Ente Ospedaliero Cantonale

Update
Ematologia

Lugano

Palazzo dei Congressi

15.10.2025

bernhard.gerber@eoc.ch

University of Zurich[UZH]

Conflitti d'interesse

Type of affiliation / financial interet	Name of the commercial company
Receipt of grant / research supports	Pfizer
Receipt of honoraria (including advisory board) or consultation fee:	Janssen, Abbvie, Sanofi
Participation in a company-sponsored speaker's bureau:	-
Stock shareholder:	-
Spouse / partner:	-
Other support (please specify):	-

Agenda

Linfoma

- M.Hodgkin: AF Herrera *NEJM* (2024); MC Pirosa *Blood* (2025)

Malattie delle plasmacellule

- iStopMM (homepage)
- PERSEUS Trial: P. Sonneveld *NEJM* (2024)
- CEPHEUS Trial: S.Z. Usmani *Nature Medicine* (2025)
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Gruppo linfomi IOSI/EOC

CLINICA

Prof. Davide Rossi
Prof. Emanuele Zucca
Prof. Anastasios Stathis
PD Dr. Maria Cristina Pirosa
PD Dr. Alden Moccia
Dr. Paolo Servida
Dr. Ilaria Romano
…

TERAPIE CELLULARI

Prof. Georg Stüssi
Dr. Alessandra Stasia
Dr. Erika Lerch
Dr. Fabio Bergamini
Dr. Guido Ghilardi
…

SPECIALISTI

PD Dr. Letizia Deantonio (Radioterapia)
PD Dr. Helmut Beltraminelli (Dermatologia)
…

DIAGNOSTICA

Prof. Luca Ceriani (Medicina nucleare)
Prof. Luca Mazzucchelli (ICP EOC)
Prof. Georg Stüssi (LEM EOLAB)
Dr. Christian Castelli
Dr. Roberta Bordone
…

Board Emato-Onco (giovedÌ)

Dr. Nicolas Fiorelli
PD Dr. Maria Cristina Pirosa

IELSG International Extranodal Lymphoma Study Group

IOR Institute of Oncology Research

REPARTO OSPEDALE SAN GIOVANNI

Dr. Eliana Souza Azambuja Fernandes
Dr. Chiara Kessler

Capi Ambulatorio

Dr. Elena Bianchi Papina (Italiano)
Dr. Elena Galfetti (Mendrisio)
Dr. Alessandra Stasia (Bellinzona)
Dr. Nicolas Fiorelli (Locarno)

18th ICML

International Conference on Malignant Lymphoma Lugano

June 17-21 2025

- ✓ 4500 partecipanti
- ✓ 600 partecipanti da remoto
- ✓ 91 paesi
- ✓ 1000 abstracts sottomessi


Davide Rossi
Bellinzona, CH
18th ICML

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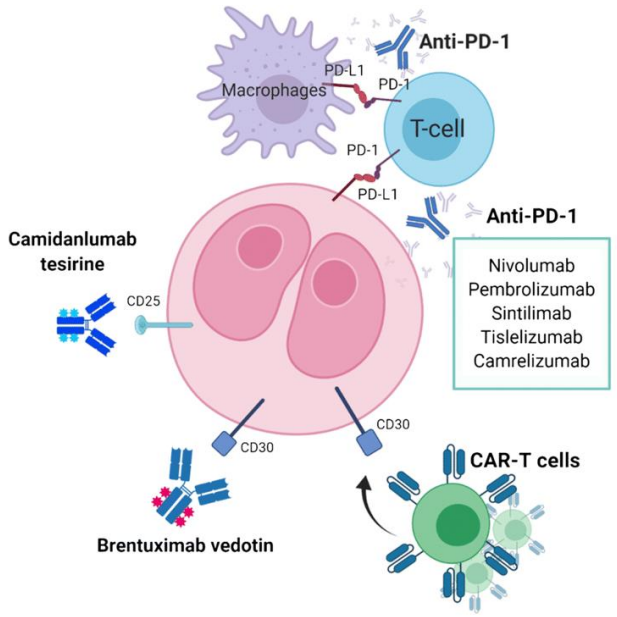
M.Hodgkin – advanced stage

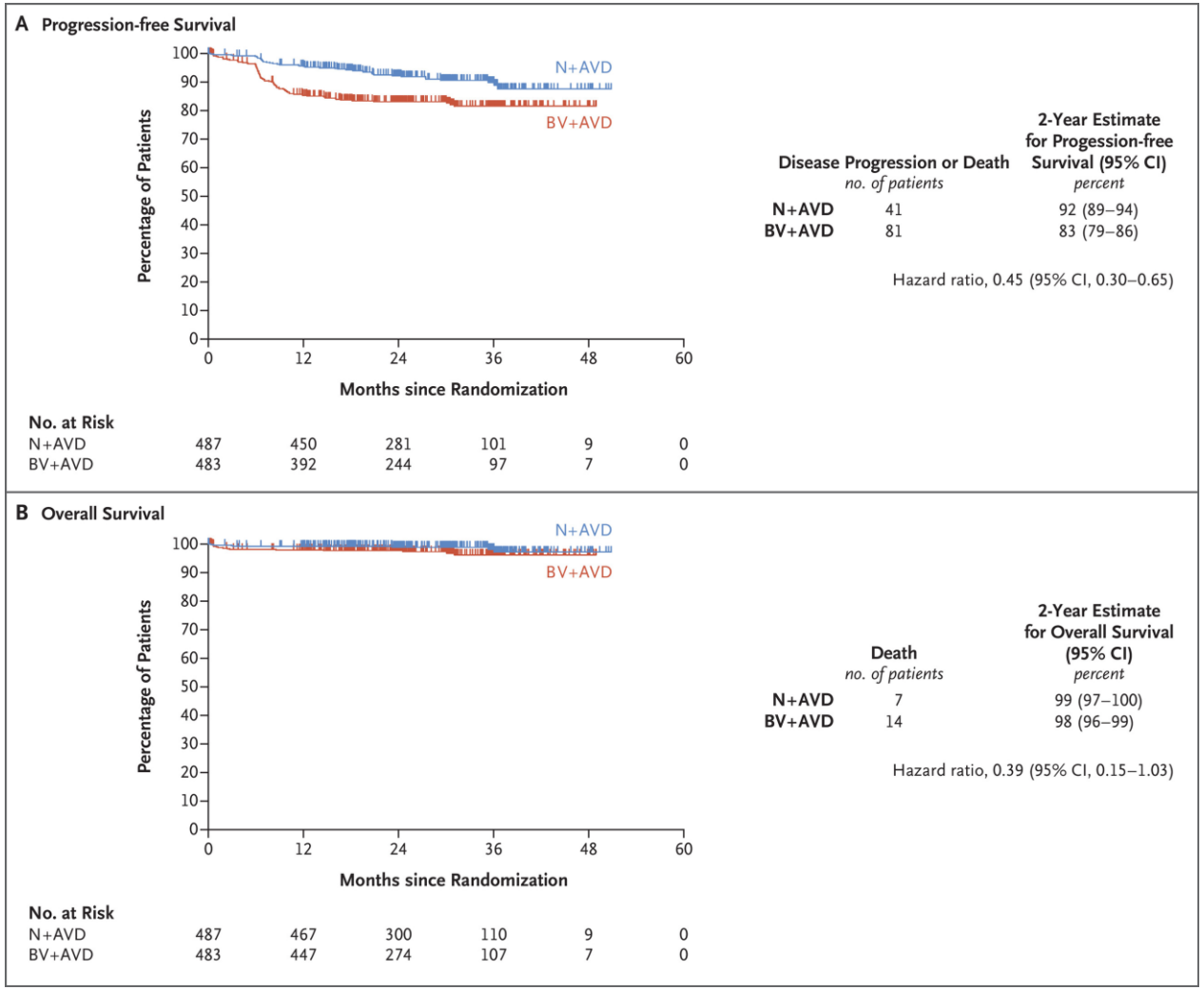
6 cicli di Terapia

Nivolumab + AVD vs Brentuximab + AVD

(AVD = doxorubicin, vinblastin, decarbazin)



Representation of a Hodgkin Reed-Sternberg cell with surface antigens that are targeted by novel therapeutic agents. Created with BioRender.com



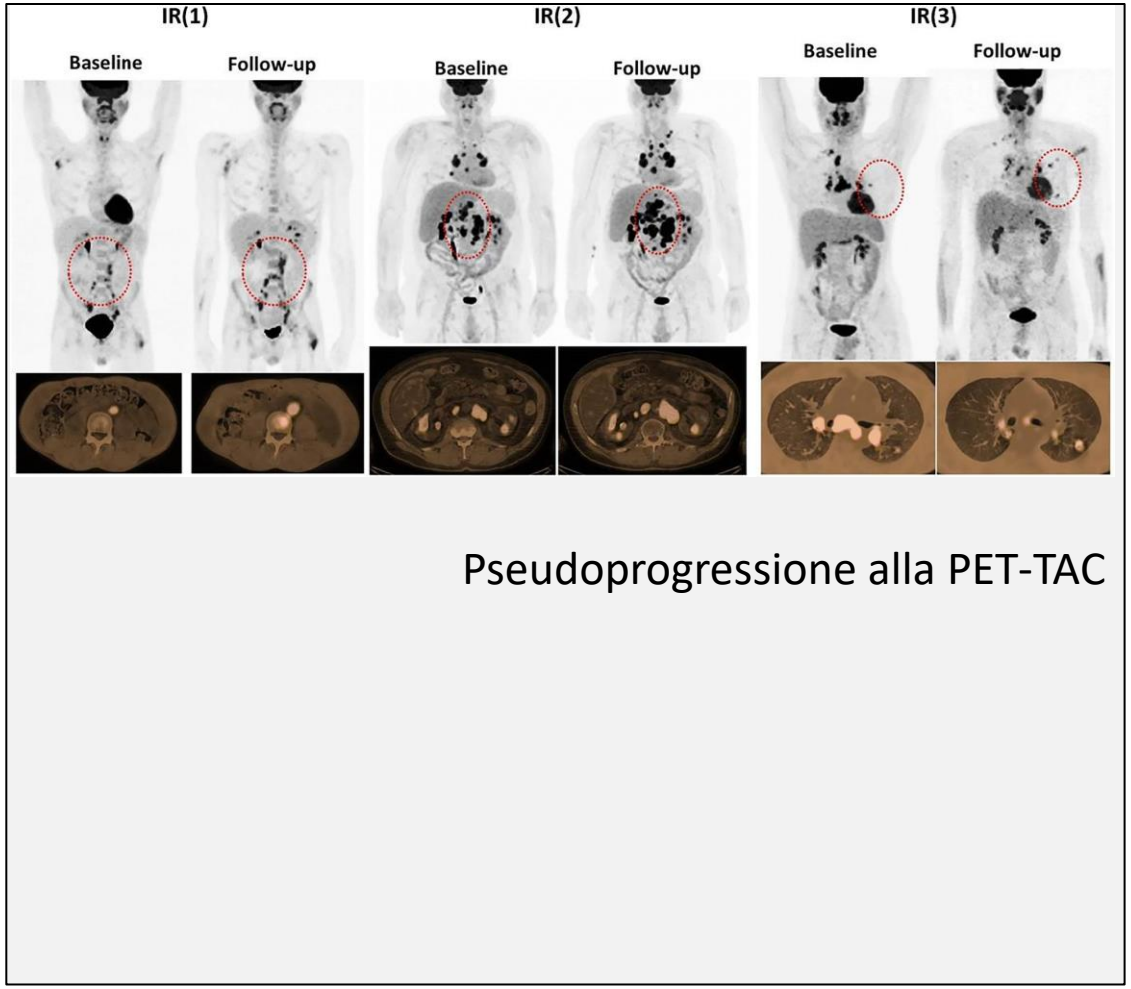
AF Herrera *NEJM* (2024)

M.Hodgkin – advanced stage

Stadio avanzato GHSG • ≤ 60 anni	**BrECADD* x 2 cicli** Discutere tutti i casi dopo interim PET (dopo 2 cicli): • se DS 1-3 BrECADD x 2 cicli (4 cicli totali) • se DS 4 o 5 senza nuove lesioni BrECADD x 4 cicli (6 cicli totali) Discutere tutti i casi dopo eot PET: • se DS 1-3 follow-up • se DS 4 o 5 senza nuove lesioni ISRT 36 Gy (In alternativa Nivolumab-AVD x 6 cicli se desiderio di preservare la fertilità)
Stadio avanzato GHSG • 60-80 anni • CIRS-G ≤5 • ECOG PS fino a 2	**Nivolumab-AVD* x 6 cicli** Discutere tutti i casi dopo eot PET: • se DS 1-3 follow-up • se DS 4 o 5 senza nuove lesioni: ISRT 36 Gy (In alternativa A-AVD x 6 cicli in schedula sequenziale)
Stadio avanzato GHSG • >80 anni e/o • CIRS-G >5 e/o • ECOG PS >2	**Checkpoint inibitore* +/- Brentuximab** (In alternativa Brentuximab + Dacarbazina)

DS = Deauville Score

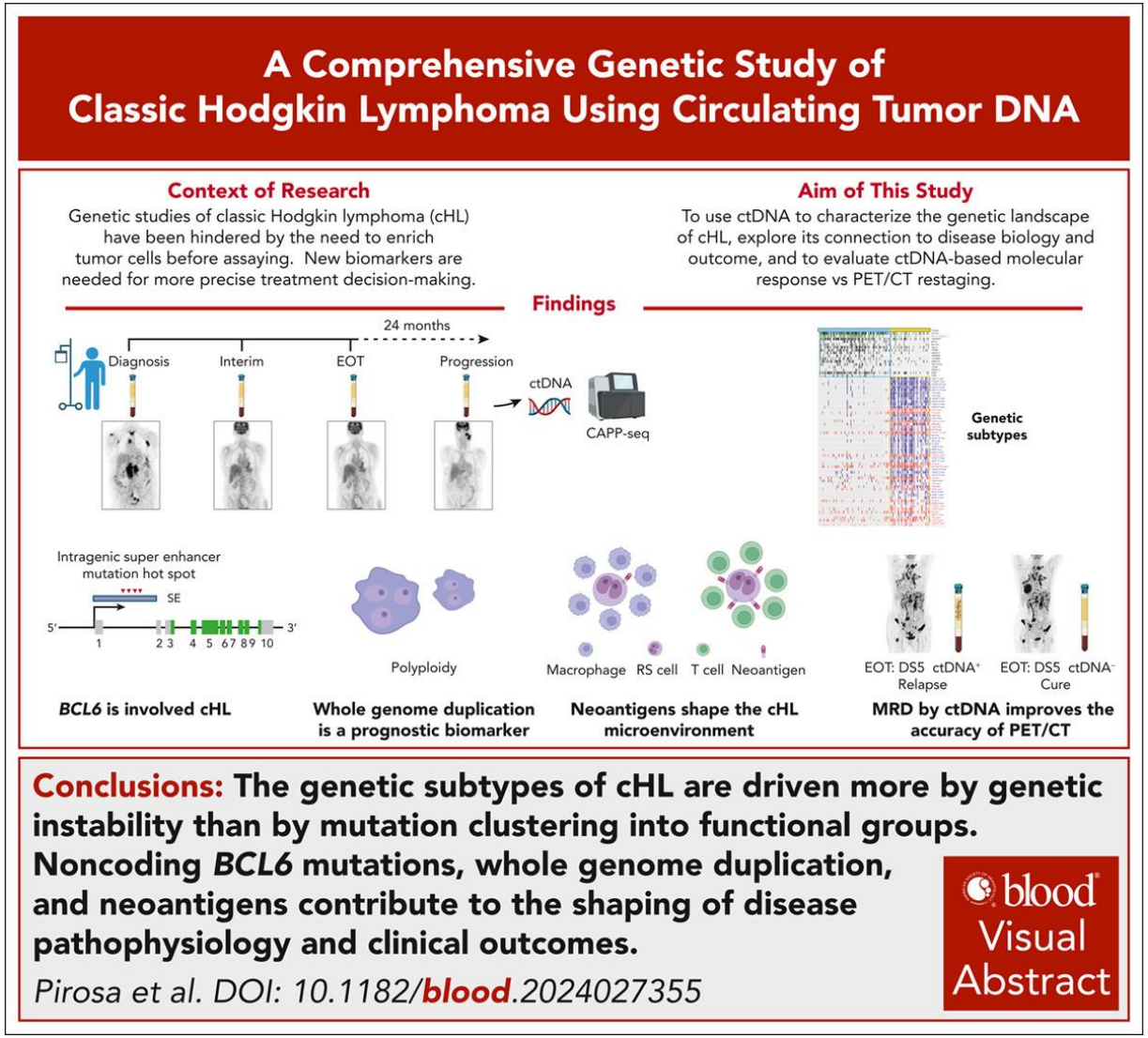
Lugano Classification (PET-guided response assessment)



Pseudoprogressione alla PET-TAC

Linee guida IOSI; *European Radiology* (2022)

M.Hodgkin – circulating tumor DNA



MC Pirosa *Blood* (2025)

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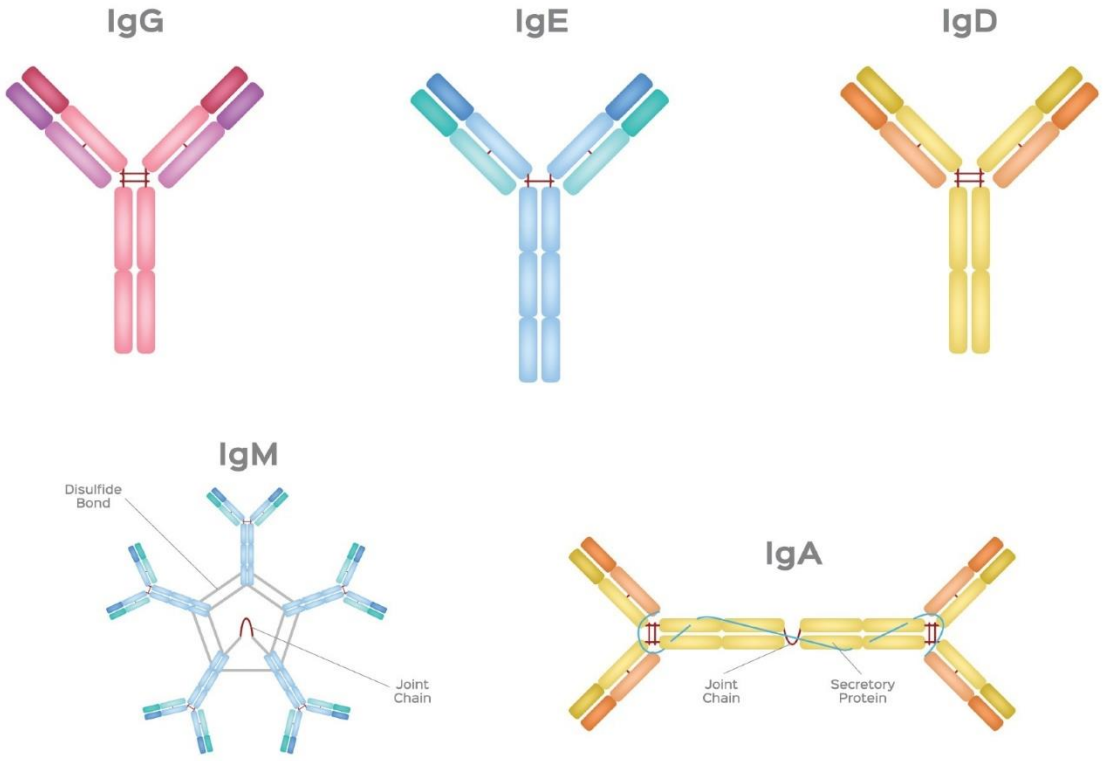
Accertamenti sierologici



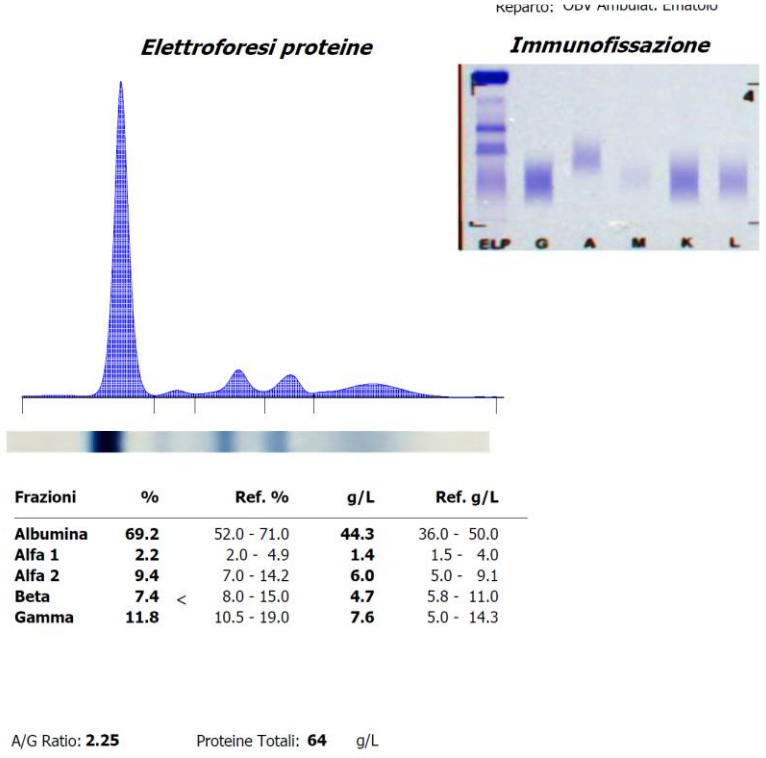
Importante: un linfocita B può esprimere/produrre o delle catene kappa o catene lambda, ma mai entrambi

Accertamenti sierologici

Elettroforesi sierica proteica (27.9 PT)

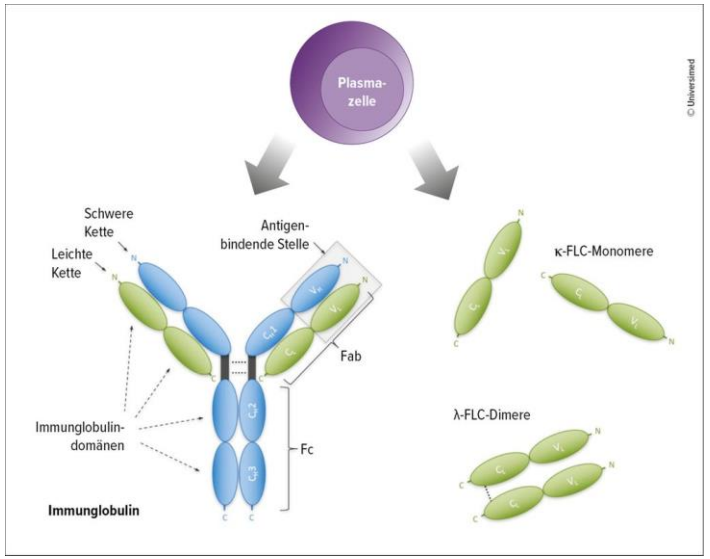
Immunofissazione (47.7 PT)

Catene leggere libere sieriche (FLC) (2 x 33.3 = 66.6 PT)



Frazioni	%		Ref. %	g/L	Ref. g/L
Albumina	69.2		52.0 - 71.0	44.3	36.0 - 50.0
Alfa 1	2.2		2.0 - 4.9	1.4	1.5 - 4.0
Alfa 2	9.4		7.0 - 14.2	6.0	5.0 - 9.1
Beta	7.4	<	8.0 - 15.0	4.7	5.8 - 11.0
Gamma	11.8		10.5 - 19.0	7.6	5.0 - 14.3

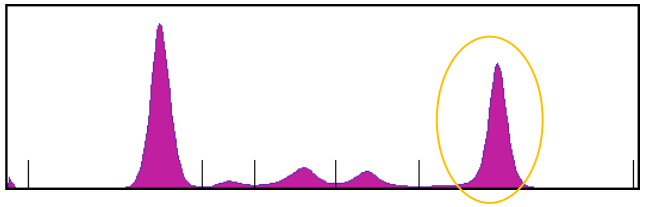
A/G Ratio: **2.25** Proteine Totali: **64** g/L



*Murray *Blood Cancer J* (2021) -> spettometria di massa; Hegen *Wien Med Wochenschrift* 2022

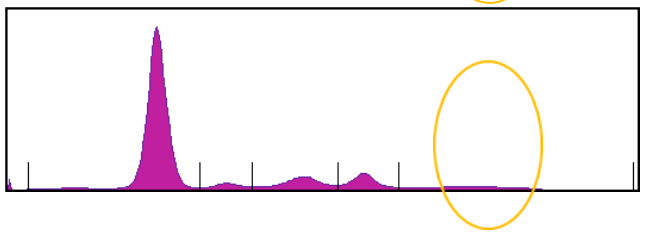
Accertamenti sierologici

ESP



Mieloma multiplo

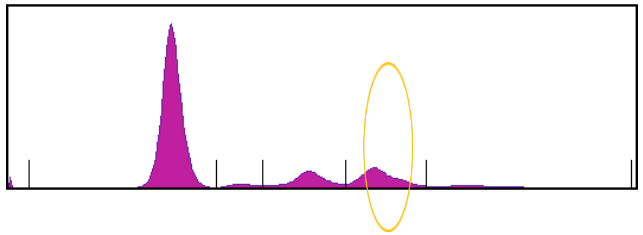
FLC



IMMUNGLOBULINE (SPEZ.)			
Immunfixation			unauffällig
Freie Kappa-Ketten	mg/L	3.30-19.40	* 652.00
Freie Lambda-Ketten	mg/L	5.71-26.30	24.30
Kappa/Lambda-Quot.frei	Koeff.	0.26-1.65	* 26.83
Immunfixation			
Ig/K-Kette	mg/l	<7.1	
Ig/L-Kette	mg/l	<4.5	
Kappa/Lambda-Koeff.	Koeff.	0.75-4.50	

Amiloidosi AL

IF



Immunfixation		pathol. (1)		
Freie Kappa-Ketten		16.00	mg/L	3.30-19.40
Freie Lambda-Ketten	*	42.50	mg/L	5.71-26.30
Kappa/Lambda-Quot.frei		0.38	Koeff.	0.26-1.65
IMMUNGLOBULINE				
Immunglobulin-IgG	*	2.8	g/l	7.0-16.0
Immunglobulin-IgA		2.0	g/l	0.7-4.0
Immunglobulin-IgM	*	<0.2	g/l	0.4-2.3

(1) In der Immunfixation erscheint eine monoklonale Komponente vom Typ IgA Lambda.

Non-IgM MGUS (IgA)

Accertamenti sierologici

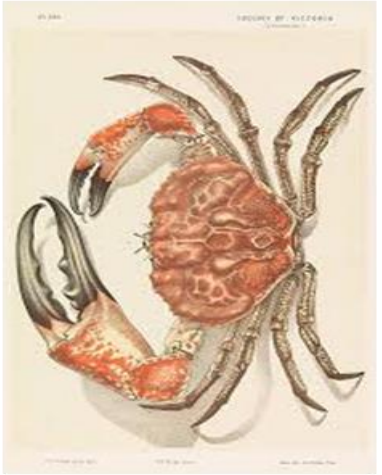
Table 2. Sensitivity of monoclonal gammopathy screening panels.

	n	All 5 tests	Serum PEL and IFE; urine IFE	Serum PEL, IFE, and FLC	Serum PEL and FLC	Serum IFE	Serum PEL	Serum FLC
Diagnosis, n								
All	1877	1851	1821	1828	1770	1632	1482	1395
MM	467	467	461	467	467	441	409	452
Macroglobulinemia	26	26	26	26	26	26	26	19
SMM	191	191	191	191	190	188	180	155
MGUS	524	524	524	509	465	486	429	222
Plasmacytoma	29	26	26	26	25	21	21	16
POEMS	31	30	30	30	23	30	23	3
Extramedullary plasmacytoma	10	2	2	1	1	1	1	1
Primary AL	581	570	547	564	559	429	383	513
LCDD	18	15	14	14	14	10	10	14
Diagnosis, %								
All		98.6	97.0	97.4	94.3	87.0	79.0	74.3
MM		100.0	98.7	100.0	100.0	94.4	87.6	96.8
Macroglobulinemia		100.0	100.0	100.0	100.0	100.0	100.0	73.1
SMM		100.0	100.0	100.0	99.5	98.4	94.2	81.2
MGUS		100.0	100.0	97.1	88.7	92.8	81.9	42.4
Plasmacytoma		89.7	89.7	89.7	86.2	72.4	72.4	55.2
POEMS		96.8	96.8	96.8	74.2	96.8	74.2	9.7
Extramedullary plasmacytoma		20.0	20.0	10.0	10.0	10.0	10.0	10.0
Primary AL		98.1	94.2	97.1	96.2	73.8	65.9	88.3
LCDD		83.3	77.8	77.8	77.8	55.6	55.6	77.8

Katzmann *Clinical Chemistry* 2009

CRAB e SLiM

HyperCalcemia
serum calcium (>0.25 mmol/L ULN, >2.75 mmol/L)
Renal failure (due to cast nephropathy)
eGFR < 40ml/min/1.73m^2 or serum creatinine >177µmol/L
Anemia >20g/L below LLN, or a hemoglobin value <100g/L
Bone lesions (osteolytic on CT or PET-CT)

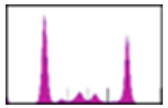
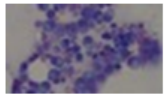


Sixty percent plasma cells or more in the bone marrow
Light chain ratio (free) involved to uninvolved ≥ 100
MRI lesions at least 2 ≥ 5mm

= risk factors for progression to CRAB criteria within 2 years

Rajkumar *Lancet* (2014)

Discrasie plasmacellulari

	Monoclonal Gammopathy of undetermined significance (MGUS)	Smoldering Multiple Myeloma (SMM)	Multiple Myeloma (MM)
Moncoclonal protein (M-protein) 	< 30g/L	≥30 g/L (and/or ≥ 10% PC)	-
Bone marrow plasma cells (PC) 	<10%	10% - 60%	≥ 10% (or biopsy proven plasmacytoma)
CRAB 	No	No	Yes (and/or SLiM)
SLiM 	No	No	Yes (and/or CRAB)

Campo *Blood* (2022); Rajkumar *Lancet (*2014)

MGUS

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Monoclonal Gammopathy of Undetermined Significance

S. Vincent Rajkumar, M.D.,[1] and Shaji Kumar, M.D.[1]

MONOCLONAL GAMMOPATHY OF UNDETERMINED SIGNIFICANCE (MGUS) is a common premalignant plasma-cell proliferative disorder that is present in approximately 5% of the general population over the age of 50 years.[1-4] This disorder is important not only because it is the precursor to plasma-cell cancers, including multiple myeloma, solitary plasmacytoma, and Waldenström's macroglobulinemia, but also because it is causally related to numerous serious non-malignant disorders, collectively referred to as monoclonal gammopathy of clinical significance (MGCS).[5] MGUS is characterized by a limited yet monoclonal proliferation of plasma cells secreting abnormal levels of immunoglobulins (antibodies) that are identical to each other, with the same amino acid sequence, referred to as monoclonal (M) proteins.[6] These secreted M proteins are best appreciated as fully functioning human antibodies present in high concentrations that fortunately lack affinity to self-antigens (autoantibody characteristics) in most persons. As a result, MGUS remains asymptomatic in the absence of malignant transformation in most people. However, there is potential for serious harm if the M protein has or develops affinity for one or more organs in the body, resulting in MGCS.

Author affiliations are listed at the end of the article. S. Vincent Rajkumar can be contacted at rajkumar.vincent@mayo.edu or at the Mayo Clinic, 200 First St. SW, Rochester, MN 55905.

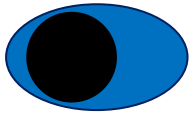
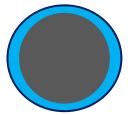
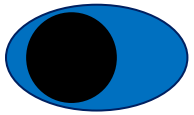
N Engl J Med 2025;393:1315-26.
DOI: 10.1056/NEJMra2412716

CME

V. Rajkumar, *NEJM* (2025)

MGUS

The International Consensus Classification of Mature Lymphoid Neoplasms

1. IgM MGUS of plasma cell type 
2. IgM MGUS NOS  → M. Waldenström
3. Non-IgM MGUS  → Mieloma multiplo MGCS

Campo *Blood 2022*;

Monoclonal gammopathies of clinical significance

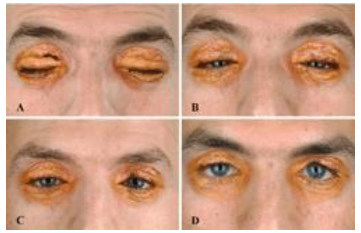
Kidney

- Monoclonal gammopathy of renal significance (MGRS)
  - light-chain Fanconi syndrome
  - proliferative glomerulonephritis
  - immunotactoid glomerulopathy
  - fibrillary glomerulonephritis
- Monoclonal immunoglobulin deposition disease (MIDD)
  - LCDD
  - HCDD

Eye (MGOS) e.g. paraproteinemic keratopathy (PPK)

Blood (vWD, heparin-like abs, CAD, VITT-like)

Skin



Nervous system

- IgM MGUS with anti-MAG (or other anti-neuronal) Abs
- IgM/IgA/IgG MGUS without anti-neuronal Abs
  - Demyelinating polyneuropathy (Type CIDP)
  - Axonal degeneration
- Cryoglobulinemia

Multi system disease

- Light-chain amyloidosis
- CANOMAD (Chronic Atactic Neuropathy with Ophthalmoplegia, IgM monoclonal gammopathy, cold Agglutinins, and Disialoganglioside antibodies)
- POEMS (Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, and Skin changes)
- TEMPI Syndrome (Telangiectasias, elevated Erythropoietin level and erythrocytosis, Monoclonal gammopathy, Perinephric-fluid collections, and Intrapulmonary shunting)
- Schnitzler syndrome (IgM, urticaria plus 2 out of 8 other)

Fermand *Blood* 2018, Bridoux *Kidney Int* 2015, Sayed *Blood* 2015, Goede *Annals Hematol* 2007; Gardert *ASH2021* #2695; EFNS/PNS PDN Guideline: *Journal of the Per Nervous System* 2010, Cochrane 2012, Cochrane 2015, Willison *J Clin Invest* 1996, Dispenzieri *Am J Hematol* 2012, Sykes *NEJM* 2011, Gusdorf *Allergy* 2017; Wang *NEJM* 2025

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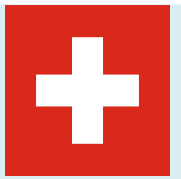
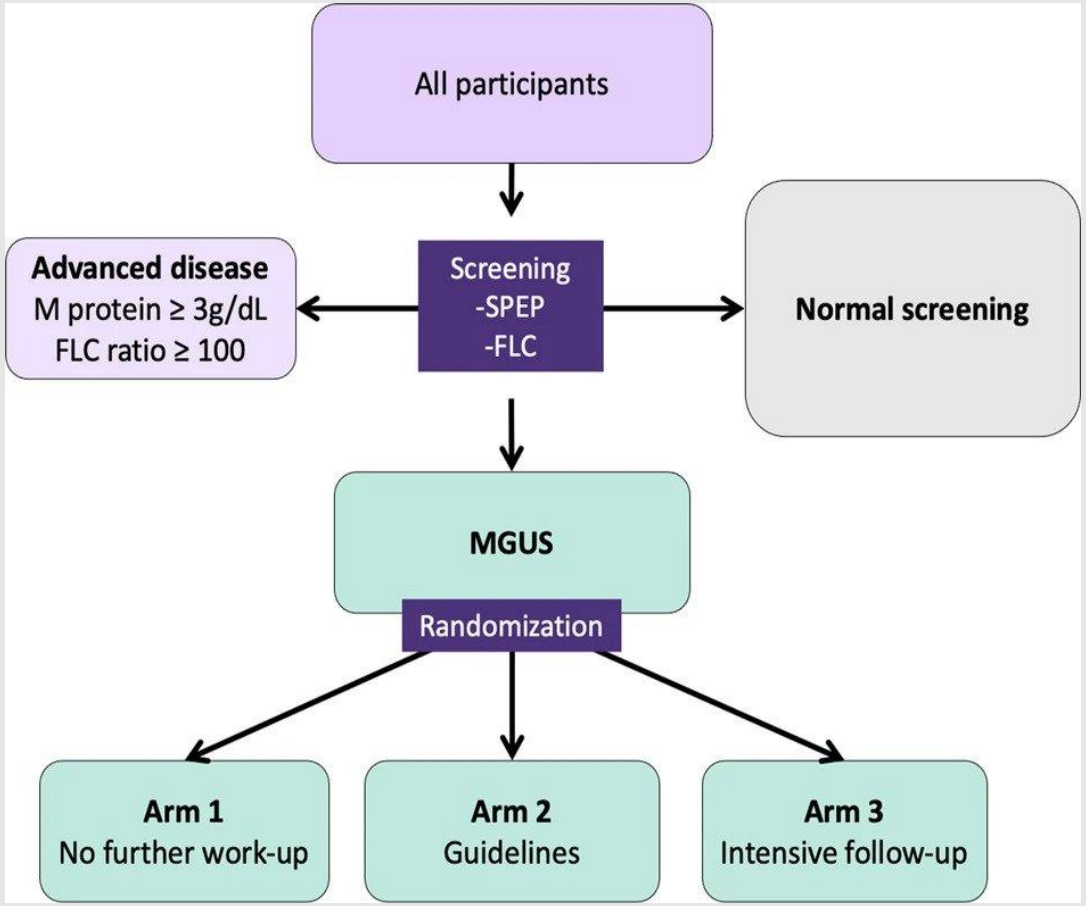
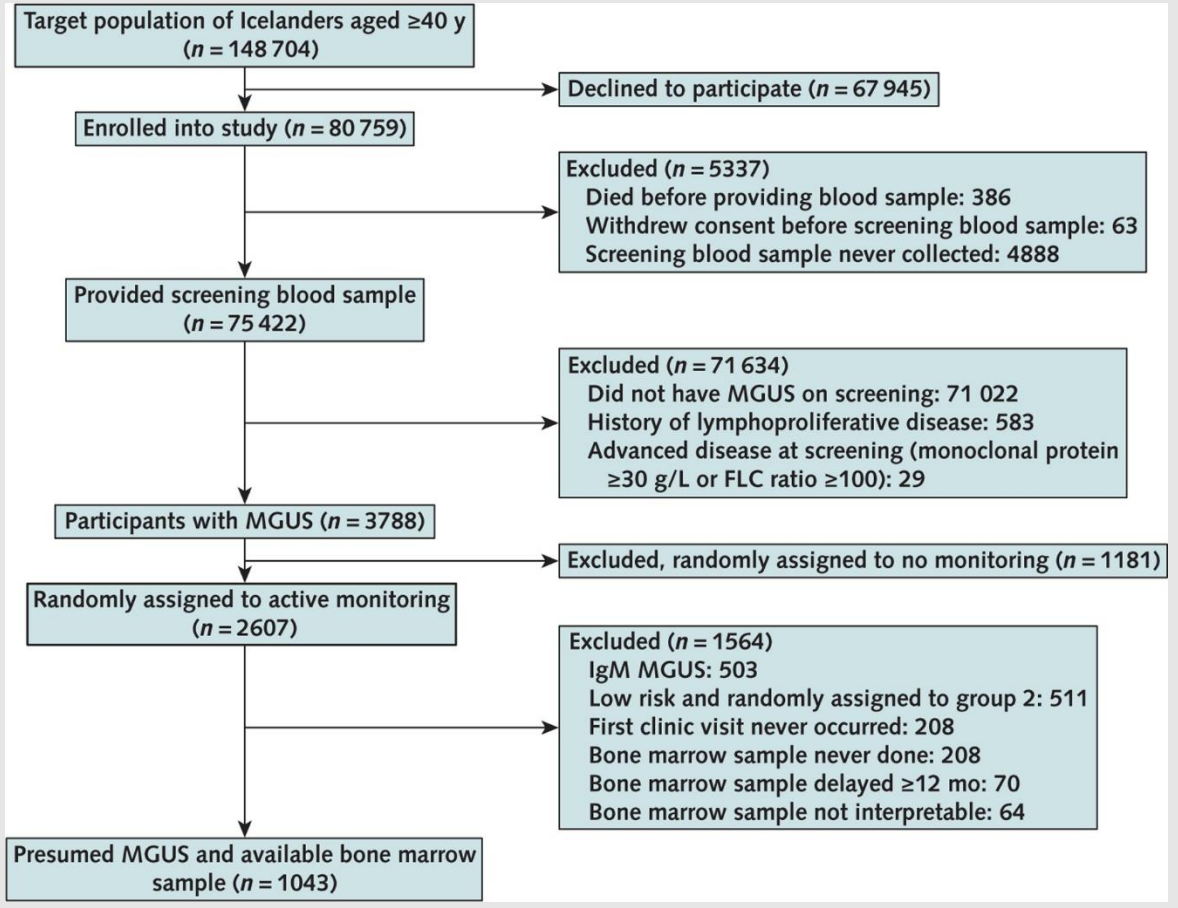
iStopMM

		
Abitanti	397’576	9’034’088
Superficie (km^2)	102’819	41’291
PIL pro capite (nominale, US$)	78’811	102’865
Medici per 1000 abitanti	4.5	4.4

https://istopmm.com; Wikipedia

iStopMM





S. Rognvaldsson *Blood Cancer J.* (2021)

iStopMM

- Valori di riferimento catene leggere libere: calcolatrice[1]
- Prevalenza MGUS 5%, mieloma asintomatico (SMM) 0.56%[2]
- Probabilitä di trovare >10% di plasmacellule nella biopsia ossea: calcolatrice[3]
- Non c‘è un‘associazione tra malattie autoimmuni e MGUS[4]
- Cause per ipercalcemia in pazienti con MGUS[5]
- Rischio elevato per eventi infettivi in pazienti con SMM[6]

[1]T. Einarsson Long *Blood Cancer J.* (2022); [2]S.Thorsteinsdóttir *Nature Medicine* (2023); [3]E. Eythorsson *Annals of Internal Medicine.*(2024); [4]I. Sverrisdottir *Annals of Internal Medicine.*(2024); [5]AH Jónsdóttir *Blood.* (2025); [6]LS Andersen Leukemia (2025)

iStopMM

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[1]T. Einarsson Long *Blood Cancer J.* (2022); [2]S.Thorsteinsdóttir *Nature Medicine* (2023); [3]E. Eythorsson *Annals of Internal Medicine.*(2024); [4]I. Sverrisdottir *Annals of Internal Medicine.*(2024); [5]AH Jónsdóttir *Blood.* (2025); [6]LS Andersen Leukemia (2025)

Catene leggere libere: valore di riferimento

istopmm.com

iStopMM

Home | The iStopMM study | Researchers | Collaborators | Publications | Risk Models and Calculators

Light chain MGUS calculator

Serum free kappa, mg/L

110

Serum free lambda, mg/L

95

Age, years

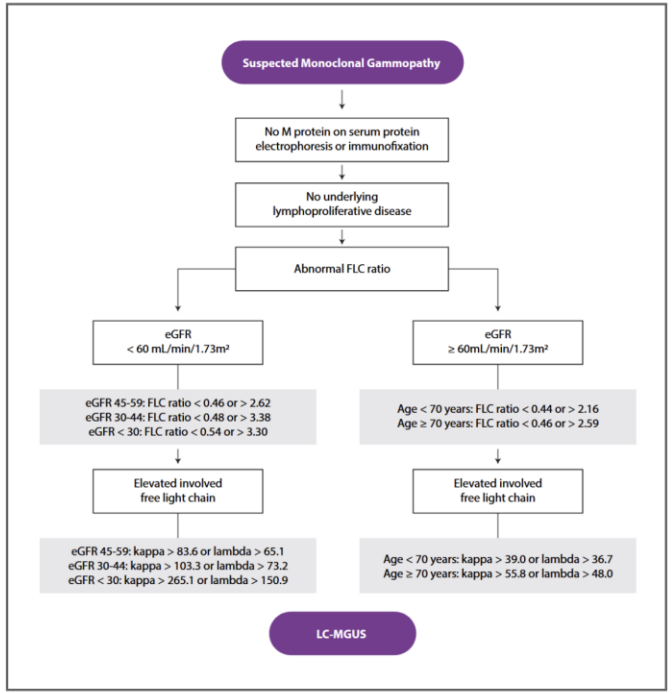
78

eGFR* mL/min/1.73m2

39

FLC (free light chain ratio) is 1.16
Based on the information provided this person **does not** have light chain monoclonal gammopathy of undetermined significance (LC-MGUS)

* Serum creatinine based CKD-EPI eGFR equation (2009) was used in the study where these reference intervals were determined. This calculator was developed based on



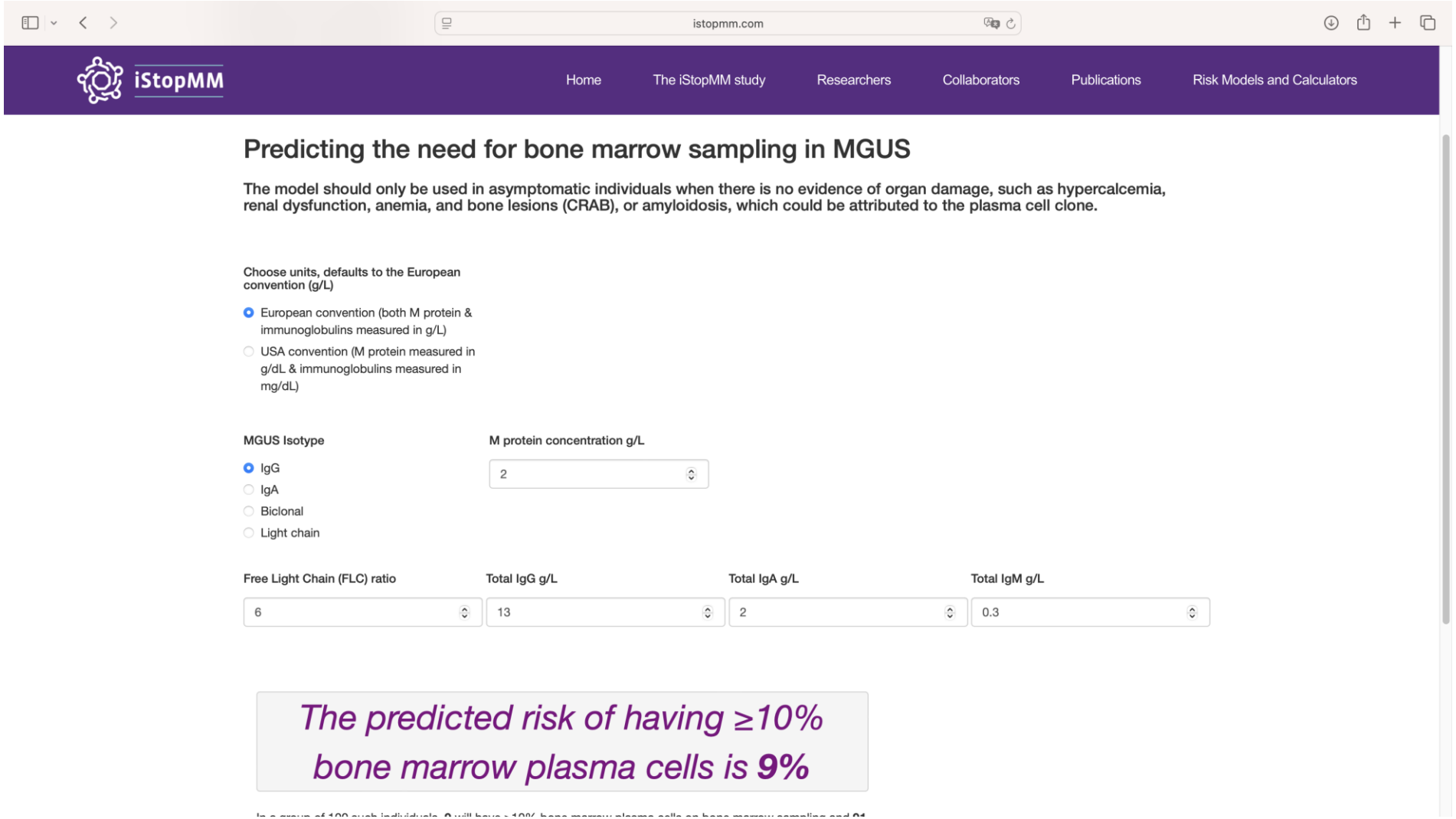
T. Einarsson Long *Blood Cancer J.* (2022); T. Einarsson Long *Blood* (2023); https://istopmm.com/lcmgus/

iStopMM

- Valori di riferimento catene leggere libere: calcolatrice[1]
- Prevalenza MGUS 5%, mieloma asintomatico (SMM) 0.56%[2]
- Probabilità di trovare >10% di plasmacellule nella biopsia ossea: calcolatrice[3]
- Non c'è un'associazione tra malattie autoimmuni e MGUS[4]
- Cause per ipercalcemia in pazienti con MGUS[5]
- Rischio elevato per eventi infettivi in pazienti con SMM[6]

[1]T. Einarsson Long *Blood Cancer J.* (2022); [2]S.Thorsteinsdóttir *Nature Medicine* (2023); [3]E. Eythorsson *Annals of Internal Medicine.*(2024); [4]I. Sverrisdottir *Annals of Internal Medicine.*(2024); [5]AH Jónsdóttir *Blood.* (2025); [6]LS Andersen Leukemia (2025)

Probabilità di trovare >10% di plasmacellule



E. Eythorsson *Annals of Internal Medicine.*(2024); https://istopmm.com/riskmodel/

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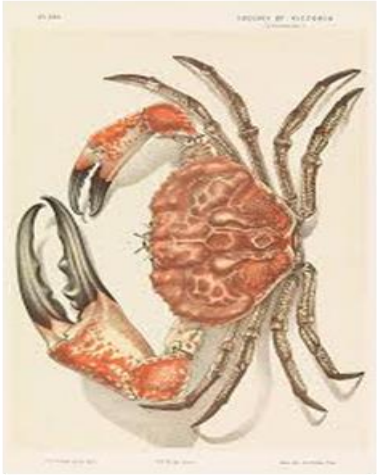
CRAB e SLiM -> CAVE la causa dev'essere il mieloma

HyperCalcemia
serum calcium (>0.25 mmol/L ULN, >2.75 mmol/L)
Renal failure (due to cast nephropathy)
eGFR < 40ml/min/1.73m^2 or serum creatinine >177µmol/L
Anemia >20g/L below LLN, or a hemoglobin value <100g/L
Bone lesions (osteolytic on CT or PET-CT)



Sixty percent plasma cells or more in the bone marrow
Light chain ratio (free) involved to uninvolved ≥ 100
MRI lesions at least 2 ≥ 5mm

= risk factors for progression to CRAB criteria within 2 years

Rajkumar *Lancet* (2014)

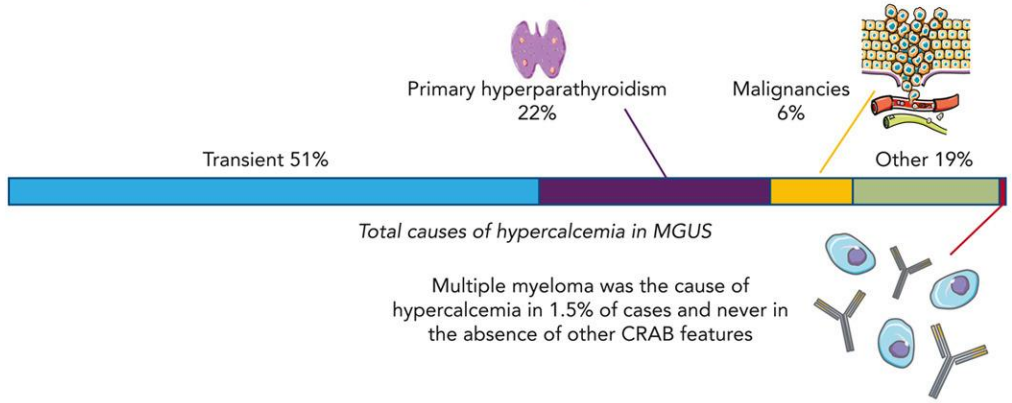
MGUS + ipercalcemia: cause

Hypercalcemia in MGUS, the Precursor to Multiple Myeloma

Context of Research: Hypercalcemia is a part of the CRAB diagnostic criteria for MGUS progression to multiple myeloma. We examined the causes of hypercalcemia in MGUS in a cohort of 2546 individuals identified by screening. In total, 191 had hypercalcemia and MGUS.

Research Question: Does hypercalcemia in MGUS mean progression to multiple myeloma?

Main Findings



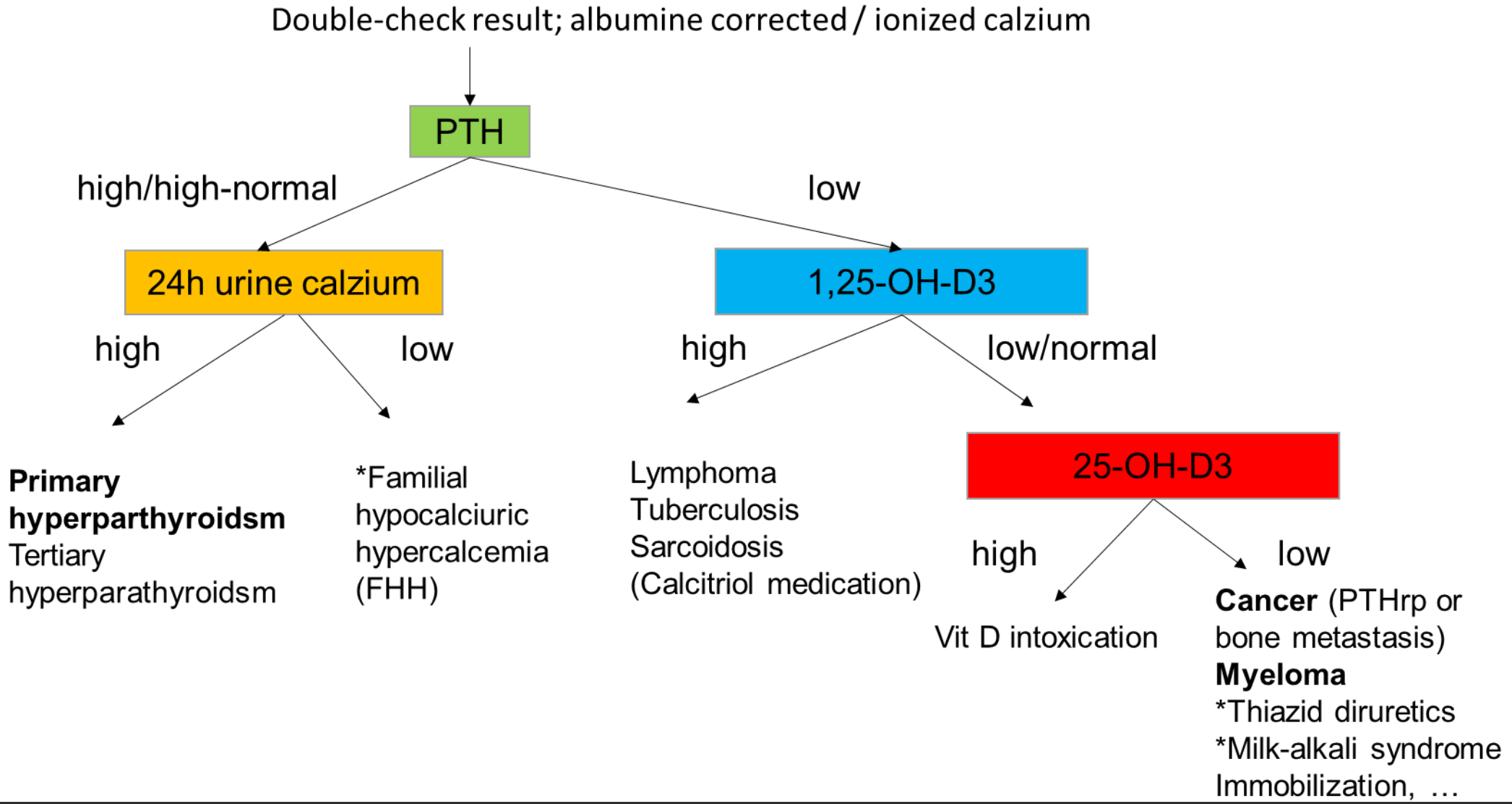
Conclusions: Hypercalcemia without other CRAB features is not a strong indicator to MGUS progression to multiple myeloma. It should be approached in the same way as in individuals without MGUS.

*Jónsdóttir et al. DOI: 10.1182/**blood**.2024025624*

blood Visual Abstract

AH Jónsdóttir *Blood.* (2025)

MGUS + ipercalcemia: cause



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Agenda

Linfoma

- M.Hodgkin: AF Herrera *NEJM* (2024); MC Pirosa *Blood* (2025)

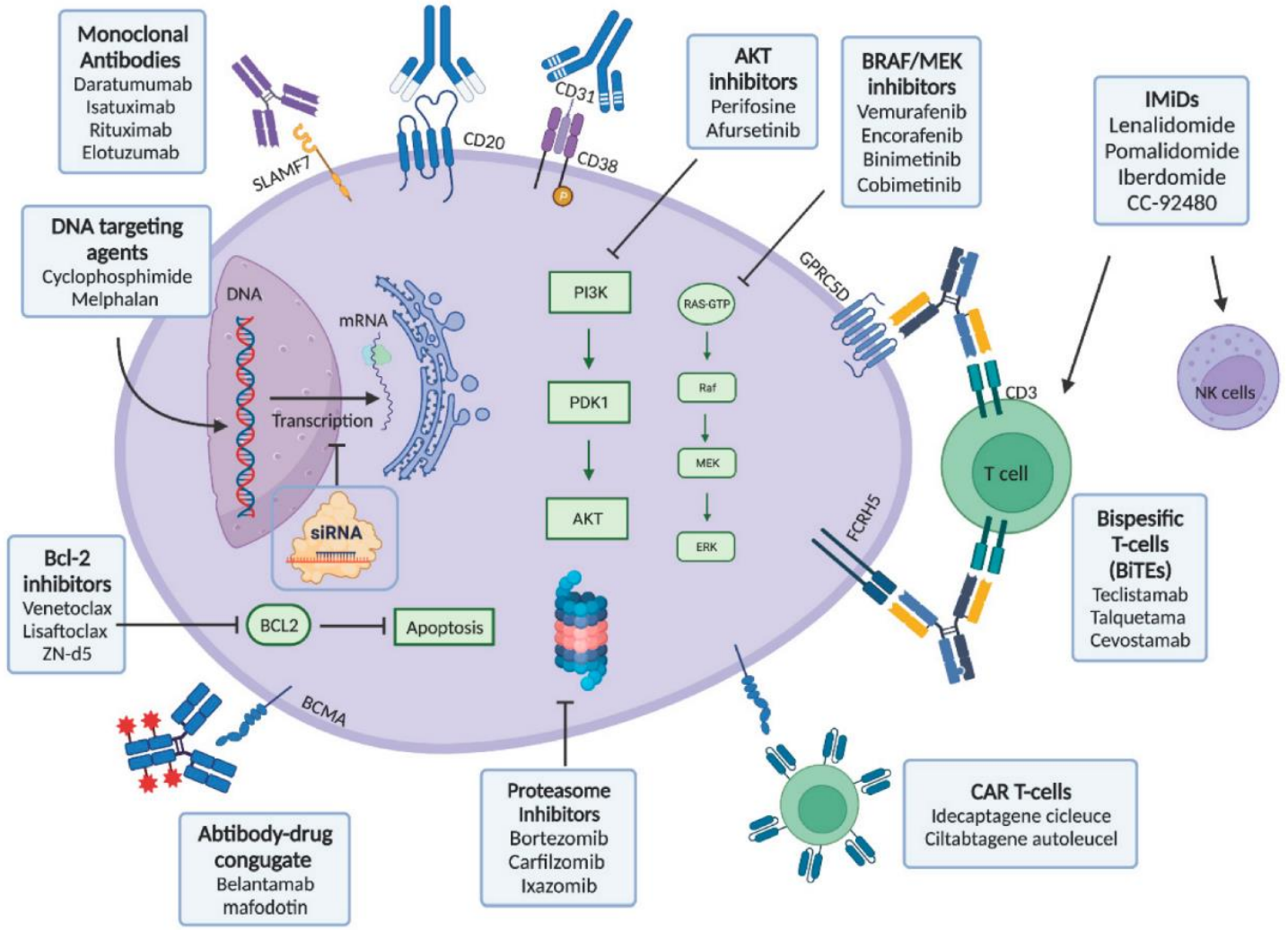
Malattie delle plasmacellule

- iStopMM (homepage)
- PERSEUS Trial: P. Sonneveld *NEJM* (2024)
- CEPHEUS Trial: S.Z. Usmani *Nature Medicine* (2025)
- MAIA Trial: T. Facon *NEJM* (2019)

Mieloma multiplo: Trattamento di prima linea 2025

Daratumumab

Lenalidomide



Corticosteroidi

Bortezomib

Theodorakakou *Hemato* 2022

Mieloma multiplo: Trattamento di prima linea 2025

Pazienti ‚fit' PERSEUS Trial

Daratumumab
Bortezomib
Lenalidomid
Dexamethasone

Melfalan
Trapianto autologo

Daratumumab
Lenalidomid

Pazienti ‚unfit fit' CEPHEUS Trial

Daratumumab
Bortezomib
Lenalidomid
Dexamethasone

Daratumumab
Lenalidomid
Dexamethasone

Pazienti ‚unfit' MAIA Trial

Daratumumab
Lenalidomid
Dexamethasone

P. Sonneveld *NEJM* (2024); S.Z. Usmani *Nature Medicine* (2025); T. Facon *NEJM* (2019)

Sopravvivenza libera da progressione

Pazienti ‚fit': PERSEUS Trial

> 15 anni

Pazienti ‚unfit fit' CEPHEUS Trial

> 8 anni

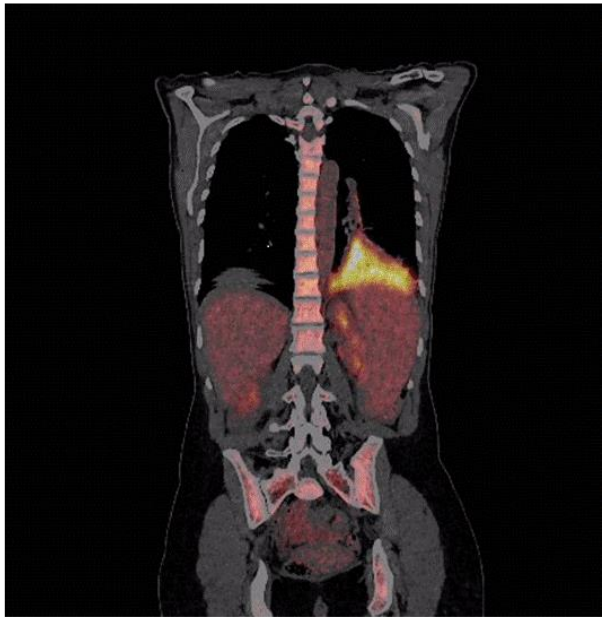
Pazienti ‚unfit' MAIA Trial

> 5 anni

P. Sonneveld *NEJM* (2024); S.Z. Usmani *Nature Medicine* (2025); T. Facon *NEJM* (2019)

Eventi infettivi (CTCAE grado 3 e 4)

Pazienti ‚fit': PERSEUS Trial	**Eventi infettivi severi 35.3%** **(10.5% polmonite)**
Pazienti ‚unfit fit' CEPHEUS Trial	**Eventi infettivi severi 40.1%** **(14.2% polmonite)**
Pazienti ‚unfit' MAIA Trial	**Eventi infettivi severi 42.6%** **(18.5% polmonite)**



P. Sonneveld *NEJM* (2024); S.Z. Usmani *Nature Medicine* (2025); T. Facon *NEJM* (2019)

Prevenzione

Informare pazienti + famigliari + medici di base

- antibiotico di riserva a casa (con attività contro pneumococco)

Vaccinazioni

- Aggiornamento vaccini di base incl. pertosse (nipotini)
- *Streptococco pneumoniae* (Prevenar20® o Vaxneuvance®)
- *Haemophilus influenzae*
- Influenza stagionale e COVID
- VZV (Shingrix)

Immunoglobuline ev o sc (anche a domicilio)

- Se IgG < 4-5 g/l + eventi infettivi e/o se terapia con anticorpi bispezifici/CAR-T

H. Ludwig *Leukemia* (2021); N.S. Raje *Lancet Haematol* (2022)

Riassunto

- Lo IOSI/EOC tratta persone con malattie linfoproliferative.
- iStopMM è un sito interessante con informazioni utili anche per il medico di base (p.es. interpretazione di risultati sierologici).
- Il trattamento di prima linea per persone con MM è diventato molto efficace.
- Collaborazione per la prevenzione e per il trattamento di eventi infettivi.
- Contattatemi per il sospetto di una gammopatia monoclonale di significato clinico.

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