presented as estimate and 95% confidence interval (95% CI).

To test CIF between histopathologic groups we the test proposed by Gray.

3 Results

3.1 Descriptive results

Parameters	Values	N	Statistics*
		284	
Age at diagnostic		284	46.5 [36;55]
Patient sex	Female	93	32.75 %
	Male	191	67.25 %
Age at diagnostic		284	46.5 [36;55]
Stage at diagnostic	I	13	6.47 %
	II	17	8.46 %
	III	45	22.39 %
	IV	126	62.69 %
	NA	83	
Stage at diagnostic	I-II	113	39.79 %
	III-IV	171	60.21 %
Subtypes	AITL	82	28.87 %
	ALCL ALK-	20	7.04 %
	ALCL ALK?	2	0.7 %
	ALCL ALK+	21	7.39 %
	ATLL	16	5.63 %
	EATL	3	1.06 %
	HS	12	4.23 %
	LGL	1	0.35 %
	NK leukemia	1	0.35 %
	NK/T nasal	16	5.63 %
	NOS	110	38.73 %
Subtypes	NOS	110	38.73 %
	AITL	82	28.87 %
	ALCL	43	15.14 %
	ATLL	16	5.63 %
	NK/T nasal	16	5.63 %
	Others	17	5.99 %
Centres	angers	8	2.82 %
	Becquerel[941]	4	1.41 %
	C.H.R.U Brest[659]	2	0.7 %
	caen	4	1.41 %
	CHU clermond ferrand	7	2.46 %
	Geneve	6	2.11 %
	Gustave Roussy[666]	3	1.06 %
	H A Michallon[270]	5	1.76 %
	H Bretonneau[272]	3	1.06 %

H Charles Nicolle[932]	1	0.35 %
H Claude Huriez[277]	8	2.82 %
H de l'ARCHET I[523]nice	3	1.06 %
H E Herriot[671]	5	1.76 %
H Haut-Leveque[267]	31	10.92 %
H Hautepierre[672]	11	3.87 %
H Jean Minjoz[233]	5	1.76 %
H La Miletrie[264]	5	1.76 %
H Mondor Hematol[252]	4	1.41 %
H Necker[160]	9	3.17 %
H Percy[665]	4	1.41 %
H Purpan[624]	8	2.82 %
H Sud/Pontchaillou[661]	7	2.46 %
H Sud[955]	1	0.35 %
Hotel Dieu[253]	32	11.27 %
liege	8	2.82 %
limoges	3	1.06 %
montpellier	10	3.52 %
nancy	1	0.35 %
Paoli Calmettes[230]	39	13.73 %
Pellegrin-Enfants[978]	1	0.35 %
Pitie-Salpetrriere[262]	8	2.82 %
St Antoine[775]	10	3.52 %
St Etienne[250]	4	1.41 %
St Louis[207]	24	8.45 %

Table 1: Patients

Parameters	Values	N	Statistics*
		284	
Previous auto	0	191	67.25 %
	1	93	32.75 %
Programme auto allo	0	257	90.49 %
	1	27	9.51 %
First graft relapse	0	219	77.11 %
	1	65	22.89 %

Table 2: Treatment before alloSCT

Parameters	Values	N	Statistics*
		284	
Age at graft		284	49.5 [38;57]

Age at graft	< 49 years	139	48.94 %
	> 49 years	145	51.06 %
Donor age		263	28 [18;39]
Donor sex	Female	114	40.71 %
	Male	166	59.29 %
	NA	4	
Delay diagnosis and allo SCT		284	378.5 [213.2;710.8]
>12 months delay	0	149	52.46 %
	1	135	47.54 %
Stage at diagnostic	I	13	6.47 %
	II	17	8.46 %
	III	45	22.39 %
	IV	126	62.69 %
	NA	83	
Disease status at transplant	CR/PR	251	88.69 %
	PD	32	11.31 %
	NA	1	
Disease status at transplant	CR	175	61.84 %
	PD	32	11.31 %
	PR	76	26.86 %
	NA	1	
Disease status at transplant	CR (?)	7	2.47 %
	CR1	94	33.22 %
	CR2	61	21.55 %
	CR3	13	4.59 %
	PD	32	11.31 %
	PR (?)	13	4.59 %
	PR1	39	13.78 %
	PR2	18	6.36 %
	PR3	5	1.77 %
	PR4	1	0.35 %
	NA	1	
Karnofsky		263	90 [80;100]
Karnofsky	100	92	34.98 %
	40	1	0.38 %
	50	4	1.52 %
	60	1	0.38 %
	70	9	3.42 %
	80	70	26.62 %
	90	86	32.7 %
	NA	21	
No of lines before alloSCT	>=4	24	9.45 %
	1	73	28.74 %

	2	92	36.22 %
	3	65	25.59 %
	NA	30	
Donnor related	0	149	52.46 %
	1	135	47.54 %
HLA match	1	231	81.34 %
	0	53	18.66 %
HLA match	Identical sibling	128	45.07 %
	Matched unrelated	103	36.27 %
	Mismatched relative	7	2.46 %
	Mismatched unrelated	13	4.58 %
	Unrelated CB	33	11.62 %
sex of patient/donnor	M/F	47	16.55 %
	Others	237	83.45 %
CMV serostatus of patient/donnor	autres	232	81.69 %
	neg/pos	52	18.31 %
Source of stem cells	BM	49	17.25 %
	CB	33	11.62 %
	PB	202	71.13 %
TBI	No	161	56.69 %
	Yes	123	43.31 %
conditioning Intensity	MAC	106	38.13 %
	NMA	27	9.71 %
	RIC	145	52.16 %
	NA	6	
Conditioning	BEAM	1	0.36 %
	BEAM + Campath	1	0.36 %
	BU CY	4	1.42 %
	BU CY + FLU+ ATG	1	0.36 %
	BU CY ATG	1	0.36 %
	EDX ATG	0	0 %
	ENX TBI 2gray	1	0.36 %
	FLU ATG	3	1.07 %
	FLU BU 1+ ATG	3	1.07 %
	FLU BU 2	1	0.36 %
	FLU BU 2+ ATG	73	25.98 %
	FLU BU 3+ ATG	21	7.47 %
	FLU BU 4+ ATG	10	3.56 %
	FLU BU EDX	8	2.85 %
	FLU BU EDX +ATG	6	2.14 %
	FLU EDX	1	0.36 %
	FLU EDX ATG	3	1.07 %
	FLU EDX MEL	1	0.36 %

	FLU ENX TBI 2gray	24	8.54 %
	FLU ENX TBI 4gray	2	0.71 %
	FLU ENX TBI 6gray	1	0.36 %
	FLU ENX TBI 6gray + campath	1	0.36 %
	FLU MEL	12	4.27 %
	FLU MEL + campath	4	1.42 %
	FLU MEL + Campath	1	0.36 %
	FLU MEL ATG	1	0.36 %
	FLU MEL TBI 2gray	1	0.36 %
	FLU TBI 2gray	21	7.47 %
	FLU TBI 2gray ATG	1	0.36 %
	FLU Tbi 8 gray	1	0.36 %
	MEL 140 TBI 10 gray	1	0.36 %
	MEL TBI VP16	1	0.36 %
	TB2F	2	0.71 %
	TBI 12 gray	1	0.36 %
	TBI 2gray	1	0.36 %
	TBI EDX	49	17.44 %
	TBI EDX +ATG	11	3.91 %
	TBI EDX FLU	5	1.78 %
	Thiotepa etoposide TBI12 gray	1	0.36 %
	NA	3	
Cells manipulation	none	275	97.86 %
	yes	6	2.14 %
	NA	3	
No of donnors	1	261	91.9 %
	2	23	8.1 %

Table 3: AlloSCT

Parameters	Values	N	Statistics*
		284	
Agvhd	0	141	49.65 %
	1	143	50.35 %
Agvhd grade	No aGvHD present (Grade 0)	141	49.65 %
	Grade I	49	17.25 %
	Grade II	46	16.2 %
	Grade III	24	8.45 %
	Grade IV	17	5.99 %
	Present, grade unknown	7	2.46 %
Cgvhd	0	187	65.85 %
	1	97	34.15 %
Cgvhd grade	deces avant J100	41	14.44 %

	extensive	38	13.38 %
	limited	55	19.37 %
	no cGvh	146	51.41 %
	unknown	4	1.41 %
Engrafted	deces avant J30	5	1.76 %
	engrafted	271	95.42 %
	lost graft	2	0.7 %
	no engraftment	6	2.11 %
Cause of death	HSCT-GVHd	21	19.63 %
	HSCT-GVHd + infection	3	2.8 %
	HSCT-infection	27	25.23 %
	HSCT-toxicity	4	3.74 %
	HSCT related	3	2.8 %
	HSCT related ILD	1	0.93 %
	HSCT related MAT	1	0.93 %
	HSCT related MOF	2	1.87 %
	HSCT related MVO	1	0.93 %
	HSCT related pneumopathie interstititelle	2	1.87 %
	HSCT related PTLD	1	0.93 %
	HSCT related SDRA	1	0.93 %
	Other	1	0.93 %
	Relapse or progression of original disease	37	34.58 %
	Secondary malignancy	1	0.93 %
	Unknown	1	0.93 %
	NA	177	
Best reponse after SCT	CR	245	86.88 %
	Not evaluable	4	1.42 %
	Not evaluated	3	1.06 %
	PD	14	4.96 %
	PR	16	5.67 %
	NA	2	
Relapse/progression	continuous progression	28	9.93 %
	No	217	76.95 %
	Non applicable	3	1.06 %
	yes	34	12.06 %
	NA	2	
Death	alive	177	62.32 %
	dead	107	37.68 %

Table 4: Post-AlloSCT Response

3.2 Survival analysis

Median follow-up from the date of AlloSCT was 20.35 (range 0.03 to 113.77). OS at 1 year was 0.68 (95 % 0.63 - 0.74), was 0.64 (95 % 0.59 - 0.7) at 2 years .OS at 4 years was 0.57 (95 % 0.5 - 0.64).
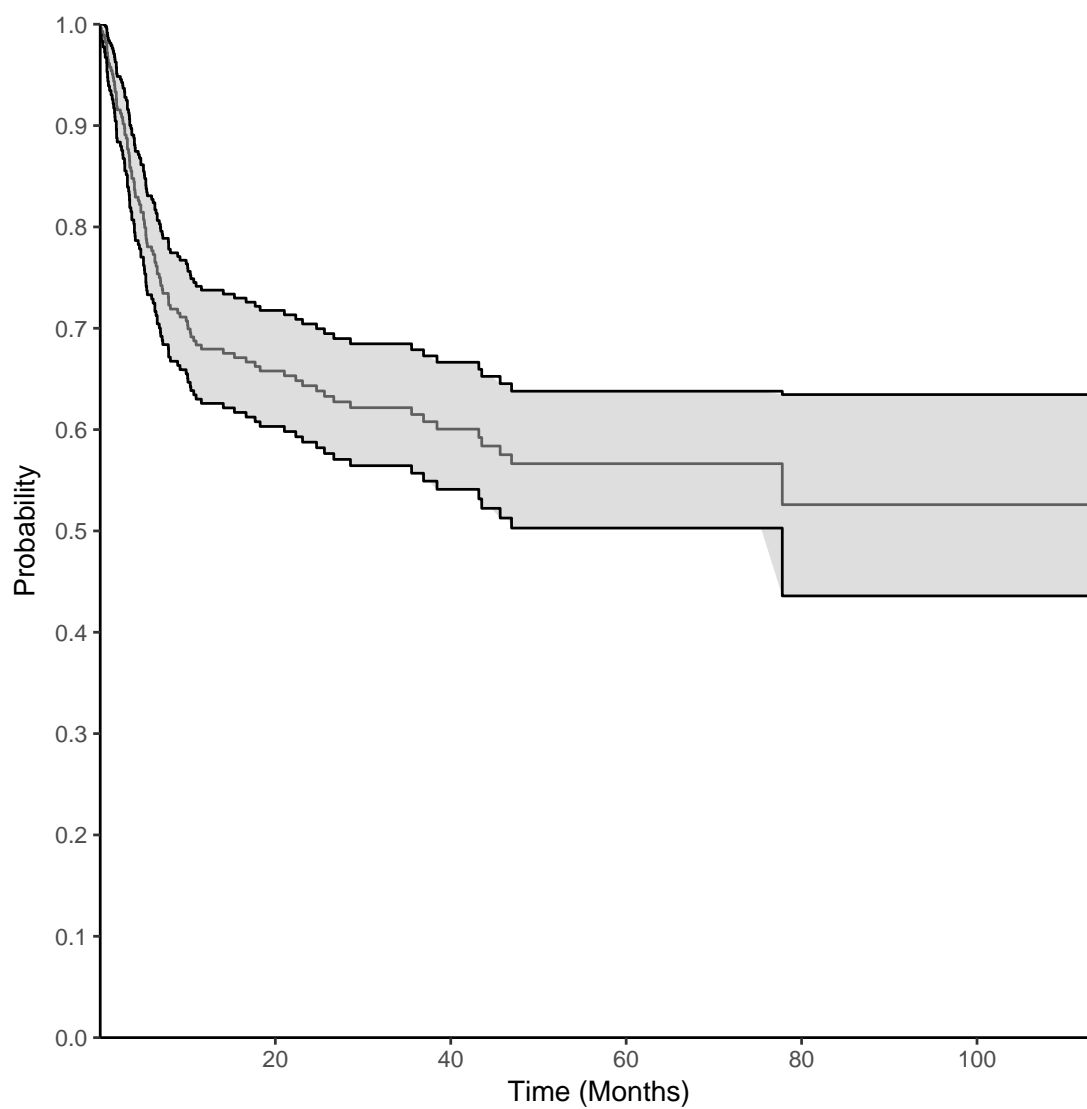

Figure 1: Overall survival

EFS at 1 year was 0.54 (95 % 0.48 - 0.6), was 0.49 (95 % 0.43 - 0.55) at 2 years. EFS at 4 years was 0.42 (95 % 0.36 - 0.5).
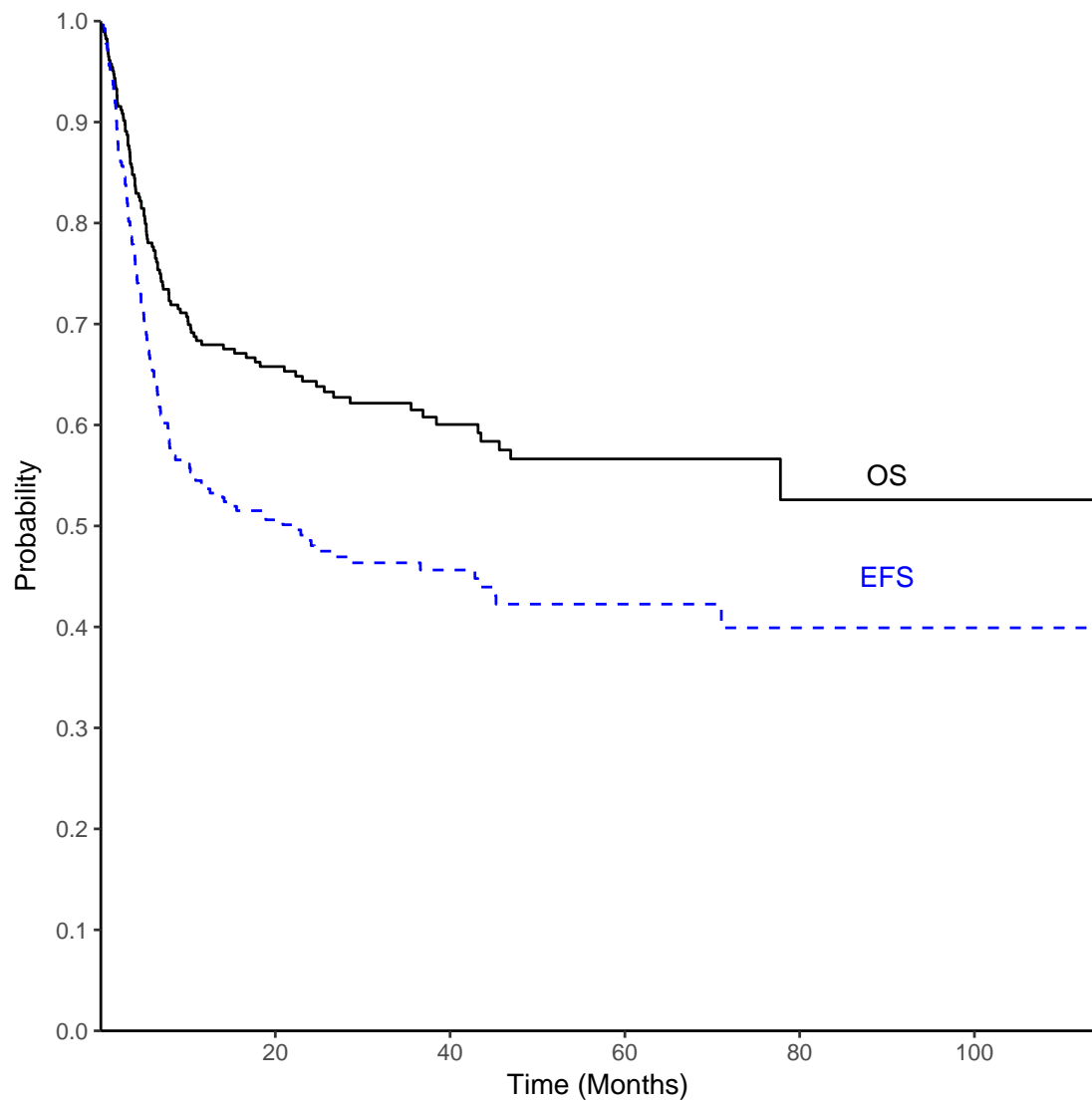

Figure 2: Event-free survival

PFS at 1 year was 0.73 (95 % 0.65 - 0.83), was 0.68 (95 % 0.59 - 0.78) at 2 years. PFS at 4 years was 0.66 (95 % 0.56 - 0.77).
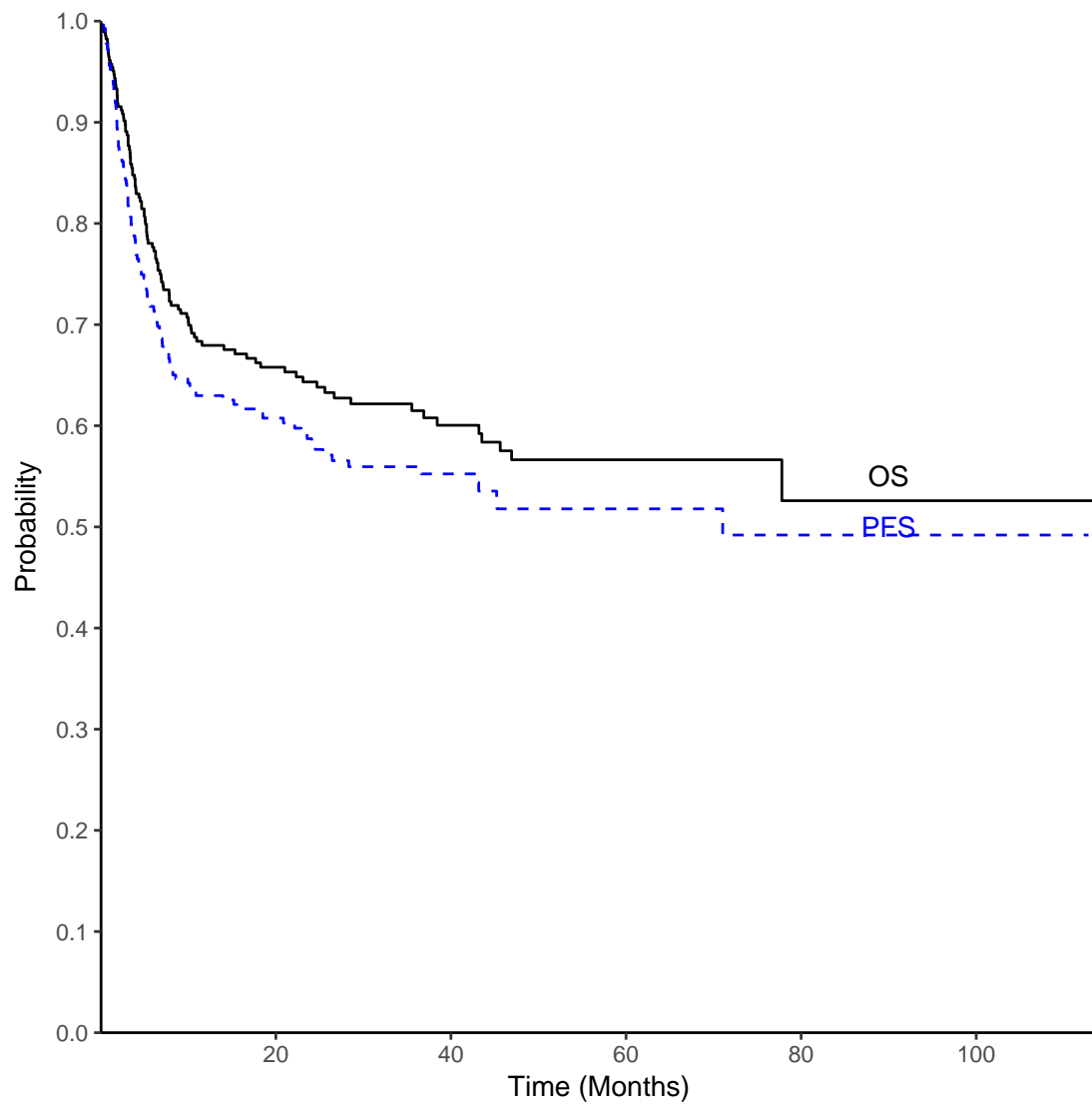
Figure 3: Progression-free survival

Relapse at 1 year was 0.87 (95 % 0.83 - 0.92), was 0.85 (95 % 0.8 - 0.9) at 2 years. Relapse at 4 years was 0.83 (95 % 0.77 - 0.89).
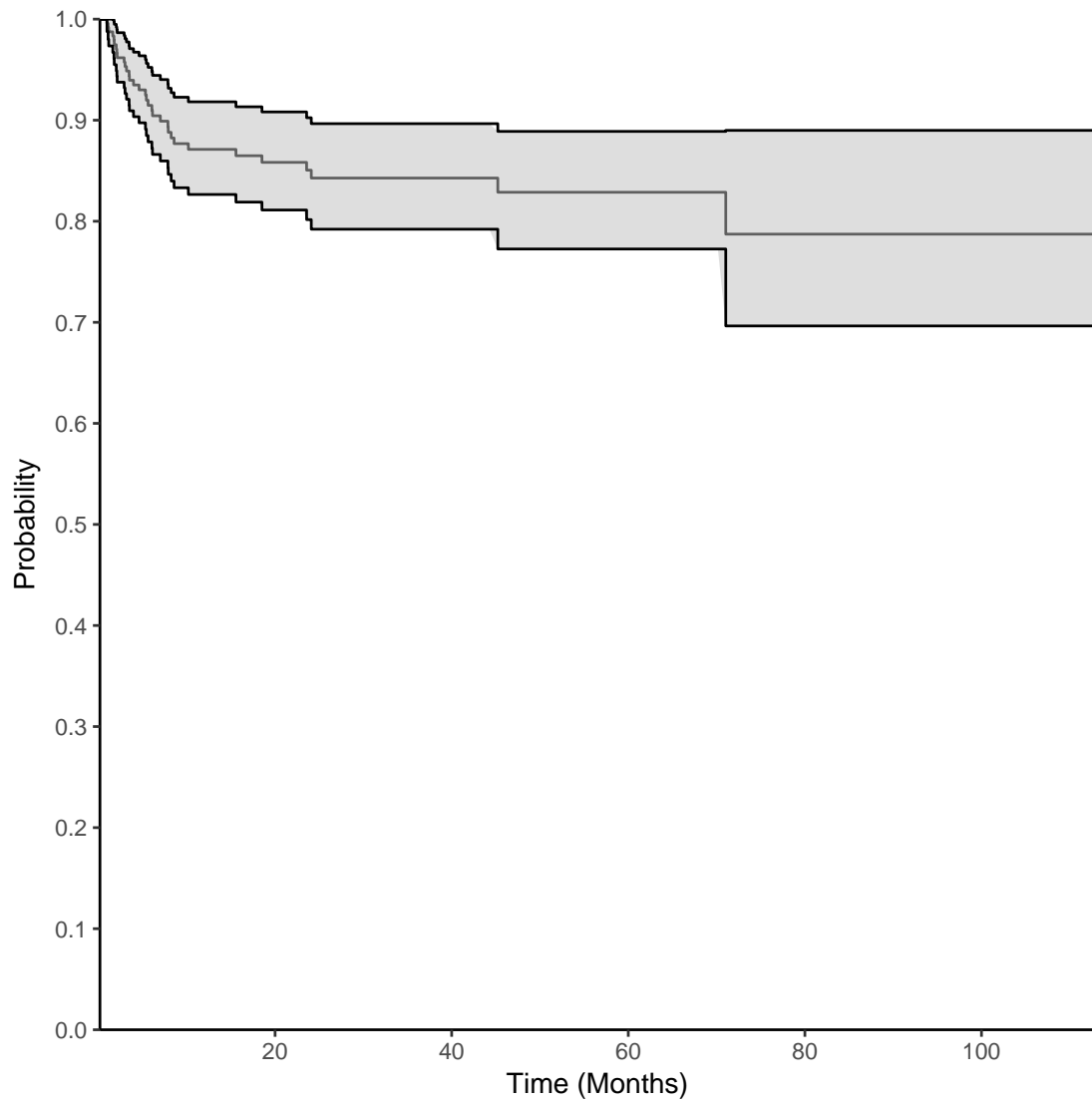
Figure 4: Relapse in patients with a complete remission post alloSCT)

CIF for related HSCT death at 1 years was 0.2, at 2 years 0.22. CIF for non-related HSCT Death at 1 years was 0.12, at 2 years 0.13.
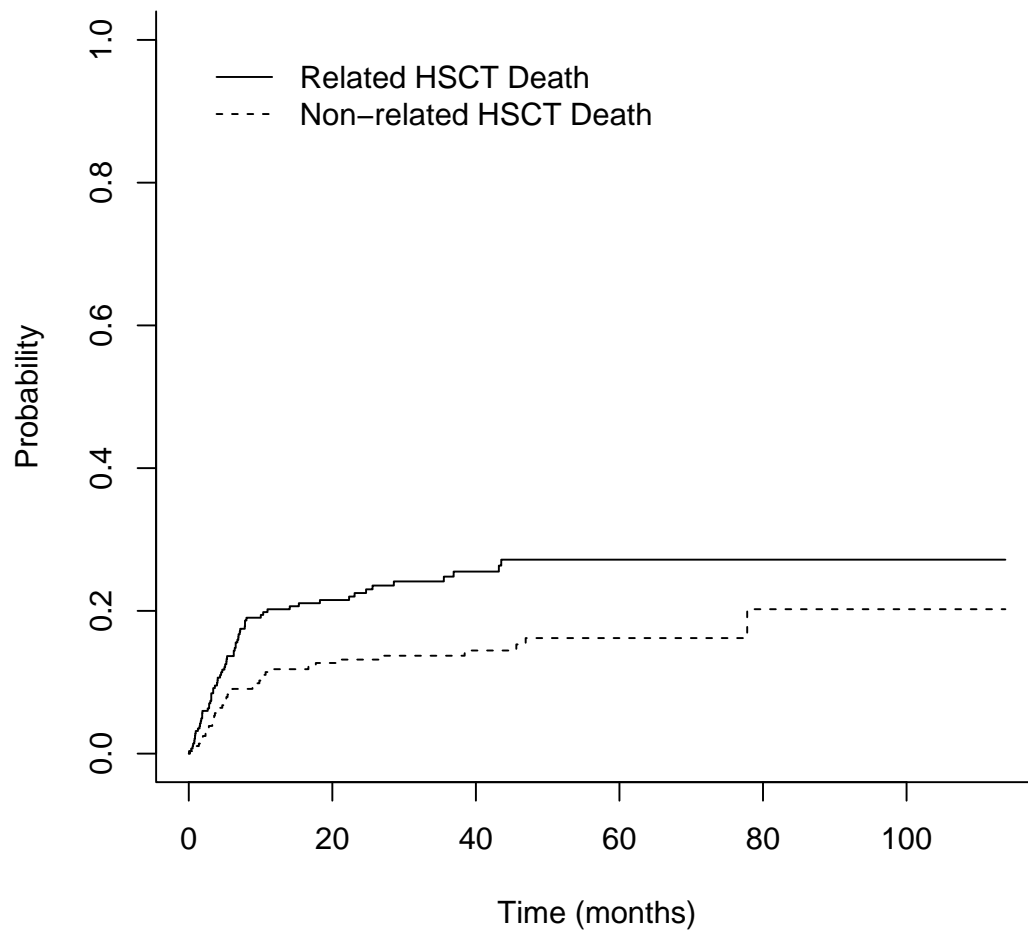
Figure 5: CIF of Related HSCT Death and Non-related HSCT Death

CIF for relapse/progression at 1 years was 0.18, at 2 years 0.19. CIF for death without relapse or progression at 1 years was 0.19, at 2 years 0.22.
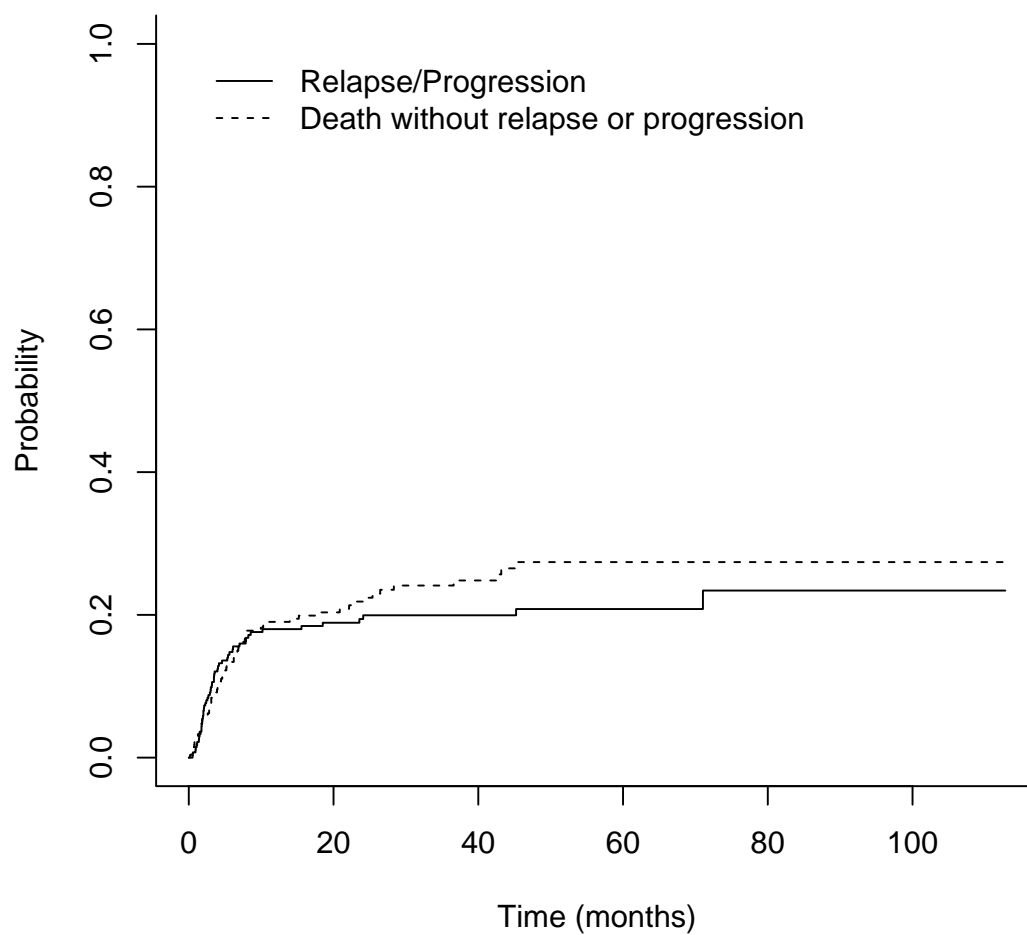

Figure 6: CIF of relapse or progression and death without relapse or progression

CIF for relapse at 1 years was 0.12, at 2 years 0.13. CIF for death without relapse at 1 years was 0.19, at 2 years 0.22.
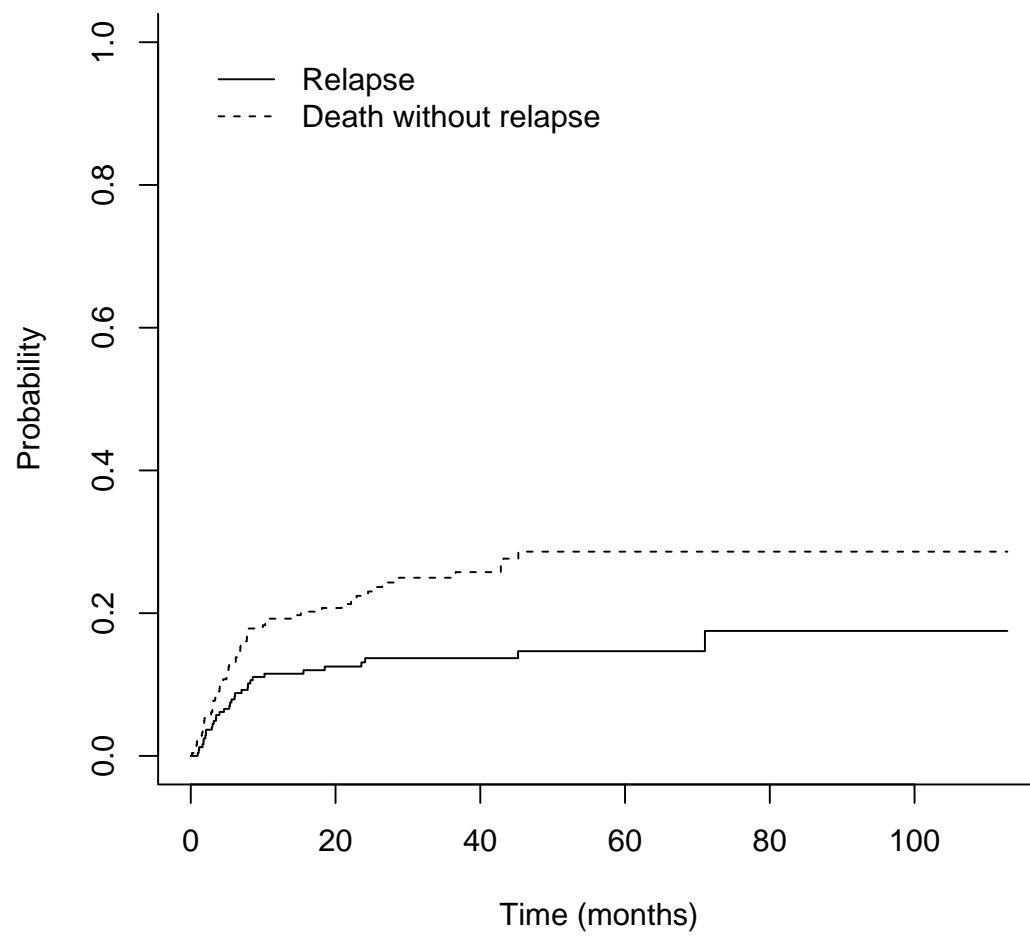
Figure 7: CIF of relapse and death without relapse (in patients with a complete remission post alloSCT)