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).

3 Results

3.1 Descriptive results

285 patients were initially selected.We excluded 1 patient that underwent two alloSCT. The final analysis was perfomed on 284 patients and 284 grafts.

3.1.1 Patients characteristics

Parameters	Values	N	Statistics*
		284	
Patient sex	Female	93	32.75 %
	Male	191	67.25 %
Age at diagnosis		284	45.01(15;68)
Stage at diagnosis	I	13	6.47 %
	II	17	8.46 %
	III	45	22.39 %
	IV	126	62.69 %
	NA	83	
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 characteristics

3.1.2 Treatments before alloSCT

Parameters	Values	N	Statistics*
		284	
Previous auto	No	191	67.25 %
	Yes	93	32.75 %
Programme auto allo	No	257	90.49 %
	Yes	27	9.51 %
First graft relapse	No	219	77.11 %
	Yes	65	22.89 %

Table 2: Treatments before alloSCT

3.1.3 Transplant conditions

Parameters	Values	N	Statistics*
		284	
Age at graft		284	46.97(16;69)
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	NO	149	52.46 %
	Yes	135	47.54 %
Disease status at transplant	CR	175	61.84 %
	PR	76	26.86 %
	PD	32	11.31 %
	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 score		263	90 [80;100]
Karnofsky score	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	
Karnofsky score	Non normal activity	15	5.7 %
	Normal activities	248	94.3 %
	NA	21	
Karnofsky score	100	92	34.98 %
	Unable to carry on normal activity	15	5.7 %
	80	70	26.62 %
	90	86	32.7 %

	NA	21	
No of lines before alloSCT		254	2 [1;3]
No of lines before alloSCT	1	73	28.74 %
	2	92	36.22 %
	3	65	25.59 %
	>=4	24	9.45 %
	NA	30	
Donnor related	Yes	149	52.46 %
	No	135	47.54 %
HLA match	Identical sibling	128	45.07 %
	Matched unrelated	136	47.89 %
	Mismatched relative	7	2.46 %
	Mismatched unrelated	13	4.58 %
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 donnor/patient	F/M	74	26.52 %
	Others	205	73.48 %
	NA	5	
CMV serostatus of donnor/patient	pos/neg	50	17.86 %
	Others	230	82.14 %
	NA	4	
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	No	275	97.86 %
	Yes	6	2.14 %
	NA	3	
No of donnors	1	261	91.9 %
	2	23	8.1 %

Table 3: Transplant conditions

3.1.4 Post-AlloSCT Response

Parameters	Values	N	Statistics*
		284	
Agvhd	No	141	49.65 %
	Yes	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	Early death	41	14.44 %
	no	146	51.41 %
	yes	97	34.15 %
Cgvhd grade	Early death (100D)	41	14.44 %
	Extensive	38	13.38 %
	Limited	55	19.37 %
	No cGvh	146	51.41 %
	grade unknown	4	1.41 %
Engrafted	Early death (30D)	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	

Table 4: Post-AlloSCT Response

3.2 Survival analysis in all patients

Median overall-survival from the date of AlloSCT was 20.35 (range 0.03 to 113.77). OS at 1 year was 0.68 (95 % 0.62 - 0.73), was 0.64 (95 % 0.58 - 0.7) at 2 years.OS at 4 years was 0.57 (95 % 0.5 - 0.63).

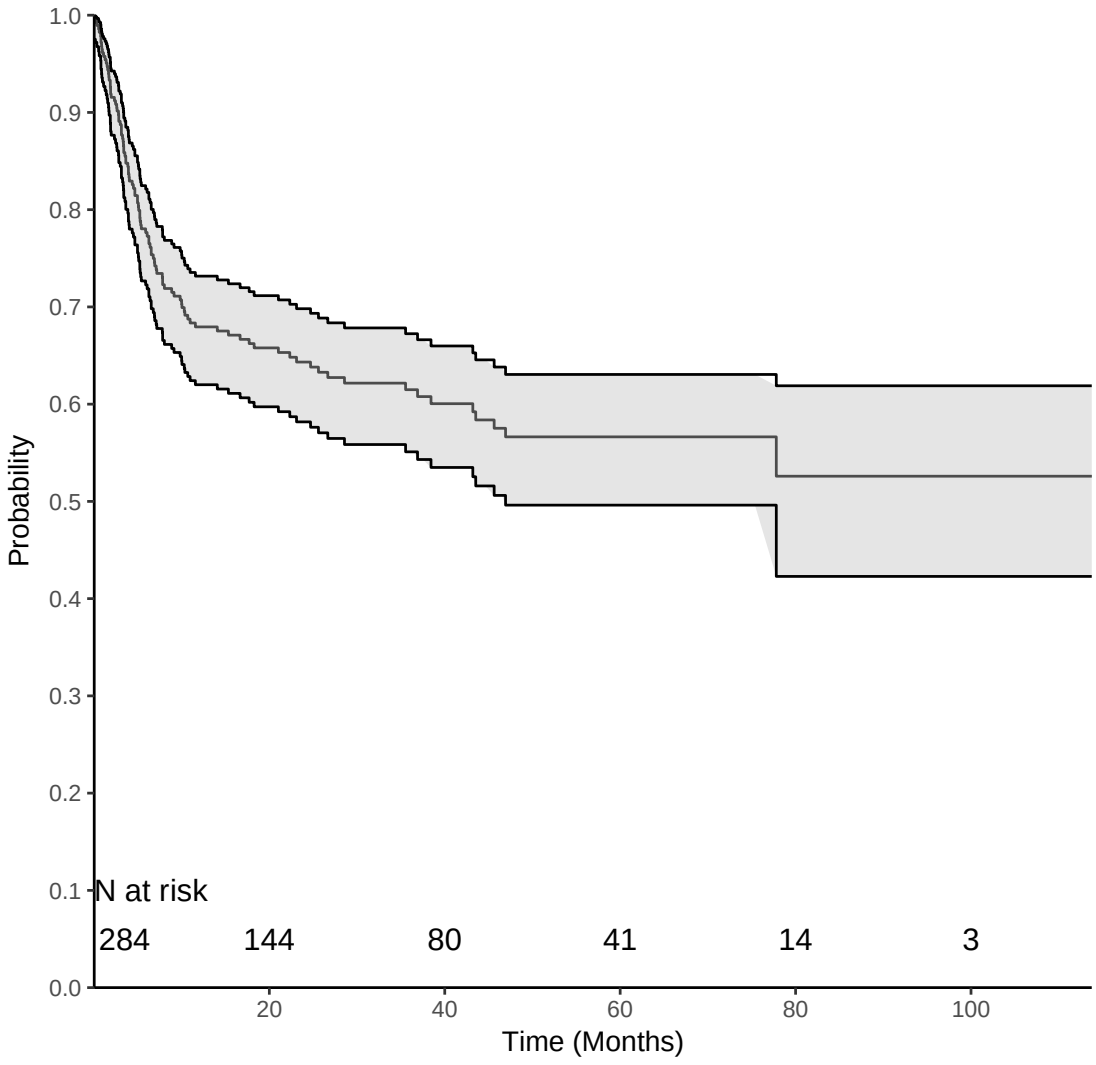

Figure 1: Overall survival

PFS at 1 year was 0.37 (95 % 0.31 - 0.44), was 0.34 (95 % 0.28 - 0.41) at 2 years. PFS at 4 years was 0.33 (95 % 0.27 - 0.4).

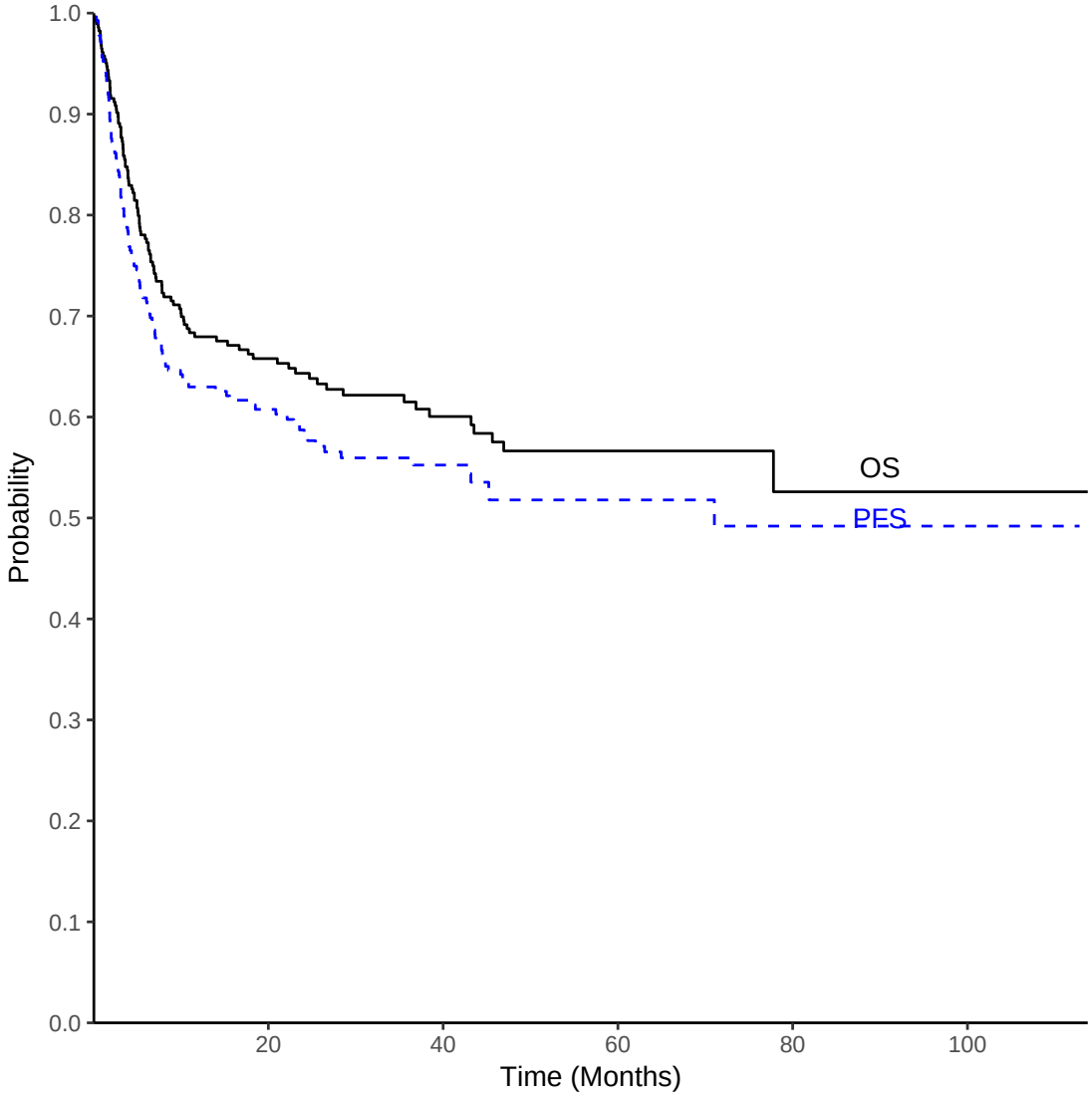

Figure 2: Progression-free survival

CIF for relapse/progression at 1 years was 0.18 (95 % 0.13 - 0.23), at 2 years 0.19 (95 % 0.15 - 0.24). CIF for death without relapse or progression at 1 year was 0.19 (95 % 0.14 - 0.24), at 2 years 0.22 (95 % 0.17 - 0.27).

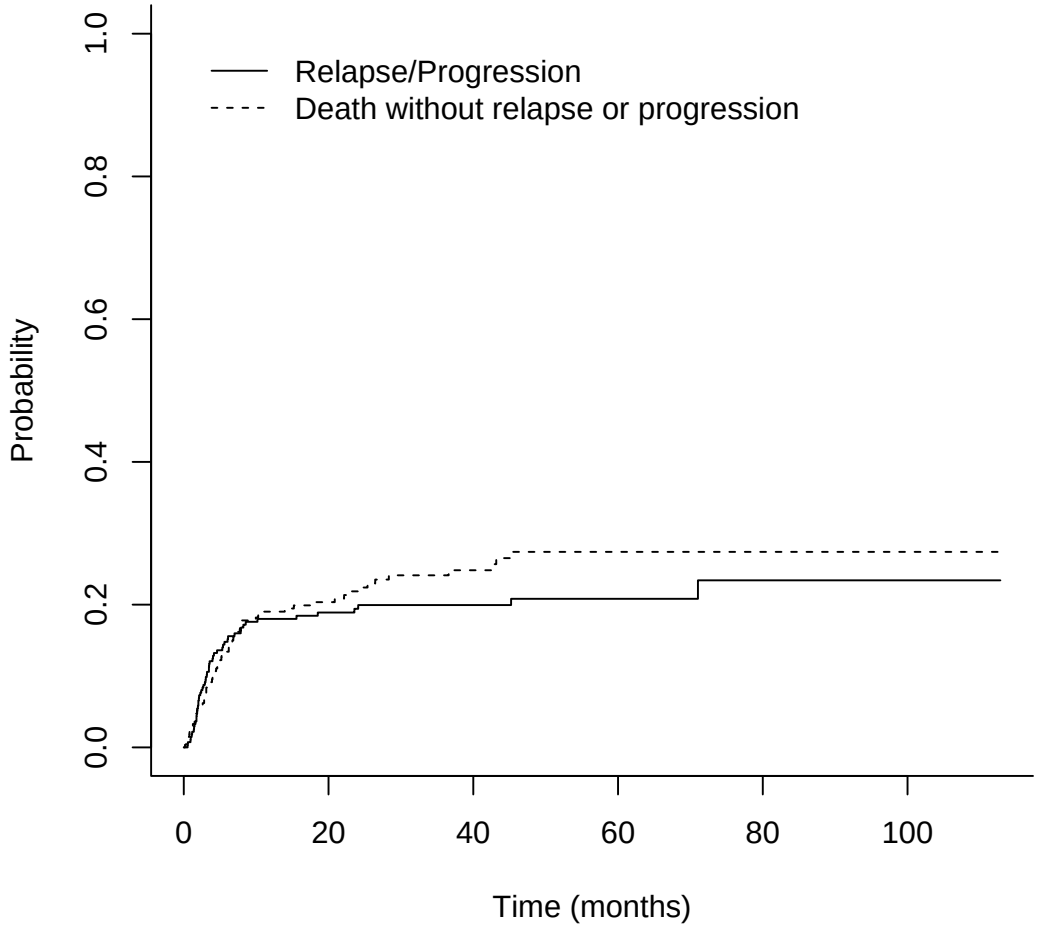

Figure 3: CIF of relapse or progression and death without relapse or progression

CIF for related HSCT death at 1 years was 0.2, at 2 years 0.23. CIF for non-related HSCT Death at 1 year was 0.12, at 2 years 0.13.

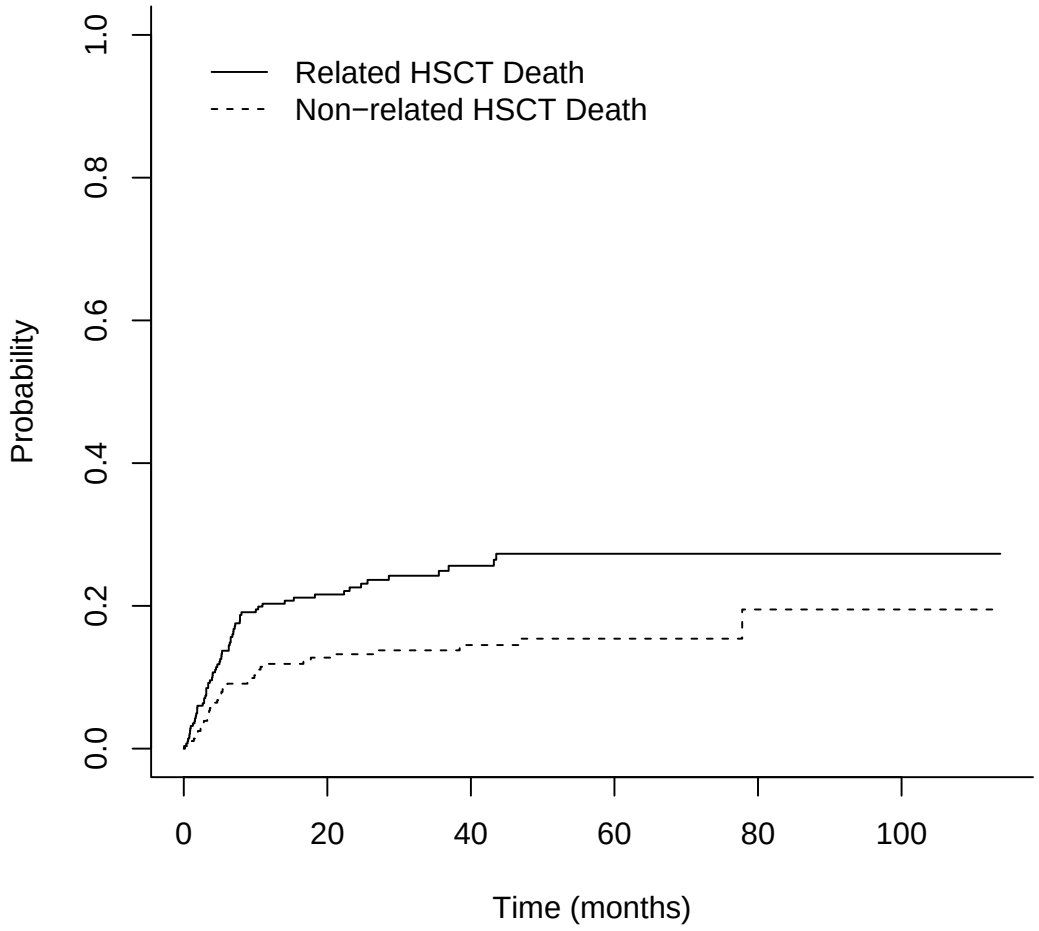

Figure 4: CIF of Related HSCT Death and Non-related HSCT Death

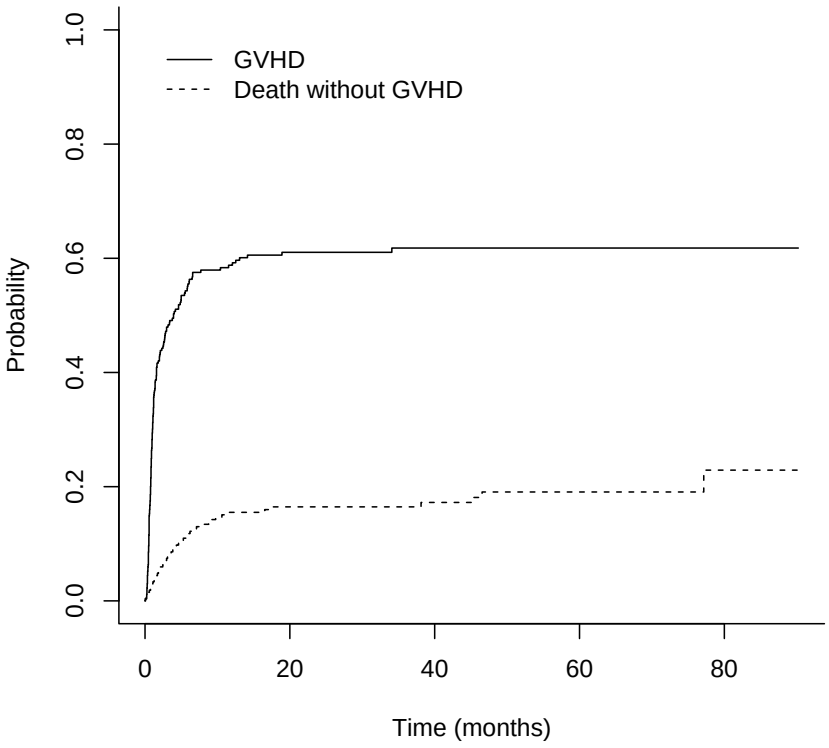

Figure 5: CIF of GVHD and Death without GVHD

3.3 Survival analysis after a complete remisson post alloSCT

245 patients whith a complete remission were included.

OS at 1 year was 0.74 (95 % 0.68 - 0.8), was 0.7 (95 % 0.64 - 0.76) at 2 years. OS at 4 years was 0.62 (95 % 0.56 - 0.7).

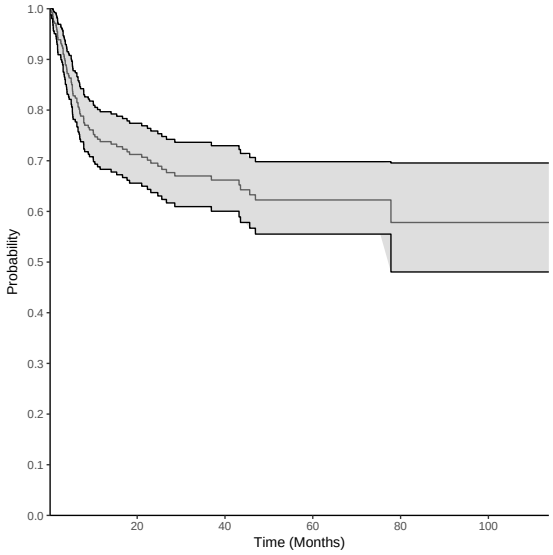

Figure 6: OS in patients with a complete remission post alloSCT

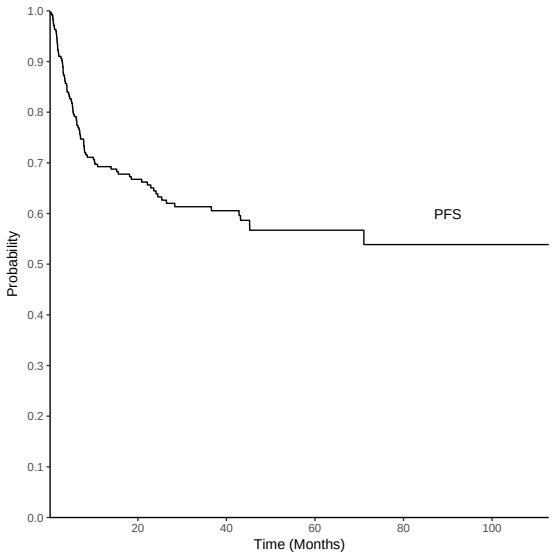

Figure 7: PFS in patients with a complete remission post alloSCT

CIF for relapse at 1 year was 0.12 (95 % 0.07 - 0.16), at 2 years 0.13 (95 % 0.09 - 0.18). CIF for death without relapse at 1 year was 0.19 (95 % 0.14 - 0.24), at 2 years 0.22 (95 % 0.17 - 0.28).

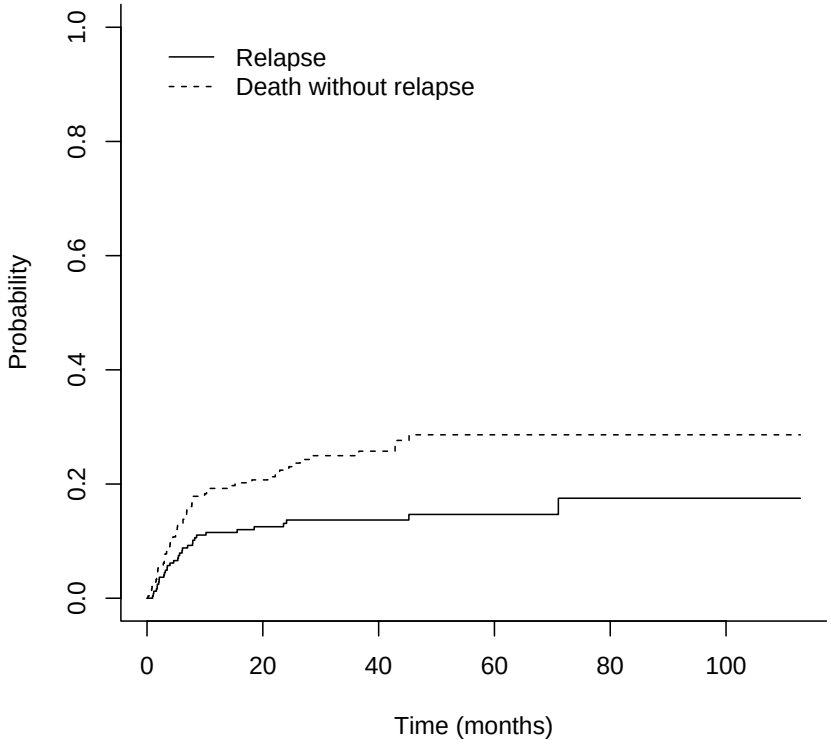

Figure 8: CIF of relapse and death without relapse (in patients with a complete remission post alloSCT)

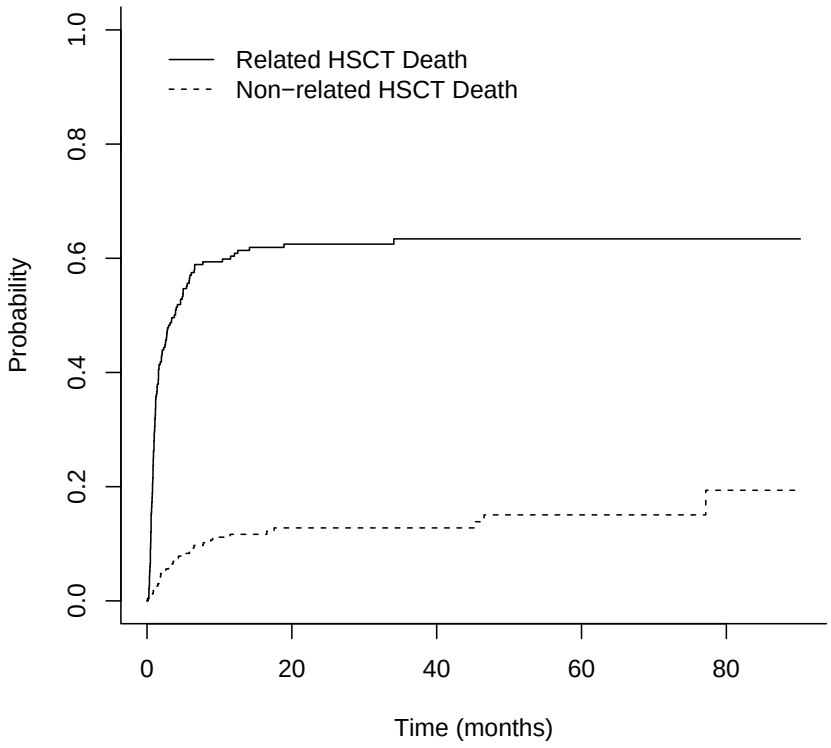

Figure 9: CIF of Related HSCT Death and Non-related HSCT Death (in patients with a complete remission post alloSCT)

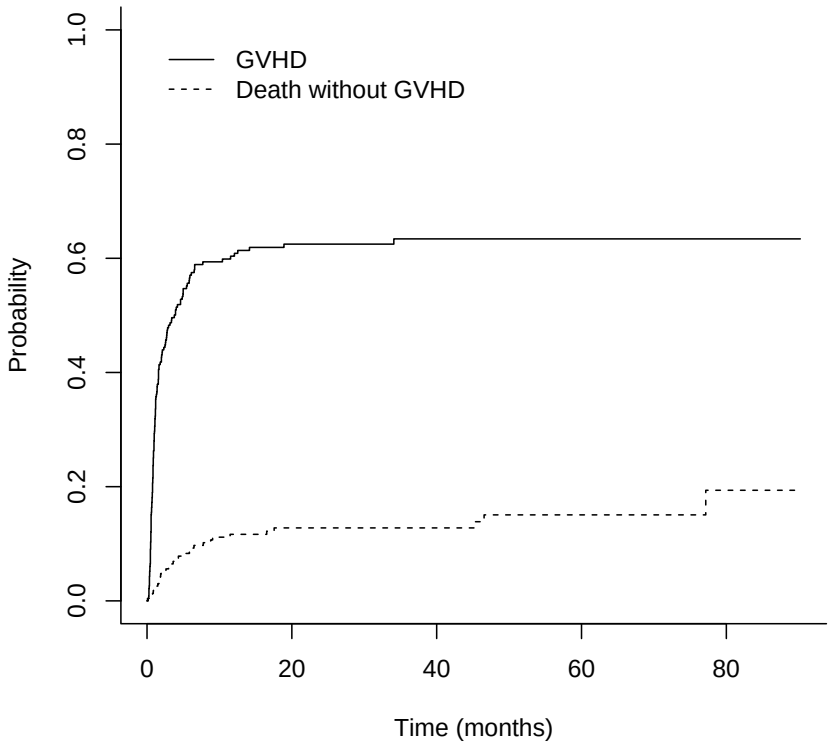

Figure 10: CIF of GVHD and Death without GVHD (in patients with a complete remission post alloSCT)