AIEOP
ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA

Presidente
A. Mastronuzzi

Segreteria Scientifica
A. Colombini, T. Perillo, A. Zibaldo

Giornate AIEOP

BOLOGNA
Zanhotel Europa

14-15 Aprile 2025

GdL Insufficienze Midollari

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Unita' di Ematologia

IRCCS – istituto Giannina Gaslini

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
No disclosures							

GdL Insufficienze Midollari

Neutropenie congenite & acquisite

Anemia Aplastica

ALPS

Anemia di BlackfanDiamond

Anemia di Blackfan-Diamond

GATA 2

Malattie del telomero

PNH

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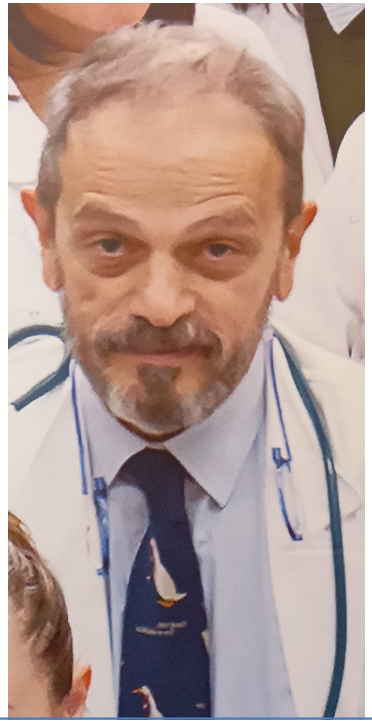
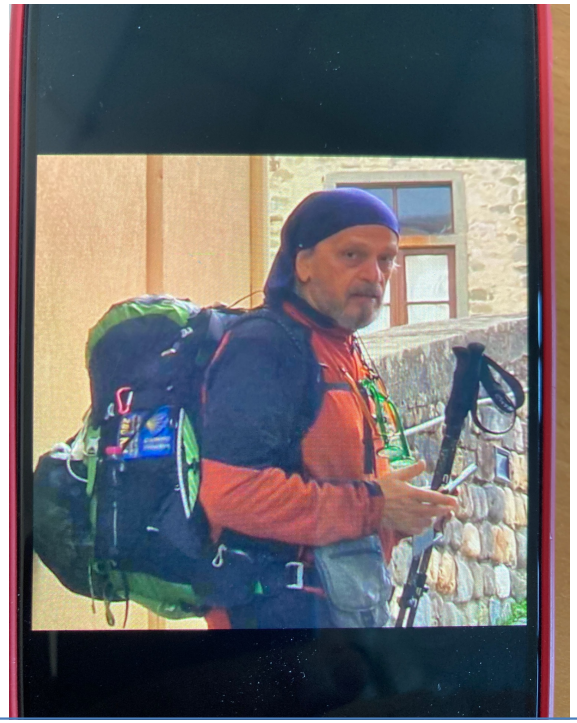
In ricordo di Fabio





https://www.youtube.com/watch?v=S3uvo9WEPWs

https://www.youtube.com/watch?v=S3uvo9WEPWs

HOT SPOT

Data base e registri
Progetti consolidati
Studi conclusi
Nuove proposte

-Studi retrospettivi/prospettici: Neutropenie, GATA2, ALPS, DBA, Malattie del Telomero, Anemia di Fanconi

- Multicentricita' : documentazione disponibile per presentazione ai comitati etici territoriali; check protocolli in uso

- Deadline compilazione delle schede registrazione & FUP

- Approccio/accesso Redcap

- Collaborazione inter GdL
- Coinvolgimento centri dell'adulto →transizione

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Received: 3 November 2024 | Accepted: 27 February 2025
DOI: 10.1002/hem3.70113

GUIDELINES - CONSENSUS-BASED

HemaSphere eha

European guidelines on treatment and supportive measures in chronic neutropenias: A consensus between the European Hematology Association and the EuNet-INNOCHRON COST Action based on a systematic evidence review

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Mavorixaflor in CN

Protocol Title:	A Phase 3, randomized, double-blind, placebo-controlled, multicenter study of mavorixafor in participants with congenital and acquired primary autoimmune and idiopathic chronic neutropenic disorders who are experiencing recurrent and/or serious infections
Brief Title:	A study to investigate efficacy, safety, and tolerability of mavorixafor in participants with congenital and acquired primary autoimmune and idiopathic chronic neutropenic disorders experiencing recurrent and/or serious infections
Compound:	Mavorixafor (X4P-001)
Indication:	Congenital and acquired primary autoimmune and idiopathic chronic neutropenic disorders

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DATABASE ITALIANO TELOMEROPATIE (DIT)

Obiettivi:

Raccolta dati clinico-molecolari + campioni biologici

Studi clinico-biologici

Approfondimenti genetici

Collaborazione tra Centri AIEOP nella gestione dei pazienti affetti

Studi collaborativi ulteriori

CRITERI DI INCLUSIONE

- TL sulle cellule mononucleate e/o linfociti patologica (< 10°p per età)

e/o

- Mutazioni TBD

e/o

- Clinica suggestiva

Almeno 3 tra:

Leucoplachia, distrofia ungueale, pigmentazione reticolare della cute, pneumopatia, epatopatia, BMF

CRITERI DI ESCLUSIONE

- Altre insufficienze midollari congenite (FA, SDS, DBA…)
- TL non patologica (> 10°p per età) *** in corso di emendamanto**
  - TBD are not inevitably associated with global short TL→ Some variants not affecting TL (but its stability) i.e.: some in the shelterin complex component POT1; biallelic variants in CTC1 and STN1 and DCLRE1B

No limiti di età

Pz afferenti a Centri AIEOP e GIMEMA !!

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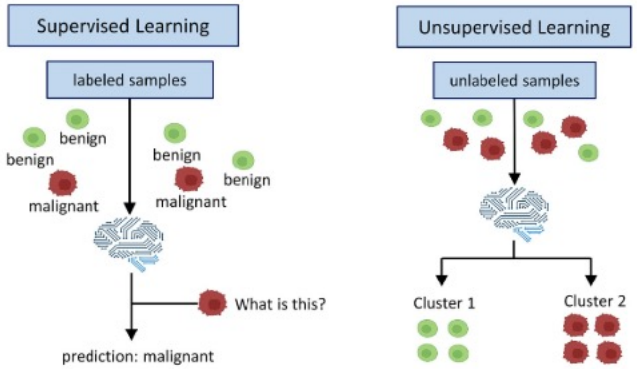
AIEOP Associazione Italiana Ematologia Oncologia Pediatrica

APPLICATION OF MACHINE LEARNING IN THE DIAGNOSTIC WORK-UP OF TELOMERE BIOLOGY DISORDERS

- Cohort of 140 patients - Hematology Unit of the Gaslini Institute 1989-2023
- Inclusion criteria: persistent cytopenia and/or features suggestive of TBD
- 85/140 males, median age of 13.28 years (range 0.25-61.29)
- Clinical, biochemical, and genetic features were collected
- Patients labeled according to molecular diagnosis (P/LP variants)
  - **"TBD" (n=20)**
  - **"Other congenital diseases" (n=27)**
  - **"Undefined diagnosis" (n=93).**
- Supervised and unsupervised ML analyses



Eckardt, J. N., et al.,
Frontiers in oncology, 12, 960984 (2022)

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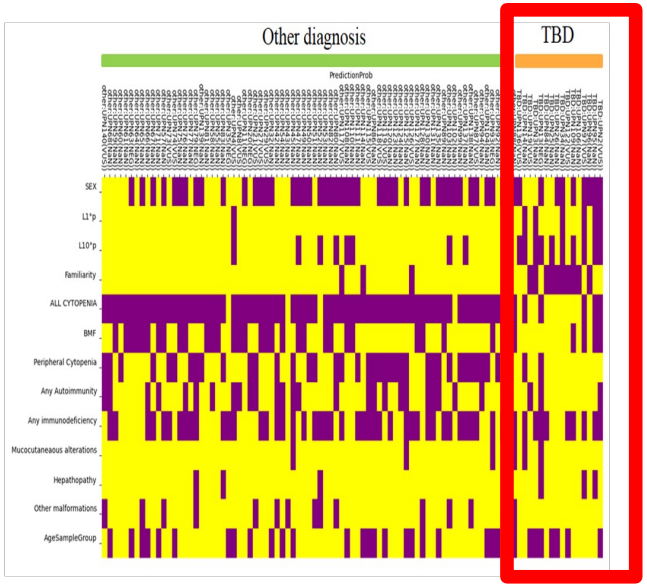
Massaccesi E et al. HemaSphere 2025, under revision

SUPERVISED ANALYSIS

1. **Training phase:** subset of patients with confirmed diagnosis (n=47, TBD + Other Dg), Random Forest model Accuracy prediction: 75% for "TBD" patients, 96% for "Other congenital diseases" patients.
2. **Testing phase**: subset of undiagnosed patients (n=93)

Predictions: 16/93 TBD - 77/93 Other congenital diseases (Fig. 1)
17.2% and 82.7% of possibly reallocated diagnoses respectively

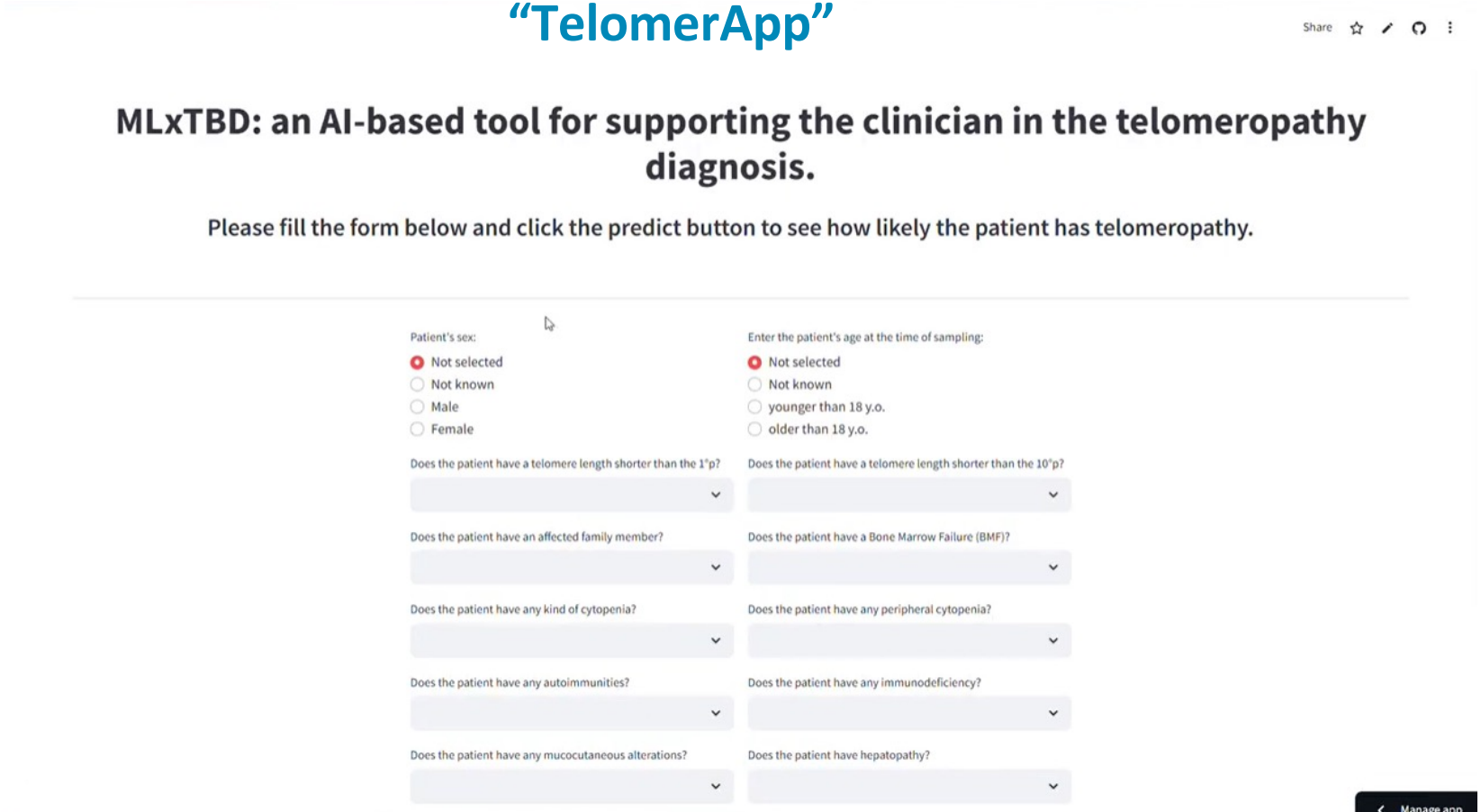


Further genetic screening indicated to reveal potential uncharacterized TBD mutations.

5/16 VUS TBD genes → HOT VUS?

Figure 1: values distribution and predictions in testing set of “Undefined diagnosis”. Features on the Y-axis, predictions on the X-axis “Other diagnosis" versus “TBD"

"TelomerApp"



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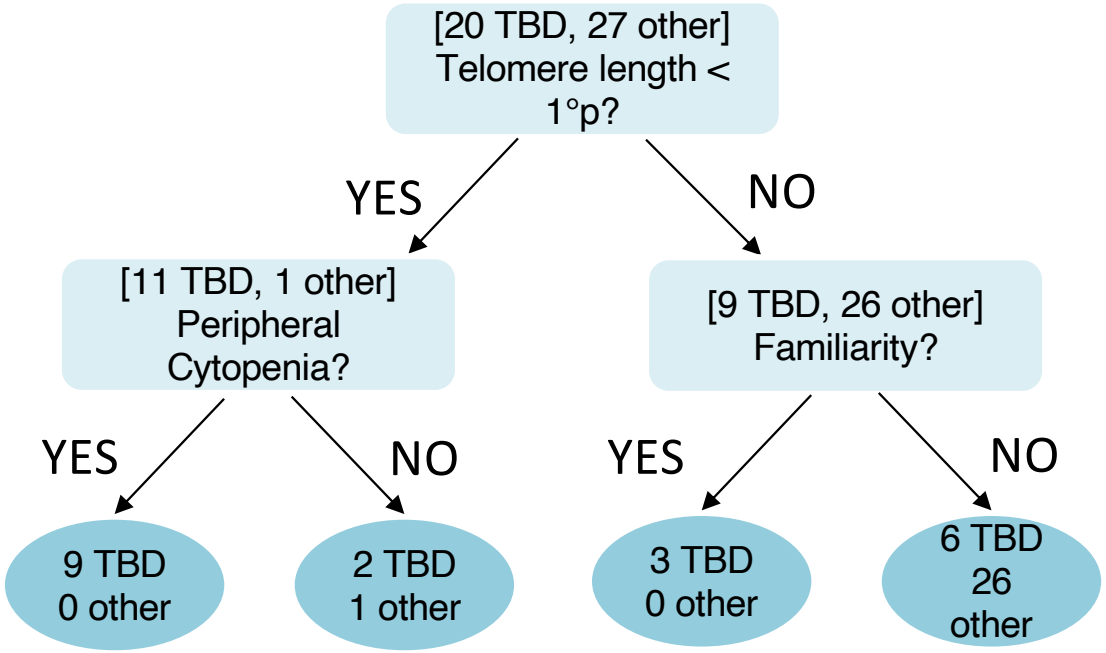
Link video:
https://drive.google.com/file/d/1l8eMksqf51g3ptukafALdXS4DymZfxmo/view?usp=sharing

What's behind it?

Example of a decision tree



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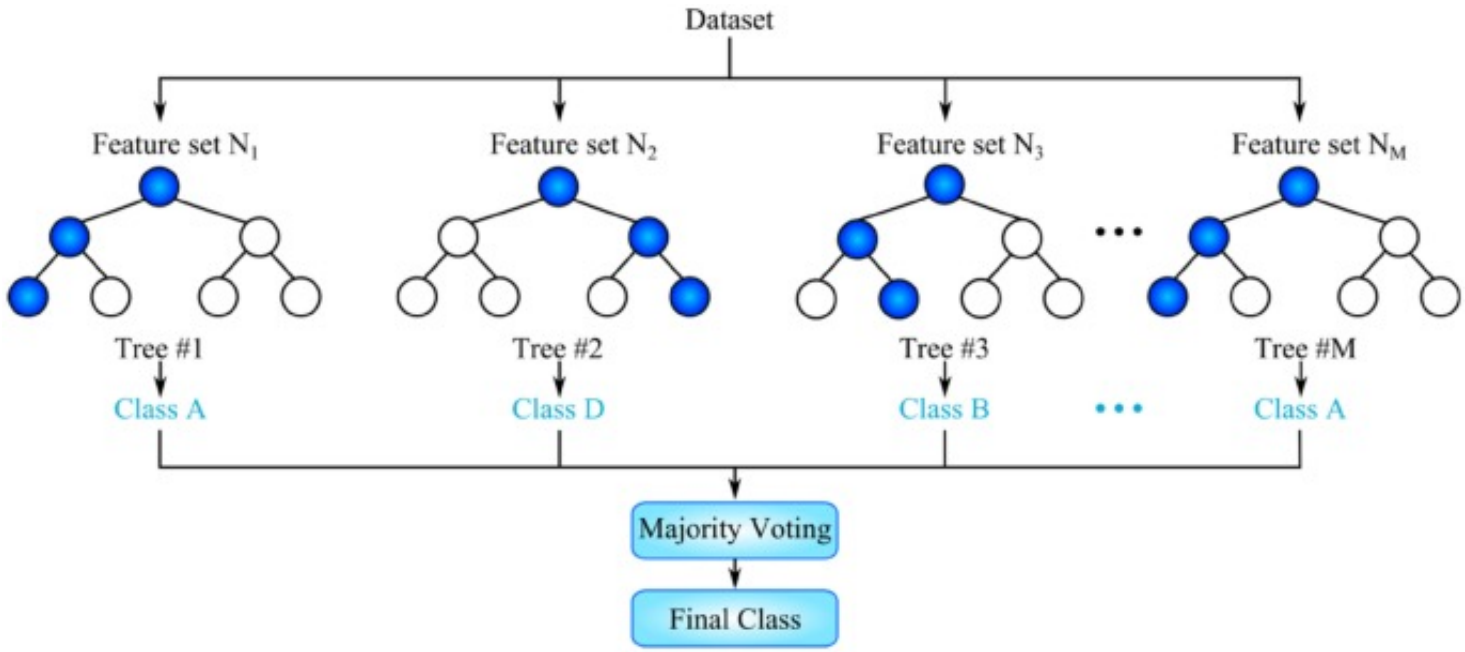
What's behind it?

Random Forest



Khozeimeh, F. et al.
Sci Rep, 12, 11178 (2022)

Advantages and considerations

- Supports clinicians in the decision-making process for ambiguous cases
- Easy to use and quick to integrate in the diagnostic workflow
- Provides an additional perspective using a data-driven approach
- Training on a larger cohort will further improve the model's robustness.

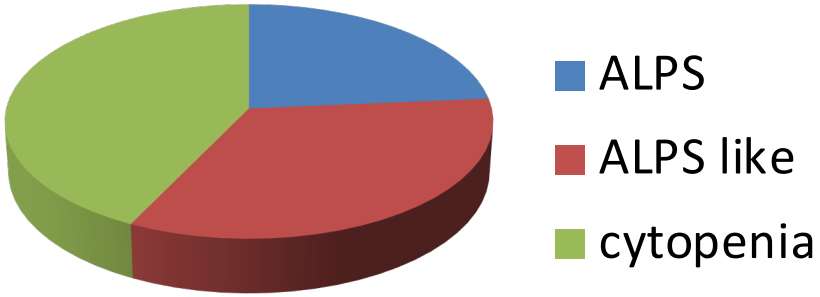
ALPS.IT.NET update gennaio 2025

381 pazienti

90 **ALPS**

128 **ALPS like**

163 **citopenia autoimmune**



ALPS.IT.NET

Redcap

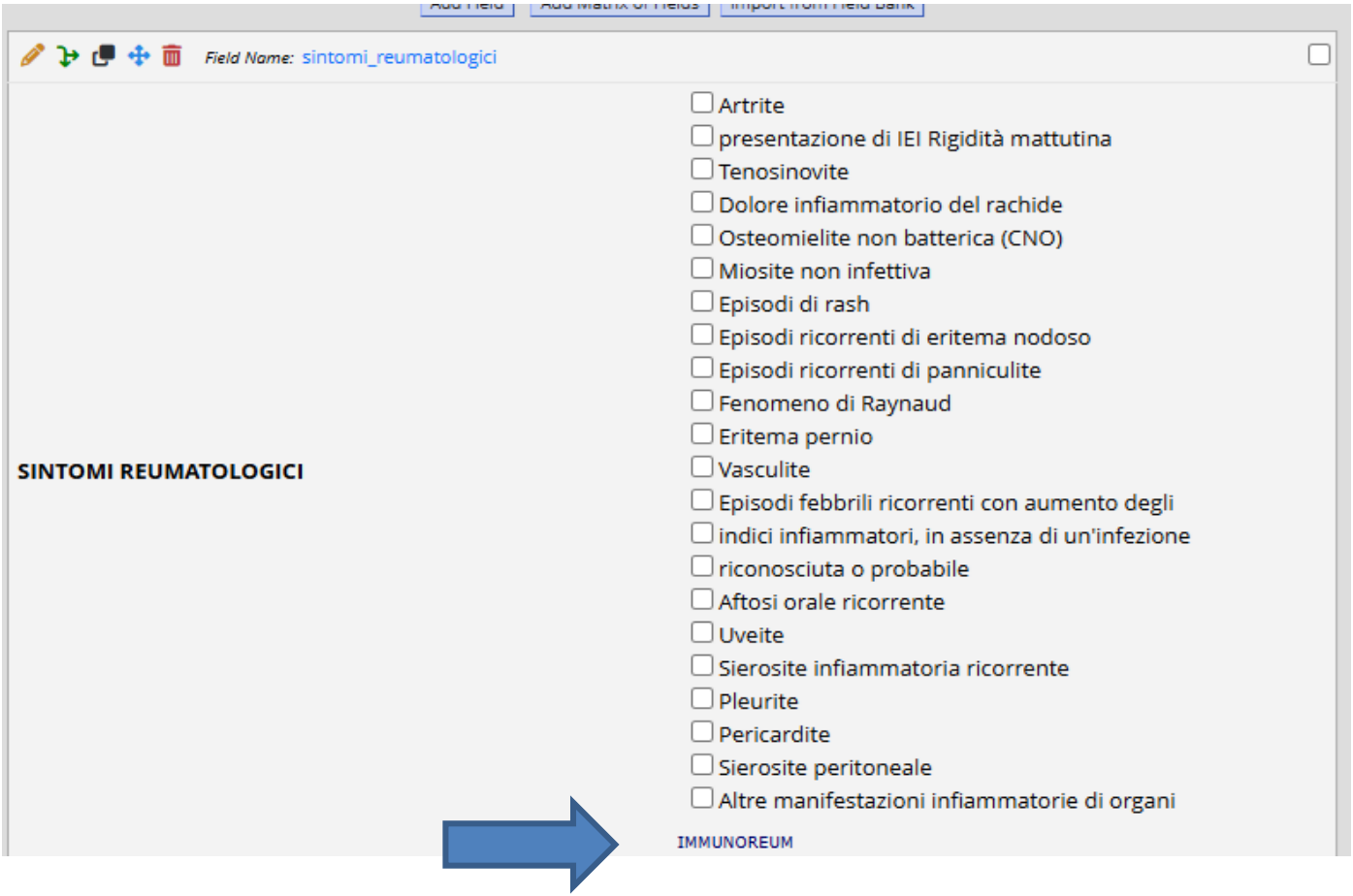
https://redcap.gaslini.org/redcap/redcap_v14.7.0/ProjectSetup/index.php?pid=61&msg=newproject

Role name (click role name to edit role)	Username or users assigned to a role (click username to edit or assign to role)	Expiration (click expiration date to edit)	Data Access Group	Project Design and Setup	User Rights	Data Access Groups
Data Entry	[No users from your group are assigned]			✗	✗	✗
Project Manager	elenapalmisani (Elena Palmisani)	never	Gaslini	✓	✓	✓

Record ID	ANAGRAFICA	CLINICA	EMOCROMO	IMMUNOGLOBULINE e SOTTOCLASSI IGG	PANNELLO ALPS	SOTTOPOPOLAZIONI LINFOCITARIE	CITOCHINE ALPS E VIT B12	TEST FUNZIONALE APOPTOSI FAS MEDIATA	MARKERS AUTOIMMUNI	TITOLI VACCINALI	GENETICA	BIOPSIA LINFONODO	ANAMNESI FAMILIARE	SINTOMI ASSOCIATI	DIAGNOSI	TERAPIA
1072-1																

Pilota: Perugia Parma Catania Genova

Insufficienze midollari/Ipinet



HOT SPOT

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Nuove proposte

CSF3R: the long Italian story

Acquired mutations in the intracellular part of *CSF3R* occur in >30% in SCN patients

>80% of SCN patients who develop MDS/AML have *CSF3R* mutations
CSF3R clones are dynamic → may disappear and reappear during G-CSF therapy

Aim of the study

observation of clones dynamic overtime in SCN italian population

Patients and methods

Retrospective observational study (**Registry based**)
Analyses performed at the **Genetics Lab** of the **Meyer Children's Hospital IRCCS**
Population → pediatric and adult patients with SCN tested for *CSF3R* somatic mutations

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Rosenberg PA BJH 2010, Klimiankou M, Ann N Y Acad Sci 2016

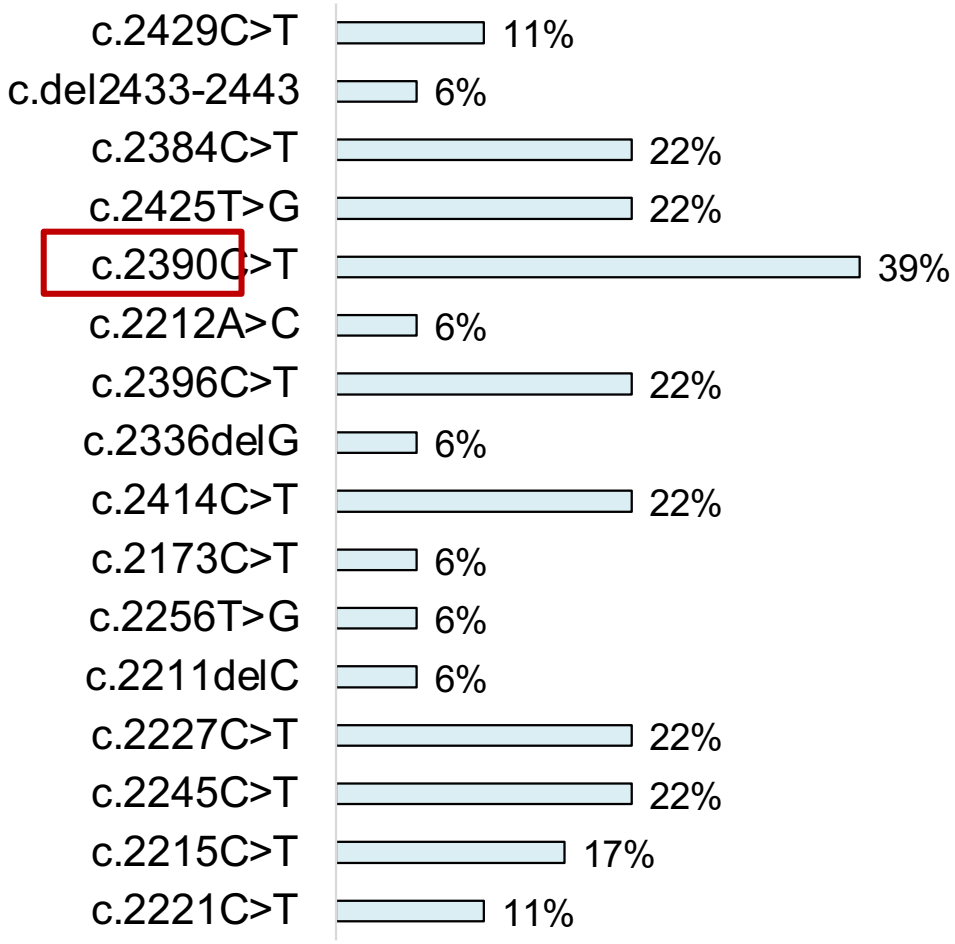
Results – *Patients*

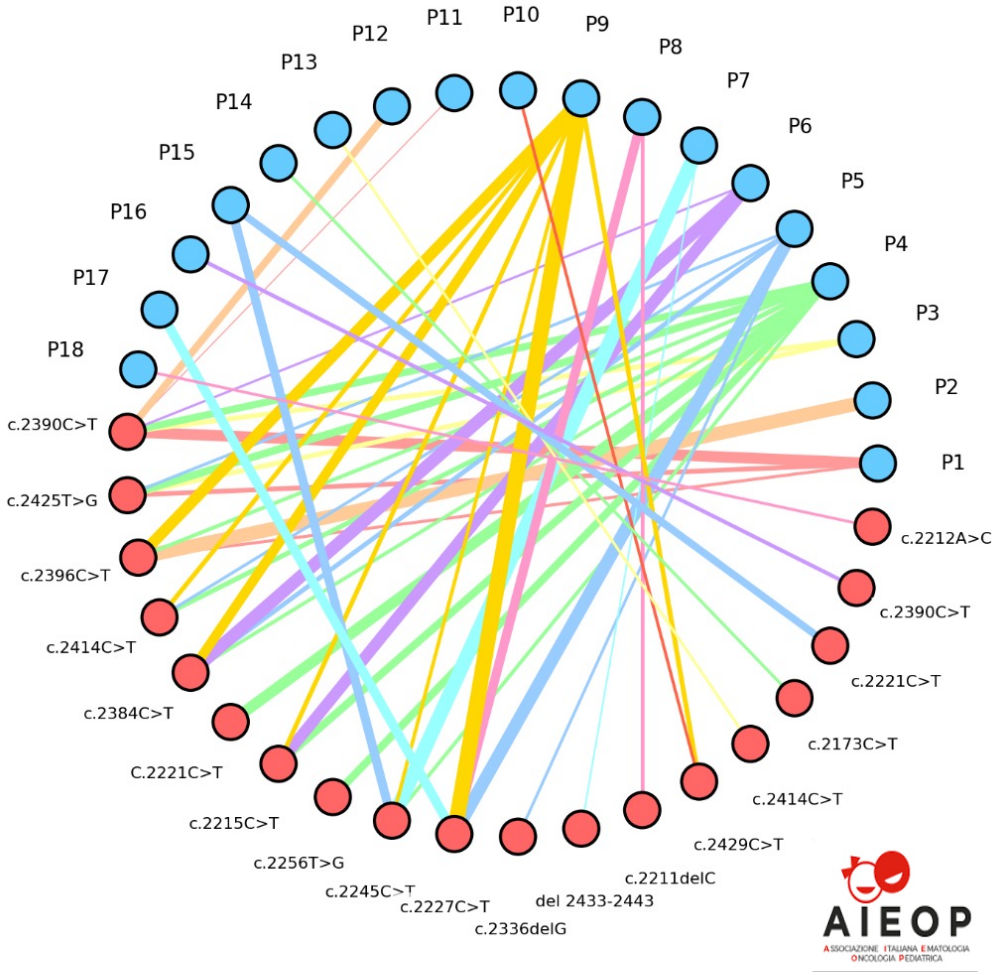
57 patients included (2004-2024)

Contributing centers	
Genova	14
Monza	12
Firenze	6
Padova	6
Bari	4
Perugia	4
Pisa	4
Brescia	2
Catania	1
Napoli	1
Palermo	1
Parma	1
Verona	1

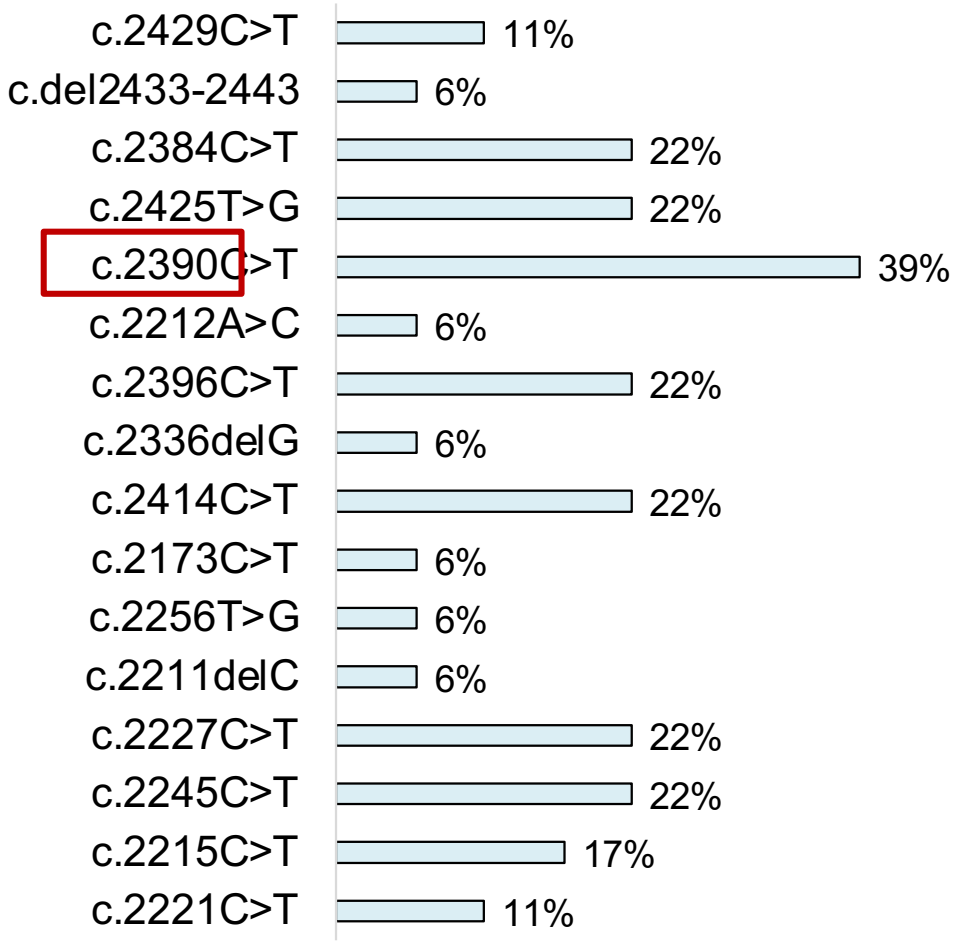
	All patients (n=57)
Female sex, n (%)	29 (51)
Median age at diagnosis, months (IQR)	12 (3-65)
SCN mutated gene, n (%) *ELANE* *HAX1* *SRP54* Gene orphan Others	 35 (61) 2 (4) 3 (5) 10 (18) 7 (12)
Median age at the beginning of G-CSF treatment, months (IQR)	12 (3-51)
Median age at the last follow-up, years (IQR)	14 (7-22)
Evolution to MDS/AML, n (%) Median age at MDS/AML, years (IQR)	6 (11) 9 (6-17)
HSCT, n (%) Median age at HSCT, years (IQR)	14 (25) 3 (2-15)
Deaths at last follow-up, n (%) Causes of death, n (%) MDS/LAM Infection TRM Others	6 (11) 1 (2) 1 (2) 3 (5) 1 (2)

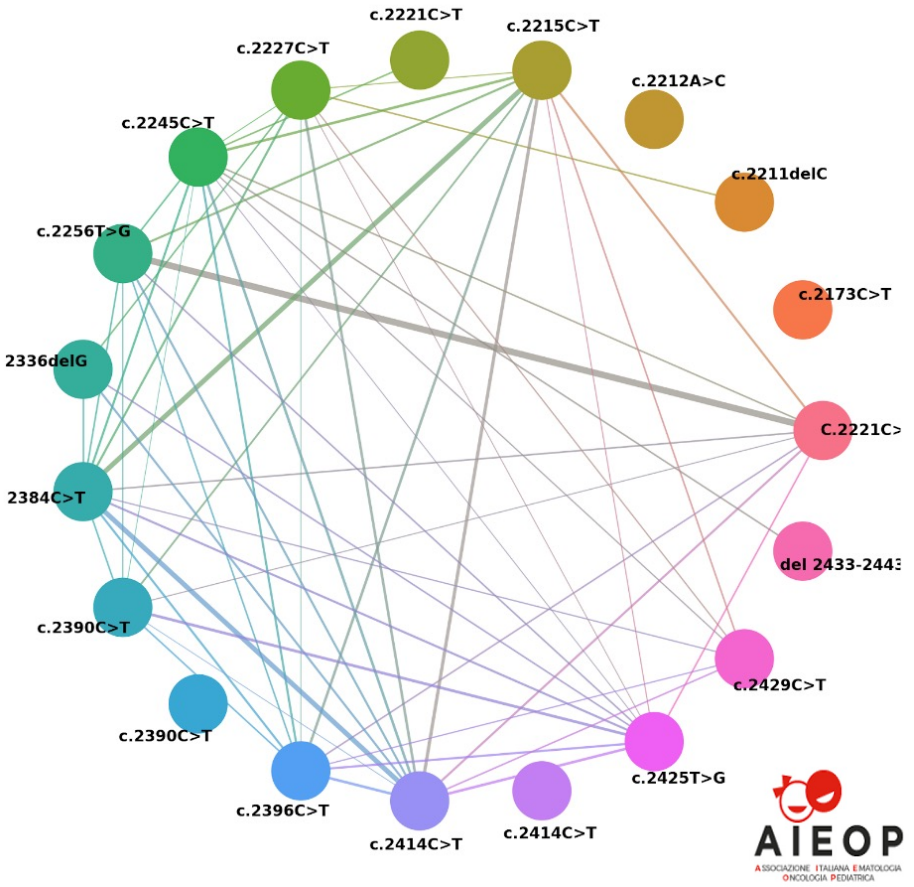
Results – *CSF3R clones*





Results – CSF3R clones



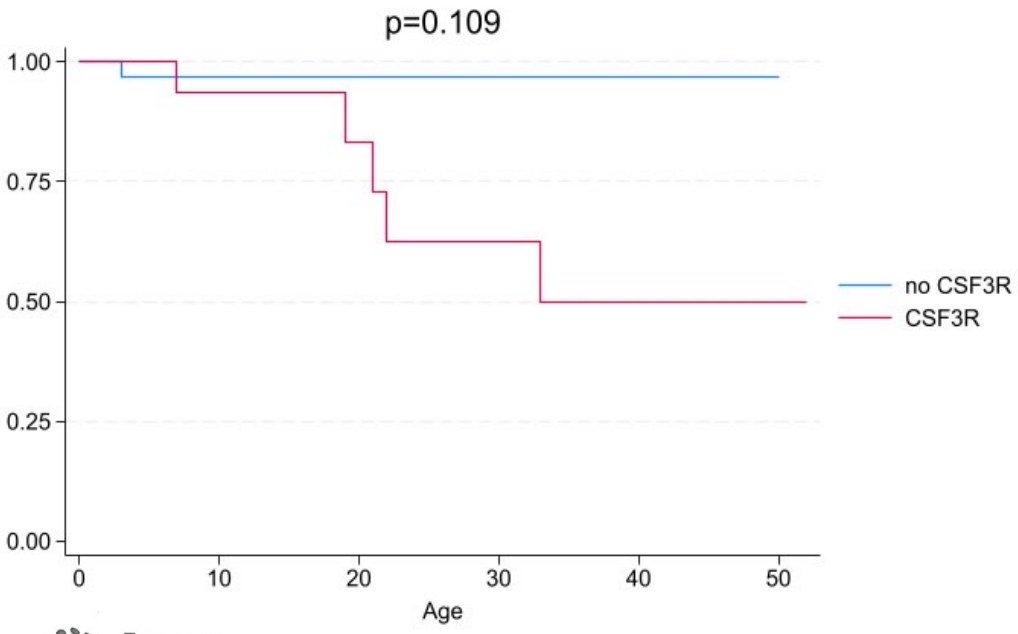


Results – *Clinical implication of CSF3R clones*

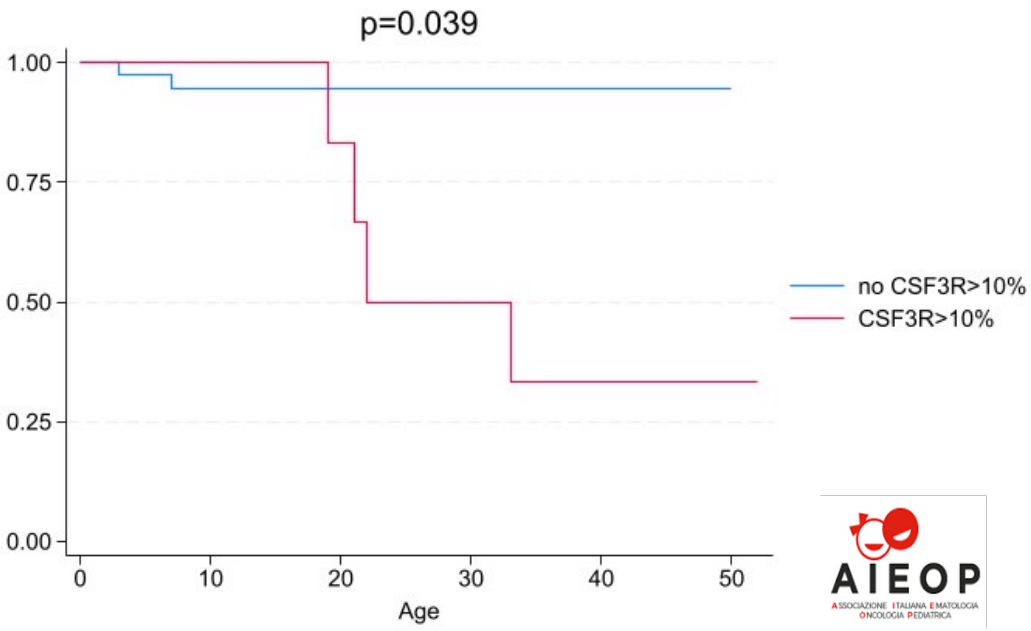
	Patients with *CSF3R* mutations (n=18)	MDS/AML evolution (n=5)	No MDS/AML evolution (n=13)	*p*-value#
Median age at the first *CSF3R* clone detection, months (IQR)	142 (72-277)	117 (83-181)	142 (72-277)	0.347
Median number of clones per patient (IQR)	2 (1-3)	2 (2-3)	1 (1-2)	0.258
CSF3R type of clone, n (%)				
c.2221C>T°	2 (11)	0 (0)	2 (15)	1.000
c.2215C>T°	3 (17)	2 (40)	1 (8)	0.172
c.2245C>T°	4 (22)	2 (40)	2 (15)	0.532
c.2227C>T°	4 (22)	1 (20)	3 (23)	1.000
c.2211delC°	1 (6)	0 (0)	1 (8)	1.000
c.2256T>G°	1 (6)	0 (0)	1 (8)	1.000
c.2173C>T°	1 (6)	0 (0)	1 (8)	1.000
c.2414C>T°°	4 (22)	1 (20)	3 (23)	1.000
c.2336delG°°	1 (6)	0 (0)	1 (8)	1.000
c.2396C>T°°	4 (22)	2 (40)	2 (15)	0.532
c.2212A>C°°	1 (6)	0 (0)	1 (8)	1.000
c.2390C>T	7 (39)	1 (20)	6 (46)	0.596
c.2425T>G	4 (22)	1 (20)	3 (23)	1.000
c.2384C>T	4 (22)	2 (40)	2 (15)	0.532
c.del2433-2443	1 (6)	1 (20)	0 (0)	0.278
c.2429C>T	2 (11)	1 (20)	1 (8)	0.490
Median value of maximum clone size per patient (IQR)	8.4 (1.2-19.3)	28.6 (21-32)	5 (1.1-9.3)	0.020

Results – *evolution-free survival*

Any clone



Clones >10%



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Conclusions and perspectives

CSF3R mutations can be detected regardless of MDS/AML transformation

Transformation likely depends on

- Type and number of clones X
- Growing / large clones V

Longitudinal monitoring is warranted

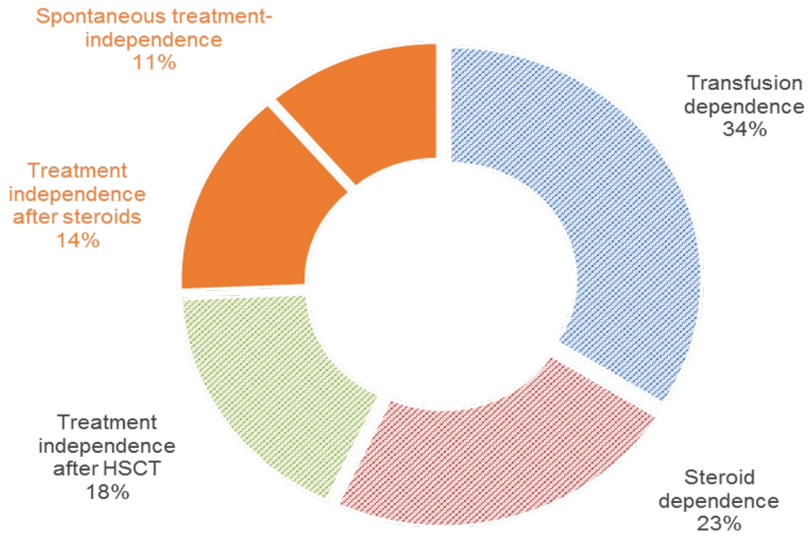
Diagnosis, treatment, and surveillance of Diamond-Blackfan anaemia syndrome: international consensus statement

Marcin W Wlodarski, Adrianna Vlachos*, Jason E Farrar*, Lydie M Da Costa, Antonis Kattamis, Irma Dianzani, Cristina Belendez, Sule Unal, Hannah Tamary, Ramune Pasauliene, Dagmar Pospisilova, Josu de la Fuente, Deena Iskander, Lawrence Wolfe, Johnson M Liu, Akiko Shimamura, Katarzyna Albrecht, Birgitte Lausen, Anne Grete Bechensteen, Ulf Tedgard, Alexander Puzik, Paola Quarello, Ugo Ramenghi, Marije Bartels, Heinz Hengartner, Roula A Farah, Mahasen Al Saleh, Amir Ali Hamidieh, Wan Yang, Etsuro Ito, Hoon Kook, MD, Galina Ovsyannikova, Leo Kager, Pierre-Emmanuel Gleizes, Jean-Hugues Dalle, Brigitte Strahm, Charlotte M Niemeyer, Jeffrey M Lipton*, Thierry M Leblanc*, on behalf of the international Diamond-Blackfan anaemia syndrome guideline panel†*

ITALIAN DBA REGISTRY

Treatment-independence (formerly remission)
Approximately 20% of patients previously treated with steroids or transfusions can become treatment-independent (ie, able to discontinue all therapy for anaemia).

25%



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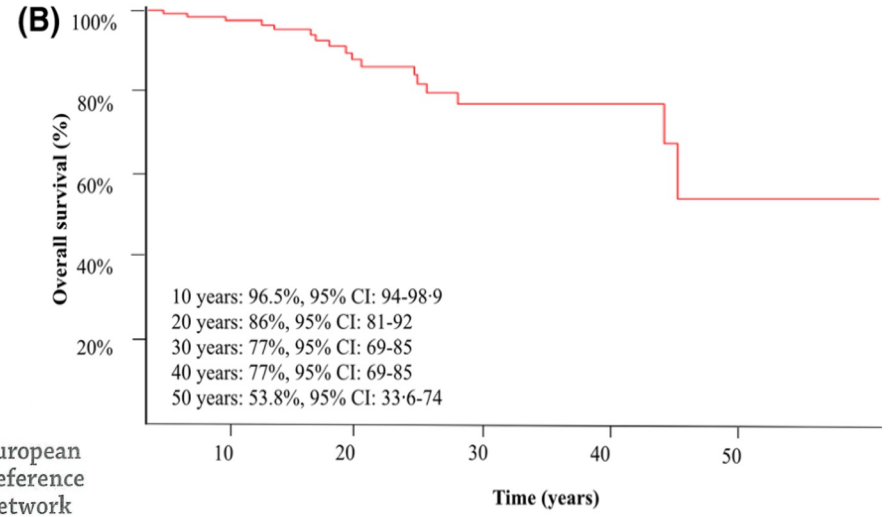
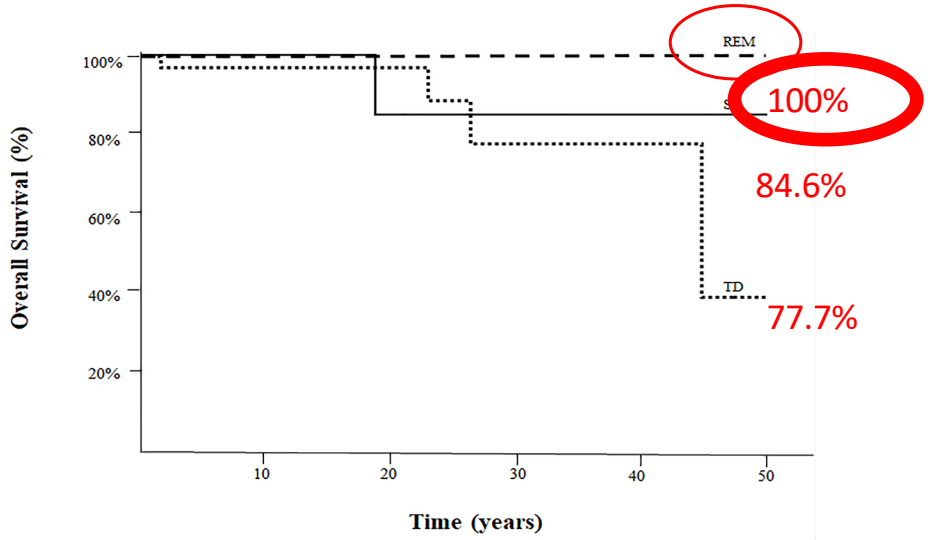
ITALIAN DBA REGISTRY

Follow-up and survival

The median duration of follow-up was 12 years (range 2 months–68 years)
The OS rate was 86% at 20 years and 77% at 30 years of age





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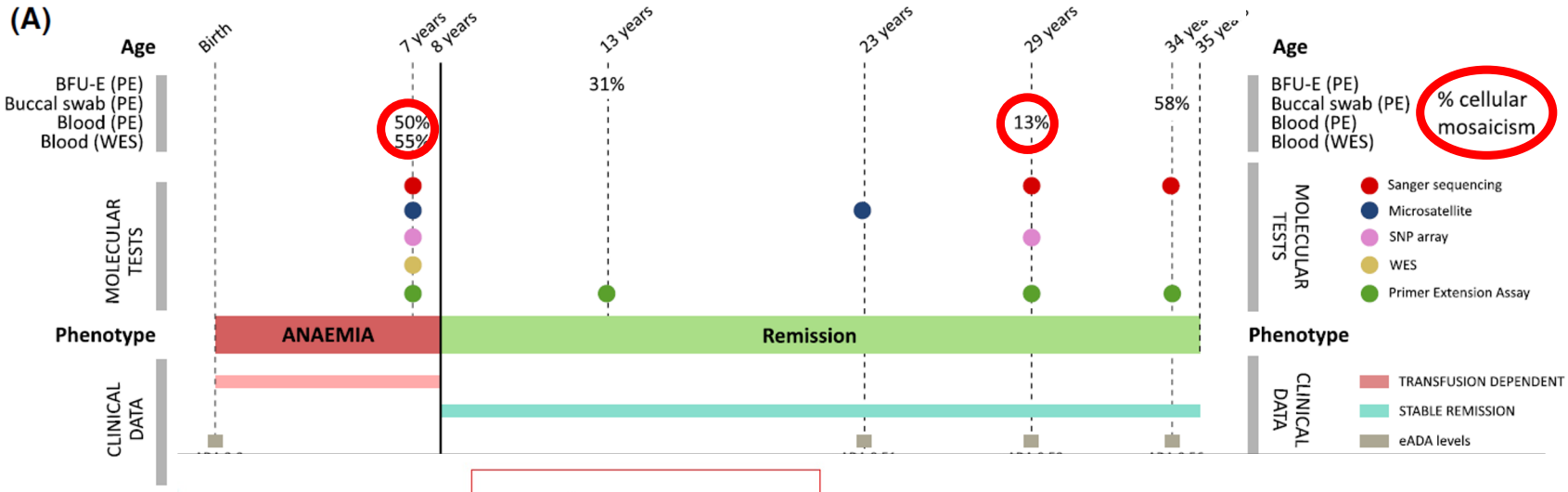
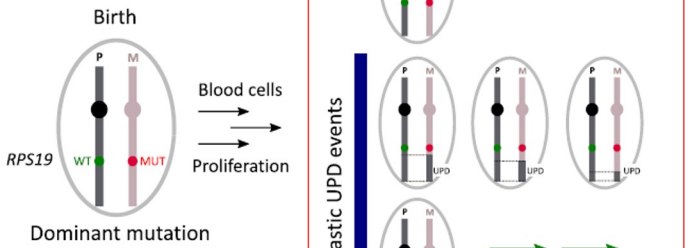
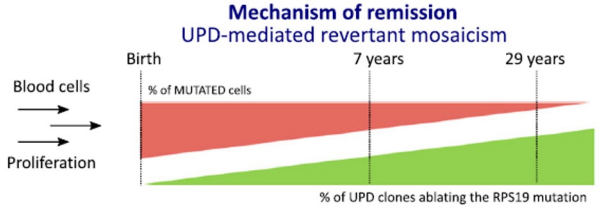
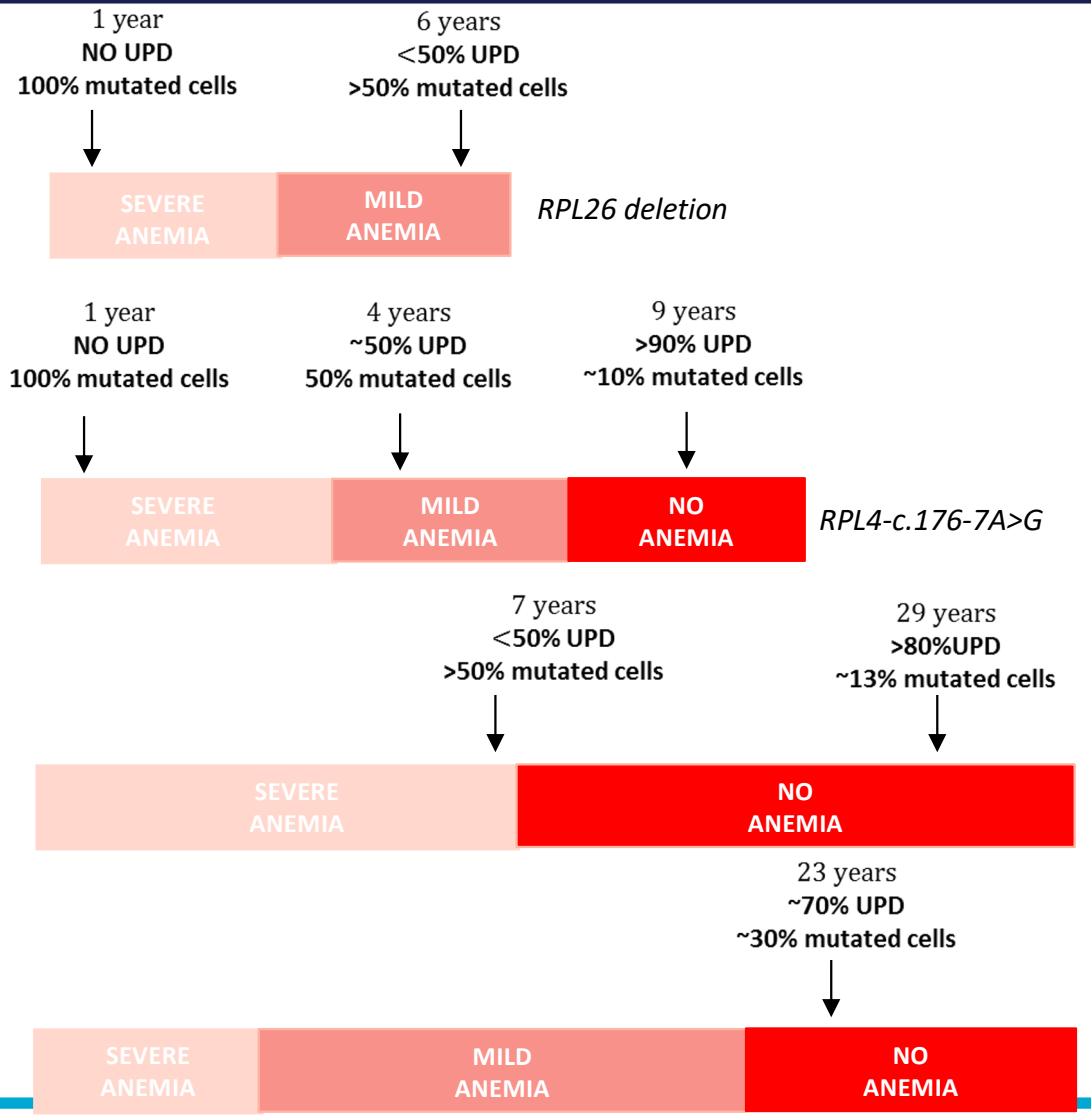






RPS19 revertant cells had a proliferative advantage and after several years, the % of UPD clones ablating the *RPS19* mutation are enough to sustain a normal red cell production



Phenotypic rescue only if mutated cells < 50%

No information about timing of the evolution of the UPD

Venugopal et al. 2017, Jongmans et al. 2018, Garelli et al. 201

Revertant mosaicism is important:

-To understand how achieving the treatment indipendence

-To understand the variable expression of phenotype /evolution of disease

OPEN QUESTIONS

How and why did the somatic genetic reversion occur?

Which factors influenced the proliferation of revertant cells?

What is the minimum percentage of revertant cells required for phenotypic rescue?

Which factors influence the timing of phenotypic rescue? Is there a correlation with specific conditions (nature of the sequence, other genetic or epigenetic factors?)

Does revertant mosaicism impact on clinical decision? How can we manage a patient with revetant nosaicism?How does the presence of revertant mosaicism influence the indication to HSCT ?

Which could be a strategy for detecting mosaicism? Should we analyze selected patisnts based on clinical evolution or molecular hints, or shoulwe analyze al patients? If yes when? At specific time points? A single diagnsois time point may not be suffcient , considering that the mosicism is a dinamic event…..

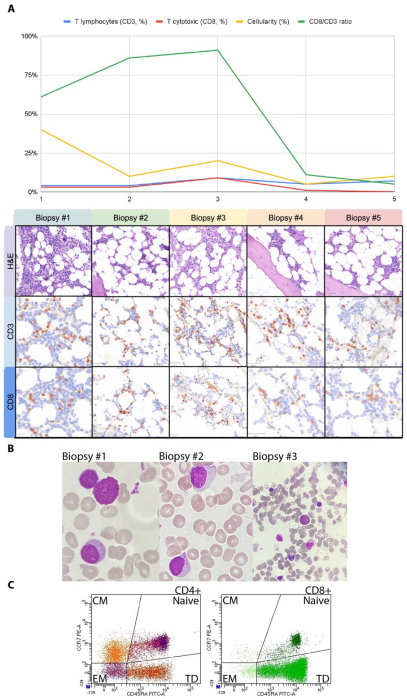
Role of CD8 in immunosurveillance of GATA2 deficiency

Journal of Clinical Immunology (2025) 45:77
https://doi.org/10.1007/s10875-025-01871-5

RESEARCH

Bone Marrow CD8 + Abundance Inversely Correlates with Progressive Marrow Fibrosis and Myelodysplastic Evolution in GATA2 Deficiency: Case Report

Francesca Vendemini[1] · Samuele Roncareggi[1] · Vincenzo L'Imperio[2] · Fabiola Guerra[1,3] · Federica Mottadelli[4] · Marco Chiarini[5] · Oscar Maglia[4] · Simona Sala[4] · Grazia Fazio[3,4] · Rocco Piazza[3] · Sonia Bonanomi[1] · Andrea Biondi[1,3,4] · Francesco Saettini[4]



While PB CD8+ remained stable over time (with an expansion of TEMRA), a notable reduction in BM CD8+ was observed in association with MDS progression.

Decrease in BM CD8+ T cells may serve as an early marker of immune surveillance escape and disease progression.

Cell

Article

LAG-3 and PD-1 synergize on CD8⁺ T cells to drive T cell exhaustion and hinder autocrine IFN-γ-dependent anti-tumor immunity

Graphical abstract

Authors

Lawrence P. Andrews, Samuel C. Butler,

Cell

Article

Intercellular nanotube-mediated mitochondrial transfer enhances T cell metabolic fitness and antitumor efficacy

Graphical abstract

Authors

Jeremy G. Baldwin,

AIEOP
ASSOCIAZIONE ITALIANA EMATOLOGIA ONCOLOGIA PEDIATRICA

Role of CD8 in GATA2 deficiency immuno-surveillance

Background: The T-cell compartment plays a critical role in the pathogenesis, maintenance, and progression of MDS, characterized by T-cell exhaustion, impaired cytotoxicity, and restricted T-cell repertoire.

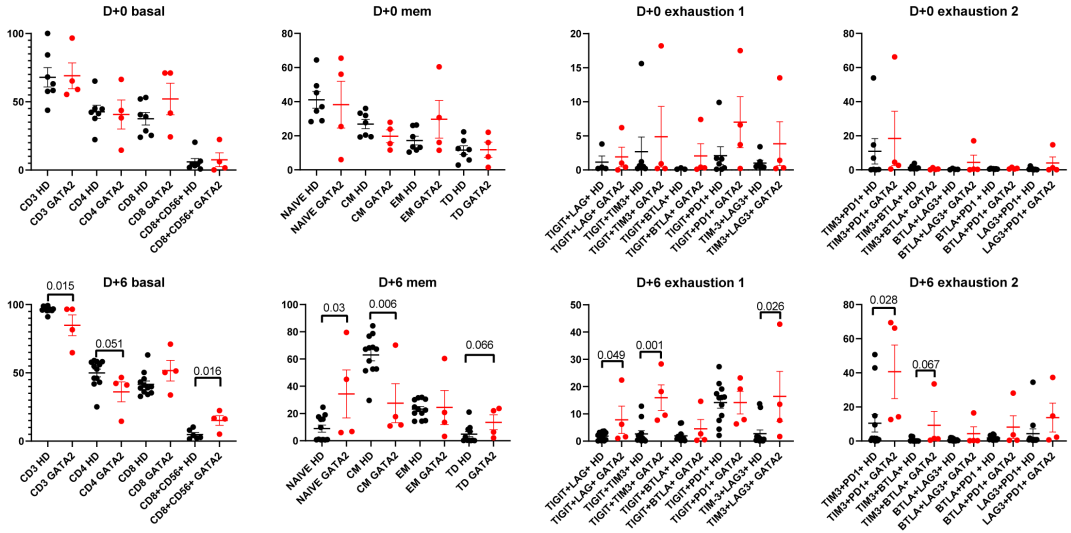
Ipotesi:

- Fenotipo esausto dei CD8+ nei pazienti GATA2?
- Alterazioni metaboliche e funzionali dei CD8+ GATA2def?

Generazione di **CIK** (Cytokine Induced Killer cells): IFNγ at day 0, anti-CD3 mAb (OKT3) and IL-2 24 hours later and by repeated addition of IL-2 every three days

Risultati preliminary: HD = 4-9, GATA2 = 4.

In Corso 4 ulteriori GATA2



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Work in progress

Development of translational read-through-inducing drugs as novel therapeutic options for patients with Fanconi anemia

16%, 21%, 31% →FANCA, FANCC, FANCF → nonsense mutations

Ataluren (PTC124)

- ✓ **Small molecule** developed in the **early 2000s**
- ✓ In 2014 authorization in the European Union for the treatment of Duchenne's Muscular Distrophy
- ✓ It forces the translational read-through of premature termination codons (PTC), by substituting the recruitment of the eukaryotic translation termination complex eRF1/eRF3 with the insertion of a near-cognate tRNA

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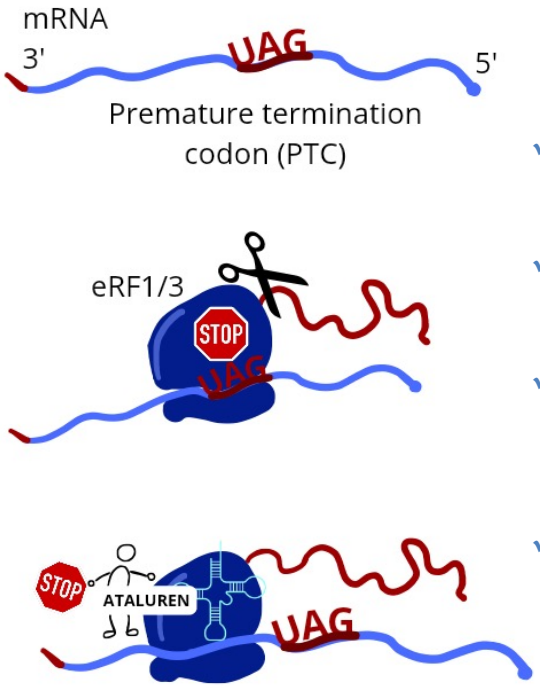

Amlexanox

- CAS 68302-57-8 **-**

- ✓ **Small molecule** developed in the **1980s** as an ocular anti-allergic drug
- ✓ FDA approved in 1996 and used in Japan to treat asthma, rhinitis and conjunctivitis
- ✓ Currently explored as potential treatment for many **metabolic and inflammatory diseases**, cancer and diabetes
- ✓ It is a potent **kinase inhibitor** that allegedly possesses **translational readthrough inducing** properties

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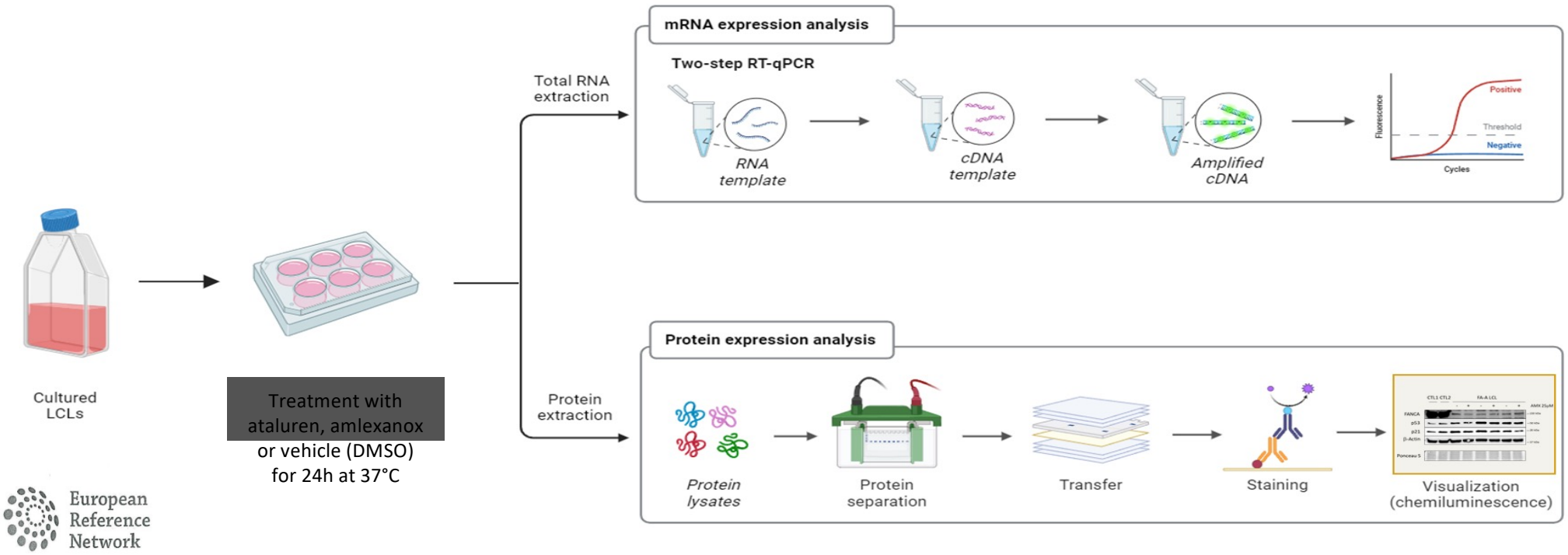
Workflow


Cultured LCLs
Treatment with ataluren, amlexanox or vehicle (DMSO) for 24h at 37°C
Total RNA extraction
Protein extraction
mRNA expression analysis
Two-step RT-qPCR
RNA template
cDNA template
Amplified cDNA
Positive
Threshold
Negative
Fluorescence
Cycles
Protein expression analysis
Protein lysates
Protein separation
Transfer
Staining
Visualization (chemiluminescence)
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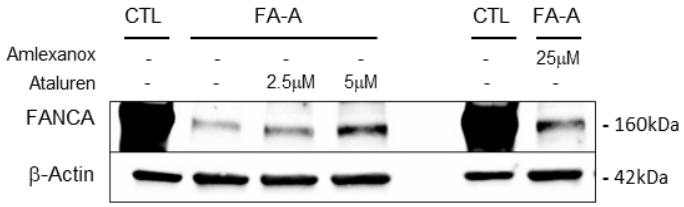
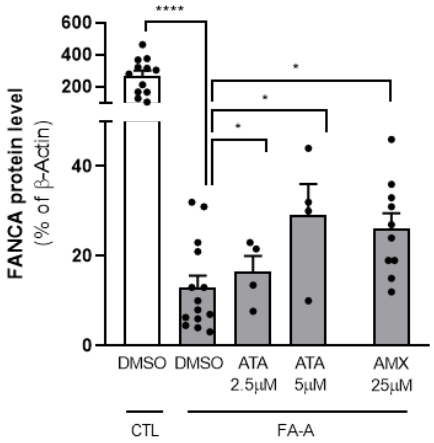
Effect of Ataluren and Amlexanox on FANCA protein levels in FA-A LCLs





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Protein expression analysis of FANCA in FA-A nonsense mutated LCLs after treatment with Ataluren (2.5 and 5mM) or Amlexanox (25mM) for 24h compared to healthy controls. Representative Western blot (left panel) and relative quantification expressed as percentage of b-Actin (right panel). *p<0.05, ****p<0.0001.

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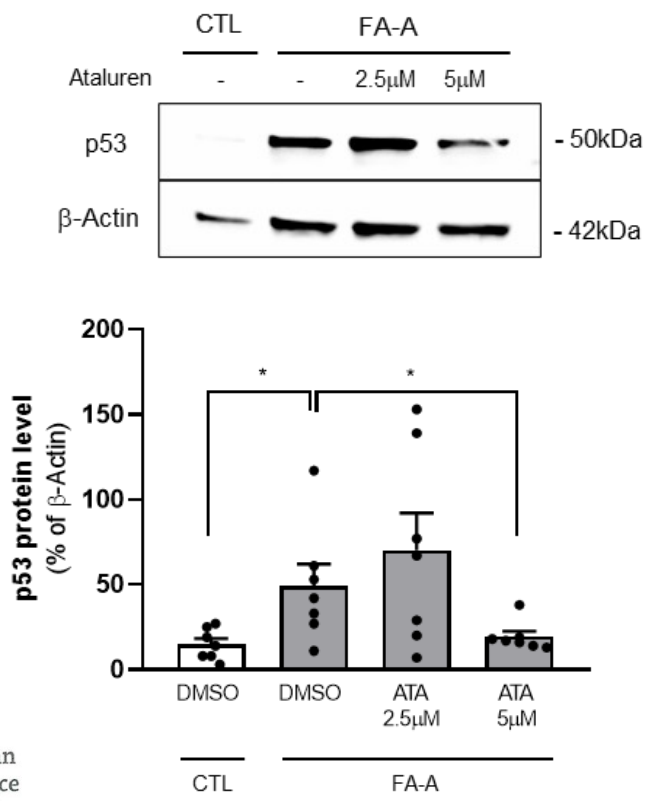
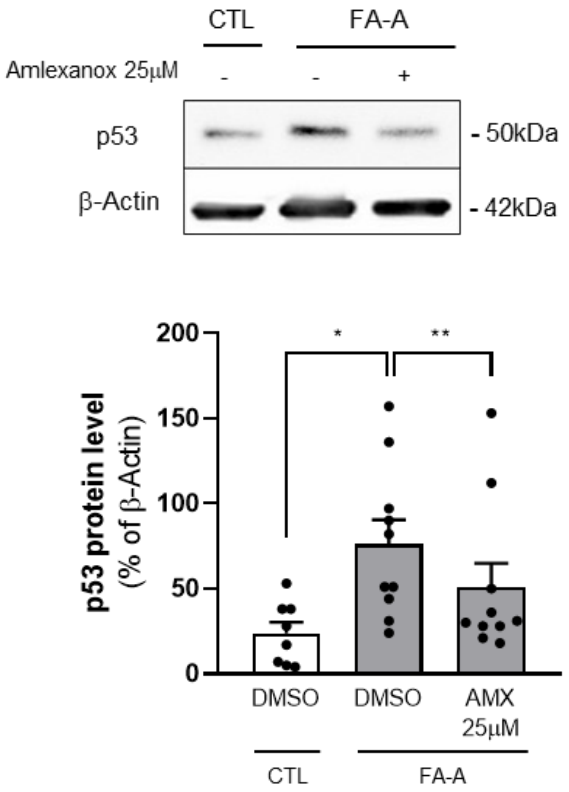
Effect of Ataluren and Amlexanox on p53 protein levels in FA-A LCLs





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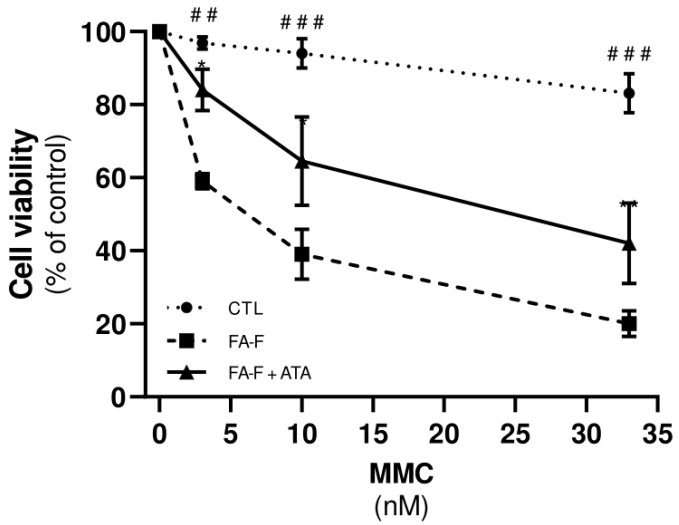
Protein expression analysis of p53 in FA-A nonsense mutated LCLs after treatment with Ataluren (2.5 and 5μM; left) or Amlexanox (25μM; right) for 24h compared to healthy controls. Representative Western blot and relative quantification expressed as percentage of β-Actin. *p<0.05, **p<0.01.

Ataluren improves cell survival upon exposure to genotoxic agent MMC



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Mitomycin C assay in FANCF (left) and FANCA (right)-mutated LCL. FA-F and FA-A cells showed a decrease of up to 76% and 58% in cell viability upon MMC treatment, respectively, displaying a dose-dependent pattern.
*p<0.05; **p<0.01; ***p<0.001.
*, comparison between basal FA condition and treated FA condition
#, comparison between healthy donors and FA

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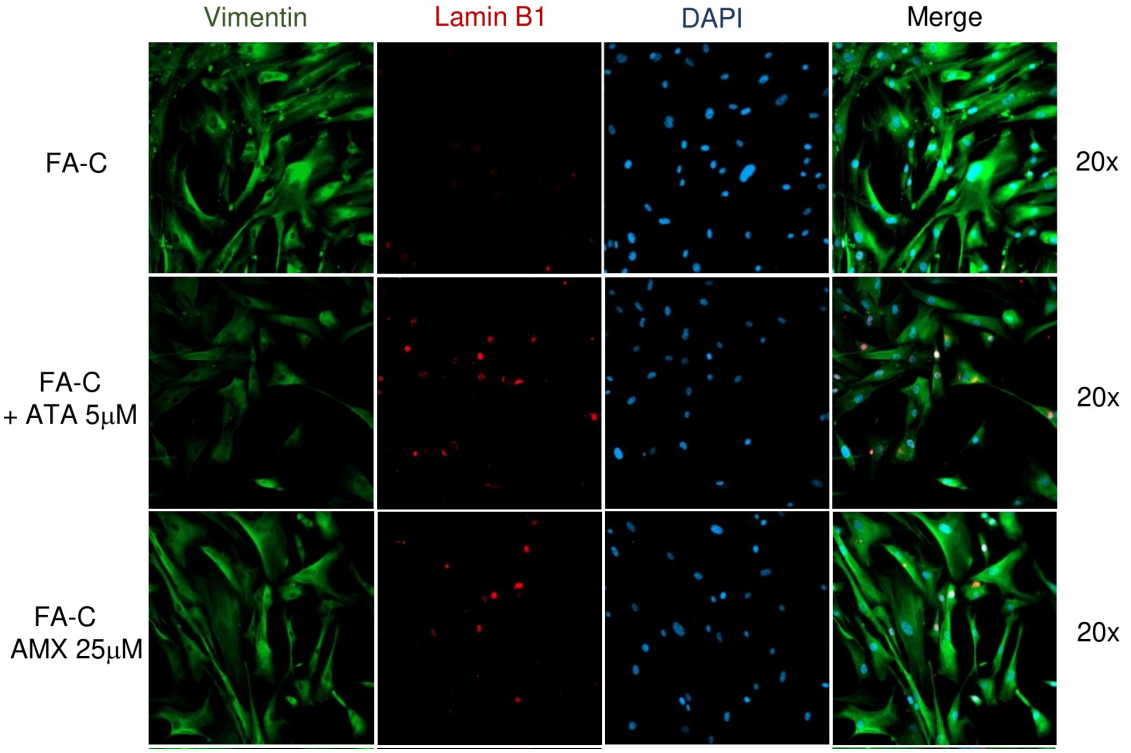
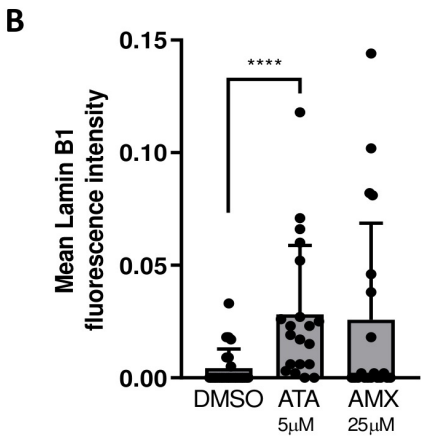
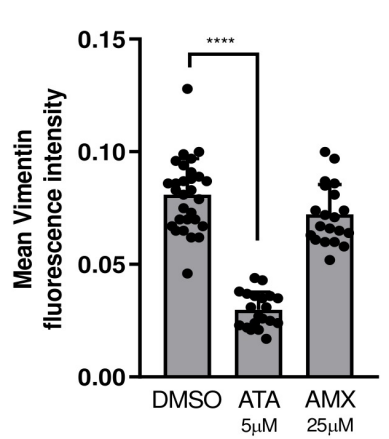
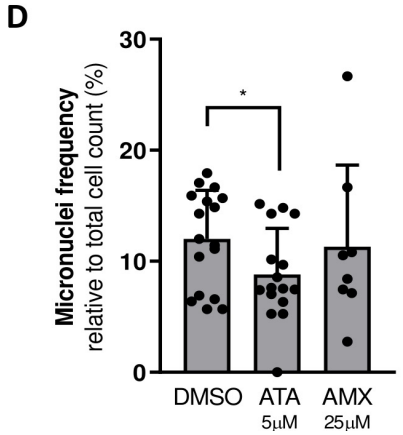
Ataluren reduces the number of micronuclei and increases LaminB1 levels, while reducing Vimentin





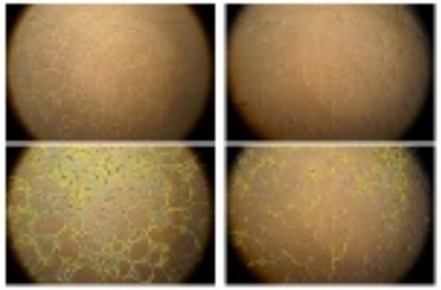




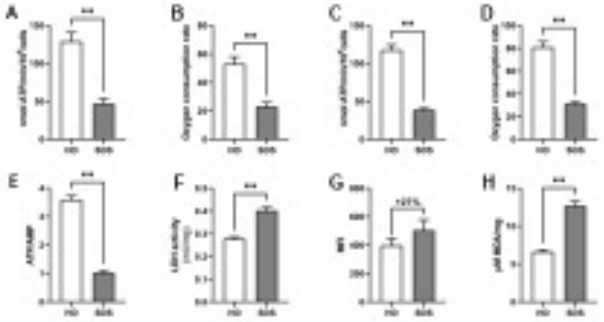
- Ataluren :
  - **Restores functional levels of FANC proteins** in patient-derived nonsense-mutated LCLs
  - **Improves the FA phenotype** by significantly reducing the abnormal **p53** levels
  - **Improves cell survival** upon exposure to MMC
  - **Reduces chromosomal aberrations** induced by DEB
  - **Reduces** the number of **micronuclei**, a hallmark of cancer and malignant transformation
  - **Increases LaminB1** levels, indicating a protective effect on the genome
- Amlexanox:
  - **Restores** FANCA protein level in FANCA-nonsense mutated LCLs
  - **Reduces** p53 levels in FANCA-mutated LCLs
  - Does not improve cell survival or chromosomal aberrations induced by MMC or DEB
  - Does not reduce the number of micronuclei
  - Does not increase levels of Lamin B1

Shwachman-Diamond Syndrome MESENCHIMAL CELLS

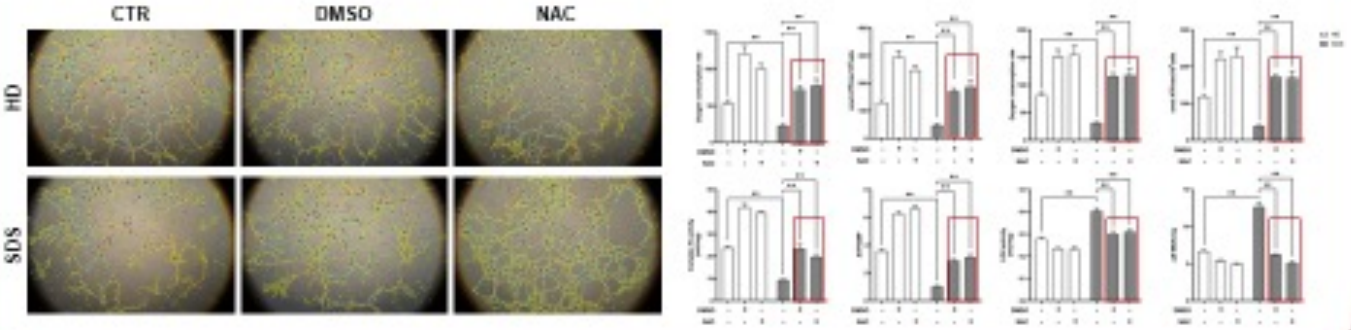
SDS-MSCs displayed impaired angiogenic potential compared to HD-MSCs



SDS-MSCs showed severe respiratory defect (A-D), decreased energy production (E-F), high oxidative damage (G-H)



Treatment with antioxidants restored the metabolic alterations and the angiogenic potential in SDS-MSCs



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SDS-MSCs showed iron overload

Received: 26 November 2020 | Revised: 17 March 2021 | Accepted: 19 March 2021
DOI: 10.1002/jcp.30383

REVIEW ARTICLE

Cellular Physiology WILEY

Role of iron and iron-related proteins in mesenchymal stem cells: Cellular and clinical aspects

Kosha J. Mehta

Research | Open access | Published: 11 September 2020

Disruption in iron homeostasis and impaired activity of iron-sulfur cluster containing proteins in the yeast model of Shwachman-Diamond syndrome

Ayushi Jain, Phubed Nilatawong, Narinrat Mamak, Laran T. Jensen & Amornrat Naranuntarat Jensen

Cell & Bioscience **10**, Article number: 105 (2020) | Cite this article

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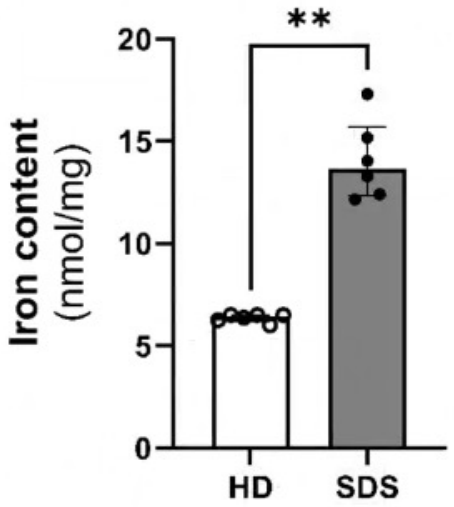
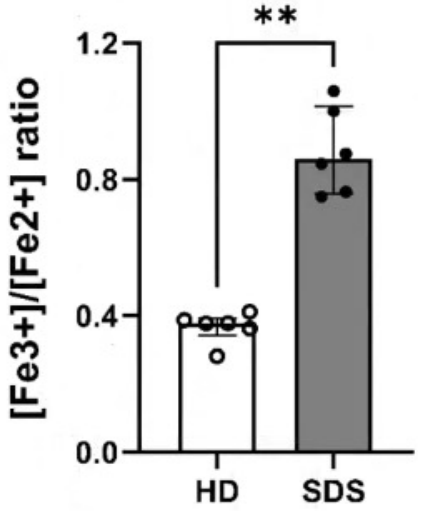
Published online 2020 Jun 8. doi: 10.1038/s41598-020-66162-y
PMCID: PMC7280296
PMID: 32514107

Iron overload alters the energy metabolism in patients with myelodysplastic syndromes: results from the multicenter FISM BIOFER study

Daniela Cilloni,[#1] Silvia Ravera,[#2,3] Chiara Calabrese,[#1] Valentina Gaidano,[1] Pasquale Niscola,[4] Enrico Balleari,[5] Daniela Gallo,[1] Jessica Petiti,[1] Elisabetta Signorino,[1] Valentina Rosso,[1] Cristina Panuzzo,[1] Federica Sabatini,[2] Giacomo Andreani,[1] Matteo Dragani,[1] Carlo Finelli,[6] Antonella Poloni,[7] Monica Crugnola,[8] Maria Teresa Voso,[9] Susanna Fenu,[10] Annamaria Pelizzari,[11] Valeria Santini,[12] Giuseppe Saglio,[1] Marina Podestà,[2] and Francesco Frassoni[#]





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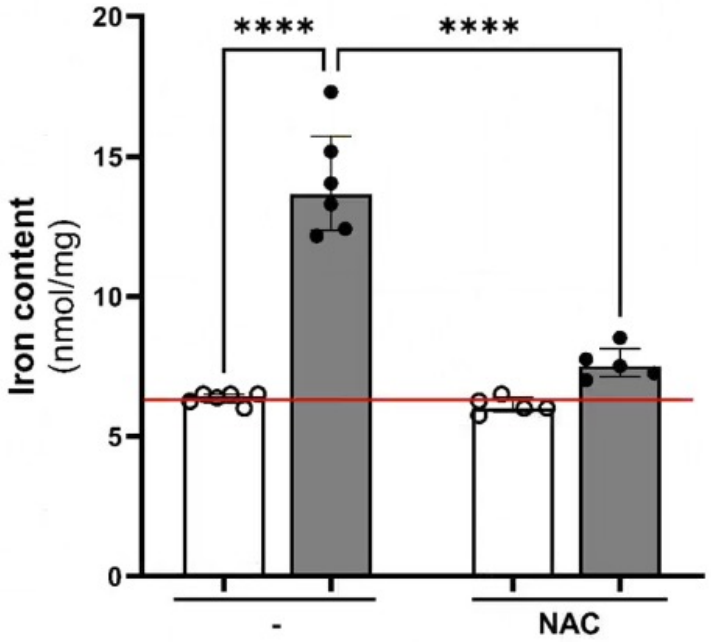
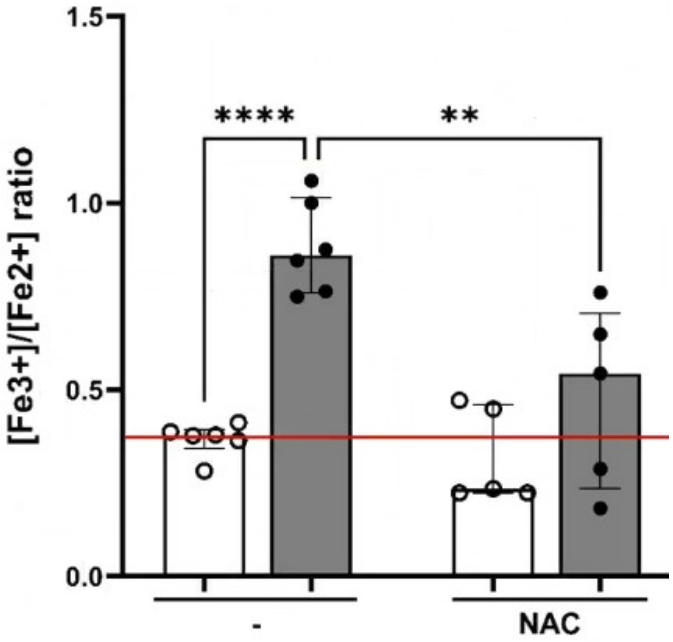
NAC treatment reduced iron level in SDS-MSCs





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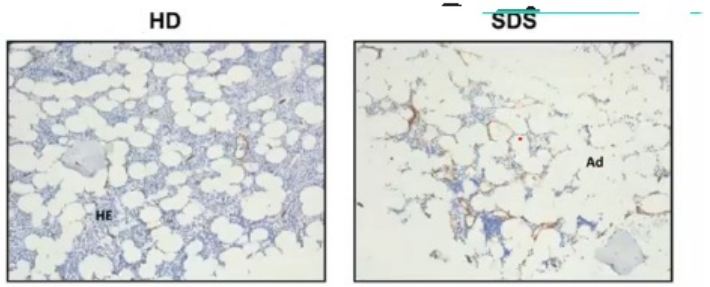
Future directions

- **Characterize vascular alterations** in SDS BM biopsies;
  - **RNA sequencing** analyses on SDS BM biopsies;
- Analyze angiogenic **molecules and metabolites in SDS BM plasma**;
- Explore the role of **iron metabolism** in SDS-MSCs

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Proposta
Riscrittura progetto SDS
Multicentrico

Adeguamento alle recenti regolamnetazioni
Firma del consenso informato

HOT SPOT

Data base e registri

Progetti consolidati

Studi conclusi

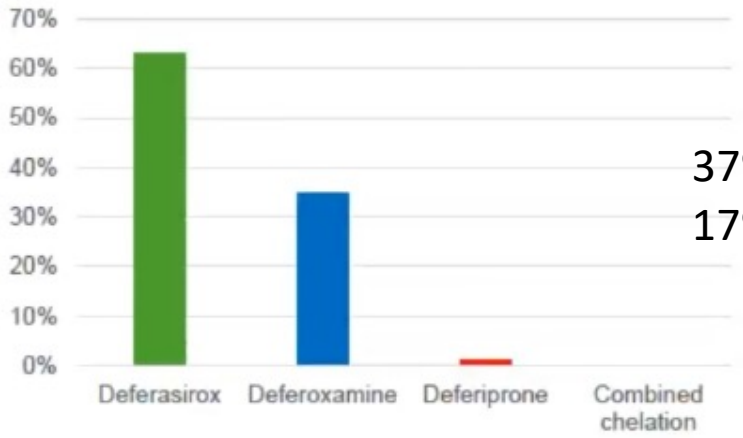
Nuove proposte

Studio «realworld» su chelazione soggetti DBA <3 anni

63 pz corte italiana (23) + francese (40). Dal 2008 al 2022

First chelator at start < 3 years

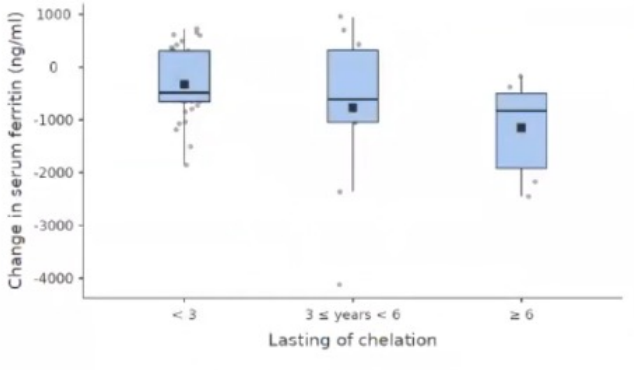
- Deferasirox: 40 patients (40/63 ; 63%)
- Deferoxamine: 22 patients (22/63 ; 35%)
- Deferiprone: 1 patient (1/63 ; 2 %)
- Combined chelation : 0 patient (0%)



37% switch
17% combined therapy

Chelation efficacy→ better efficacy for prolonged therapy (monitoring ferritin)

Ferritin starting from 1400 ng/mL



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Studio «realworld» su chelazione soggetti DBA <3 anni

Stop chelation → No compliance (desferoxamine)

Adverse effect → Liver toxicity: hypertansaminasemia

Coufounding factors : high iron overload, familiar hypertransaminasemia, viral infections

No renal toxicity (tubulopathy!! To check)

Deferasirox, good efficacy and rare toxicity

Not only ferritin, but liver/heart MRI

Accurate check of renal toxicity

Real life data are in line with DBAS 2024
Safety and efficacy of chelation in this age group

- ✓ Deferasirox, good efficacy and rare toxicity
- ✓ Timing and management to be improved . Not only ferritin, but liver/heart MRI
- ✓ Accurate check of renal toxicity

A Gut Feeling: Gut Microbiome Dysbiosis Is Associated with Metabolite and Lipidome Alterations in GATA2 Deficiency

Inclusion criteria

- No ATB in the preceding three months

Additional criteria for the post-HSCT group:

- No cGVHD
- full donor chimerism
- no immunosuppressive treatment for at least six months prior to enrollment.

GATA2 group, n = 12

age range 19-46 years, M:F = 5:7

- No HSCT, n = 5
- HSCT, n = 7

HD group, n = 24

age range 14-44, M:F = 9:15

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Roncareggi et al, under review

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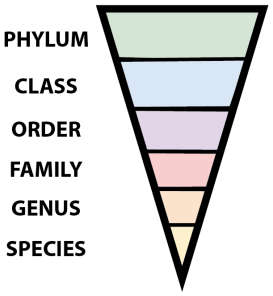

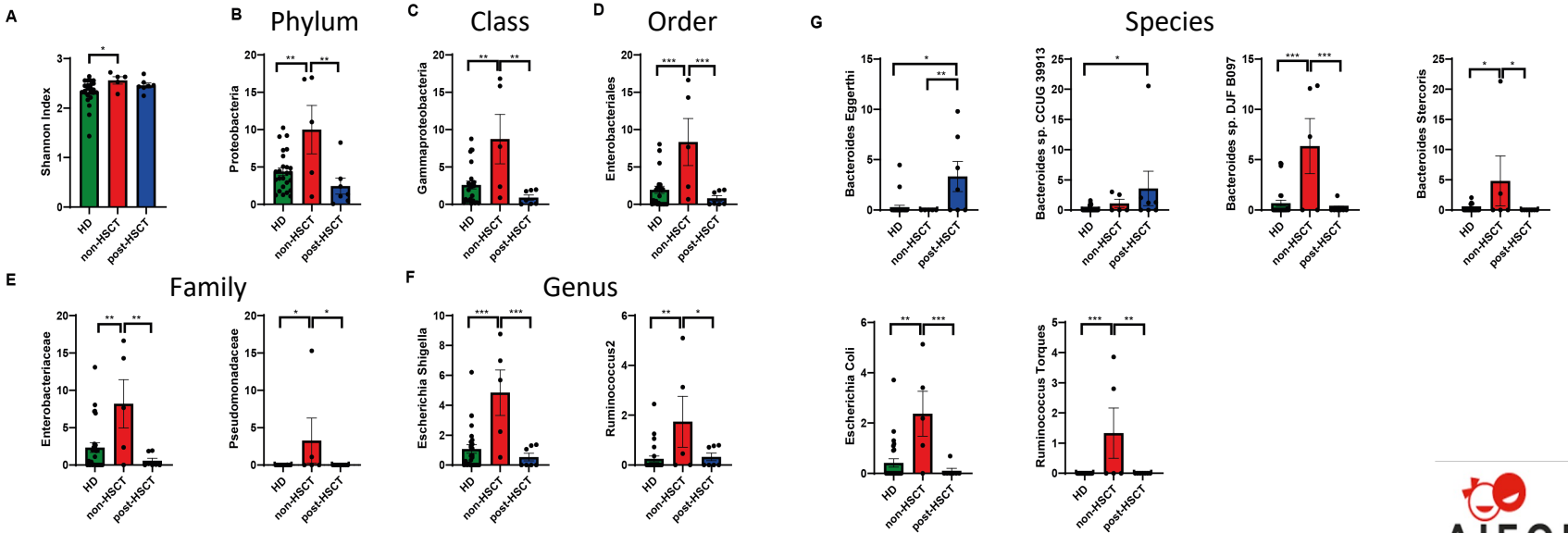

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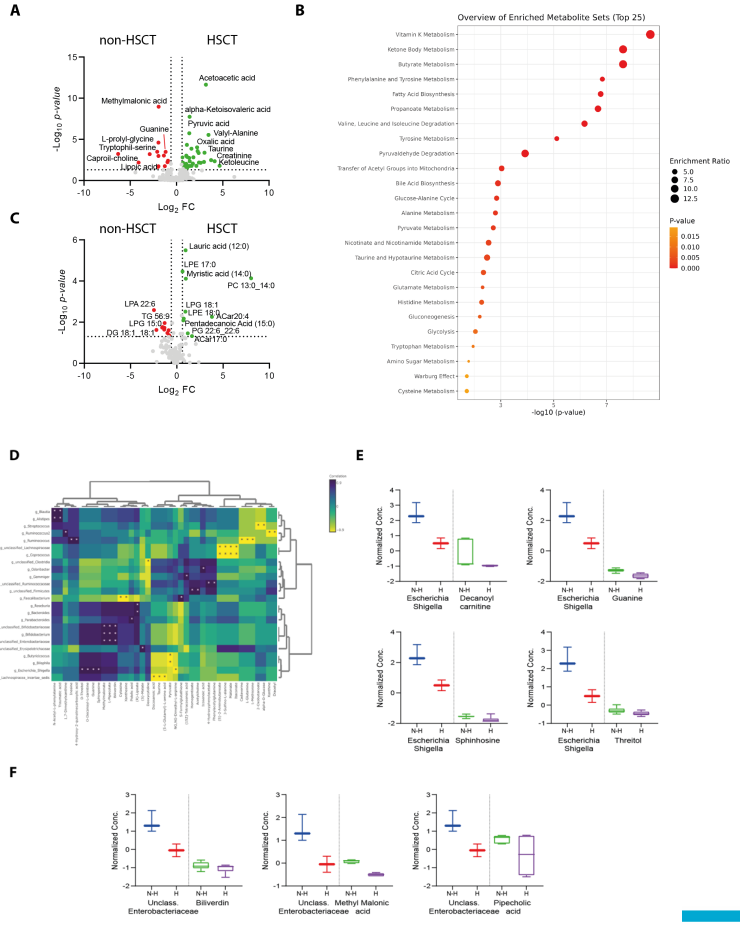

- integrative analysis of the GM and metabolome (non-HSCT = 3, HSCT = 2): correlation with inflammatory and nitrogen metabolism-related metabolites. *Enterobacteriaceae*: nitrogen metabolism and mitochondrial function. *Escherichia/Shigella*: oxidative stress and metabolic dysfunction.

Conclusions:

- evolutionary relationship from phylum to species level. *Proteobacteria* and related taxa , gram- with LPS in the outer membrane, mirroring findings in MDS and IEI
- increased inflammatory metabolites and pro-inflammatory lipids potentially impacting BM niche and HSC. Expansion of *Enterobacteriaceae* family and dysregulated fatty acids metabolism may influence hematopoiesis, Treg and signaling pathways involved in inflammation, including BM homeostasis and oxidative stress.

Roncareggi et al, under review

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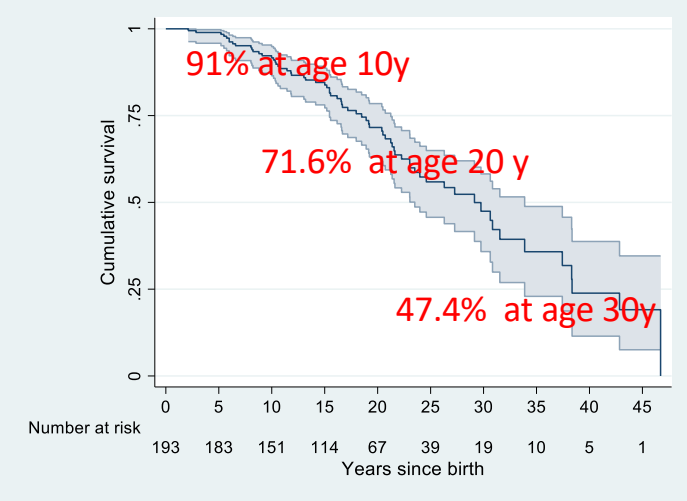
Long-term outcome of Fanconi anemia patients from the Italian Registry on behalf of the Marrow Failure Study Group of the AIEOP (Italian Association for Pediatric Hematology-Oncology)

193 Fanconi pts between 1982 and 2021
Median age at diagnosis 7.1 years (y) (IQR: 4.3-10.5y, range 0-35.7y)
Median follow-up time 6.9 years (IQR 2.5-13.3 y)

Cumulative OS from birth



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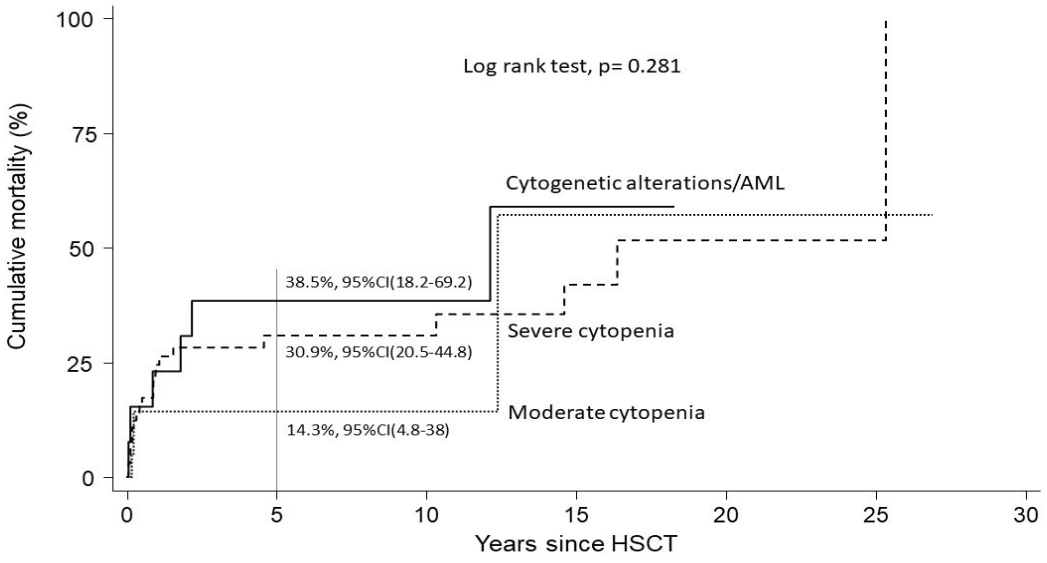
Ricci E et al,under revision AJH

TMO 130 pts #2000 #2010

Cumulative mortality



TRM

26.9% fino 2000
23.7 % 2000-2010
14.5 % >2010

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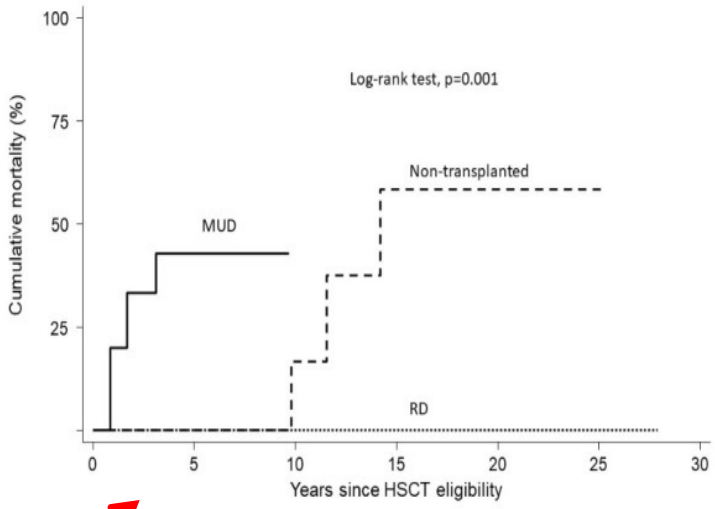
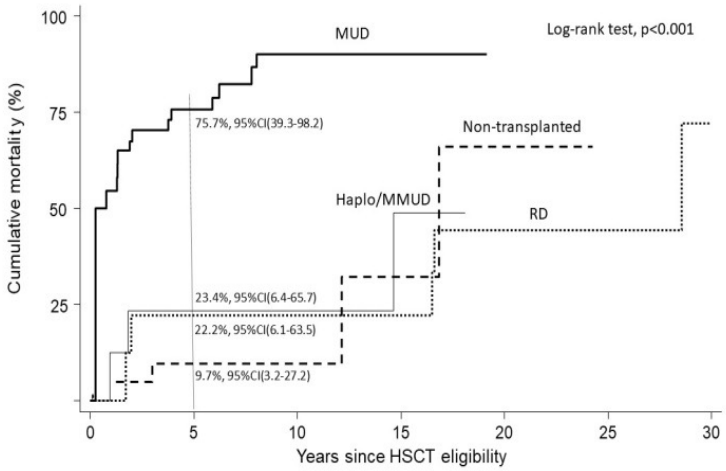
TMO vs non TMO since eligibility

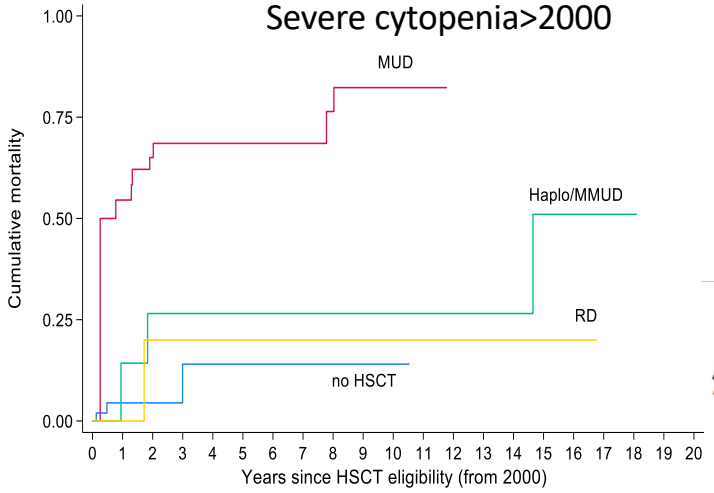
Moderate cytopenia



Severe cytopenia



Severe cytopenia>2000



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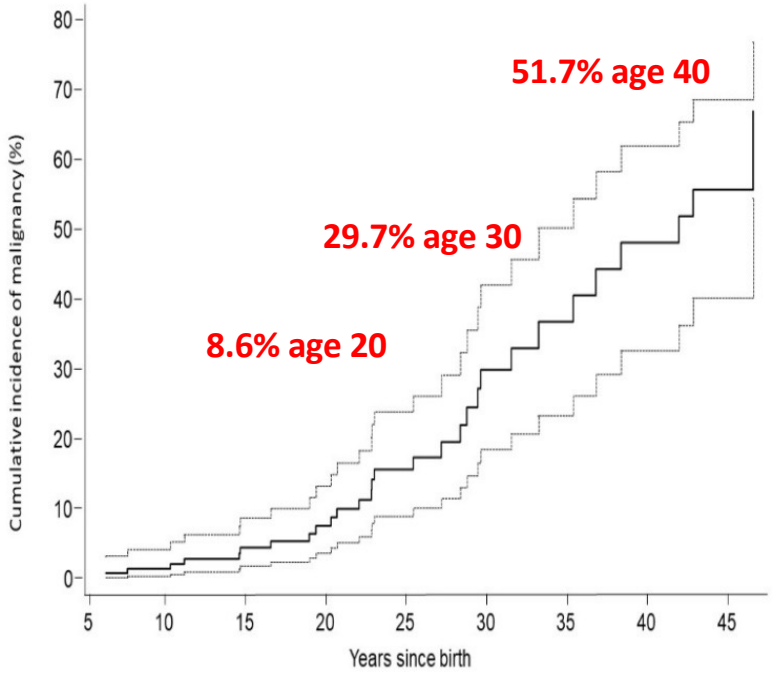
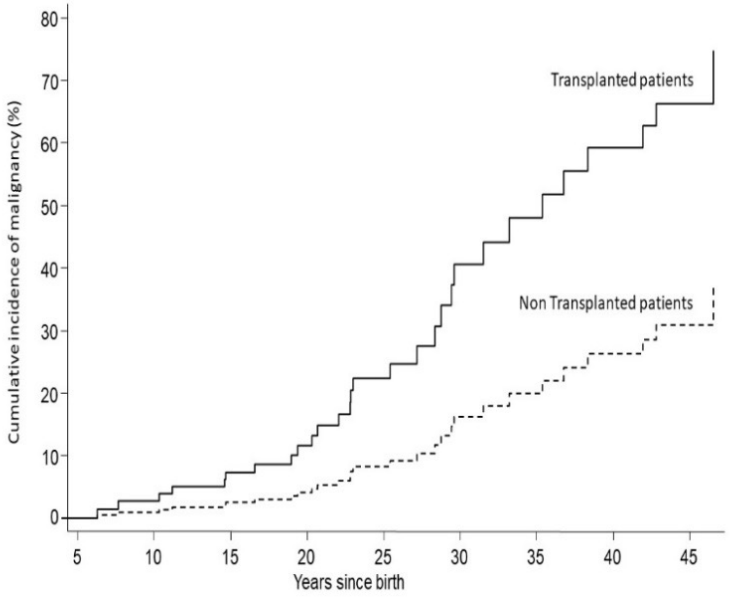
Cancer

29/175 (16.6%) pts



Rapid increase after age 20



Higher occurrence in transplated pts (22/29)

TAKE HOME MESSAGES

- ✓ HCT remains the best treatment option, but it does not revert the systemic phenotype of FA patients
- ✓ A proportion of marrow failure patients can survive long-term even without HCT
- ✓ Negative effect of HCT on tumors
- ✓ Cancer emerging issue. Prevention still the strongest measure.
- ✓ Overall, monitoring currently the most powerful tool for reducing morbidity

HOT SPOT

Data base e registri

Progetti consolidati

Studi conclusi

Nuove proposte

Anomalie SNC rilevate tramite imaging di RM o TAC in DBA

- ✓ RM o TC cranio/distretto facciale dei pazienti spedire tramite wetransfer *immacolata.tartaglione@unicampania.it.*
- ✓ Alla ricezione rimandato breve form per raccogliere informazioni cliniche
- ✓ Arruolamento aprile-settembre 2025
- ✓ Padova e Salerno→ RM in regime gratuito previo contatto con i colleghi proponenti

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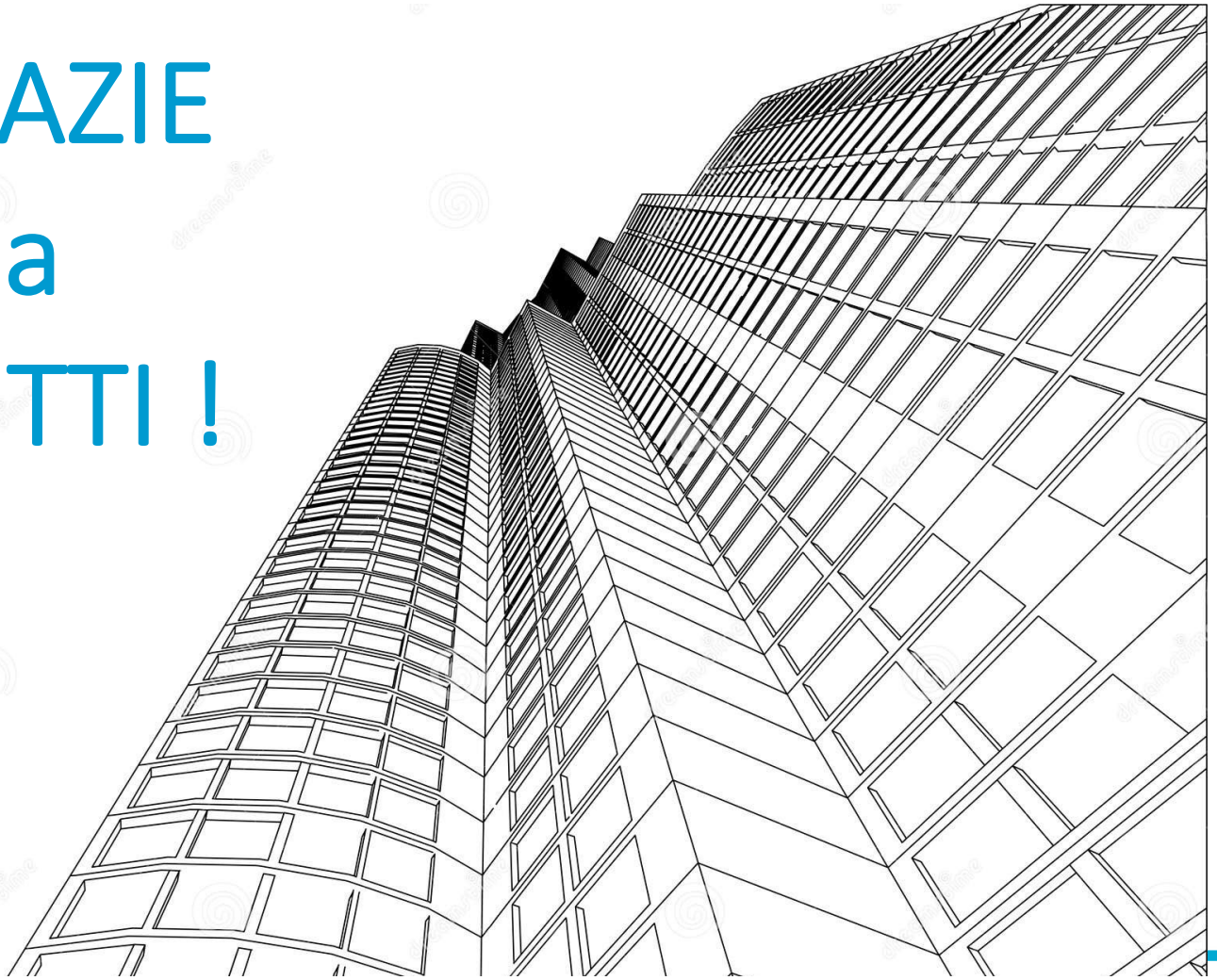
Proposta di raccolta dati su PNH
→ aggiornamento dati dal 2017

I centri AIEOP riceveranno una survey i prossimi giorni, con deadline di compilazione il 30 aprile 2025

GRAZIE a TUTTI !



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Anna Pegoraro , Valentino Bezzerri Growth Charts for Shwachman-Diamond Syndrome at Ages 0 to 18 YearsDOI: 10.3390/cancers16071420

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