GRUPPO DI LAVORO COMMISSIONE GITMO – MUD:
Secondi Trapianti Allogenici

Dr. Simona Piemontese
IRCCS Ospedale San Raffaele, Milano - UTMO

2nd allo da UD? → PASSAGGIO DALLA COMMISSIONE ALLOGENICO

Italian Bone Marrow Donor Registry

Form CT309 (V 6 2/4 agosto 2021)

WMDA Accredited

Richiesta di ***ulteriore*** *donazione (post-trapianto)*

INFORMAZIONI RELATIVE AL I TRAPIANTO:

Numero di trapianti precedenti:

Data dell'ultimo trapianto:

Manipolazione (es : deplezione cellule T, rimozione plasma etc.)

Sorgente di CSE utilizzata per il precedente trapianto:

☐ Sangue Midollare ☐ PBSC ☐ Cord Blood

Dose cellulare infusa al paziente:	Midollo x 10^8 / kg (MNC)	PBSC x 10^6 / kg (CD34+)
Regime di condizionamento:	Mieloablativo ☐	Intensità ridotta ☐

[redacted]

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Richiesta di ***ulteriore*** *donazione (post-trapianto)*

STATO CLINICO ATTUALE DEL PAZIENTE:

Valutazione clinica: (principali dettagli) .....

Attuale terapia: .....

Se il paziente assume terapia immunosoppressiva, specificare:

Data inizio del tapering:..... Data prevista sospensione:.....

Precisare se il paziente è in terapia intensiva (specificare, es: ventilazione, dialisi etc..):

.....

STATO CLINICO ATTUALE DEL PAZIENTE (TEST DI LABORATORIO):

Inserire i valori solo se al di fuori della norma

[redacted]

Italian Bone Marrow Donor Registry

Form CT309 (V6 4/4 agosto 2021)

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Richiesta di ***ulteriore*** *donazione (post-trapianto)*

INFORMAZIONI RELATIVE AL NUOVO TRAPIANTO DI CSE PROGRAMMATO:

Trattamento previsto al paziente (specificare date):

E' prevista manipolazione?: ☐ SI ☐ NO

Se sì, descrivere brevemente la manipolazione prevista:

Profilassi per la GVHD:

E' disponibile un back-up autologo? ☐ SI ☐ NO

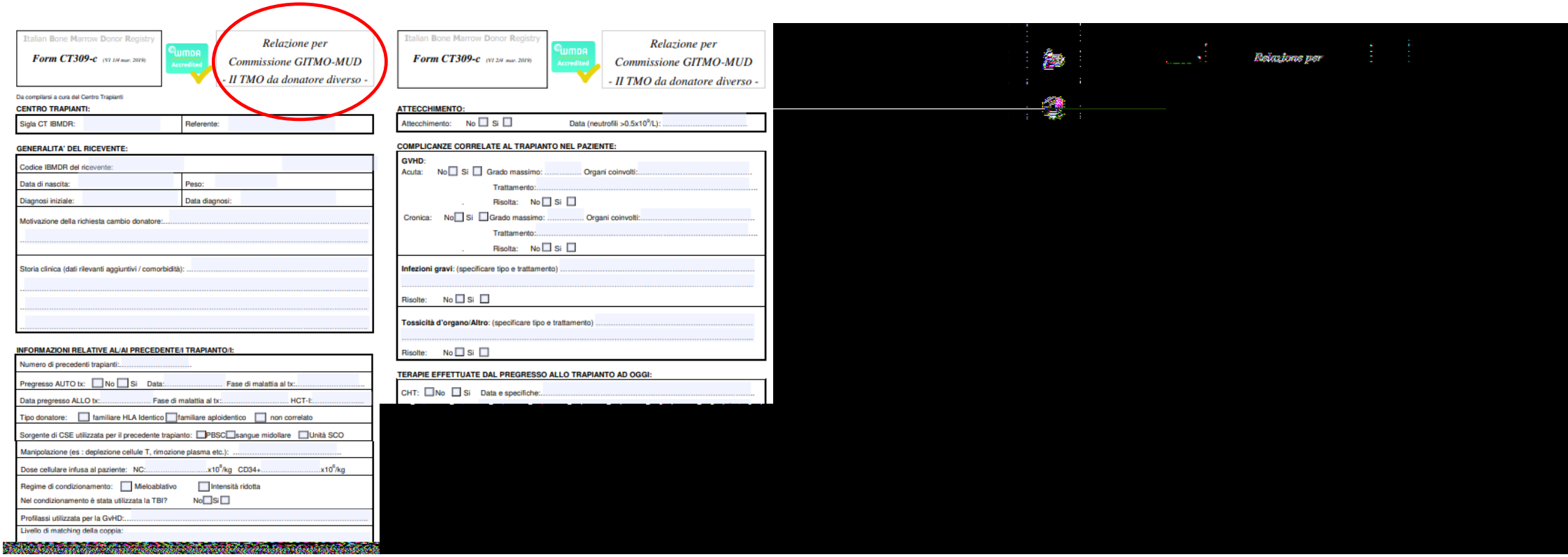
Si dispone di un donatore famigliare di back up? ☐ SI ☐ NO

Si dispone di un donatore non famigliare (adulto/SCO) di back up? ☐ SI ☐ NO

Ulteriori informazioni disponibili:

[redacted]

2nd allo da UD? → PASSAGGIO DALLA COMMISSIONE ALLOGENICO



Italian Bone Marrow Donor Registry

Form CT309-c (V1 1/4 mar. 2019)

WMDA Accredited

Relazione per
Commissione GITMO-MUD
- Il TMO da donatore diverso -

Da compilarsi a cura del Centro Trapianti

CENTRO TRAPIANTI:

Sigla CT IBMDR: | Referente:

GENERALITA' DEL RICEVENTE:

Codice IBMDR del ricevente:

Data di nascita: | Peso:

Diagnosi iniziale: | Data diagnosi:

Motivazione della richiesta cambio donatore:

Storia clinica (dati rilevanti aggiuntivi / comorbidità):

INFORMAZIONI RELATIVE AL/AI PRECEDENTE/I TRAPIANTO/I:

Numero di precedenti trapianti:

Pregresso AUTO tx: ☐ No ☐ Si Data: Fase di malattia al tx:

Data pregresso ALLO tx: Fase di malattia al tx: HCT-I:

Tipo donatore: ☐ familiare HLA Identico ☐ familiare aploidentico ☐ non correlato

Sorgente di CSE utilizzata per il precedente trapianto: ☐ PBSC ☐ sangue midollare ☐ Unità SCO

Manipolazione (es : deplezione cellule T, rimozione plasma etc.):

Dose cellulare infusa al paziente: NC: x10^6/kg CD34+ x10^6/kg

Regime di condizionamento: ☐ Mieloablativo ☐ Intensità ridotta

Nel condizionamento è stata utilizzata la TBI? No ☐ Si ☐

Profilassi utilizzata per la GvHD:

Livello di matching della coppia:

Italian Bone Marrow Donor Registry

Form CT309-c (V1 2/4 mar. 2019)

WMDA Accredited

Relazione per
Commissione GITMO-MUD
- Il TMO da donatore diverso -

ATTECCHIMENTO:

Attecchimento: No ☐ Si ☐ Data (neutrofili >0.5x10^9/L):

COMPLICANZE CORRELATE AL TRAPIANTO NEL PAZIENTE:

GVHD:

Acuta: No ☐ Si ☐ Grado massimo: Organi coinvolti:

Trattamento:

Risolta: No ☐ Si ☐

Cronica: No ☐ Si ☐ Grado massimo: Organi coinvolti:

Trattamento:

Risolta: No ☐ Si ☐

Infezioni gravi: (specificare tipo e trattamento)

Risolte: No ☐ Si ☐

Tossicità d'organo/Altro: (specificare tipo e trattamento)

Risolte: No ☐ Si ☐

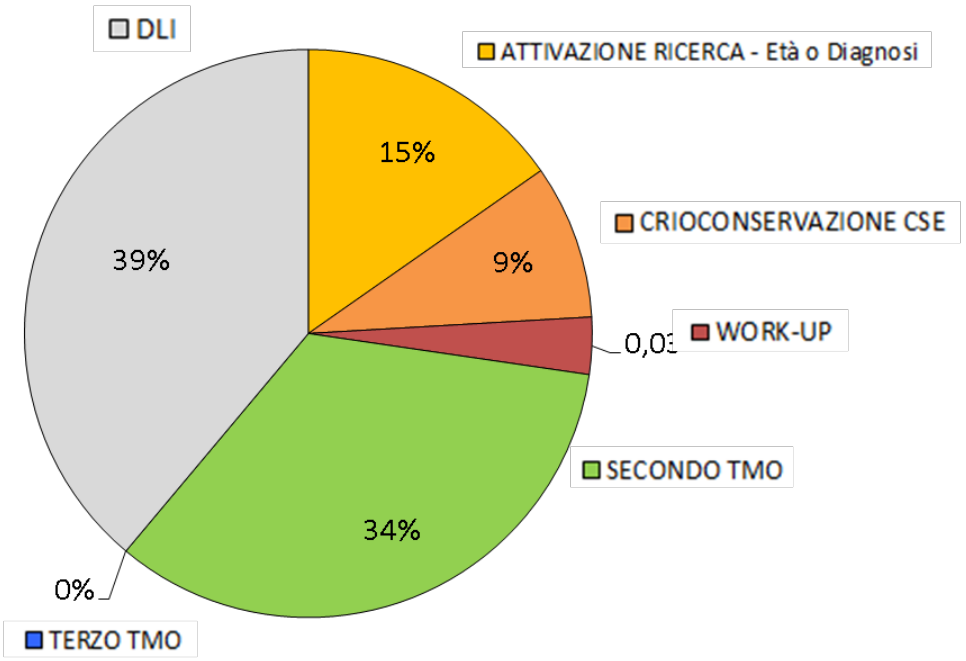
TERAPIE EFFETTUATE DAL PREGRESSO ALLO TRAPIANTO AD OGGI:

CHT: ☐ No ☐ Si Data e specifiche:

Relazione per

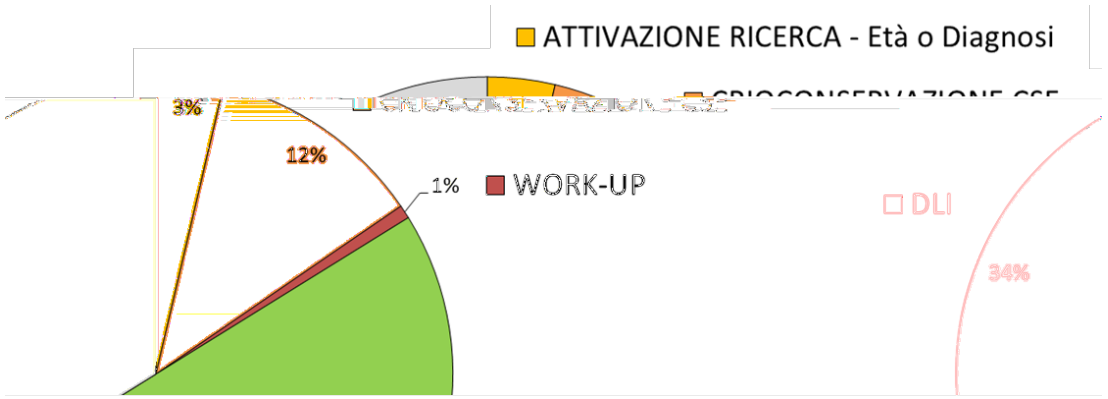
Causa di attivazione della Commissione per Pazienti italiani: differenze 2019 - 2022

2019



n=216

2022



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Courtesy of IBMDR- Dr.ssa Simona Pollichieni

PERCHè PENSARE AL SECONDO allo-SCT?

- "Several studies have shown that relapsed AML postallografting is generally associated with poor outcomes with a reported median survival of ~3 months" *(Bone Marrow Transplantation (2020) 55:325–331)*

- "The survival of ALL patients who relapse after an allo-HCT remain poor, with long-term leukaemia-free survival (LFS) <10%"

  (Fielding et al, 2007; Spyridonidis et al, 2012).

- "Relapse is still a major cause of failure after alloHSCT for lymphoma, and in the absence of effective salvage options in this situation these patients have a poor outlook"

  (Bone Marrow Transplantation (2015) 50, 790–794)

COSA VALUTIAMO QUANDO PENSIAMO A UN SECONDO allo-SCT?

- Quali pazienti candidare?
- Intensità del regime di condizionamento?
- C’è un vantaggio nel cambiare donatore?

COSA VALUTIAMO QUANDO PENSIAMO A UN SECONDO allo-SCT?

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COSA CI DICE LA LETTERATURA?

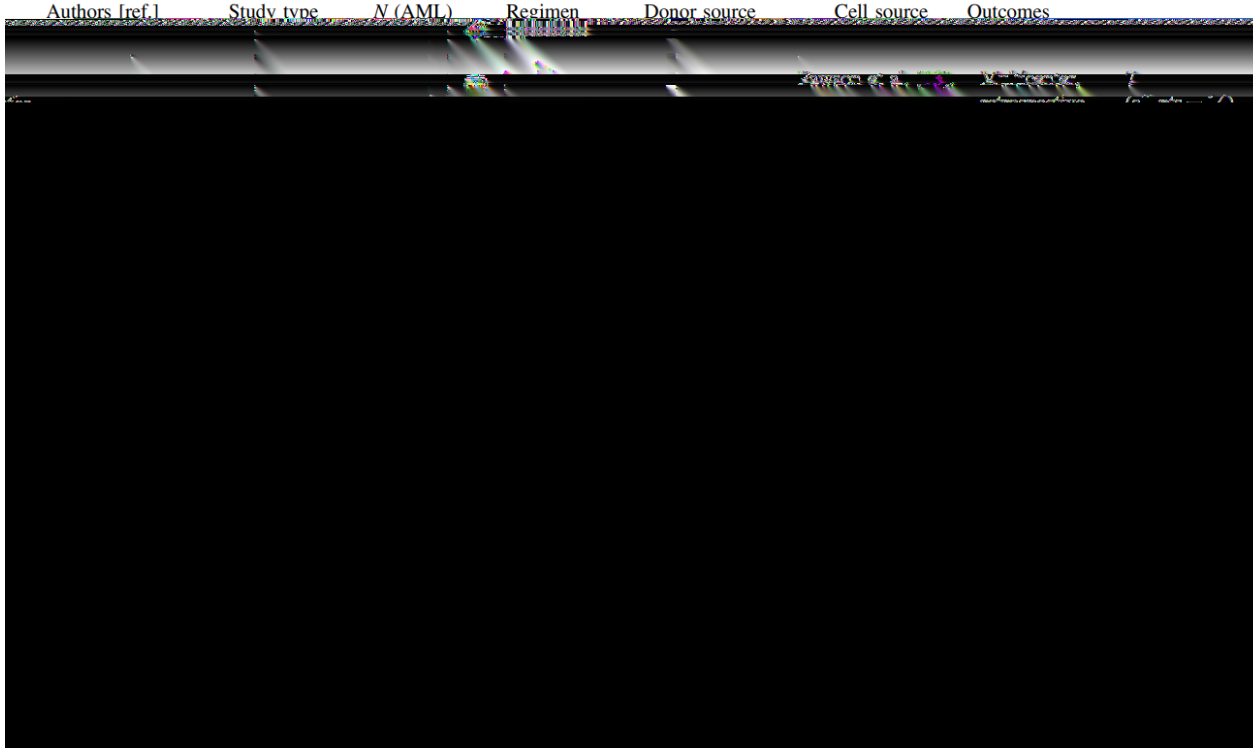
No RCT has ever been conducted comparing the efficacy of a second allo-HCT against other treatments. Available published data are mainly from observational studies (single or multi-institution) or registry data.

Bone Marrow Transplantation (2020) 55:325–331

SECONDO allo-SCT in AML: single institution or multicenter studies

Table 1 Selected single institutions or multicenter studies evaluating a second allo-HCT in relapsed AML

Authors [ref.]	Study type	*N* (AML)	Regimen	Donor source	Cell source	Outcomes



→ 1995-1999

→ 2000-2010, AML

→ 1979-2011, AML, MDS, MPN

→ 2002-2015, AML e ALL

→ 1980-2016, AML, ALL, AA, CML

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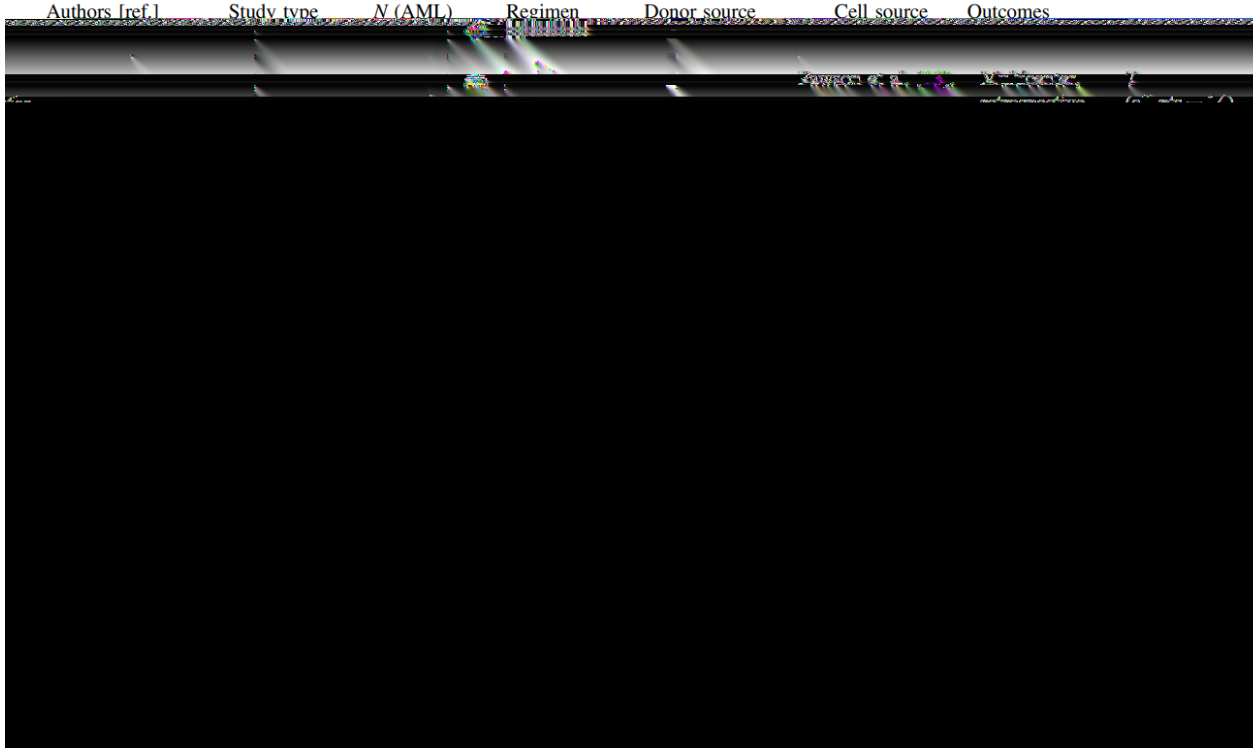

- 1995-1999
- 2000-2010, AML
  Age <65y, 1st allo – Rel > 12mo,
- 1979-2011, AML, MDS, MPN
  CR e 1st allo- 2nd allo ≥ 430gg
- 2002-2015, AML e ALL
  CR, allo-allo > 6mo, cGvHD post 2nd allo
- 1980-2016, AML, ALL, AA, CML
  1st allo – Rel/BM failure > 12mo

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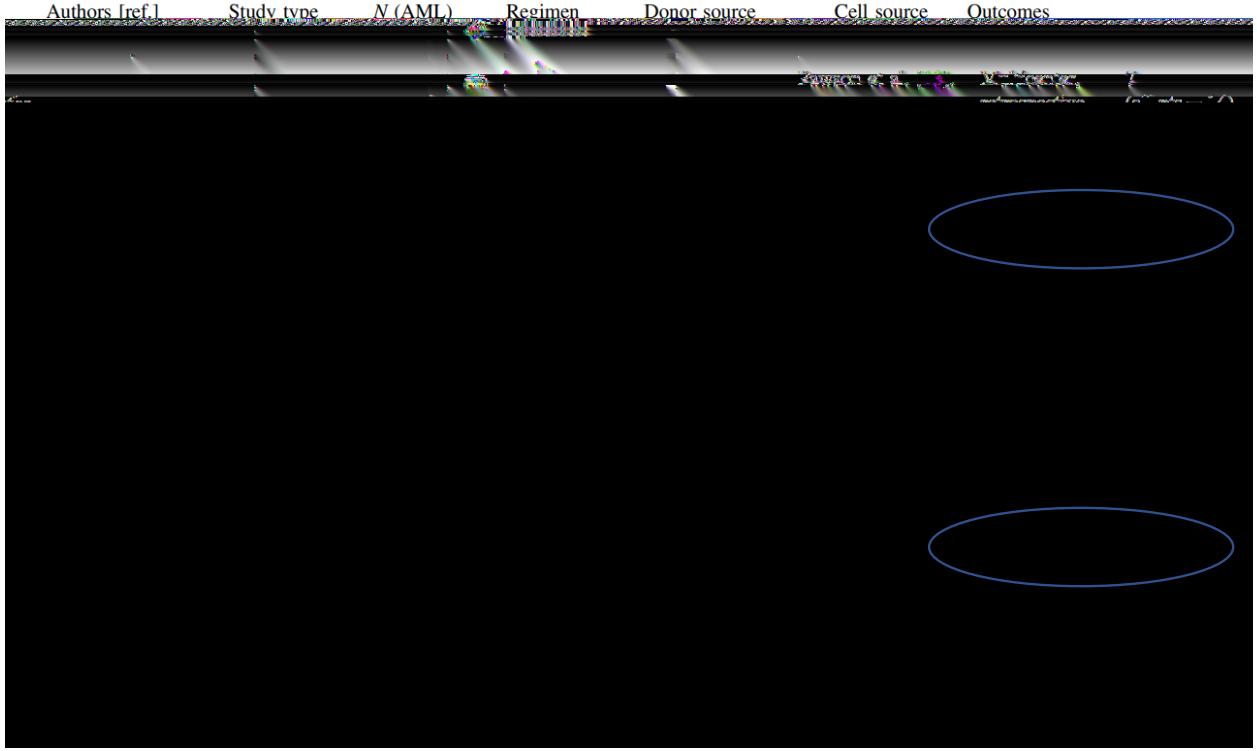

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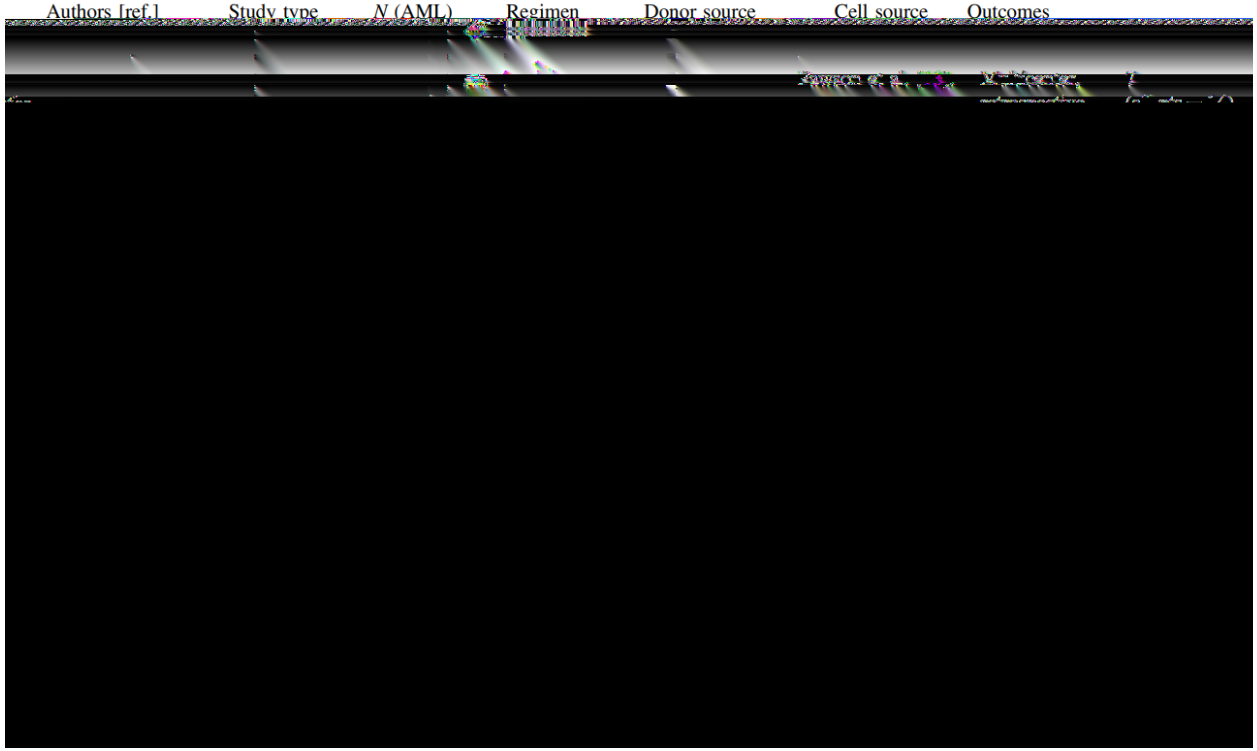

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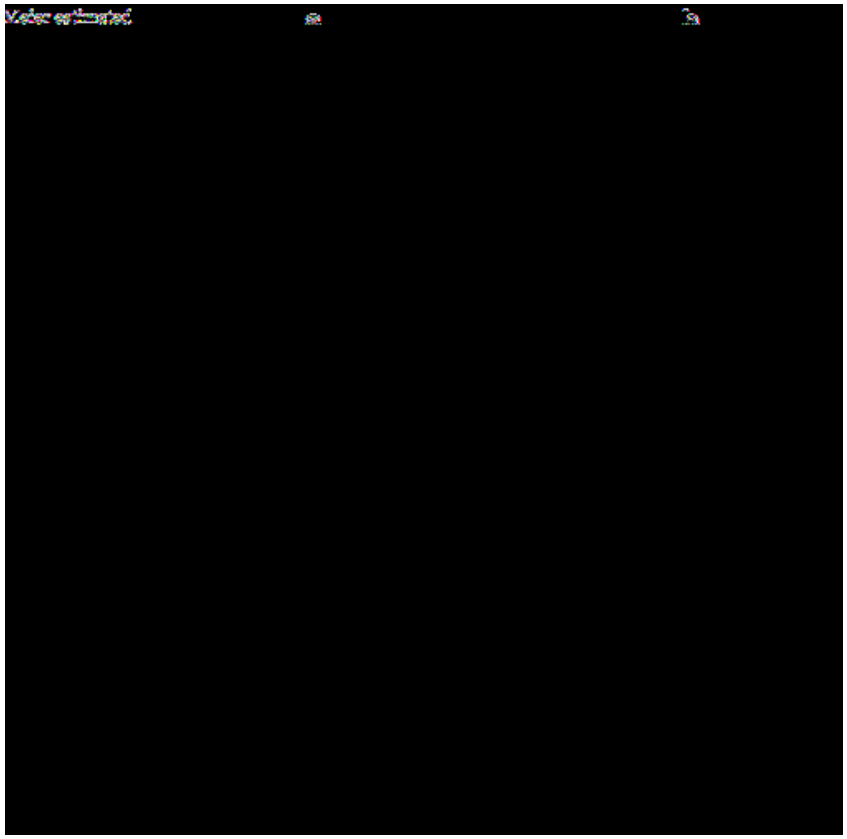
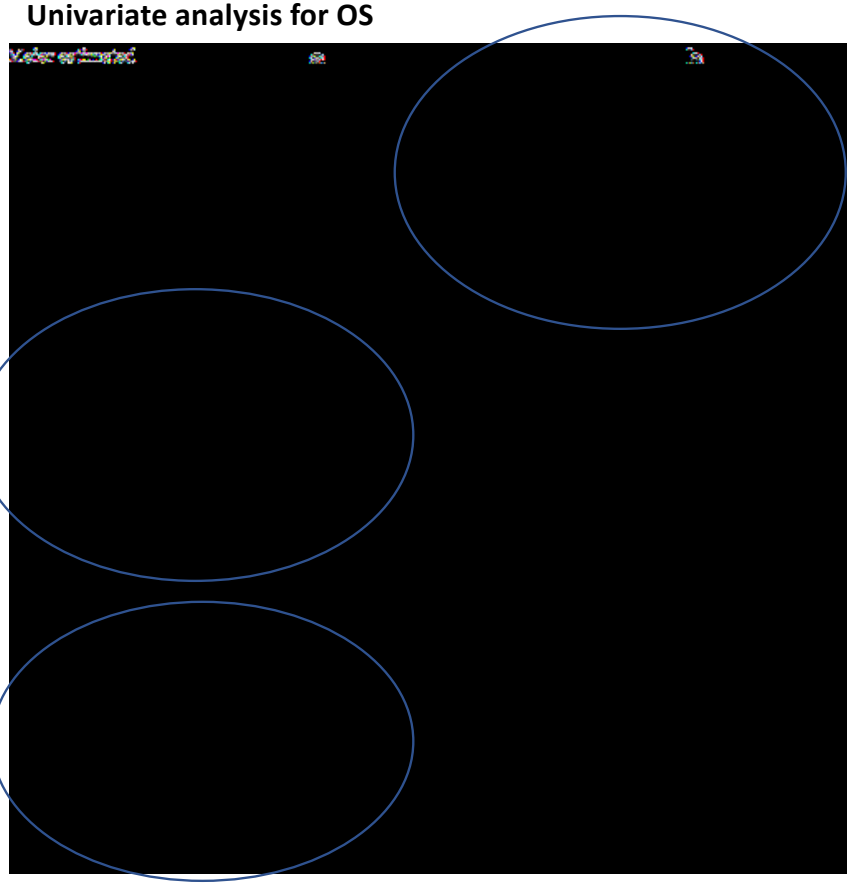
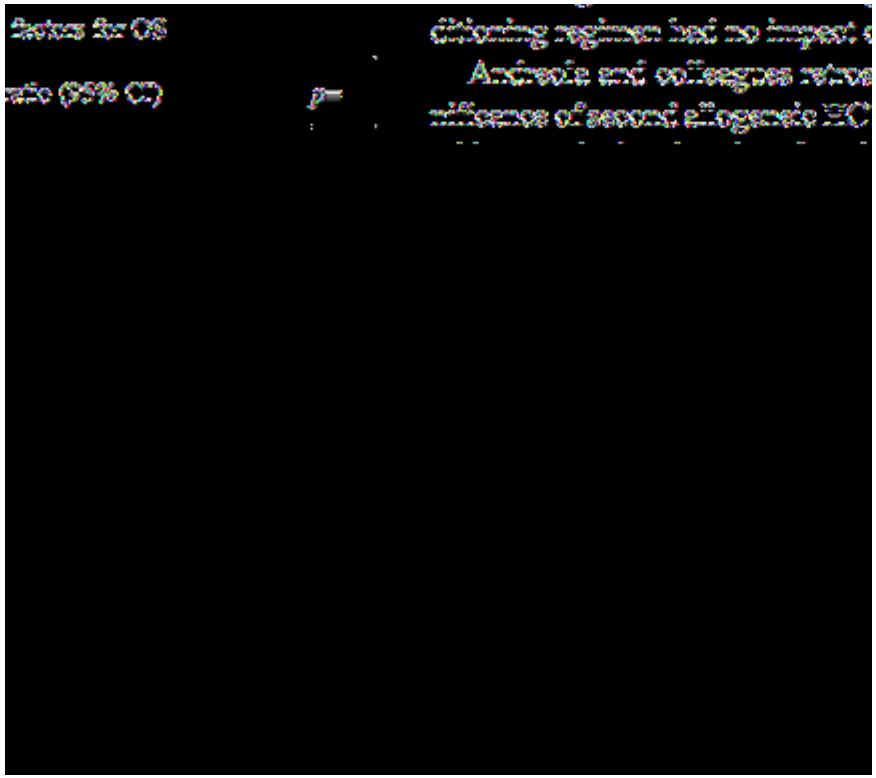
Univariate analysis for OS



Schneidawind C et al., Annals of Hematology (2018) 97:2491–2500

Univariate analysis for OS





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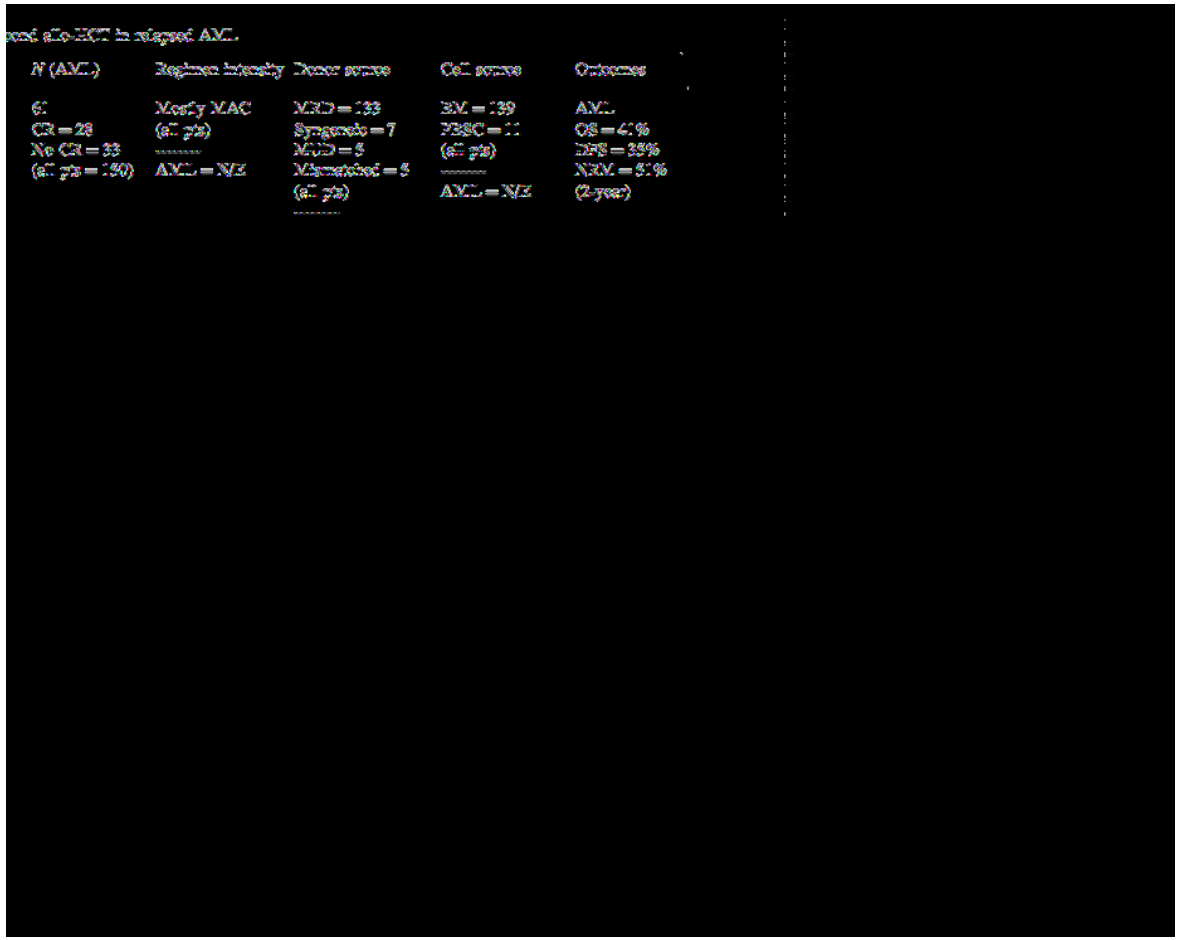
SECONDO allo-SCT in AML: registries studies



→ 1984-1996, AML, ALL, CML

→ 1983-2000, AML

→ pub 2008, AML, MDS, MPN, ALL, CML, NHL, MPN, MM

→ 1994-2009, all diseases

→ 1990-2010, AML

→ 2015-2017, AML

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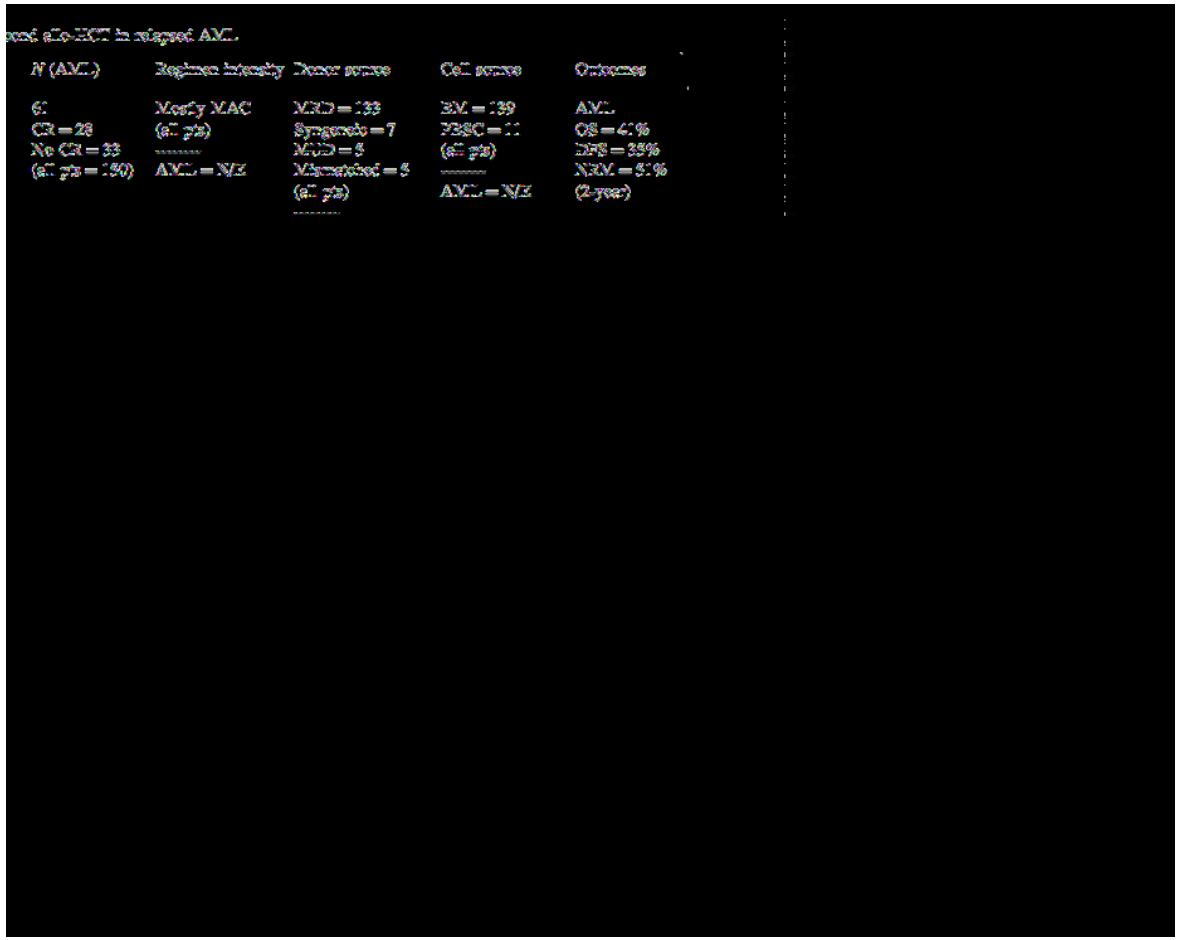
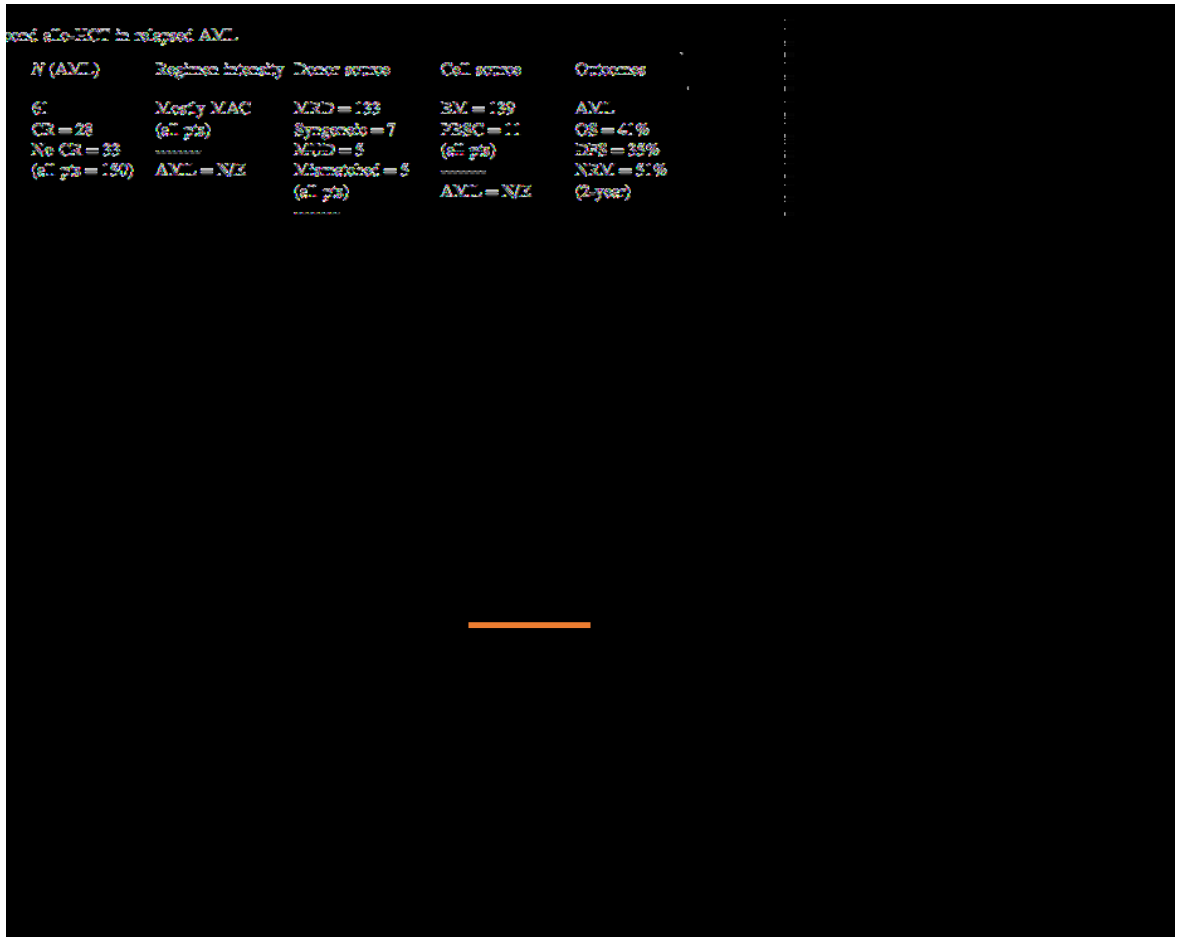


- 1984-1996, AML, ALL, CML
  1st allo – Rel > 12mo, age <16y, cGvHD post 2nd allo
- 1983-2000, AML
  1st allo – Rel > 6mo, CR
- pub 2008, AML, MDS, MPN, ALL, CML, NHL, MPN, MM
  No RF
- 1994-2009, all diseases
  CR, 1st allo – Rel > 4mo, cGvHD post 2nd allo …
- 1990-2010, AML
  1st allo – Rel > 6mo, age < 41y
- 2015-2017, AML
  1st allo – Rel > 6mo, CR

SECONDO allo-SCT in AML: registries studies



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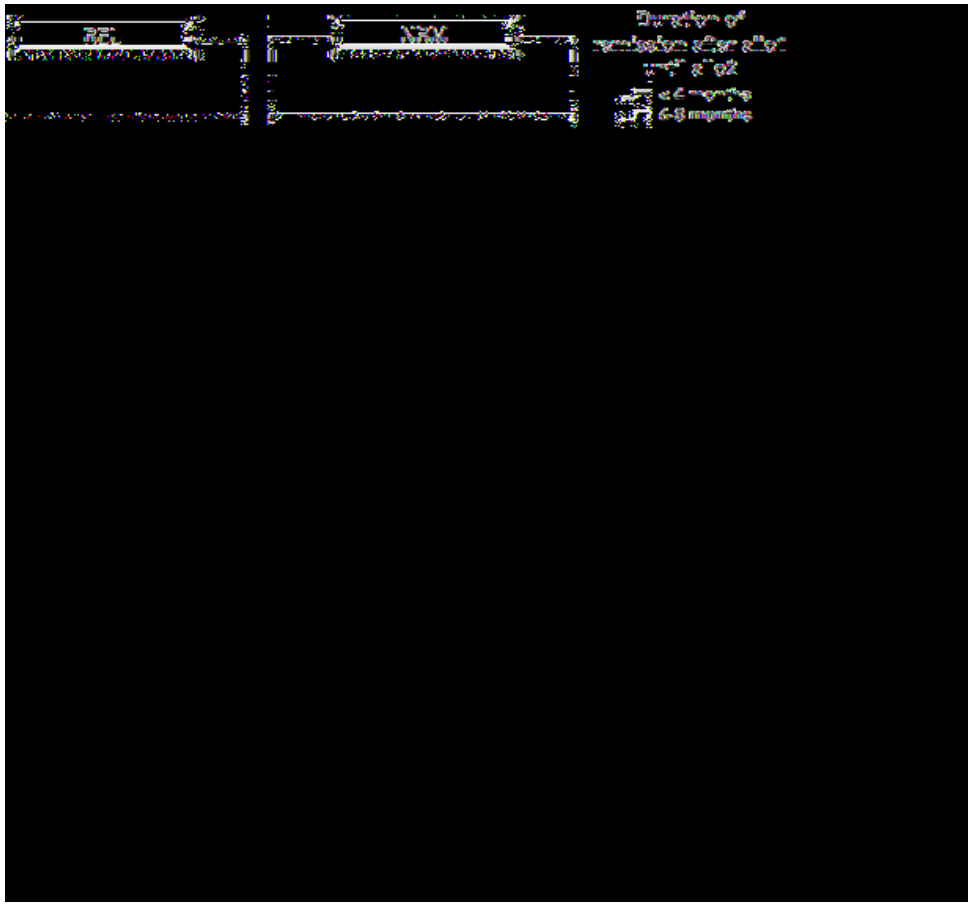
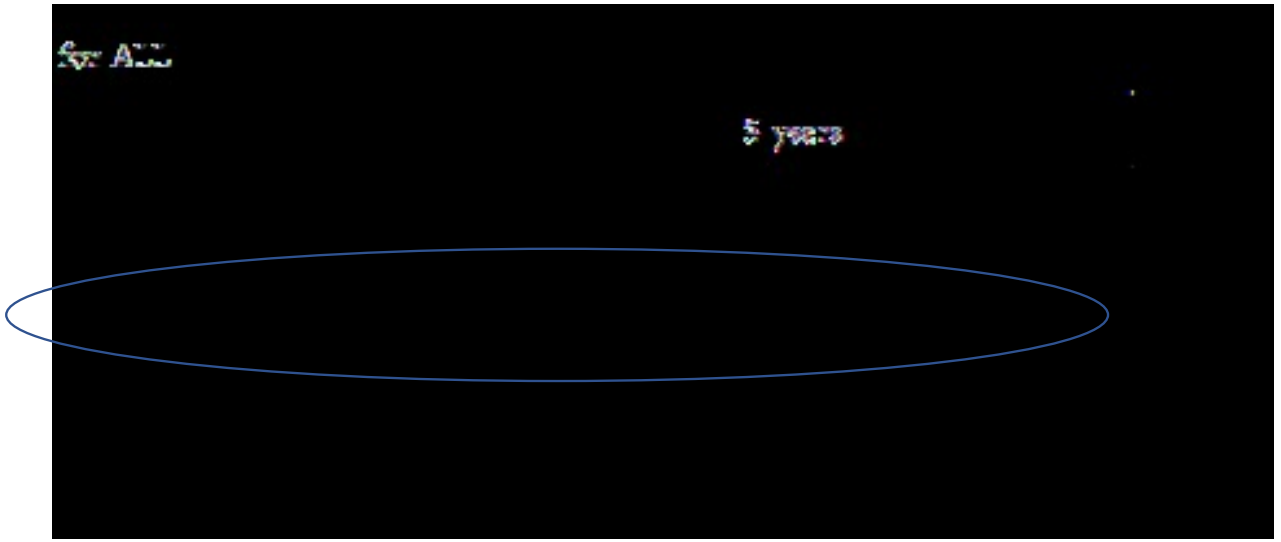


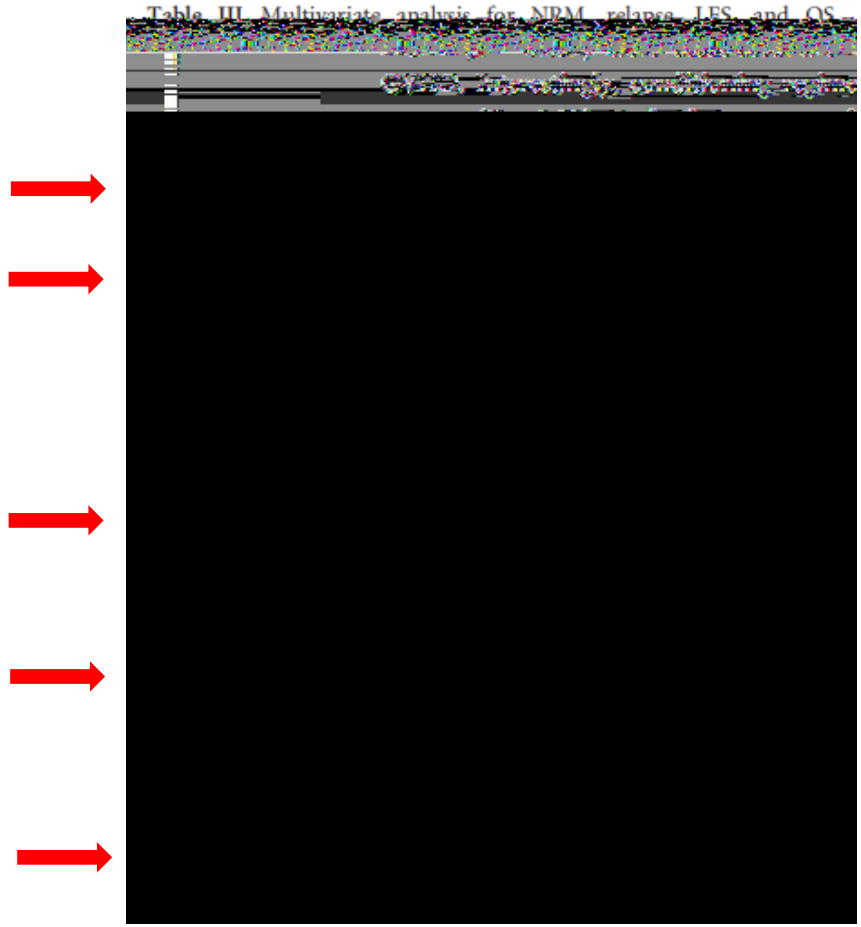
Ruutu T, et al. Bone Marrow Transplantation (2015) 50, 1542–1550

SECONDO allo-SCT in ALL: dati EBMT, 2000-2017, 245 pts



Nagler et al. BJH, 2019: 245pz dal 2000 al 2017

SECONDO allo-SCT in ALL: dati EBMT, 2000-2017, 245 pts



Time 1st allo – Rel: per mese

Nagler et al. BJH, 2019: 245pz dal 2000 al 2017

SECONDO allo-SCT in ALL: dati EBMT, 2000-2017, 245 pts

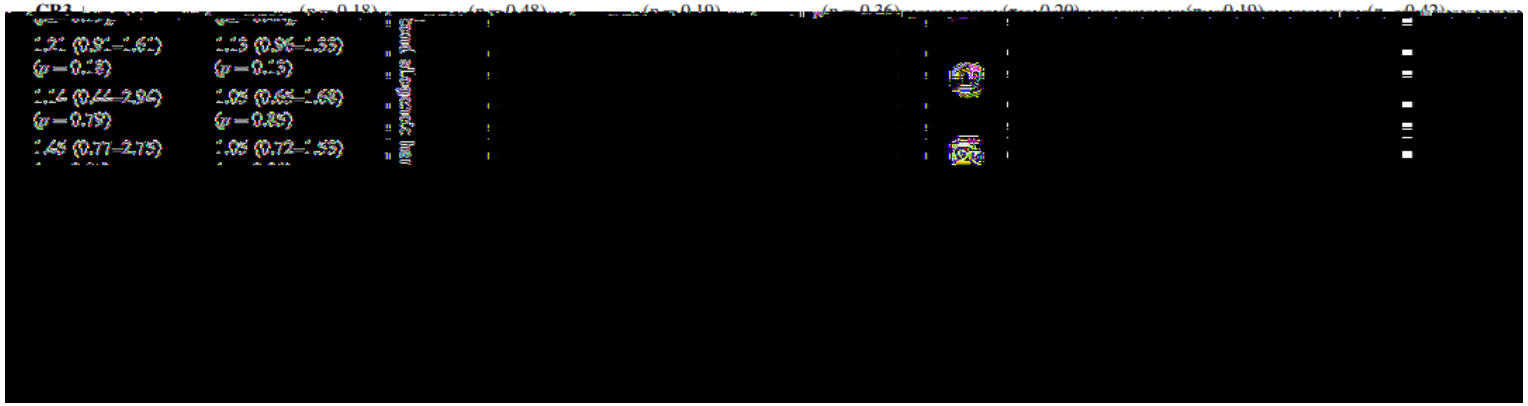
2y OS CR vs no CR
33 vs 23% p 0.001
in analisi univariata

Associazione tra CR e time to 2nd allo

Nagler et al. BJH, 2019: 245pz dal 2000 al 2017

Table 3 Multivariable analysis.

	OS HR (95%CI) (*P*-value)	LFS HR (95%CI) (*P*-value)	RI HR (95%CI) (*P*-value)	NRM HR (95% CI) (*P*-value)	Acute GVHD (Grade 2–4) HR (95%CI) (*P*-value)	Chronic GVHD (Any grade) HR (95%CI) (*P*-value)	GRFS HR (95% CI) (*P*-value)
Haploidentical vs. MUD	0.69 (0.4–1.17) ($p = 0.17$)	0.82 (0.51–1.32) ($p = 0.41$)	0.74 (0.41–1.34) ($p = 0.32$)	0.98 (0.45–2.14) ($p = 0.96$)	1.23 (0.57–2.67) ($p = 0.60$)	0.77 (0.35–1.69) ($p = 0.52$)	0.77 (0.49–1.21) ($p = 0.25$)
Active disease vs. CR2/ CR3	1.40 (0.86–2.29)	1.18 (0.75–1.85)	1.45 (0.83–2.55)	0.82 (0.37–1.82)	1.4 (0.68–2.88)	1.68 (0.77–3.67)	1.20 (0.78–1.84)



M. A. Kharfan-Dabaja et al.

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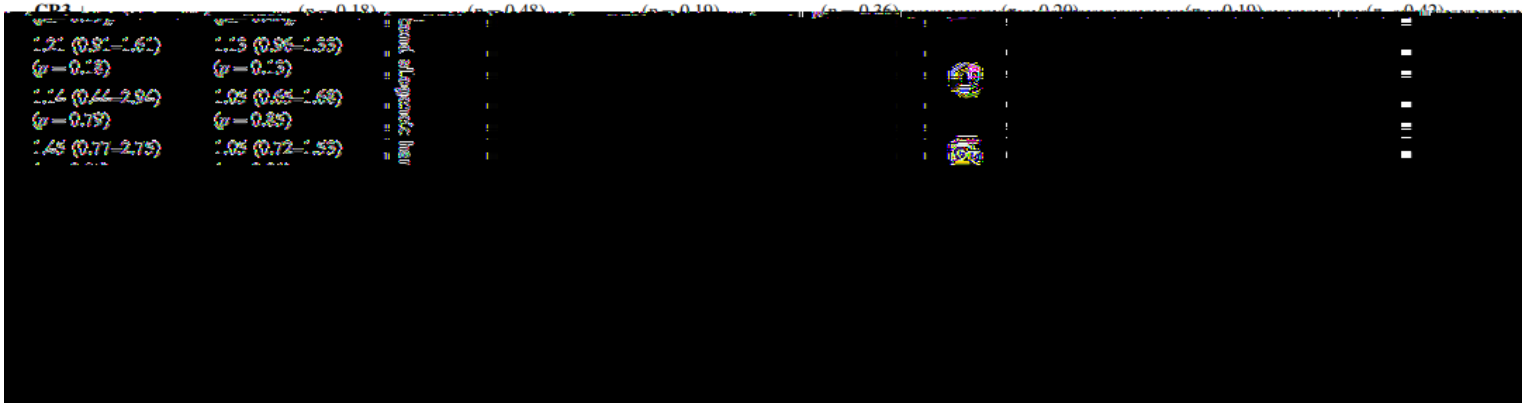


We identified a ≤ 6 months cutoff, from first allo-HCT to relapse, as the threshold to define high risk patients undergoing a second allo-HCT

1- year LFS 5% vs. 49%, p = 0.001
1-year OS 17% vs. 64%, p = 0.001
2-year OS 7% vs. 50%, p = 0.001

M. A. Kharfan-Dabaja et al.

Second allo-SCT in patients with lymphoma relapse after a first allogeneic transplantation. A retrospective study of the EBMT Lymphoma Working Party

K Korstmann, A Boumendil, J Finke, H Finel, E Kanfer, G Milone, N Russell , A Bacigalupo, Y Chalandon, JL Diez-Martin, N Ifrah, M Jurado Chacon and P Dreger

Table 2. Multivariate Cox proportional hazard model of PFS and OS

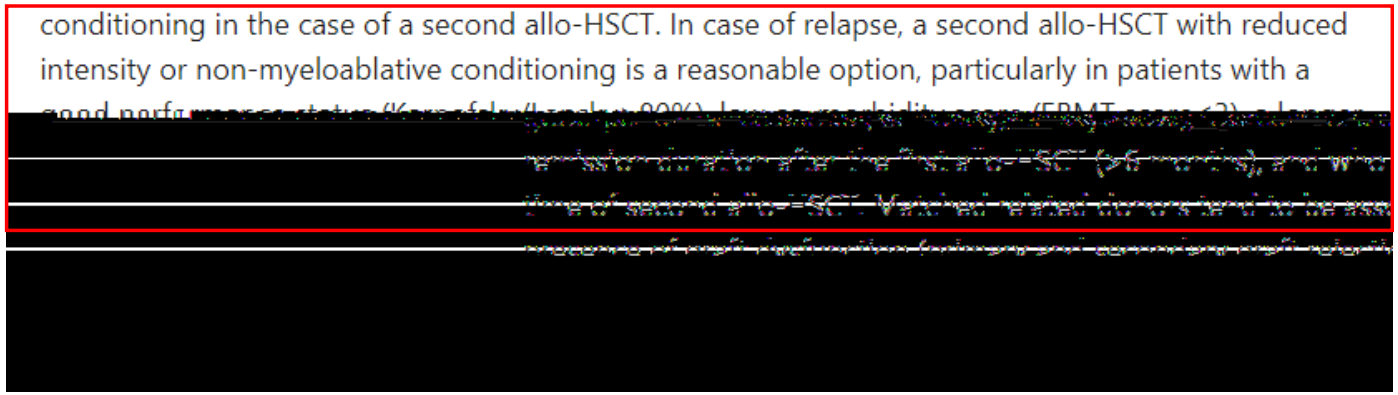
Endpoint	*Variable*	*Hazard ratio*	*Lower CL*	*Upper CL*	*P-value*
PFS					
	Interval alloHSCT_1 to alloHSCT_2 >12 months	0.63	0.41	0.97	0.034
	Disease status refractory or unknown at alloHSCT_2	1.60	1.04	2.45	0.033
	Unrelated donor	1.17	0.765	1.81	0.48
OS					
	Interval alloHSCT_1 to alloHSCT_2 >12 months	0.54	0.35	0.84	0.0065
	Disease status refractory or unknown at alloHSCT_2	1.51	0.98	2.32	0.064

K Korstmann, et al. Bone Marrow Transplantation (2015) 50, 790–794

2nd allo-SCT: line guida della SFGM

[Second allogeneic hematopoietic stem cell transplant: Guidelines from the francophone Society of bone marrow transplantation and cellular therapy (SFGM-TC)]

Disease recurrence and graft dysfunction after allogeneic hematopoietic stem cell transplantation (allo-HSCT) currently remain among the major causes of treatment failure in malignant and non-malignant hematological diseases. A second allo-HSCT is a valuable therapeutic option to salvage those situations. During the 8th annual harmonization workshops of the french Society of bone marrow transplantation and cellular therapy (SFGM-TC), a designated working group reviewed the literature in order to elaborate unified guidelines on feasibility, indications, donor choice and conditioning in the case of a second allo-HSCT. In case of relapse, a second allo-HSCT with reduced intensity or non-myeloablative conditioning is a reasonable option, particularly in patients with a



- 1st allo – Rel > 6 mo
- Low disease burden at 2nd allo-SCT
- PS > 80%
- EBMT score ≤ 3

Yafour N, et al. Bull Cancer. 2019 Jan;106(1S):S40-S51.

COSA VALUTIAMO QUANDO PENSIAMO A UN SECONDO allo-SCT?

- Quali pazienti candidare?

- Tempo 1st allo-SCT – Recidiva > 6 mesi
- Leucemie acute in remissione, Linfomi non in progressione
- Pazienti con PS > 80%

- Intensità del regime di condizionamento?

- C'è un vantaggio nel cambiare donatore?

COSA VALUTIAMO QUANDO PENSIAMO A UN SECONDO allo-SCT?

- Quali pazienti candidare?
- Intensità del regime di condizionamento?
- C’è un vantaggio nel cambiare donatore?

C’è UN VANTAGGIO UTILIZZANDO UN NUOVO DONATORE?

- No benefit in changing *(Bone Marrow Transplantation (2020) 55:325–331)*
- No improvement but not detrimental *(J Clin Oncol. 2013 Sep 10;31(26):3259-71)*
- Same donor increase aGvHD 2-4, a different donor is associated with better GRFS e NRM *(BJH, 2019: 245pz dal 2000 al 2017)*
- An allograft with a new mismatched haplotype may improve outcomes after second BMTs for relapsed hematologic malignancies *(Biol Blood Marrow Transplant 23 (2017) 1887–1894)*

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- Incidence of HLA Loss in a Global Multicentric Cohort of Post-Transplantation Relapses: Results from the Hlaloss Collaborative Study *(Blood, Volume 132, Supplement 1, 29 November 2018, Page 818)*

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- No improvement but not detrimental *(J Clin Oncol. 2013 Sep 10;31(26):3259-71)*
- Same donor increase aGvHD 2-4, a different donor is associated with better GRFS e NRM *(BJH, 2019: 245pz dal 2000 al 2017)*
- An allograft with a new mismatched haplotype may improve outcomes after second BMTs for relapsed hematologic malignancies

(Biol Blood Marrow Transplant 23 (2017) 1887–1894)

- Incidence of HLA Loss in a Global Multicentric Cohort of Post-Transplantation Relapses: Results from the Hlaloss Collaborative Study *(Blood, Volume 132, Supplement 1, 29 November 2018, Page 818)*

In total, we detected 51 HLA loss post-transplantation relapses out of the 396 cases analyzed (12.8%).

35 occurred after haploidentical HSCT (22.6% of relapses in this setting)

12 after MMUD HSCT (11.9%),

4 after 10/10 MUD HSCT (4.3%)

none after UCB HSCT

LE NOSTRE PROPOSTE

- Riattivazione diretta della ricerca MUD se recidiva avvenuta > 6 mesi dal 1st allo-SCT
- Richiesta diretta del WU se ottenimento di RC o malattia chemiosensibile (linfomi) al momento del Work-up
- Karnofsky > 80% al momento del WU (?)

Se tali criteri non sono rispettati resta necessario il passaggio dalla

Commissione allogenico

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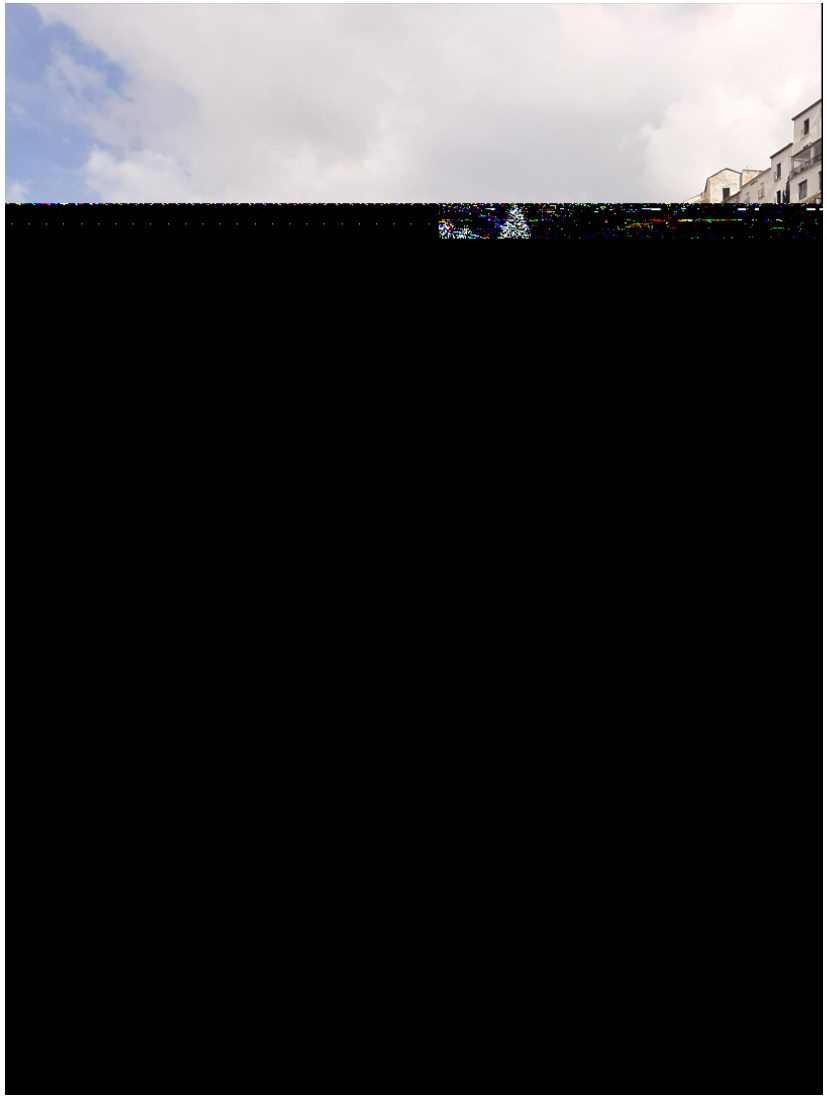

... voi tutti per l' attenzione!