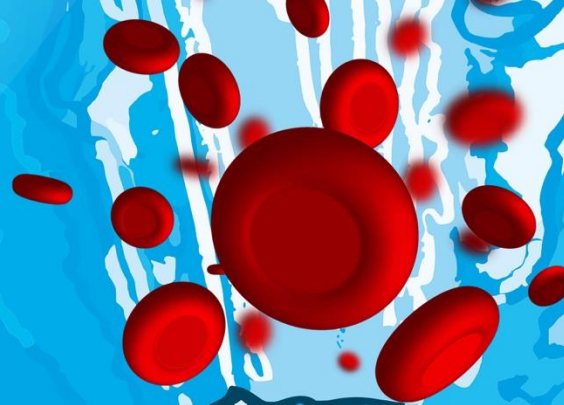




*Diagnosi di talassemia non trasfusione dipendente:
risultati di un progetto pilota su pazienti con anemia microcitica
in età adulta*

Immacolata Tartaglione, MD PhD

Meeting del CLUB DEL

**Globulo
Rosso** 2026

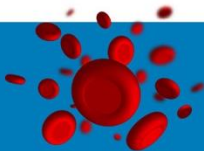
NAPOLI

28-29 SETTEMBRE 2026

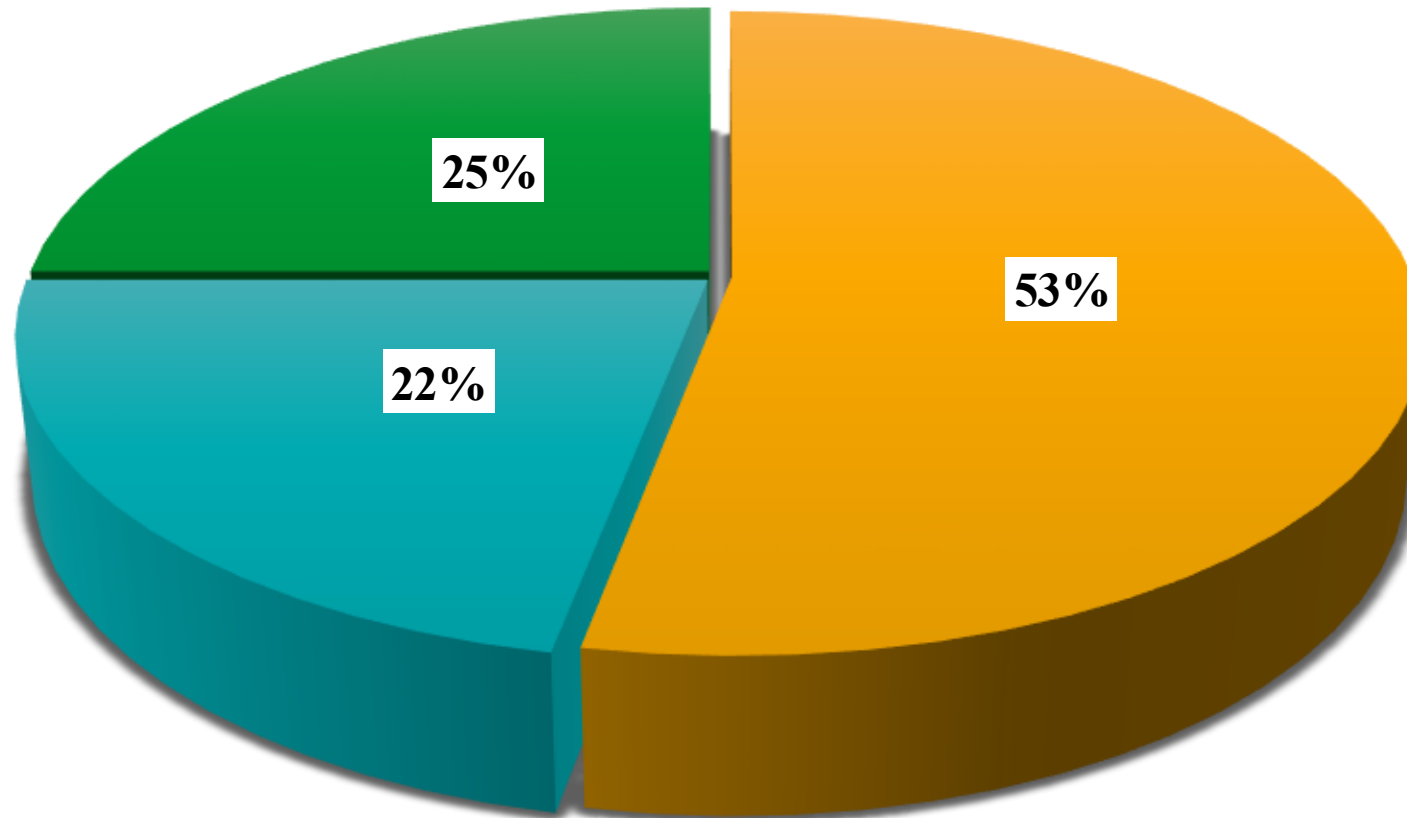
Complesso dei SS. Marcellino e Festo

Disclosures

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
BMS	x					x	
Vertex						x	
Agios					x		

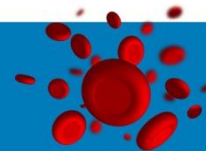


Modalità di Diagnosi nei nostri pz NTDT

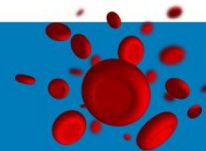
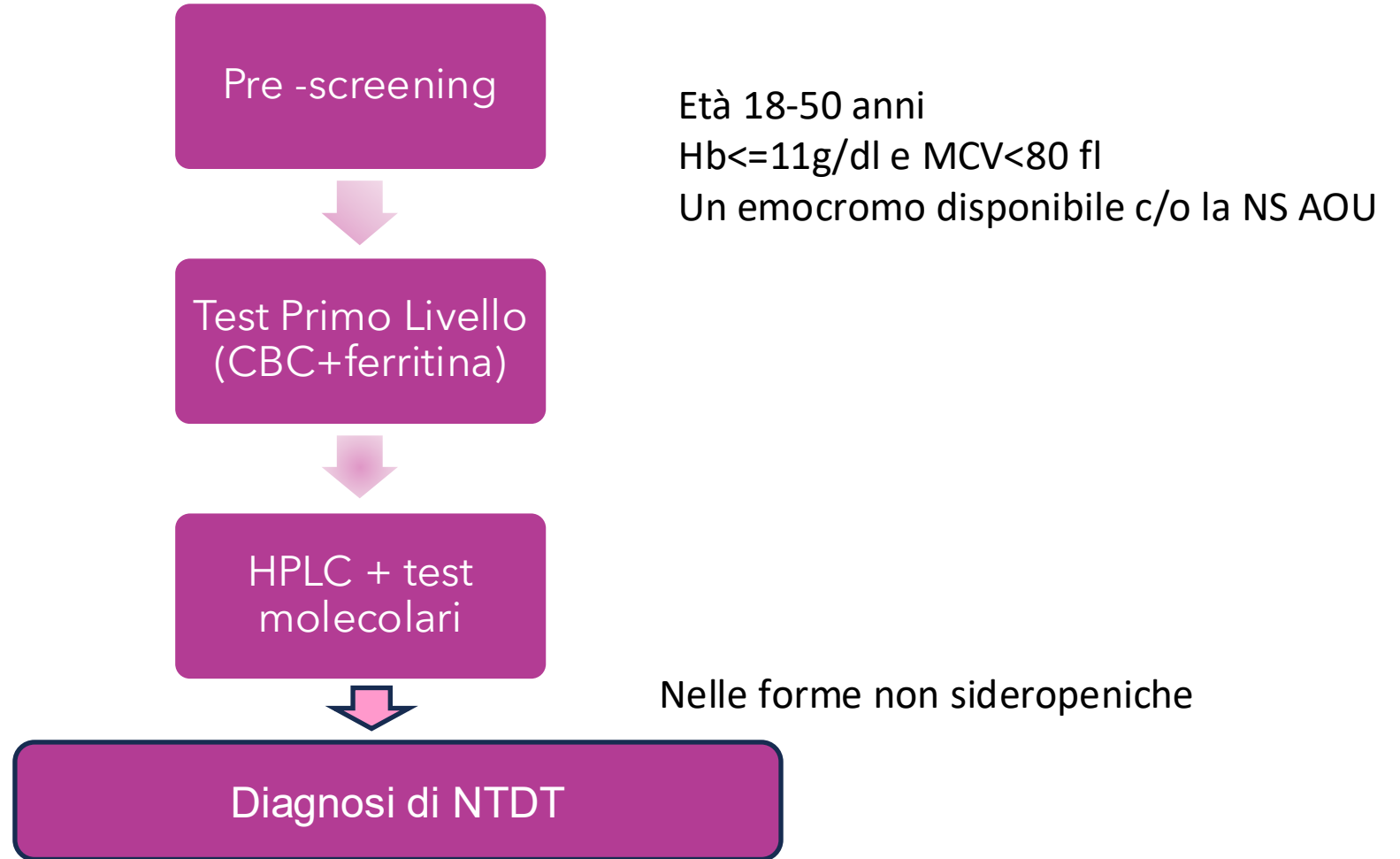


■ Diagnosi errata come portatore sano ■ Diagnosi eseguita per familiarità ■ Diagnosi eseguita correttamente

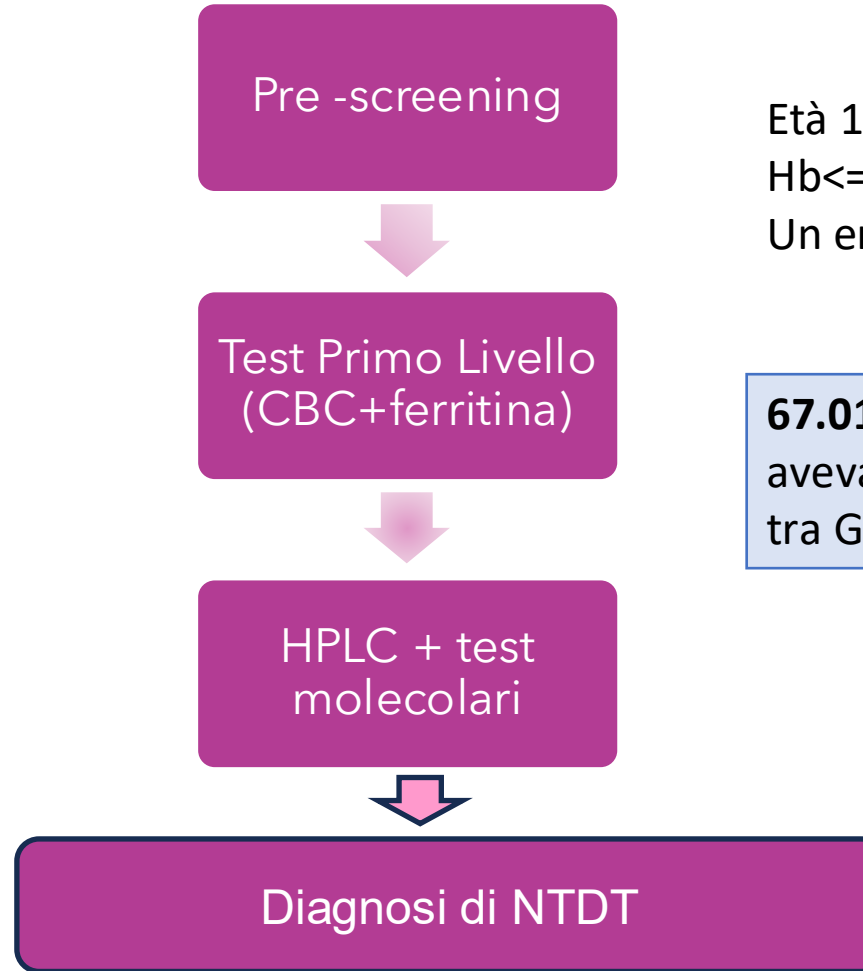
Personal data, unpublished



Progetto pilota Università Vanvitelli

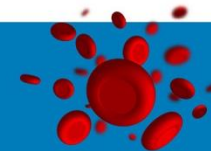


Progetto pilota Università Vanvitelli

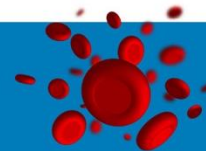
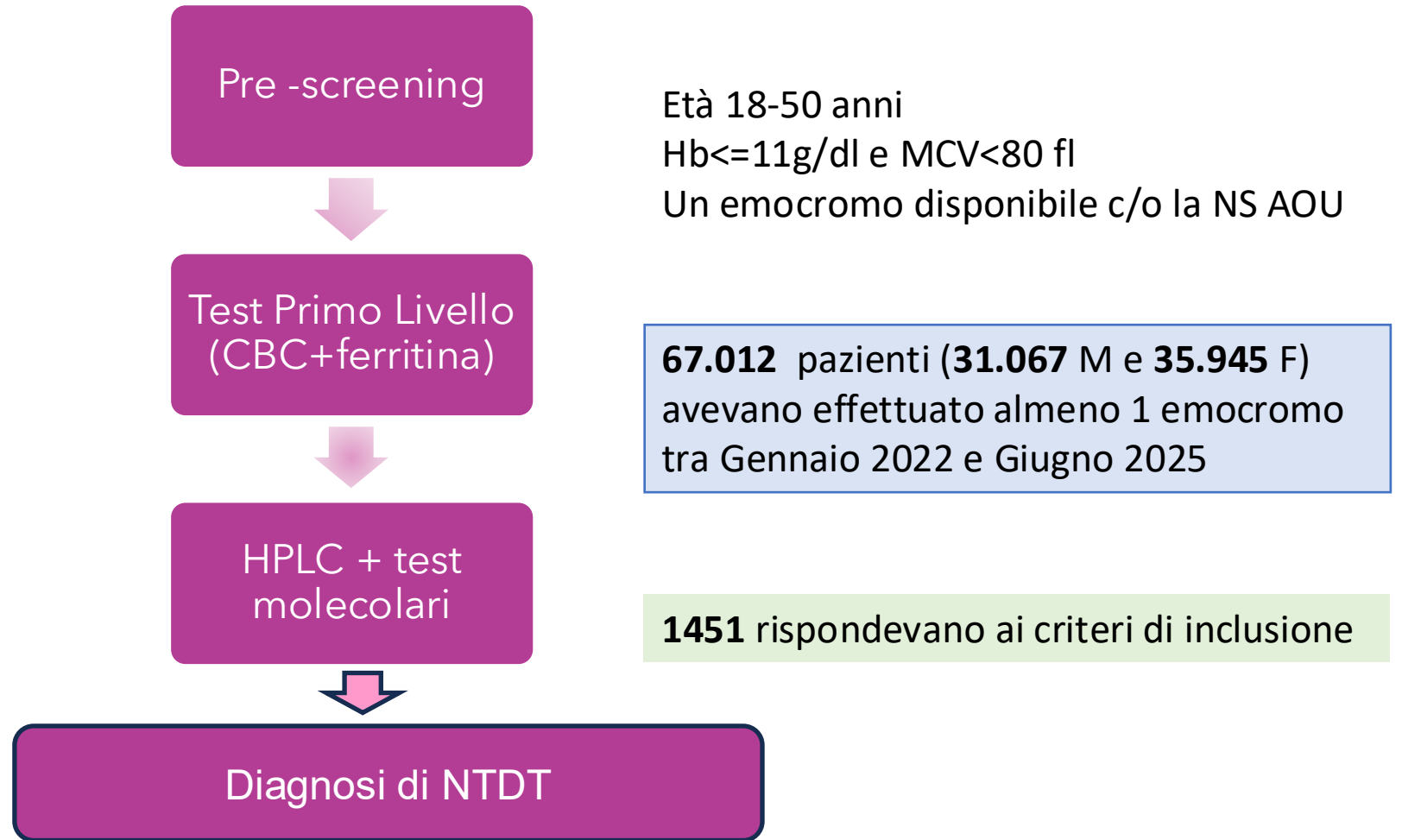


Età 18-50 anni
Hb $\leq$ 11g/dl e MCV $<$ 80 fl
Un emocromo disponibile c/o la NS AOU

67.012 pazienti (**31.067** M e **35.945** F)
avevano effettuato almeno 1 emocromo
tra Gennaio 2022 e Giugno 2025



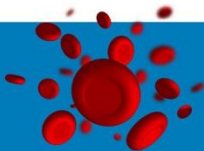
Progetto pilota Università Vanvitelli



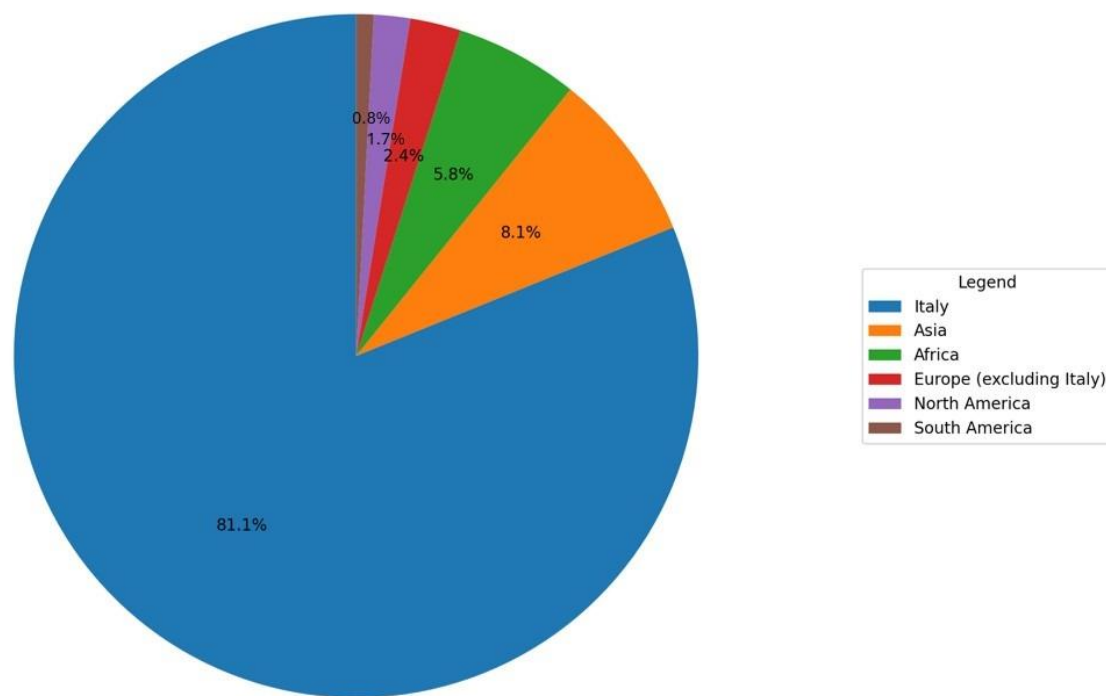


Variable	Overall N = 1451	Not enrolled N = 1011	Enrolled N = 440	SMD	p-value
Sex				0.069	0.240
Male	121 (8.3%)	90 (8.9%)	31 (7.0%)		
Female	1330 (91.7%)	921 (91.1%)	409 (93.0%)		
Age (years)	34.9 ± 8.3	34.4 ± 8.3	36.2 ± 8.4	0.220	<0.001
Hb (g/dL)	9.9 [9.0, 10.6]	10.0 [9.1, 10.6]	9.9 [9.0, 10.5]	0.034	0.509
MCV (fL)	74.7 [68.8, 78.2]	75.0 [69.8, 78.4]	74.0 [66.6, 77.9]	0.186	0.003

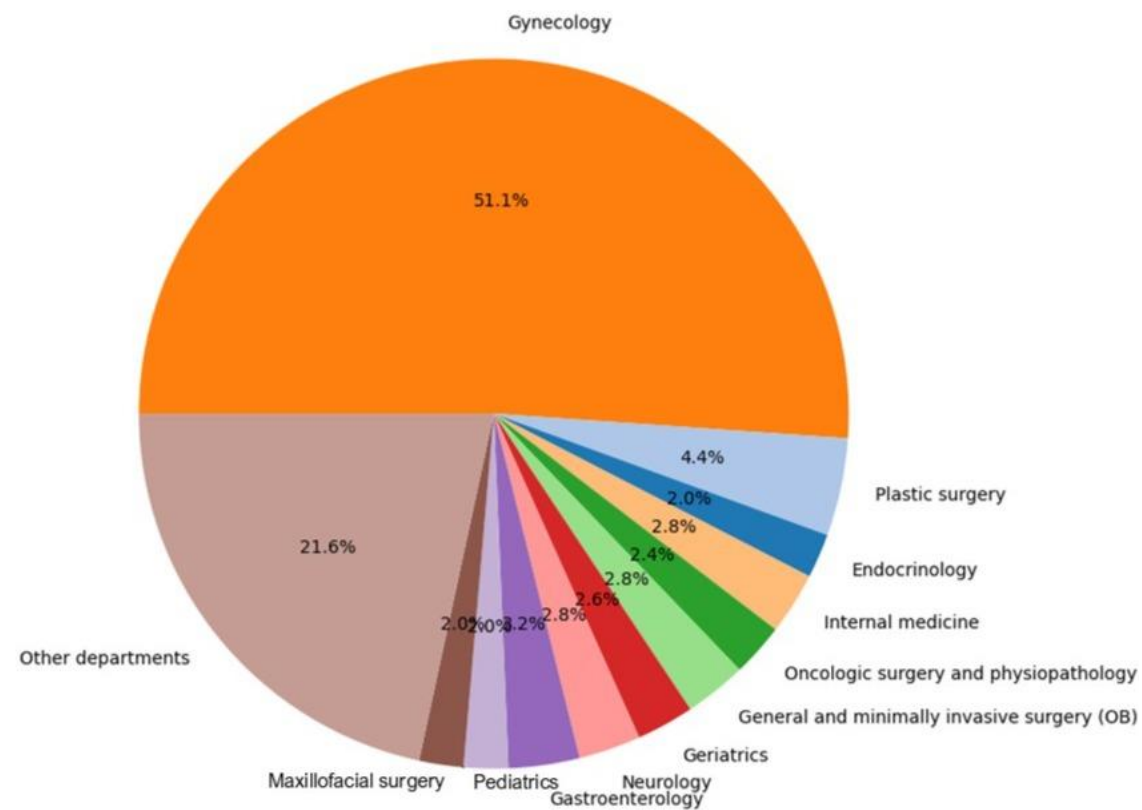
Note: Data are presented as n (%) for sex, mean ± SD for age, and median [Q1, Q3] for Hb and MCV. P-values were derived from the chi-square test for sex, the t-test for age, and the Mann-Whitney U test for Hb and MCV. Because of the large overall sample size, p-values are sensitive to clinically trivial differences; SMD, which is independent of sample size, is therefore the primary metric for assessing between-group balance. An |SMD| < 0.10 is conventionally interpreted as a negligible difference (balanced groups), whereas values of approximately 0.20, 0.50, and 0.80 denote small, moderate, and large differences, respectively. Abbreviations: SMD, standardized mean difference; Hb, hemoglobin; MCV, mean corpuscular volume; SD, standard deviation; Q1, first quartile; Q3, third quartile.



Provenienza dei pz



A: Paesi di origine

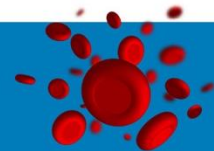


B: Reparti di provenienza ("Other departments" refers to all the departments with distribution <2%)

Variable	Not anemic N = 238	Anemic N = 202	Effect size	95% CI Effect size	p-value
Sex			0.007	[-0.041, 0.055]	0.774
Male	16 (6.7%)	15 (7.4%)			
Female	222 (93.3%)	187 (92.6%)			
Age (years)	36.6 ± 8.1	35.6 ± 8.7	1.011	[-0.572, 2.593]	0.210
Hb (g/dL)	10.0 [9.1, 10.6]	9.9 [8.9, 10.4]	0.061	[-0.047, 0.167]	0.273
MCV (fL)	76.3 [71.5, 78.8]	69.0 [63.7, 75.6]	0.428	[0.325, 0.521]	<0.001

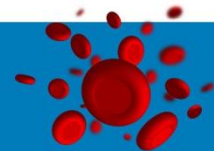
Note: Group assignment was based on anemia status at the second complete blood count, whereas all variables shown refer to the first assessment. Data are presented as n (%) for sex, mean ± SD for age, and median [Q1, Q3] for Hb and MCV. Effect sizes are reported with 95% confidence intervals and were computed as the difference in proportions for sex, the difference in means for age, and Cliff's delta, δ , for Hb and MCV. The difference in proportions and the difference in means are expressed in their original units and are therefore interpreted directly. In contrast, Cliff's delta is a unit-free effect size ranging from -1 to 1; positive values indicate systematically higher values in group 1 ("Not anemic") than in group 2 ("Anemic"), negative values the converse. The magnitude of δ was interpreted using conventional thresholds: $|\delta| < 0.147$, negligible; $|\delta| < 0.33$, small; $|\delta| < 0.474$, medium; $|\delta| \geq 0.474$, large. P-values were derived from the chi-square test for sex, the t-test for age, and the Mann-Whitney U test for Hb and MCV.

Abbreviations: Hb, hemoglobin; MCV, mean corpuscular volume; SD, standard deviation; Q1, first quartile; Q3, third quartile.

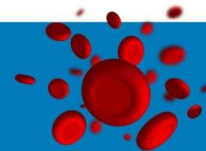
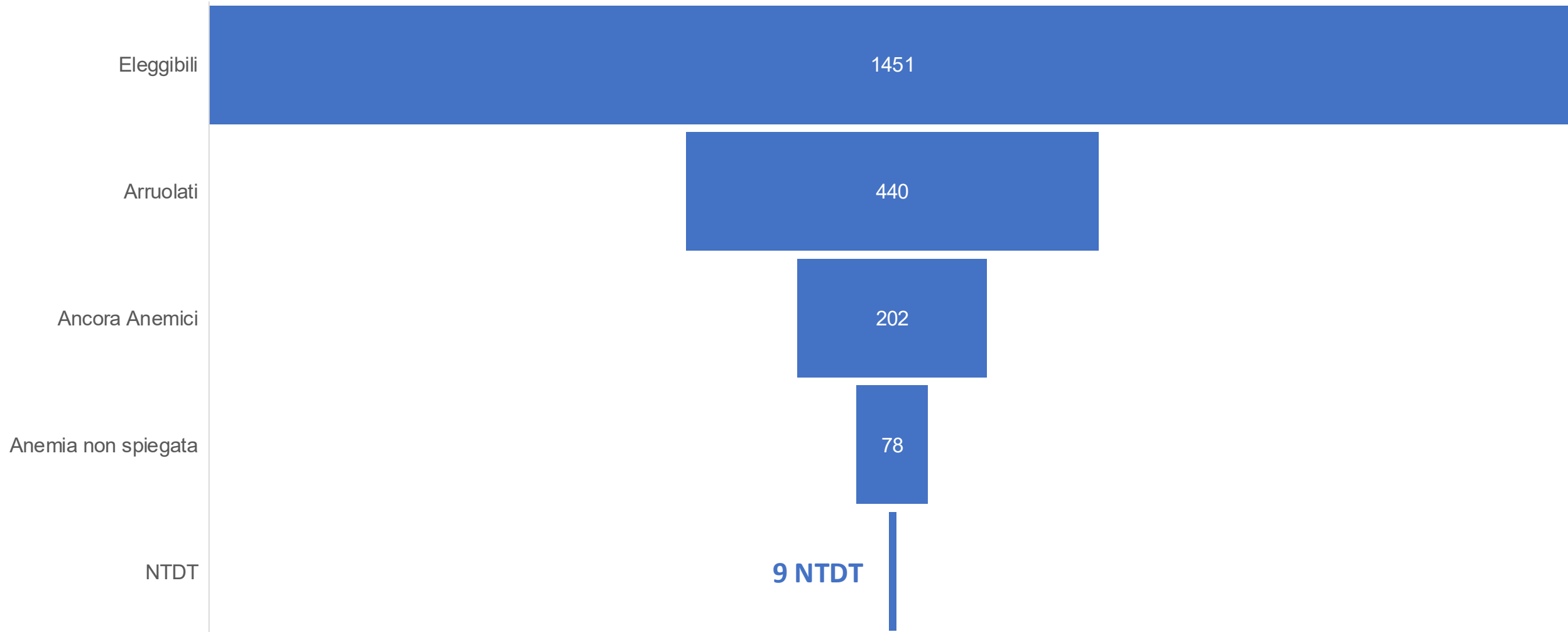


Final diagnostic groups	N	%
Pure IDA	113	55.9
Pure carriers*	56	27.7
NTDT	9	4.5
Carriers with IDA*	13	6.4
Other anemias	11	5.4

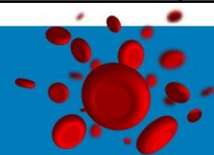
***25 dei 69 carriers non sapevano di esserlo**



Distribuzione dei pazienti durante lo studio



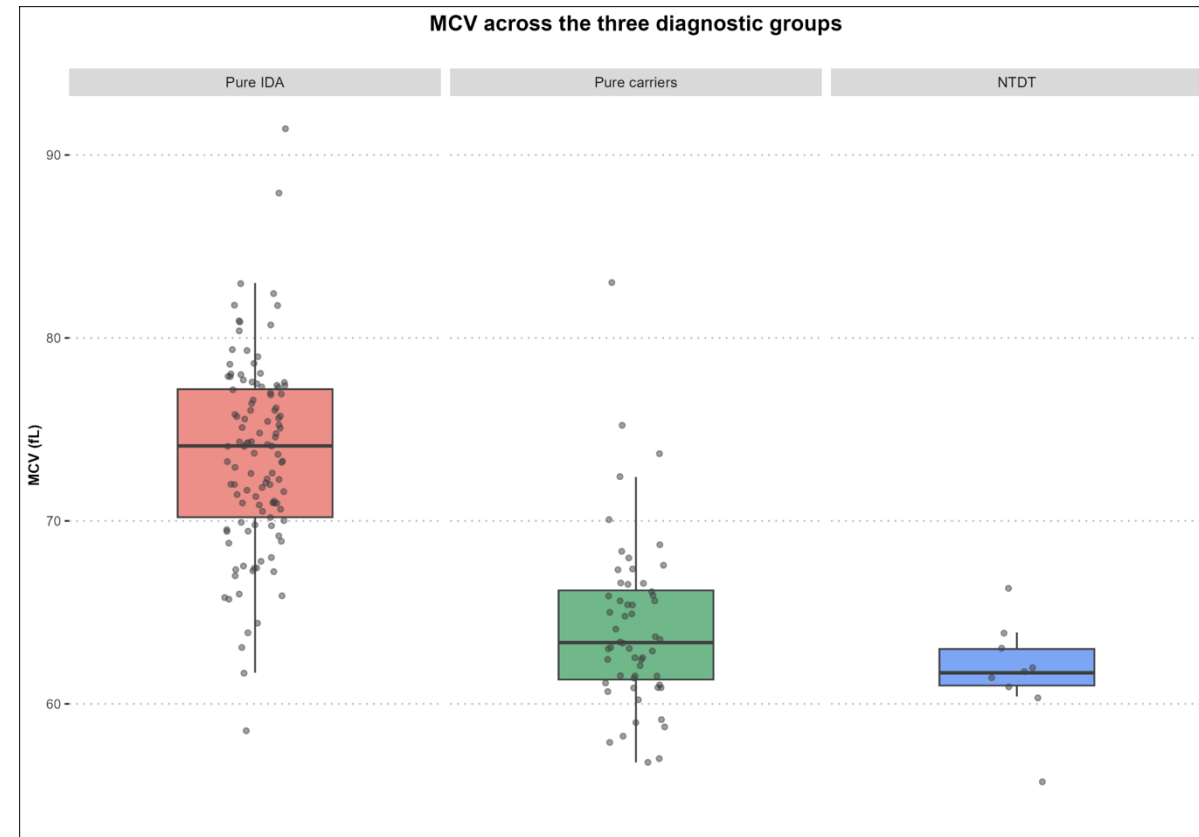
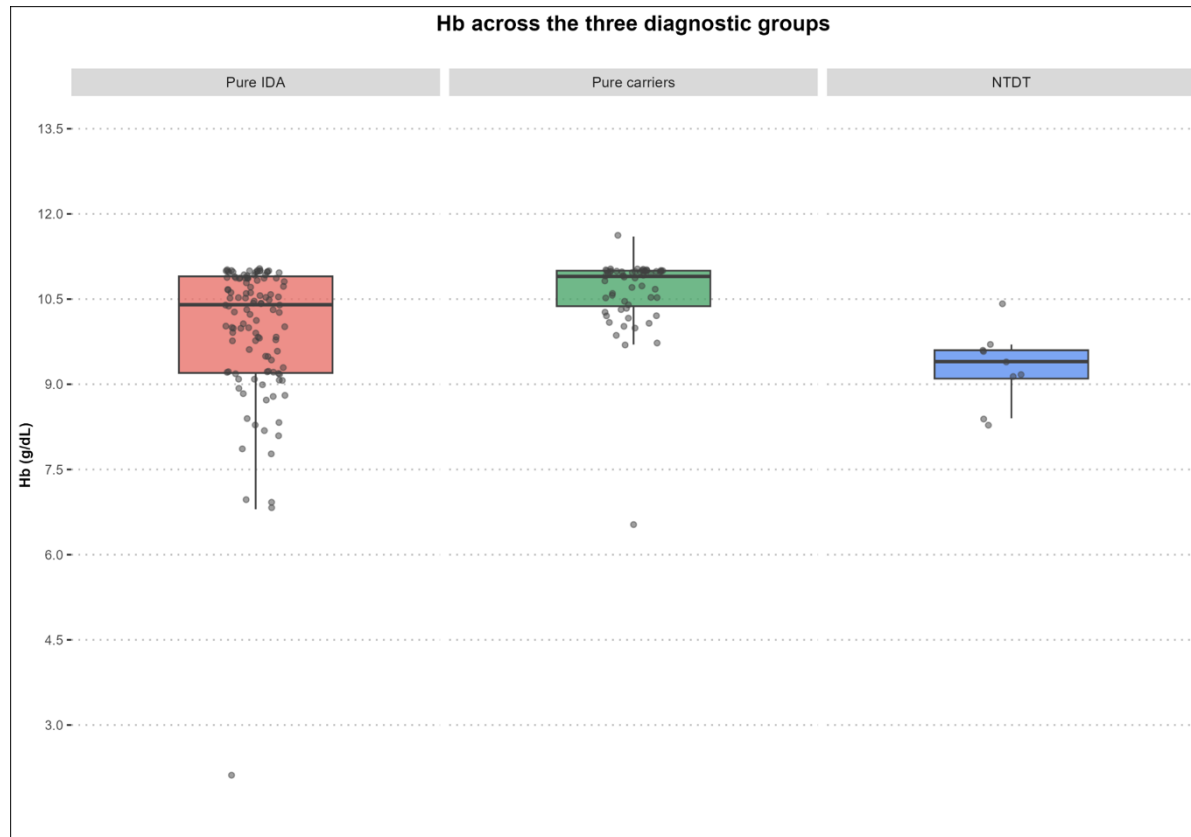
Variable	Pure IDA N = 113	Pure carriers N = 56	NTDT N = 9	Carriers with IDA N = 13	Other anemias N = 11
Female	109 (96.5%)	50 (89.3%)	8 (88.9%)	13 (100.0%)	7 (63.6%)
Age (years)	37.0 [32.0, 44.0]	36.5 [27.8, 42.0]	32.0 [31.0, 39.0]	38.0 [34.0, 42.0]	38.0 [26.5, 40.0]
Hb (g/dL)	10.4 [9.2, 10.9]	10.9 [10.4, 11.0]	9.4 [9.1, 9.6]	10.2 [8.7, 10.6]	10.0 [8.9, 10.7]
MCV (fL)	74.1 [70.2, 77.2]	63.4 [61.3, 66.2]	61.7 [61.0, 63.0]	59.5 [58.6, 62.0]	77.5 [68.0, 81.4]
RBC ($\times 10^{12}/L$)	4.5 [4.2, 4.8]	5.5 [5.1, 5.8]	4.8 [4.6, 4.9]	5.4 [5.1, 5.7]	4.3 [3.6, 4.5]
RDW-SD (fL)	43.9 [40.3, 46.4]	35.3 [33.4, 38.0]	35.4 [34.4, 36.5]	34.8 [33.8, 39.6]	47.7 [45.0, 51.2]
RDW-CV (%)	16.4 [15.1, 17.5]	16.2 [15.4, 17.3]	16.1 [15.3, 17.8]	17.9 [16.5, 19.8]	17.5 [15.6, 19.0]
Presence of NRBC	2 (1.8%)	7 (13.5%)	2 (22.2%)	2 (15.4%)	0 (0.0%)
Ferritin (ng/mL)	7.0 [5.0, 10.2]	53.7 [20.6, 78.3]	75.3 [55.0, 92.0]	10.0 [5.8, 12.0]	118.0 [12.8, 249.5]
TSAT(%)	5.0 [4.0, 7.8]	24.0 [19.0, 31.0]	27.0 [24.0, 31.0]	7.0 [5.0, 9.0]	25.0 [22.5, 27.5]



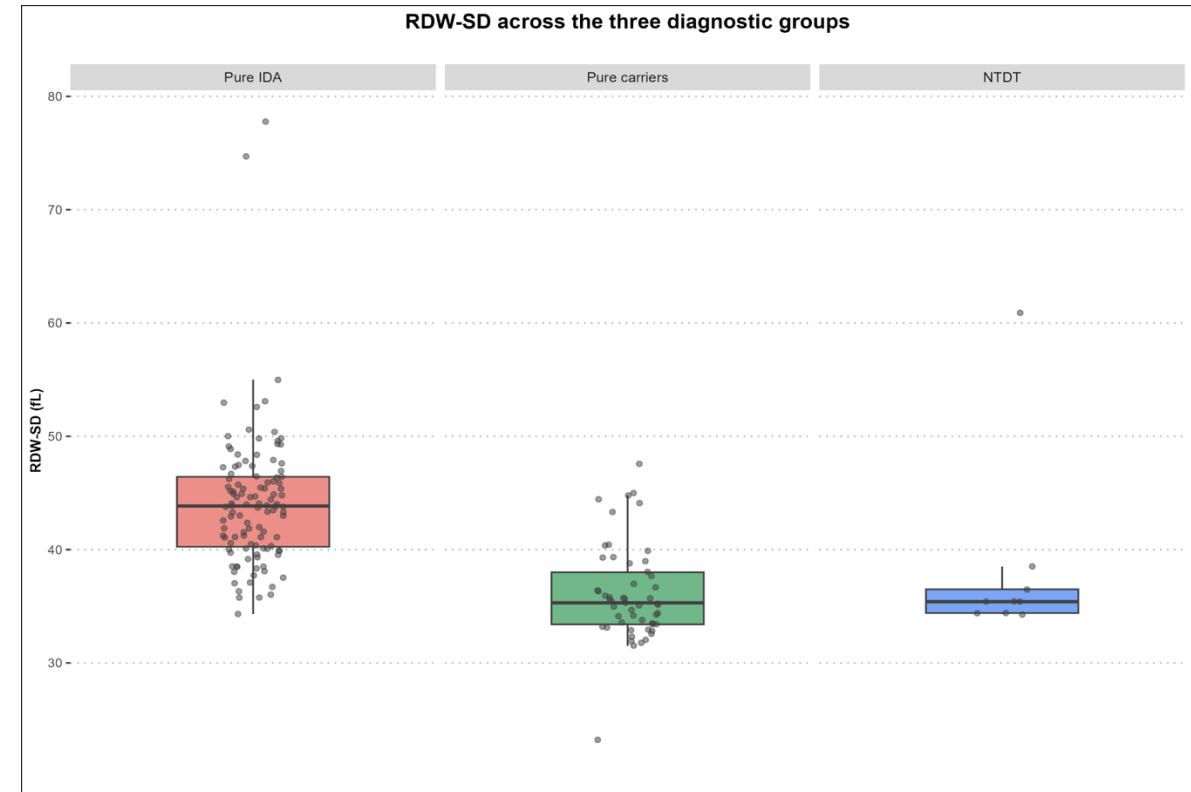
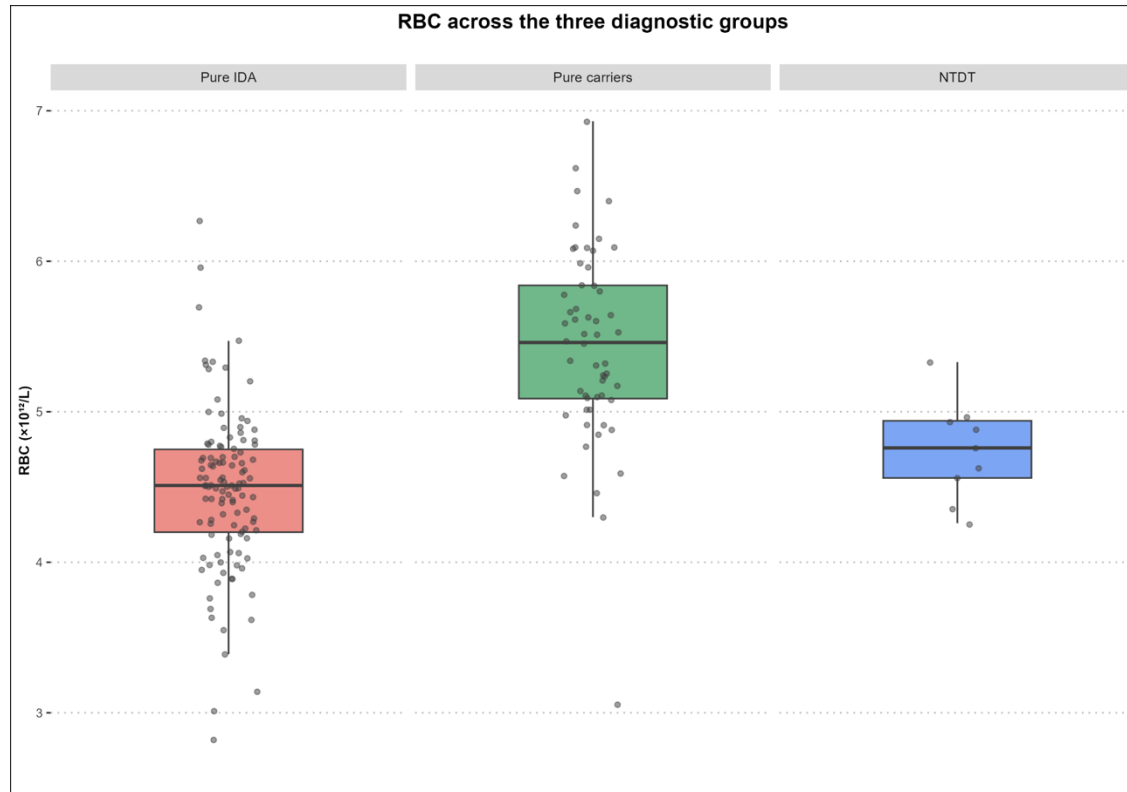
	NTDT1	NTDT2	NTDT3	NTDT4	NTDT5	NTDT6	NTDT7	NTDT8	NTDT9
Age	41	32	36	30	28	41	38	28	31
Gender	F	F	F	M	F	F	F	F	F
Hb (g/dl)	10,4	8,4	9,6	8,3	9,4	9,2	9,6	9,1	9,7
MCV (fl)	61,7	61	63	55,8	61,5	63,9	60,4	66,3	61,9
RBC (10 ⁶ /μL)	5,3	4,3	4,9	4,6	4,8	4,6	5	4,4	5
nRBC (n/μL)	0	20	50	0	0	0	0	0	0
PLT (10 ³ /μL)	282	232	310	116	220	234	238	267	180
Ferritin (ng/ml)	92	69	75,3	194	544	8,1	82	5	55
TSAT (%)	27	28	39	35	24	19	31	3	25
HbF (%)	1,4	<1	4,7	4,6	<1	1	<1	2,1	2,9
HbA2 (%)	5	4,8	5,7	1	5,3	5,3	5,7	12,7	5,4
Genotype	β ⁰ /ααα	β ⁺ /ααα	β ⁰ /ααα	α ⁺ /α ⁰	β ⁺ /ααα	β ⁰ /ααα	β ⁰ /ααα	Lepore/ααα	β ⁰ /ααα
Genetics	CD 39 (CAG>TAG)/α αα	IVS II-745 C>G/ααα	IVS II-1 G>A/ααα	-3,7/-20,5	IVS II-745 C>G/ααα	CD 39 (CAG>TAG)/α αα	CD 39 (CAG>TAG)/α αα	g.63290_70702d el/ααα	CD 39 (CAG>TAG)/ ααα
Comorbidities	Connective tissue disease	ND	hypothyroidism, Gilbert's syndrome	nodular goiter, chronic glomerulo nephritis	splenomegaly	chronic asthenia, bone pain, splenomegaly	ND	IDA, splenomegaly	ND
iron supplementation	No	Yes	No	Yes	Yes	Yes	No	Yes	No
Known carrier status	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

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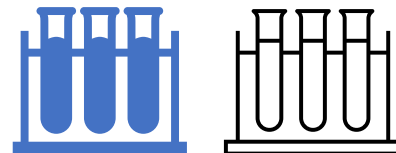
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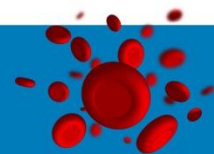
NTDT: 15% tra MCV <65 e 8.3% tra MCV <70



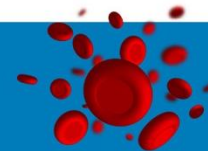
HPLC a confronto



- La percentuale di pz con $HbF < 1\%$ non differiva significativamente tra carriers e NTDT ($p=0.718$)
- I livelli di $HbA2$ erano paragonabili tra i due gruppi ($p=0.814$)



E i pz con anemia non IDA e non Thal?



È in corso studio NGS con R. Russo e colleghi per i casi non risolti...

KIF23
BMP6
ATP11C
GSR
GSS PKLR
CDAN1
FTCD
SPTB
NT5C3A
HFE
PIEZO1
RPL15
ABCB6
SPTA1
RPL15
BMP6
ATP11C

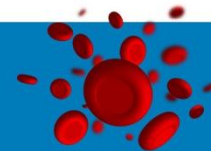
CDAIII
DBA
Pyrimidine 5' nucleotidase deficiency
Susceptibility to iron overload
Glutathione reductase deficiency
Glutathione synthetase deficiency
PKD

CDAI
Formiminoglutamic aciduria
HS2

GLUT1 deficiency

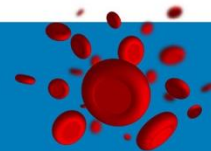
Conclusioni (I)

- «Tratto talassemico» e NTDT sono responsabili del 38.6% delle anemie microcitiche in età adulta; la NTDT del 4.5% tra tutti e del 15 % tra MCV<70.
- Carenza di ferro e Talassemia possono coesistere
I quadri ematologici di portatori e NTDT possono essere sovrapponibili:
MCV, HbF e HbA2 paragonabili tra i due gruppi
- Soltanto l'analisi molecolare può permettere la diagnosi differenziale
- L'applicazione dell'algoritmo diagnostico ci ha permesso di identificare 9 soggetti affetti da NTDT e 25 carriers inconsapevoli



Conclusioni (II)

- Il coinvolgimento dei reparti di provenienza ci ha consentito di sensibilizzare i colleghi circa la condizione di NTDT, poco o per nulla conosciuta
- È necessario fare un lavoro di awareness della patologia, sia tra i clinici che tra la popolazione generale, perché anche questa forma di Talassemia sia conosciuta, accettata e riconosciuta

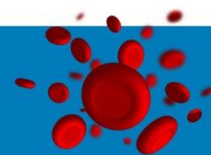


SHINE THE LIGHT ON THALASSEMIA



 **8**
MAY
INTERNATIONAL **THALASSAEMIA** DAY

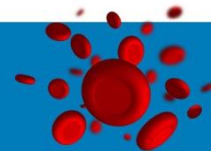
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Finding the Undiagnosed. Supporting the Unseen.



GRAZIE



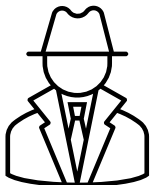
Claudia Sica
Marcella Contieri



Saverio Scianguetta



Teresa Palma
Fara Vallefucolo
Velia D'Angelo
Antony Cardone



Angelo Perrotta
Gelsomina Simeone
Domenico Roberti
Sofia Matarese

Rosa Manca
Laura Pinfildi

Fulvio della Ragione
Adriana Borriello

Silverio Perrotta

Immacolata.tartaglione@unicampania.it

