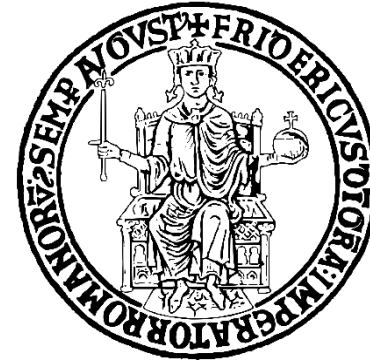


Leucemia Linfoblastica Acuta Ph+

Esperienza di pratica clinica nel paziente Fit



Francesco Grimaldi
AOU Federico II di Napoli

08.04.2026



Due piccoli casi...





CASO CLINICO

Nº1



P. F. ♀ 60aa

Luglio 2021: diagnosi di LLA Ph-positiva

IF: 30% CP CD45- HLA-DR+ CD34+ CD19+ CD10+ CD22+ CD24+ CD33- CD13- CD117-

Citogenetica: 46, XX, t(9;22)(q34;q11.2), der(3)t(1;3)(q21;q29)

Bio molecolare: BCR/Abl p190, trascritto e1a2

Emocromo: WBC 5440/mmc; Hb 9.5 g/dl; PLT 7000/mmc

APR: Appendicectomy (1978) Ablazione del nodo seno-atriale (1996)

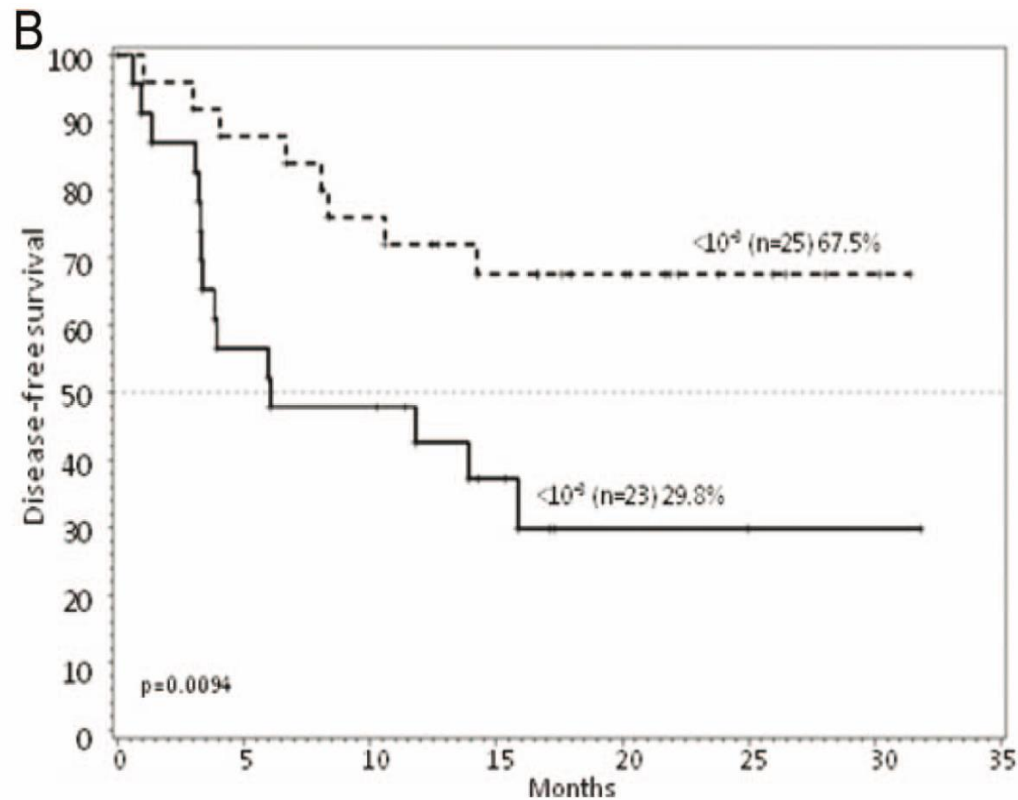
Discectomia D4 + Tunnel carpale (2007)

START: **DASATINIB** + Prednisone + I.T. (MTX+desa)



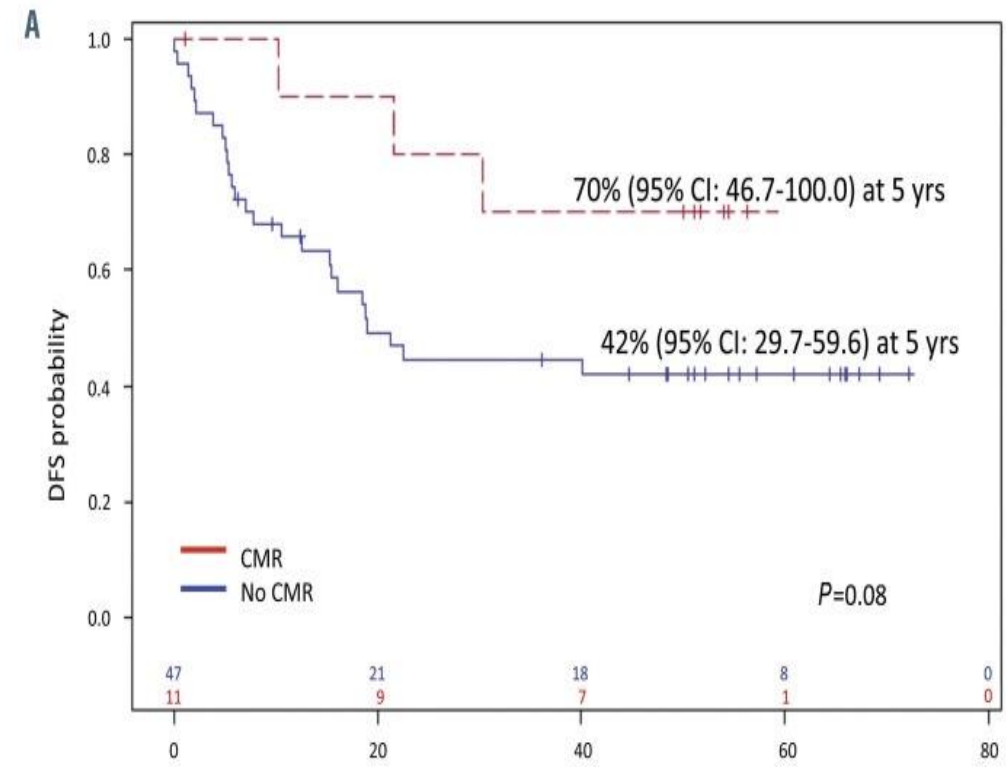
LAL PH+, INDUZIONE CON DASATINIB

GIMEMA 1205



Foa R et al., *Blood*. 2011

GIMEMA 1509



Chiaretti S et al., *Hematologica*. 2021



TERAPIA DI INDUZIONE

31 Agosto 2021 (+43): RC, IF MRD-neg, BCR/ABL ratio 0.219

08 Ottobre 2021: Spondilodiscite da MRSA → Daptomicina + Rifampicina

15 Ottobre 2021 (+88): **BCR/ABL ratio 0.007**

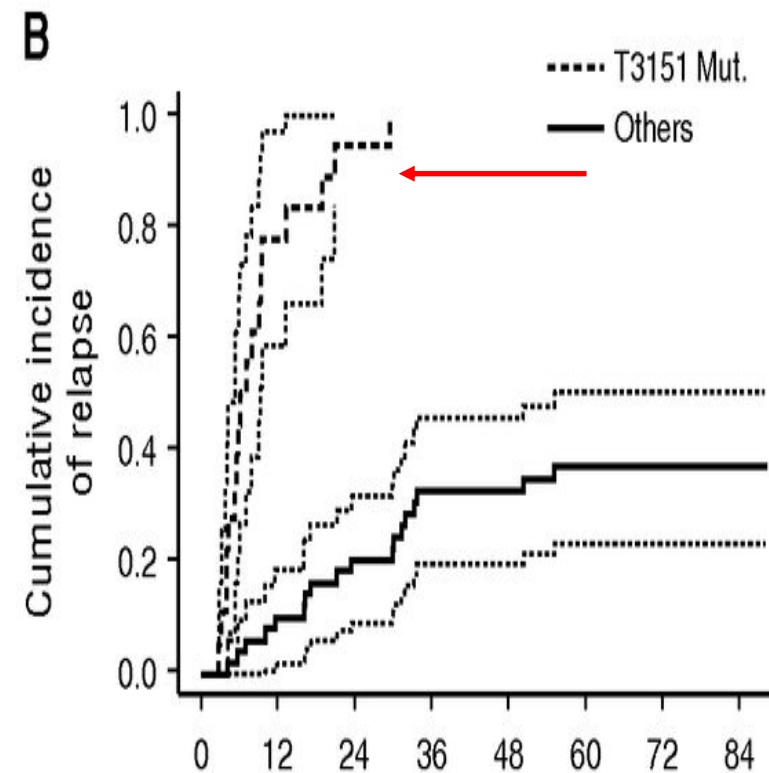
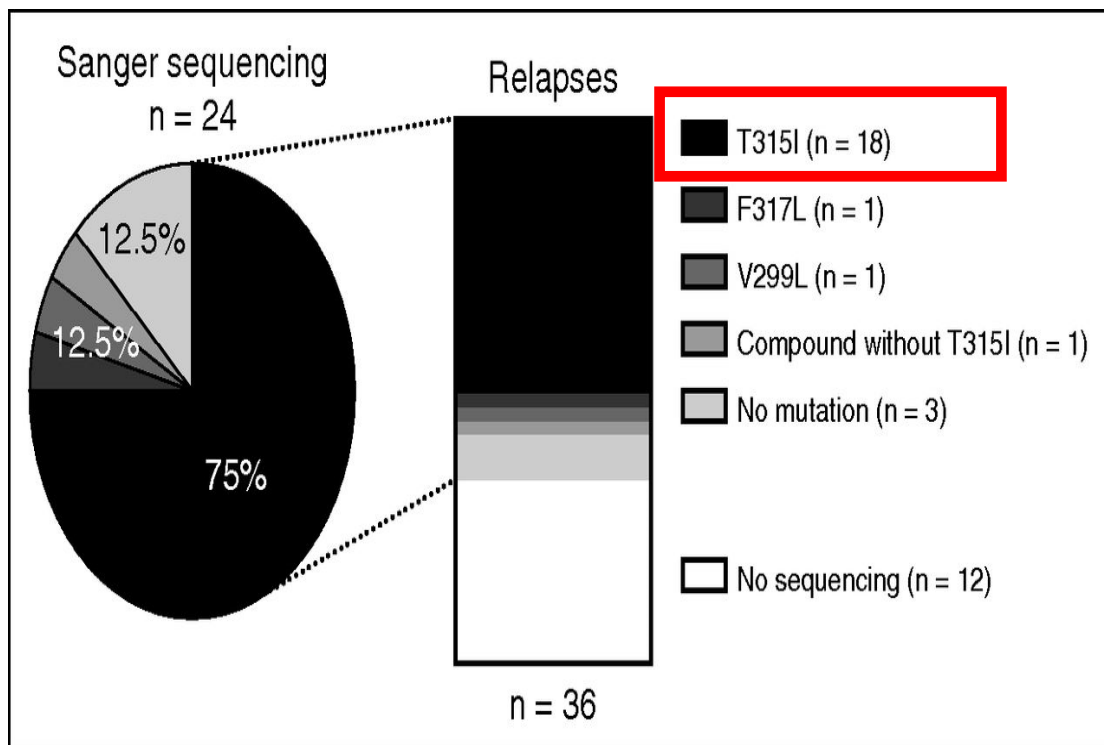
Identificato un donatore familiare sibling HLA-identico

03/12/2021 (+5,5 mesi): **PRIMA RECIDIVA** → 70% CP, BCR-ABL 75.899

T315I +



T315I E RECIDIVA di MALATTIA





TERAPIA DI II LINEA

6 Dicembre 2021: **PONATINIB** + I.T.

11 Gennaio 2022 (+36): RC2 → BCR/ABL ratio 0.006

28 Febbraio 2022 (+84): **BCR/ABL ratio 0.037**

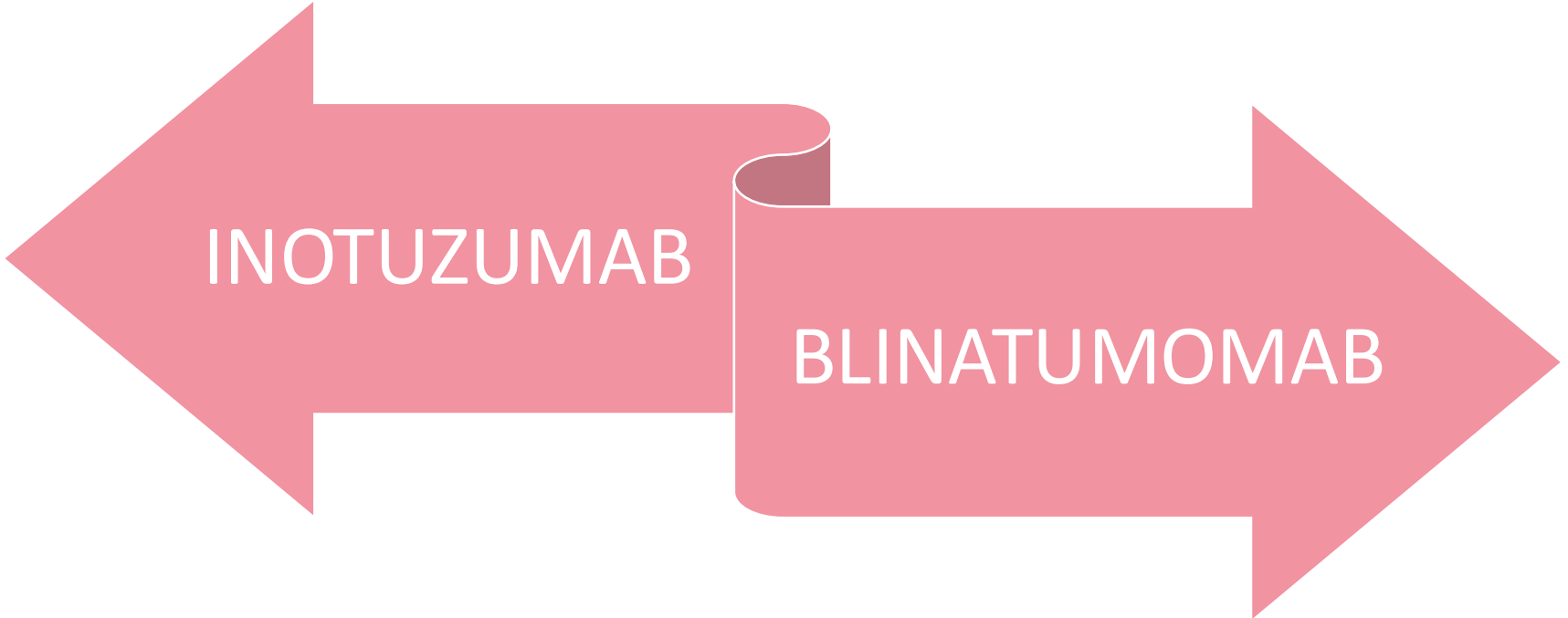
26 Aprile 2022 (+4.5 mesi): **BCR/ABL ratio 0.091**

Maggio 2022: Colecistite Acuta → Piperacillina/Tazobactam + Tigeciclina

09/06/2022 (+6 mesi): **SECONDA RECIDIVA → 12% CP, BCR-ABL 47.023 + CNS pos**



IMMUNOTERAPIA PER LLA PH+ post 2 TKi



INOTUZUMAB

BLINATUMOMAB

**Available studies in 2021 on activity of INOTUZUMAB in relapsed/refractory PH+ ALL**

STUDY	N of pts	ORR (%)	HSCT (%)	mOS	REF
INOVATE	14	78%	41%*	7.7 mo*	Kantarjian HM, et al. N Engl J Med, 2016 Aug 25;375(8):740-53. doi:10.1056/NEJMoa1509277.
INOVATE long-term f-up	22	72%	42%*	8.7 mo*	Kantarjian HM, et al. Cancer, 2019 Jul 15;125(14):2474-2487. doi:10.1002/cncr.32116.
1010 study + INOVATE	38	73%	41%	8.7 mo	Stock W, et al. Cancer, 2021 Mar 15;127(6):905-913. doi:10.1002/cncr.33321.
Real World	22	73%	27%*	11.5 mo*	Badar T, et al. Clin Lymphoma Myeloma Leuk. 2020 Aug;20(8):556-560. doi:10.1016/j.clml.2020.03.004.
INO+Bosutinib NCT02311998	16	83%	33%	14 mo	Jain N, et al. Am J Hematol, 2021 Aug 1;96(8):1000-1007. doi: 10.1002/ajh.26238.

**Dal 30/3 survey per
RACCOLTA**

CAMPUS ALL



*** Data not available for PH+ patients**

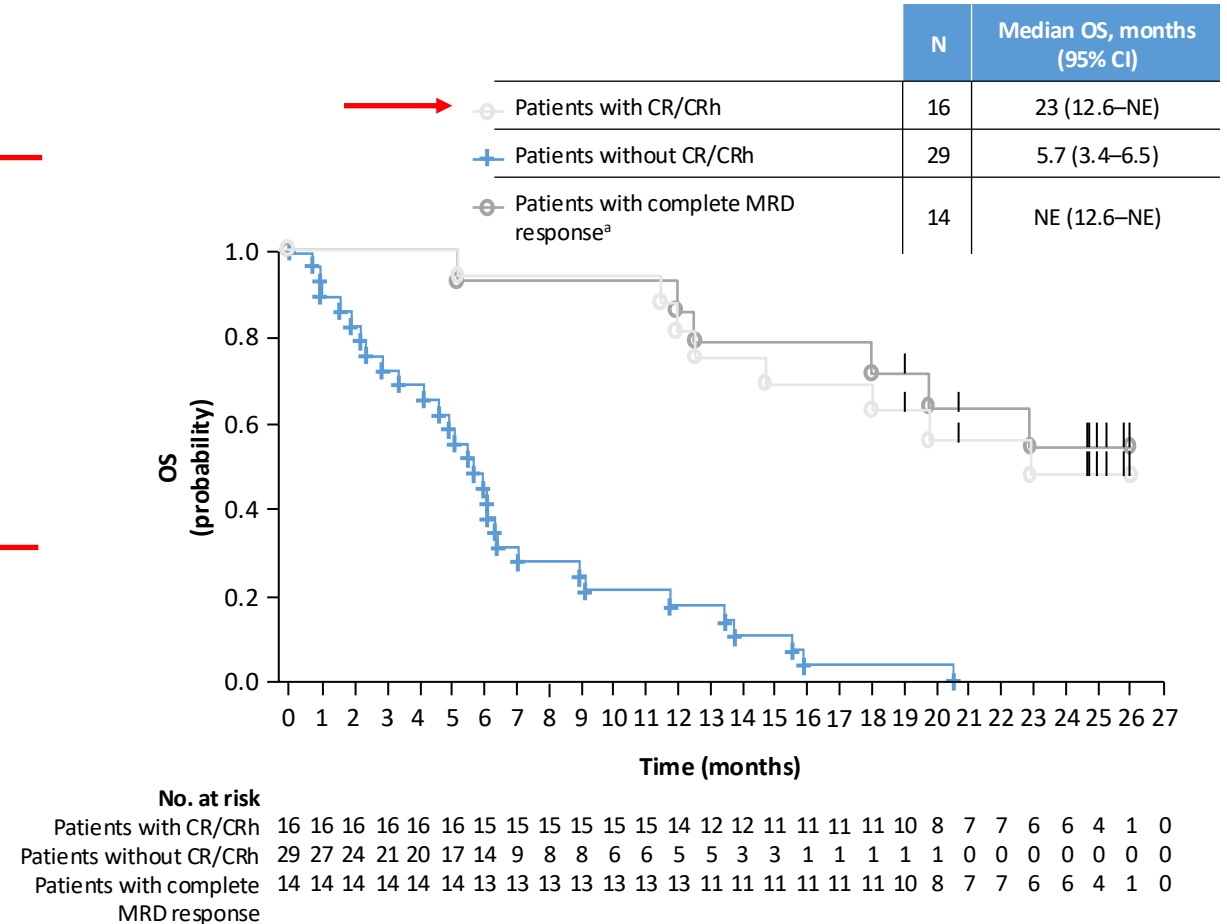


STUDIO ALCANTARA (45 pts)

	n/N	%
Median age (range), years	55 (23–78)	
Age group		
18 to < 55 years	22/45	49
≥ 55 years	23/45	51
No. of prior TKI treatments ^b		
1	7/45	16
2	21/45	47
3	13/45	29
4	4/45	9

	n/N	%
Ponatinib	23/45	51
Bone marrow blasts (central review)		
< 10%	2/45	4
10% to < 50%	9/45	20
50% to < 75%	6/45	13
≥ 75%	28/45	62

CR 36%, T315I CR 40%, CR MRD-neg 80%





IMMUNOTERAPIA PER LLA PH+ post 2 TKi

70% CR,

mOS 11.5 mo

INOTUZUMAB

BLINATUMOMAB

36% CR,

mOS 23 mo





TERAPIA DI III LINEA

14 Giugno 2022: Terapia I.T. (ARA-c+MTX+Dexa) x6

24 Giugno 2022: CTX 300 mg/mq x3 gg

8 Luglio 2022 (+84): I CICLO BLINATUMOMAB

NO CRS, NO Neurotox → dal G+8, infusione con pompa domiciliare

SETTEMBRE 2022: 3 RC, **MRD-Mol NEGATIVA** dopo 2 CICLI di BLINATUMOMAB



TRAPIANTO ALLOGENICO

Dicembre 2022, ricovero in C.S. **(POST 4 cicli di BLINA)**

Donatore: Sibling 9/10 → Midollo

Condizionamento: TB2F

Profilassi GvHD: ATG + 3 dosi MTX + CSA

G+28: midollo post TMO → RC (100% Donor, MRD-neg)

Follow-up – No GvHD

+3 mesi → RC (100% Donor, MRD-neg), inizia PONATINIB mantenimento

Settembre 2023 (+10 mesi): TERZA RECIDIVA → 40% CP (CNS neg)



TERAPIA DI IV LINEA

Ottobre 2023: Riferita AST Papa Giovanni XXIII Bergamo

INOTUZUMAB x 1 ciclo → **RC3 MRD+**

20 Novembre 2023: infusione **CAR-ClK** (FT03-CARClK) → **RC3 MRD Mol-neg**

11 Gennaio 2024: **BCR/ABL ratio 0.103** → Riprende PONATINIB 15 mg

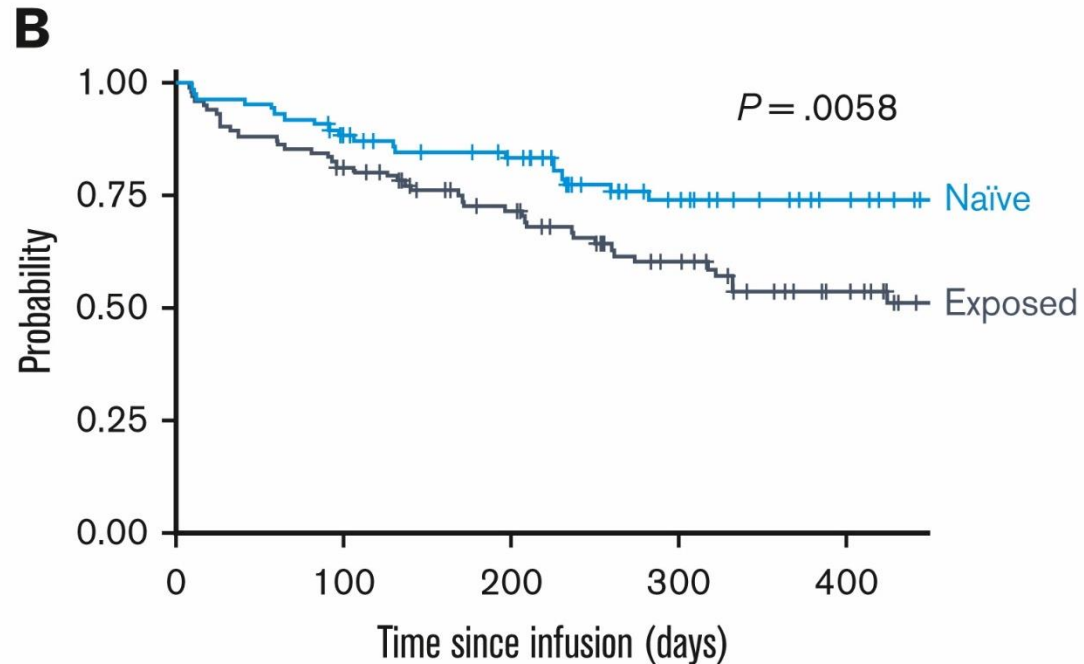
14 Marzo 2024: **IF 1,2%** → PONATINIB 30 mg

Aprile 2024: **V LINEA** → **II HSCT (MUD 10/10)** Fludara, Melphalan, TBI 200 cGy

Sepsi E. Faecium
+ sinusite micotica

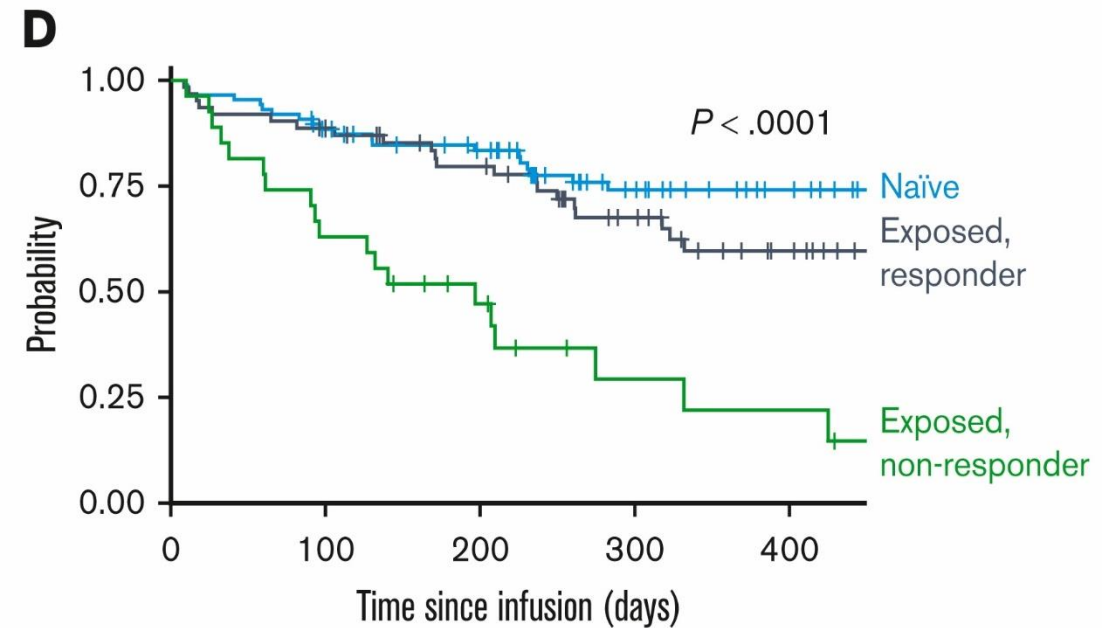


Impact of prior Inotuzumab Ozogamicin treatment on Brexucel outcomes



No. at risk

87	74	62	40	29
102	82	62	41	26



No. at risk

87	74	62	40	29
62	54	43	29	17
27	17	10	4	3



TERAPIA DI VI LINEA

10 Giugno 2024 (+3 mesi post II allo-HSCT): QUARTA RECIDIVA → 10% CP T315I (CNS neg)

20 Giugno 2024: ASCIMINIB + DLI → progressione

8 Luglio 2024: arruolamento in protocollo BLINA SC - 70% CP T315I (snc NEG)

I ciclo BLINA SC: CRS G1 → RC MRD negativa (IF + BCR/ABL-neg)

II ciclo BLINA SC: CRS G1 + ICANS G2 + cGVHD intestinale G4 → RC MRD negativa (STOP BLINA)

Ottobre 2024: QUINTA RECIDIVA → palliazione a domicilio (Exitus Nov 2024, +40 mesi)



CASO CLINICO

Nº2



N. G. ♀ 18aa

Ottobre 2024: diagnosi di LLA Ph-positiva

IF: 80% CP CD45- HLA-DR+ CD34+ CD19+ CD10+ CD22+ CD79a+ CD33- CD13- CD117-

Citogenetica: NV (Assenza di metafasi)

Bio molecolare: BCR/Abl p190, trascritto e1a2

Emocromo: WBC 1240/mmc; Hb 7.5 g/dl; PLT 15.000/mmc

APR: muta

ARRUOLATO Gimema LAL2820: Inizia 16/10 **PONATINIB** + Prednisone + I.T. (Ara-c +MTX +dexa)



CASO CLINICO N°2

N. G. ♀ 18aa PONA IND(70dd) + BLINA x5 + PONA MANT + TIT x15

TOT Emoderivati

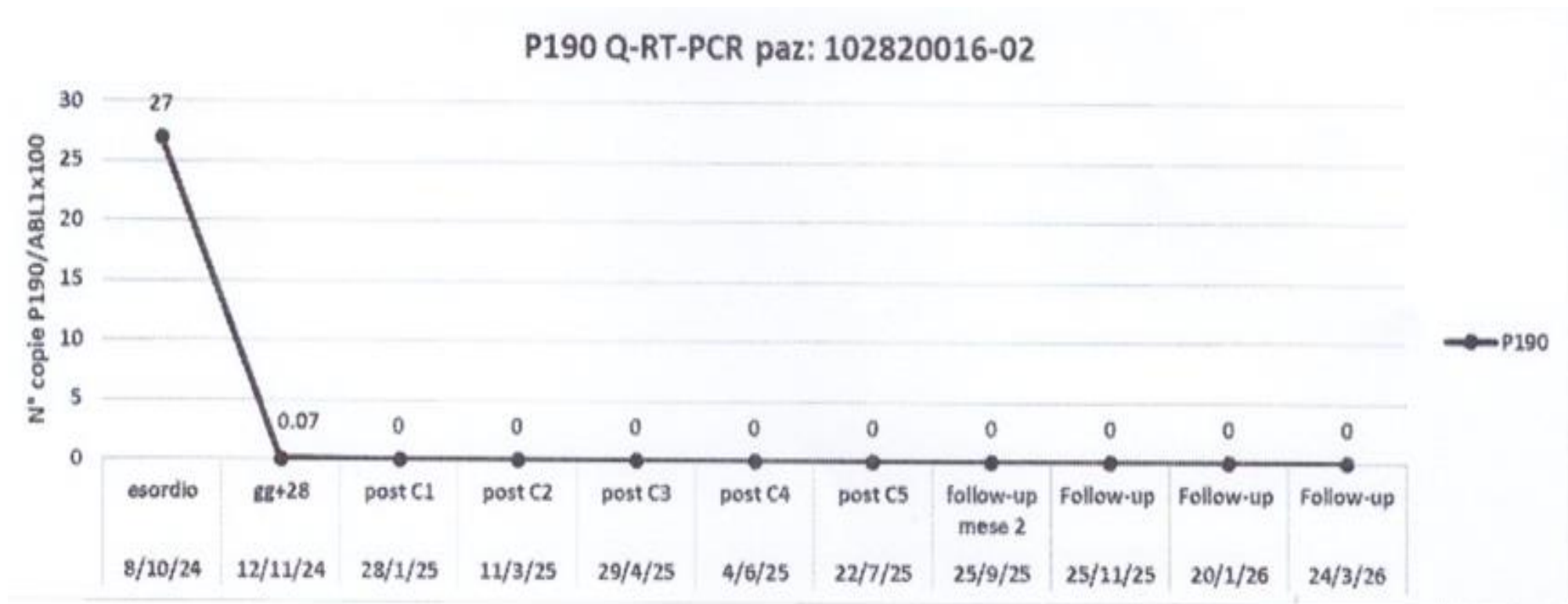
3 ED

TOT giorni ricovero

21 + 8

Complicanze osservate

Dermatite + CRS G½





UN CONFRONTO ALL' AMERICANA

	P.F. ♀ 60aa	N.G. ♂ 18aa
BCR/Abl inhibitors	DASA, PONA, ASCIMINIB	PONATINIB
Linee immunoterapia	BLINA, INOTUZUMAB	BLINATUMOMAB
Terapia cellulare	CAR-CIK	nessuna
Trapianto	1 Sibling + 1 MUD	nessuno
Complicanze infettive	5	nessuna
Emoderivati trasfusi	<i>Ho perso il conto</i>	3 unità
Giorni di degenza	<i>Ho perso il conto</i>	29 gg
Durata prima remissione	5,5 mesi	≈18 mesi



DASATINIB

PONATINIB

ASCIMINIB

BLINATUMOMAB

INOTUZUMAB



TISACEL

BREXUCEL

OBECEL

CAR-CIK

HD-Ara-C (?)

HSCT (?)



A word cloud featuring the phrase "Thank You" in numerous languages and scripts. The words are arranged in a circular pattern, with "Thank You" in the center. The words are in various colors and sizes, representing different languages and cultures. The languages include English, Spanish, French, Italian, German, Dutch, Swedish, Norwegian, Danish, Finnish, Polish, Czech, Slovak, Hungarian, Romanian, Bulgarian, Serbian, Croatian, Slovenian, Macedonian, Albanian, Greek, Turkish, Persian, Urdu, Hindi, Bengali, Tamil, Telugu, Malay, Indonesian, Vietnamese, Thai, Lao, Khmer, Burmese, Sinhala, and many others. The words are also in different fonts and styles, adding to the visual diversity of the cloud.