FONDAZIONE ITALIANA SINDROMI MIELODISPLASTICHE

CONVEGNO FISiM

Firenze, CSF Montedomini
"Il Fuligno"
24-25 ottobre 2025

LINEE GUIDA SIE NELLE MDS - UPDATE

MARCHETTI Monia

Disclosures of Monia Marchetti

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
NOVARTIS					ϒ	ϒ	
ROCHE						ϒ	
BMS						ϒ	
BEIGENE						ϒ	
MENARINI						ϒ	
ASTRA ZENECA						ϒ	
MSD					ϒ		
OTSUKA					ϒ		
GSK							ϒ

MILESTONES

ottobre 2025

1- Do we need a support to our clinical decisions?

Quesions & Domains

Figura 1. Processo decisionale e preparatorio

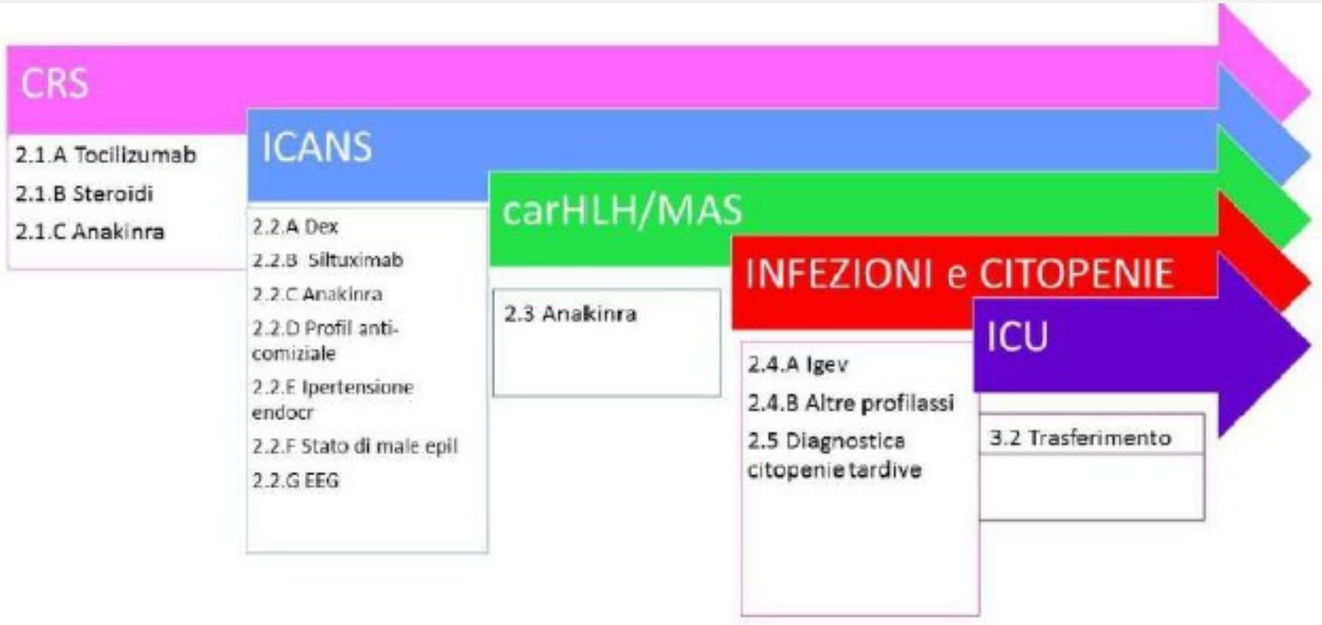
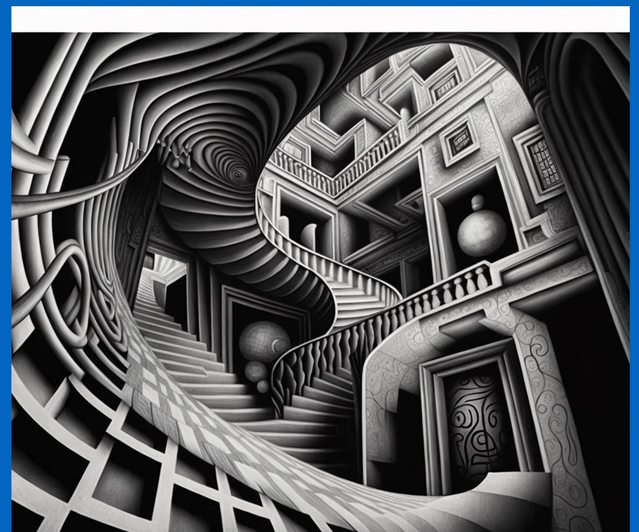


Figura 2. Gestione delle complicanze

2- Can we access robust and trustable decisional supports?

CPGs



A robust support to clinical decisions needs to be **systematically** and **transparently** built onto available scientific evidence

bjh guidelines

British Society for Haematology guidelines for the management of adult myelodysplastic syndromes

Sally B. Killick,[1] Wendy Ingram,[2] Dominic Culligan,[3] Helen Enright,[4] Jonathan Kell,[2] Elspeth M. Payne,[5] Pramila Krishnamurthy,[6] Austin Kulasekararaj,[6] Manoj Raghavan,[7] Simon J. Stanworth,[8] Simone Green,[9] Ghulam Mufti,[6] Lynn Quek,[6] Catherine Cargo,[10] Gail L. Jones,[11] Juliet Mills,[12] Alex Sternberg,[13] Daniel H. Wiseman[14] and David Bowen[10]

A trustable support to clinical decisions needs to be authored by a **scientific community/society**

- SIE 2002 (Haematologica)

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2025 Myelodysplastic Syndromes

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

Myelodysplastic syndromes: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†☆

Linee Guida (LG)

Le Linee Guida (LG) di pratica clinica sono uno strumento di supporto decisionale finalizzato a consentire che, fra opzioni alternative, sia adottata quella che offre un migliore bilancio fra benefici ed effetti indesiderati, tenendo conto della esplicita e sistematica valutazione delle prove disponibili, commisurandola alle circostanze peculiari del caso concreto e condividendola-laddove possibile- con il paziente o i *caregivers*.

Procedure di invio e valutazione di Linee Guida per la pubblicazione nel SNLG

Manuale operativo

CENTRO NAZIONALE
ECCELLENZA CLINICA, QUALITÀ E SICUREZZA DELLE CURE

ıdations screened

Countries	Institution	Links and references
USA	NCCN	https://www.nccn.org/professionals/physician_gls/default.aspx#site
Germany, Austria, Switzerland	DGHO, OeGHO, SGH-SHH	https://www.onkopedia.com/de/onkopedia/guidelines/myelodysplastische-syndrome-m guideline/html/index.html
Scandinavia	NMDSG	https://www.nmds.org/index.php/guidelines
France	GFM	http://www.gfmgroup.org/recommandations.php
Europe	EBMT, ELN, BMT-CTN	Allo-HSCT for MDS and CMML: recommendations from an international expert panel[5]
Europe	ESMO	European Society for Medical Oncology MDS guidelines[51]
2013 Europe	ELN	European LeukemiaNet MDS guidelines[52]
2013 The Netherlands/ Belgium	HOVON	https://hematologienederland.nl/kwaliteit/richtlijnen/
2013 UK	BCSH	British Committee for Standards in Haematology MDS guidelines[53]
2012 Spain	GESMD	https://www.gesmd.es/
2011 Italy	FISiM	https://www.fismonlus.it/en/about-fism/
G/Rs from cancer care certification/ accreditation programs, n = 6		
Annual updates	UK	NICE https://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers#path=view%3 pathways/blood-and-bone-marrow-cancers/blood-and-bone-marrow-cancers-overvie xml&content=view-index
2018	Germany	DKG https://www.krebsgesellschaft.de/deutsche-krebsgesellschaft-wtrl/deutsche-krebsgese zertifizierung/erhebungsboegen/onkologische-zentren.html
2017	USA	ASCO/QOPI https://practice.asco.org/quality-improvement/quality-programs/qopi-certification-progr
2016	USA	ACS/CoC https://www.facs.org/quality-programs/cancer/coc/standards
2013	Switzerland	SCN https://www.sgmo.ch/qualitaetssicherung/dokumentation/
1999	Europe	OECI/ACOE http://www.acoe.be/About-ACOE/Mission-and-Objectives

2021 UK BCSH

Valutazione di eleggibilità della LG proposta

Pre-requisito: iscrizione al Registro del Ministero della Salute

- È una LG?
- Rispecchia le priorità dell'SNLG?
- Esistono già LG di alta qualità sull'argomento?
- ...

Analisi Allegato A compilato dal produttore

LG eleggibile? — No → Stop

Si → Inserimento nel sito SNLG del titolo della LG, produttore, data presentazione

Valutazione del Quality of Reporting (QoR)

- Verifica della corretta compilazione dell'AGREE quality of reporting checklist compilata dal produttore

QoR soddisfacente? — No → Correzione carenze/ discrepanze

Si

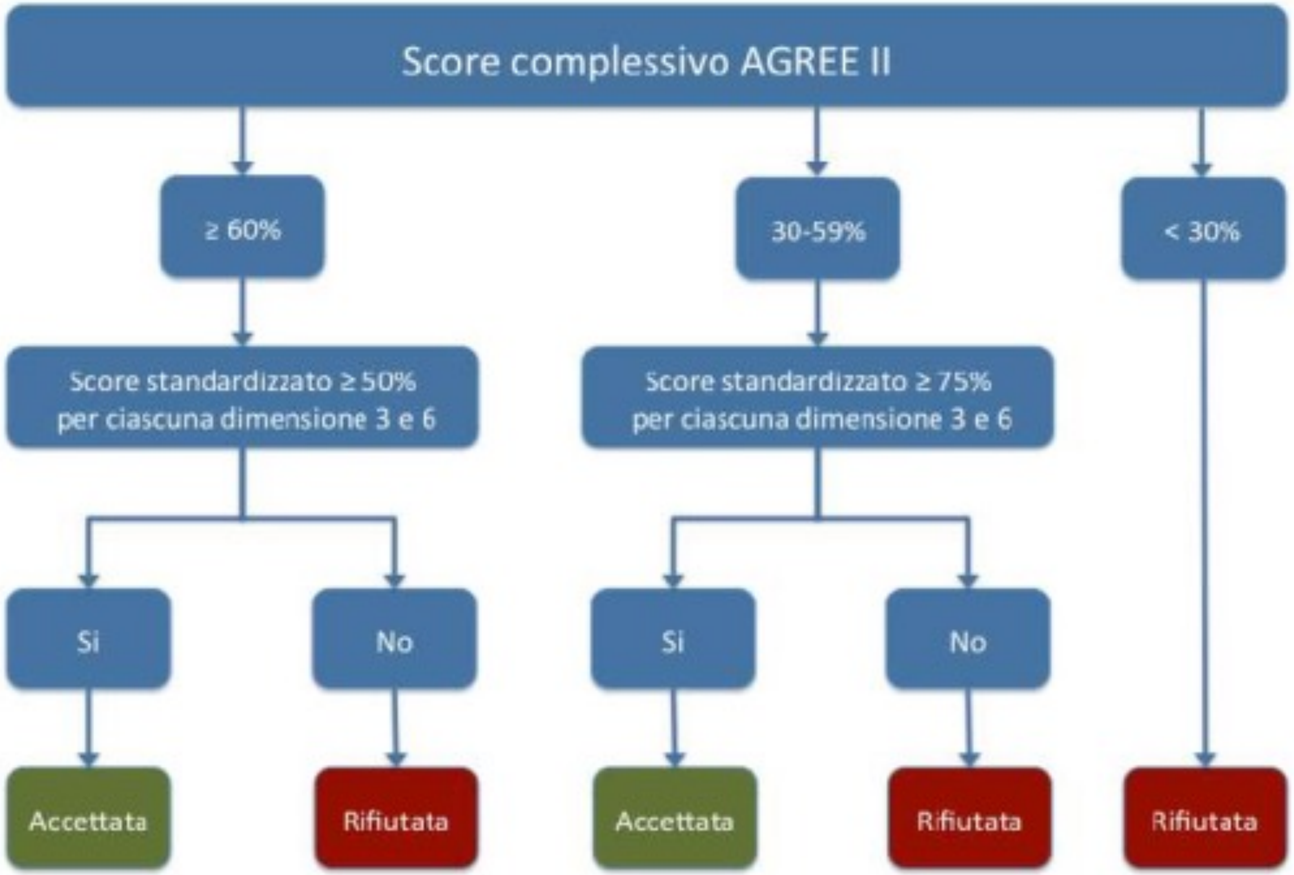
Valutazione della qualità metodologica e dei contenuti

- Strumento CNEC per lo screening preliminare di LG affidabili
- AGREE II, versione italiana
  Criteri preferenziali: GRADE, *patients oriented outcomes*, multimorbidità, ricadute organizzative e di costi, indicatori di audit, schemi di PDTA

Qualità e contenuti soddisfacenti? — No → Correzione carenze

Si

Pubblicazione della LG nell'SNLG



Tradotto da: European Commission Initiative on Breast Cancer. Evaluation of existing evidence of desired AGREE II thresholds for considering guidelines as reliable in national and international contexts. University of Warwick and GIMBE

Procedure di invio e valutazione di Linee Guida per la pubblicazione nel SNLG

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CENTRO NAZIONALE ECCELLENZA CLINICA, QUALITÀ E SICUREZZA DELLE CURE

APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II

AGREE II

Checklist per la Valutazione delle Linee Guida

DIMENSIONE 3

RIGORE METODOLOGICO

7. Sono stati utilizzati metodi sistematici per ricercare le evidenze scientifiche
8. La linea guida descrive con chiarezza i criteri utilizzati per selezionare le evidenze scientifiche
9. La linea guida descrive con chiarezza i punti di forza e i limiti delle evidenze scientifiche
10. La linea guida descrive con chiarezza i metodi utilizzati per formulare le raccomandazioni
11. Nella formulazione delle raccomandazioni sono stati presi in considerazione benefici e rischi conseguenti alla loro applicazione
12. Esiste un legame esplicito tra le raccomandazioni e le evidenze scientifiche che le supportano
13. Prima della pubblicazione la linea guida è stata valutata da esperti esterni
14. È descritta la procedura per l'aggiornamento della linea guida

11. BENEFICI E RISCHI *Riportare benefici, effetti avversi e rischi considerati nella formulazione delle raccomandazioni.*	☐ Analisi dei benefici, con relativi dati a supporto ☐ Analisi dei rischi/effetti avversi/danni, con relativi dati a supporto ☐ Bilancio (*trade off*) tra benefici e rischi/effetti avversi/danni ☐ Raccomandazioni che riflettono tutte le considerazioni effettuate sui benefici e sui rischi/effetti avversi/danni
12. LEGAME ESPLICITO TRA EVIDENZE E RACCOMANDAZIONI *Descrivere il legame esplicito tra evidenze scientifiche e raccomandazioni.*	☐ Metodologia con cui il gruppo che ha elaborato la linea guida ha collegato e utilizzato le evidenze per formulare le raccomandazioni ☐ Legame esplicito tra ciascuna raccomandazione e le principali evidenze che la supportano (descrizione testuale e/o lista di voci bibliografiche) ☐ Legame esplicito tra le raccomandazioni e le tabella delle evidenze nella sezione dei risultati della linea guida

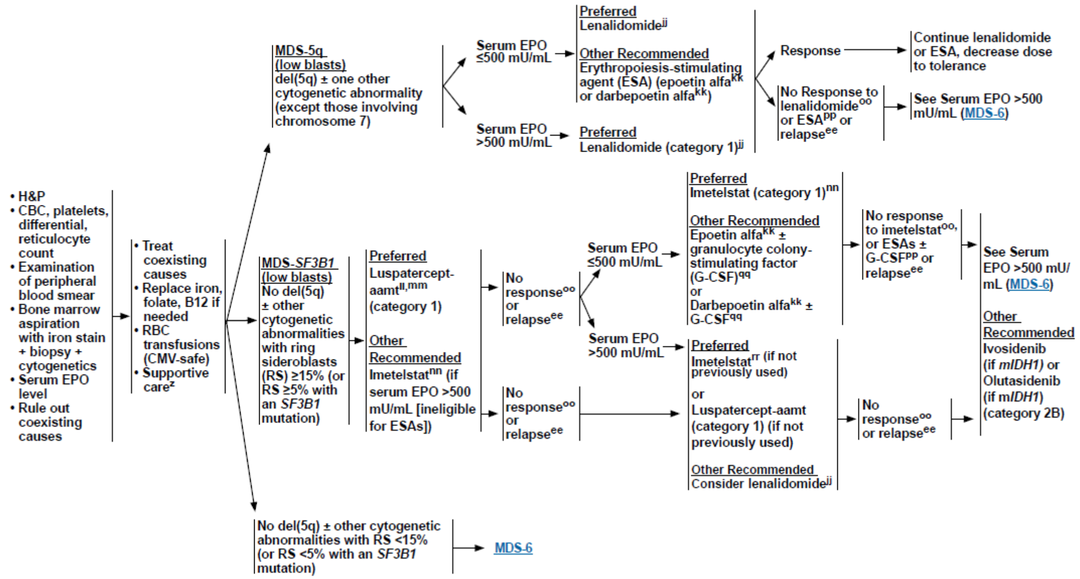
National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2025
Myelodysplastic Syndromes

NCCN Guidelines Index
Table of Contents
Discussion

MANAGEMENT OF LOWER-RISK DISEASE (IPSS-R VERY-LOW-, LOW-, INTERMEDIATE-RISK DISEASE)[w,x,y]

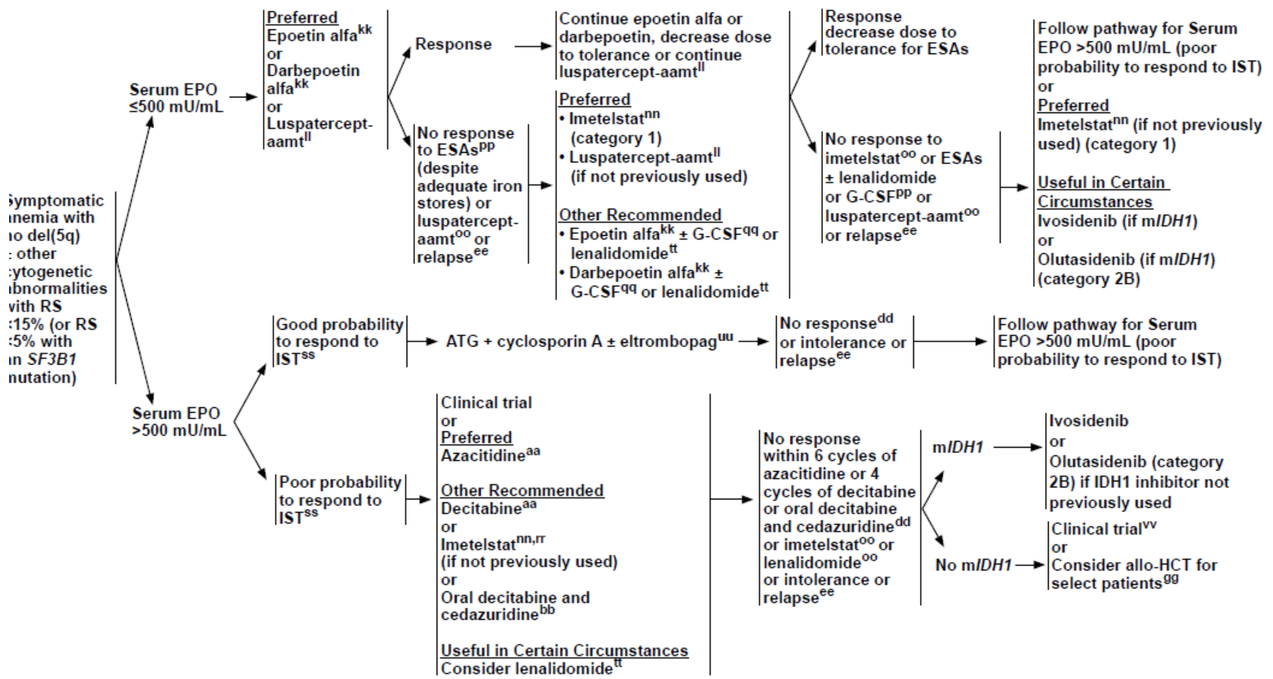
EVALUATION OF RELATED ANEMIA | TREATMENT OF SYMPTOMATIC ANEMIA[hh,ii] | FOLLOW-UP



Note: All recommendations are category 2A unless otherwise indicated.

Footnotes on MDS-6A

TREATMENT OF SYMPTOMATIC ANEMIA[nn,ll]



[xx] Allogeneic HCT from the most suitable donor (ie, HLA-matched sibling or unrelated donor, HLA-haploidentical family member or cord blood). Early referral for transplant evaluation is recommended to allow moving to transplant efficiently. Pre-transplant debulking therapy to reduce marrow blasts to <5% with the goal of reducing post-transplant relapse (see footnote yy and Discussion) is recommended, although the optimum strategy (ie, azacitidine, decitabine, induction-type chemotherapy) has not been determined. To reduce the disease burden pre-transplant is particularly important in patients who will receive a reduced-intensity conditioning regimen (Festuccia M, et al. Biol Blood Marrow Transplant 2016;22:1227-1233). At some centers, failure to achieve <5% blasts with cytoreduction should not preclude patients from proceeding to transplant, as these patients appeared to derive survival benefit from transplant (Nakamura R, et al. J Clin Oncol 2021;39:3328-3339; Schroeder T, et al. Biol Blood Marrow Transplant 2019:25;1550-1559). Strategies for patients with specific mutations are under investigation. Patients with TP53 mutations, particularly biallelic, have a poor prognosis even with transplantation. These cases should be discussed with a transplant physician and patients should be enrolled in a clinical trial whenever possible.

EVIDENCE BLOCKS FOR TREATMENT OF SYMPTOMATIC ANEMIA

MDS-5q (low blasts): del(5q) ± one other cytogenetic abnormality (except those involving

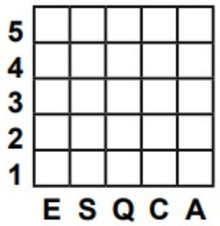
Primary treatment		
	Serum EPO ≤500 mU/mL	Serum EPO >50
Preferred regimen		
Lenalidomide	▦	▦
Other recommended regimens		
Epoetin alfa	▦	—
Darbepoetin alfa	▦	—

EVIDENCE BLOCKS FOR TREATMENT OF SYMPTOMATIC ANEMIA

MDS-*SF3B1* (low blasts): No del(5q) ± other cytogenetic abnormalities with RS ≥15% (or RS ≥5% with an *SF3B1* mutation)

Primary treatment		
Preferred regimen		
Luspatercept-aamt	▦	
Other recommended regimens		
Imetelstat	▦	
Epoetin alfa	▦	
Darbepoetin alfa	▦	
Subsequent treatment		
	Serum EPO ≤500 mU/mL	Serum EPO >500 mU/mL
Preferred regimens		
Imetelstat	▦	▦
Luspaterce	—	▦

NCCN EVIDENCE BLOCKS CATEGORIES AND DEFINITIONS



E = Efficacy of Regimen/Agent
S = Safety of Regimen/Agent
Q = Quality of Evidence
C = Consistency of Evidence
A = Affordability of Regimen/Agent

Quality of Evidence

No del(5q) ± other cytogenetic abnormalities with RS <15% (or RS <5% with an *SF3B1* mutation) with serum EPO ≤500 mU/mL

Primary treatment	
Preferred regimens	
Epoetin alfa	▦
Darbepoetin alfa	▦
Luspatercept-aamt	▦
Subsequent treatment	
Preferred regimens	
Imetelstat	▦
Luspatercept-aamt	▦

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guideline production according to GRADE: STEPS of the process

Step	
Search and selection of existing guidelines (and recommendations) for potential ADOLOPMENT	1
Key questions listing and refinement	2
Key questions classification and priorization: evidence-based (EBQ) vs good-practice (GPQ) questions	3
Outcome listing and ranking (prioritisation) for EBQ [PICO framework]	4
Literature search for EBQ	5
Selection of systematic reviews and randomized clinical trials – PRISMA 1	6
Additional search and appriasal of non-randomized studies – PRISMA 2	7
Evidence profiles for EBQ [Summary of Findings Table] and GPQ [narrative review]	8
Evidence-to-decision tables for EBQ	9
Recommendations: proposed statements, consensus-based approval, possible changes, strength (EBQ)	10

International Journal of Hematology (2025) 121:294–317
https://doi.org/10.1007/s12185-024-03906-w

GUIDELINE

JSH practical guidelines for hematological malignancies, 2023: leukemia-6. Myelodysplastic syndromes (MDS)

Yasushi Miyazaki[1]

References

1. Italian Cooperative Study Group for rHuEpo in Myelodysplastic Syndromes.; Ferrini PR, et al. A randomized double-blind placebo-controlled study with subcutaneous recombinant human erythropoietin in patients with low-risk myelodysplastic syndromes. Br J Haematol. 1998;103(4):1070–4. (**1iDiv**)

2. Fenaux P, et al. A phase 3 randomized, placebo-controlled study assessing the efficacy and safety of epoetin-α in anemic patients with low-risk MDS. Leukemia. 2018; 32(12):2648–58. (**1iDi, iv**)

3. Park S, et al. Outcome of Lower-Risk Patients With Myelodysplastic Syndromes Without 5q Deletion After Failure of Erythropoiesis-Stimulating Agents. J Clin Oncol 2017;35(14):1591–7. (**3iiiA**)

CQ4 Is cytokine therapy recommended for cytopenia in patients with lower risk MDS?

Recommendation grade: Category 2A

Treatment with an erythropoiesis-stimulating agent (ESA; erythropoietin [EPO] or darbepoetin alfa) corrects anemia in lower risk MDS patients with low serum erythropoietin (< 200 U/L or < 500 U/L) who are RBC transfusion-independent or mildly transfusion-dependent (only darbepoetin alfa is covered by Japanese NHI)

Recommendation grade: Category 2B

Granulocyte colony-stimulating factor (G-CSF) corrects neutropenia and reduces infection risk. G-CSF may be considered in combination with antibiotics as a short-term treatment in patients with marked neutropenia or at the onset of any infection, while monitoring for side effects on systemic conditions, such as G-CSF-induced exacerbation of inflammation. G-CSF is not currently known to increase risk of progression to AML

Recommendation grade: Category 2B

Addition of G-CSF enhances responsiveness to ESAs, but has not been shown to improve quality of life (QOL). Use of G-CSF for this purpose is not covered by Japanese NHI

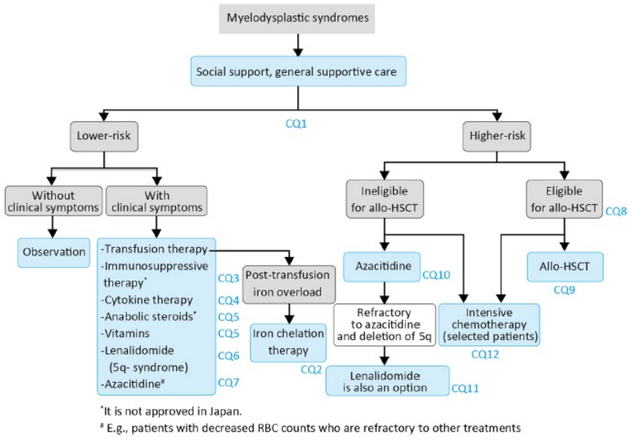
Recommendation grade: Category 1

Luspatercept is beneficial for correcting anemia in lower risk MDS-RS patients, but it is not approved in Japan

Recommendation grade: Category 2B

Thrombopoietin receptor agonists (TPO-RAs) increase platelet count and reduce the incidence of serious bleeding in lower risk MDS patients with thrombocytopenia, but are not covered by Japanese NHI. It is not currently known whether they increase risk of progression to AML or negatively impact prognosis

gorithm



VIA MEDICA

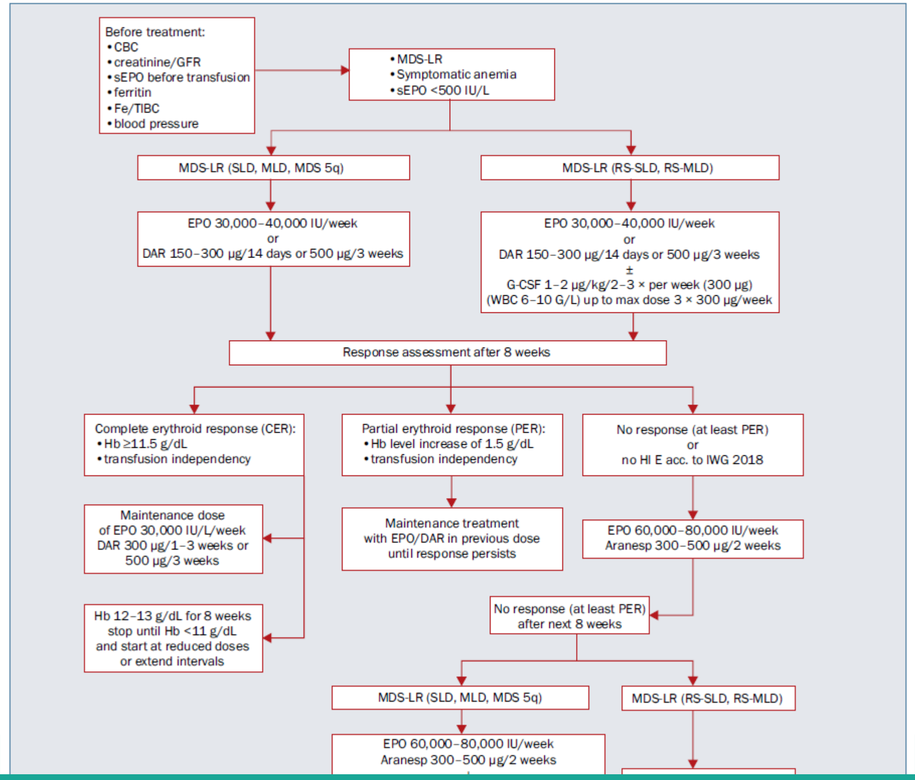
GUIDELINES/EXPERT CONSENSUS

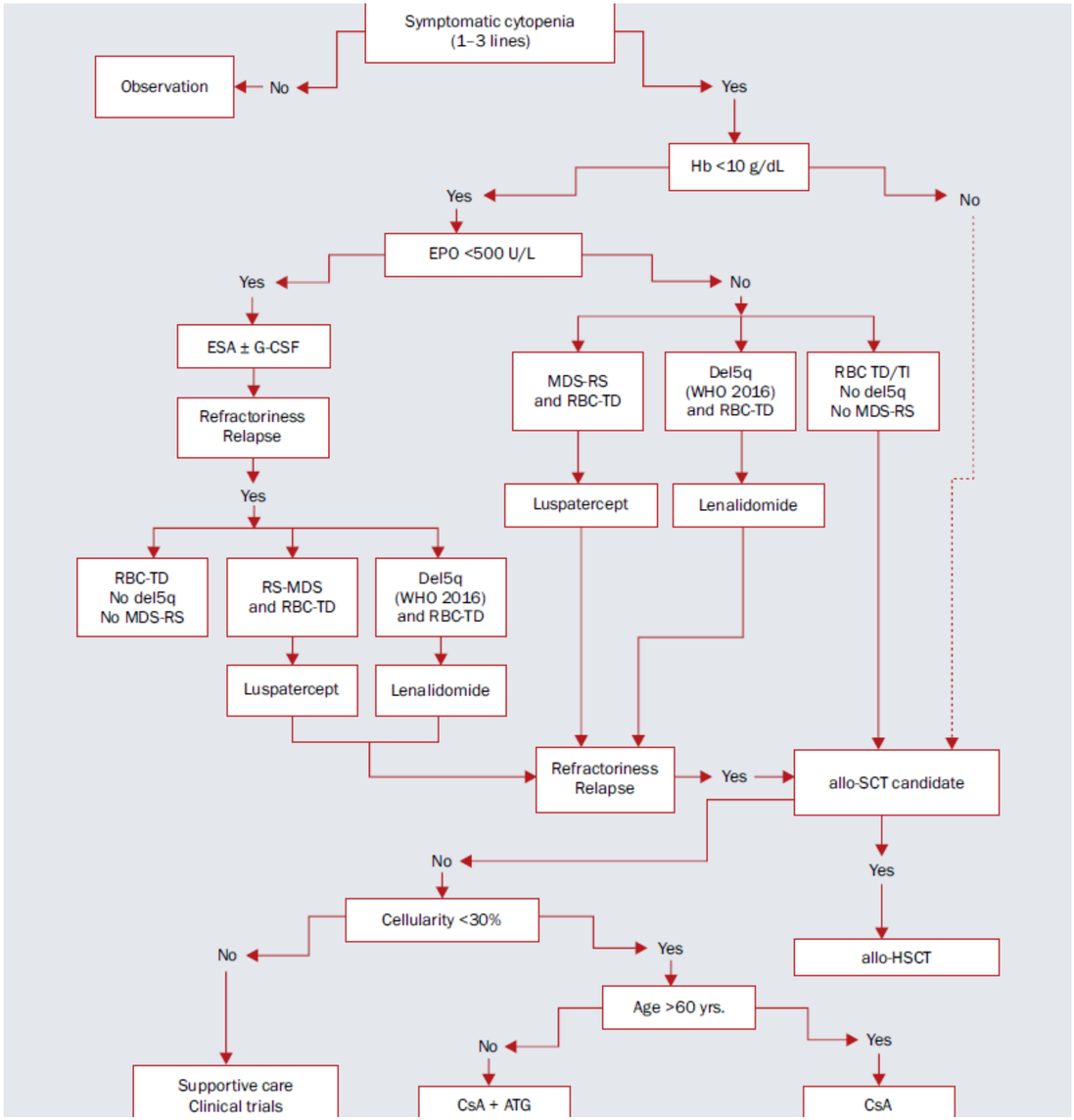
Acta Haematologica Polonica 2022
Number 2, Volume 53, pages 75–93
DOI: 10.5603/AHP.a2022.0009
ISSN 0001–5814
e-ISSN 2300–7117

Treatment recommendations of Polish Adult Leukemia Group (PALG) for management of myelodysplastic syndromes (MDS) and other MDS-related conditions in Poland

Krzysztof Mądry[1*], Bożena Katarzyna Budziszewska[2], Karol Lis[1], Joanna Drozd-Sokołowska[1].

Krzysztof Mądry et al., **Recommendations for the management of MDS and other MDS-related conditions in Poland**





Procedure di invio e valutazione di Linee Guida per la pubblicazione nel SNLG

Manuale operativo

CENTRO NAZIONALE ECCELLENZA CLINICA, QUALITÀ E SICUREZZA DELLE CURE

ADOLOPT? = HARMONIZE?

APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II

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BIGG, the international database of GRADE Guidelines

Marcela Torres,[a] Martin Ragusa,[a] Veronica Abdala,[a] Eva Brocard,[a] Holger Schunemann,[b,c,d,e,f] Sebastian Garcia-Saiso,[a] and Ludovic Reveiz,[a,]*

[a]Evidence and Intelligence for Action in Health Department, Pan American Health Organization
[b]Department of Health Research Methods, Evidence and Impact, McMaster University, 1280 Main St West, Hamilton, ON, L8S 4L8, Canada.
[c]Michael G. DeGroote Cochrane Canada & McMaster GRADE Centres; Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON, Canada
[d]Department of Medicine, McMaster University, Hamilton, ON, Canada
[e]Dipartimento di Scienze Biomediche Humanitas University, Milan, Italy
[f]Institute for Evidence in Medicine, Medical Center & Faculty of Medicine, University of Freiburg, Freiburg, Germany

The Lancet Regional Health - Americas 2022;6: 100099
Published online 30 November 2021
https://doi.org/10.1016

Health and equity have a central place in the 2030 Agenda for Sustainable Development that was adopted by all United Nations Member States. Implementation of evidence-based practice (EBP) principles has resulted in major advances in improving

indexed and hard to find which threatens the extent evidence is used.

Several scientific repositories such as Health Systems Evidence, Epistemonikos or Trip database are available for those interested in public health or clinical practice. BIGG[4]

UPDATED

Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation

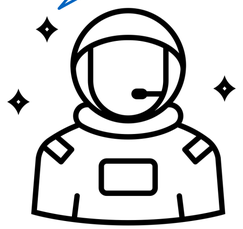
Olaf Penack*, Monia Marchetti*, Mahmoud Aljurf, Mutlu Arat, Francesca Bonifazi, Rafael F Duarte, Sebastian Giebel, Hildegard Greinix, Mette D Hazenberg, Nicolaus Kröger, Stephan Mielke, Mohamad Mohty, Arnon Nagler, Jakob Passweg, Francesca Patriarca, Tapani Ruutu, Hélène Schoemans, Carlos Solano, Radovan Vrhovac, Daniel Wolff, Robert Zeiser, Anna Sureda, Zinaida Peric

Graft-versus-host disease (GVHD) is a major factor contributing to mortality and morbidity after allogeneic Lancet Haematol 2024;

Focusing

2024

Monitoring



EUROPEAN RESPIRATORY JOURNAL
ERS OFFICIAL DOCUMENTS
S. BOS ET AL.

ERS/EBMT clinical practice guidelines on treatment of pulmonary chronic graft-*versus*-host disease in adults

Saskia Bos [1,2], John Murray[3], Monia Marchetti[4], Guang-Shing Cheng[5], Anne Bergeron[6], Daniel Wolff[7],

Transfusion and Apheresis Science 63 (2024) 103990

Contents lists available at ScienceDirect

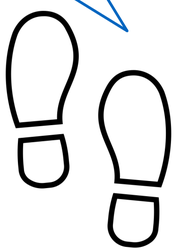
Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Treatment of acute and chronic graft-versus-host disease with extracorporeal photopheresis: Update of best practice recommendations from Italian Society of Hemapheresis and Cell Manipulation (SIdEM) and the Italian Transplant Group for Bone Marrow Transplantation, Hematopoietic Stem Cells and Cell Therapy (GITMO)

Anna Colpo [a,*], Monia Marchetti [b], Irene Bianco [c], Fabio Cruciani [d], Francesco Ipsevich [e],

Rebooting



Prophylaxis and management of graft versus host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation

Olaf Penack, Monia Marchetti, Tapani Ruutu, Mahmoud Aljurf, Andrea Bacigalupo, Francesca Bonifazi, Fabio Ciceri, Jan Cornelissen, Ram Malladi, Rafael F Duarte, Sebastian Giebel, Hildegard Greinix, Ernst Holler, Anita Lawitschka, Stephan Mielke, Mohamad Mohty, Mutlu Arat, Arnon Nagler, Jakob Passweg, Hélène Schoemans, Gerard Socié, Carlos Solano, Radovan Vrhovac, Robert Zeiser, Nicolaus Kröger, Grzegorz W Basak

Graft-versus-host disease (GVHD) is a major factor contributing to mortality and morbidity after allogeneic stem-cell transplantation. Because of the small number of results from well designed, large-scale, clinical studies there is Lancet Haematol 2020; 7: e157–67

Extracorporeal photopheresis for the treatment of acute and chronic graft-versus-host disease in adults and children: best practice recommendations from an Italian Society of Hemapheresis and Cell Manipulation (SIdEM) and Italian Group for Bone Marrow Transplantation (GITMO) consensus process

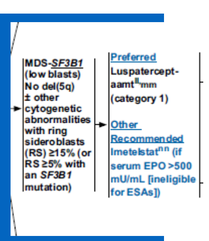
Luca Pierelli, Paolo Perseghin, Monia Marchetti, Chiara Messina, Cesare Perotti,

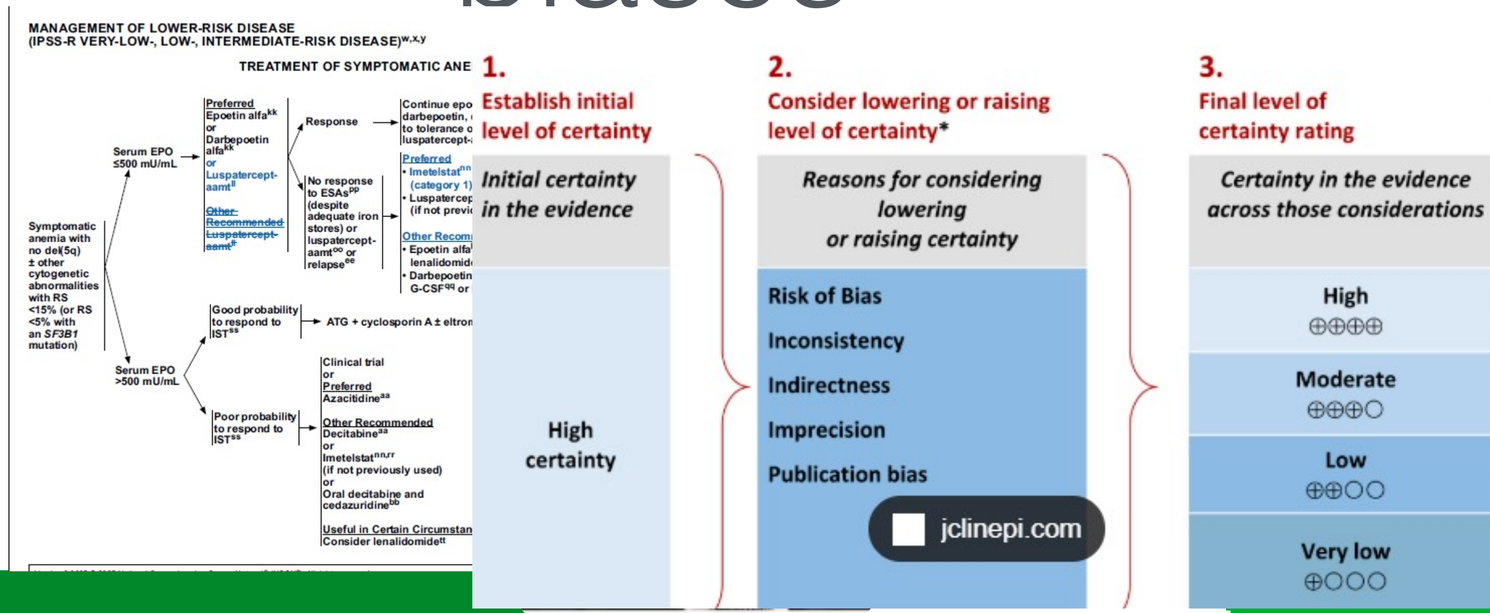
2020 -- 2013

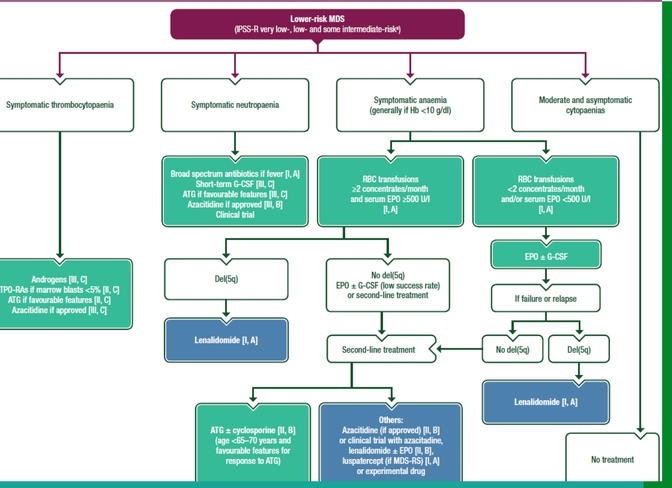
Hemonc CPG cognitive biases

NEW DRUGS

No trust for CPG not including last approved drugs







SIMPLE & COMPLETE

FLOWCHARTS; TABLES (edu, tools) … KOL mediates pending CPG recommendations

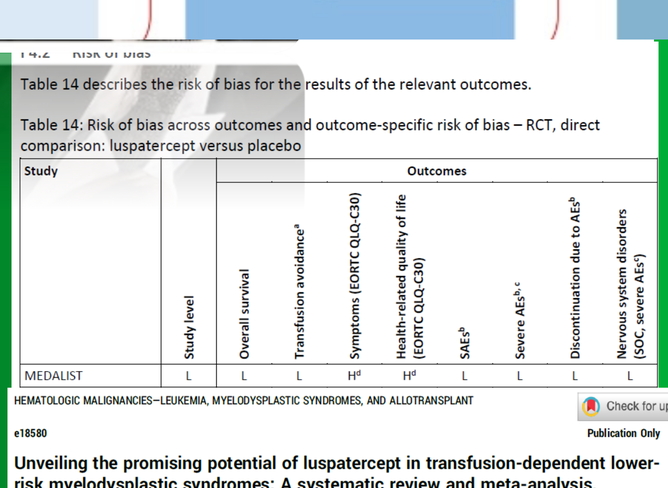


Table 14 describes the risk of bias for the results of the relevant outcomes.

Table 14: Risk of bias across outcomes and outcome-specific risk of bias – RCT, direct comparison: luspatercept versus placebo

Study	Study level	Outcomes								
		Overall survival	Transfusion avoidance[a]	Symptoms (EORTC QLQ-C30)	Health-related quality of life (EORTC QLQ-C30)	SAEs[b]	Severe AEs[b,c]	Discontinuation due to AEs[b]	Nervous system disorders (SOC, severe AEs[c])
MEDALIST	L	L	L	H[d]	H[d]	L	L	L	L

HEMATOLOGIC MALIGNANCIES—LEUKEMIA, MYELODYSPLASTIC SYNDROMES, AND ALLOTRANSPLANT
e18580
Publication Only

Unveiling the promising potential of luspatercept in transfusion-dependent lower-risk myelodysplastic syndromes: A systematic review and meta-analysis.

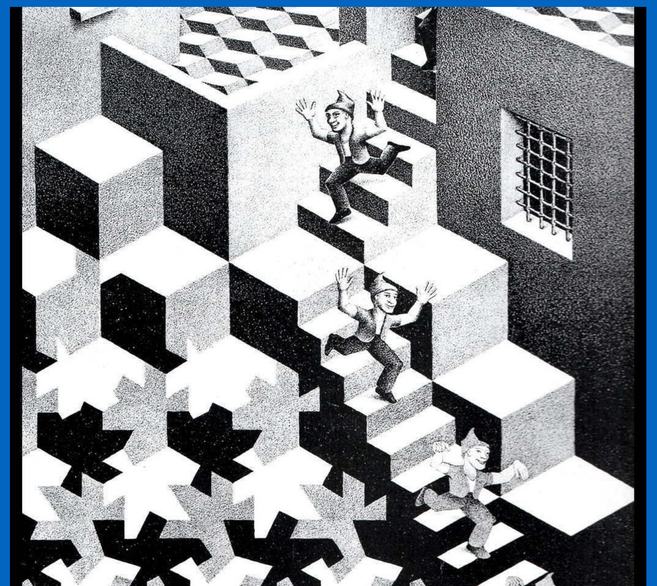
Shamikha Cheema, Hassan Ijaz, Sai Sushrutha Mudupula Vemula, Muhammed Faique Hassan, Jabez David John, Muhammad Shaheer Bin Faheem, Umaima Cheema,

REIMBURSED = RECOMMENDED

Any Agency indication is a recommendation to use the drug

Is the CPG robust = TRANSPARENT ?

Grading of Recommendations, Assessment, Development, and Evaluation



QUESITO 1.1.A: È raccomandata una terapia con CD19 CAR- T per i pazienti adulti con DLBCL, tFL, PMBCL, tMZL recidivati/refrattari dopo due linee di terapia precedente al fine di ottimizzare il rapporto tra esiti non desiderati (CRS, neurotssicità) ed esiti desiderati (sopravvivenza, PFS, qualità di vita)?

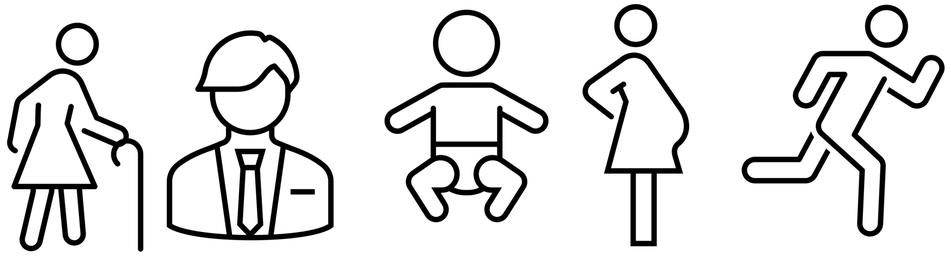
GRADE

PICO 1.1.A

		Note
POPOLAZIONE	Adulti con DLBCL, HGBCL, tFL o PMBCL recidivati o refrattari dopo almeno 2 linee di terapia	*I criteri di esclusione sono discussi nelle Domande Narrative dedicate*
INTERVENTO	CAR-T anti CD19	*Si intendono Axicabtagene ciloleucel e Tisagenlecleucel Axicabtagene ciloleucel (attualmente rimborsate in Italia)*
COMPARATORE	Migliore terapia disponibile (BAT)	*Include terapie cellulari non CAR-T*
ESITI DESIDERABILI	Sopravvivenza libera da progressione[11] Sopravvivenza globale Qualità della vita	
ESITI non-DESIDERABILI	Sindrome da rilascio citochinico grado 3-4 Neurotossicità (ICANS) grado 3-4	
SETTING	Ospedaliero II livello	
PROSPETTIVA	Singolo paziente	

PICO

Population



Host

Disease

TD MDS-RS

Prior therapies

ESA refract or inelegible

Intervention

Luspatercept

Comparator

Transfusions

Outcome

Transf-Indep

QoI

Improved survival and enhanced quality of life through anaemia correction in lower risk myelodysplastic syndromes: meaningful insights from an EUMDS Registry study

The focus of a study by Hege Kristin Gravdahl Garelius and ... The main outcomes of their study were the evaluation of ...

- 2448 pts low/int1 IPSS mdn fup 3.9 yrs
- ESAs OS 44·9 months [95% CI 40·2–50·5] vs 34·8 months [28·6–39·2]
- the absence of RBCT correlated to markedly better HRQoL, regardless of ESA exposure.
- Gravdahl Garelius HK, Bagguley T, Taylor A, et al. Survival and quality of life in patients with lower risk myelodysplastic syndromes exposed to erythropoiesis-stimulating agents: an observational cohort study. *Lancet Haematol* 2025; **12:** e128–37.

ELSEVIER

Blood 138 (2021) 64–67

63rd ASH Annual Meeting Abstracts

ORAL ABSTRACTS

637.MYELODYSPLASTIC SYNDROMES - CLINICAL AND EPIDEMIOLOGICAL

The EQ-5D-5L Predicts Treatment Outcomes and Provides Added Value to the R-IPSS in Patients with MDS, CMML or AML Treated within the Austrian Azacitidine Registry - a Prospective Cohort Study By the AGMT Study Group

Lisa Pleyer[1,2,3], Sonja Heibl[4,2], Christoph Tinchon[5,2], Sonja Vallet[6,2], Branka Petricevic[2,7], Michael Leisch[8,2,3],

bjh research paper

Development of a core outcome set for myelodysplastic syndromes – a Delphi study from the EUMDS Registry Group

U. Rochau *et al.*

Table 4. Definitions of the MDS core outcomes.

Health-related quality of life	General definition: Quality of life is described 'as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad-ranging concept affected in a complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment'[61]
Treatment-related mortality	Any unexpected cause of death, which cannot be contributed to the disease itself, but can be explained by one of the applied MDS therapeutic interventions. This may include early death after induction or septicaemia due to prolonged cytopenia after drug therapy. The actual cause of death should be specified, if possible. Those deaths which can be explained by other conditions (e.g., stroke, heart attack, other malignancies, suicide, etc.) should be excluded
Overall survival	The length of time from the first MDS diagnosis until death, irrespective of the cause
Performance status	General definition: 'The performance status describes the status of symptoms and functions with respect to ambulatory status and need for care'[38]
Safety	General definition: Safety can include assessment of the 'adverse events, laboratory evaluations, vital signs'[60], physical examinations, etc.
Haematological improvement	Definition according to the MDS IWG response criteria until the ongoing improvements become available

Received: 19 January 2022 | Revised: 30 September 2022 | Accepted: 16 November 2022

DOI: 10.1002/cam4.5487

RESEARCH ARTICLE

Cancer Medicine Open Access WILEY

Raising the standards of patient-centered outcomes research in myelodysplastic syndromes: Clinical utility and validation of the subscales of the QUALMS from the MDS-RIGHT project

Fabio Efficace[1] | Karin Koinig[2] | Francesco Cottone[1] | David Bowen[3] |

guideline production according to GRADE: STEPS of the process

Step	
Search and selection of existing guidelines (and recommendations) for potential ADOLOPMENT	1
Key questions listing and refinement	2
Key questions classification and priorization: evidence-based (EBQ) vs good-practice (GPQ) questions	3
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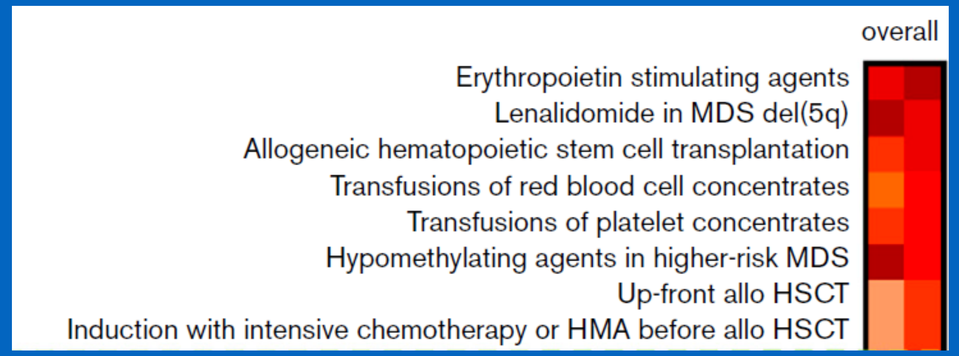
Additional search and appriasal of non-randomized studies – PRISMA 2	7
Evidence profiles for EBQ [Summary of Findings Table] and GPQ [narrative review]	8
Evidence-to-decision tables for EBQ	9
Recommendations: proposed statements, consensus-based approval, possible changes, strength (EBQ)	10

Is the question RELEVANT?



REGULAR ARTICLE

blood advances

Guideline-based indicators for adult patients with myelodysplastic syndromes

Kristina Stojkov,[1,2,*] Tobias Silzle,[3,*] Georg Stussi,[4] David Schwappach,[5,6] Juerg Bernhard,[7] David Bowen,[8] Jaroslav Čermák,[9] Avinash G. Dinmohamed,[10-12] Corien Eeltink,[12] Sabrina Eggmann,[13] Pierre Fenaux,[14] Ulrich Germing,[15] Manuel Haschke,[16,17] Eva Hellstrom-Lindberg,[18] Monika Heger,[1,7] Arjan A. van de Loosdrecht,[12] Jakob Passweg,[19] Michael Pfeilstöcker,[20] Uwe Platzbecker,[21,22] Luca Malcovati,[23,24] António Medina de Almeida,[25] Moshe Mittelman,[26] Christine Morgenthaler,[1,7] David P. Steensma,[27] Valeria Santini,[28,29] Reinhard Stauder,[30] Argiris Symeonidis,[31] Sämi Schär,[32] Charlotte Maddox,[32] Theo de Witte,[33] Julia Bohlius,[6] and Nicolas Bonadies,[1,2] on behalf of the Swiss MDS Study Group and the Swiss Group of Clinical Cancer Research (SAKK)

Final set of 29 GBIs

Domain 1: *Diagnosis* (n=14)
Diagnostic work-up:
- Cytogenetic analysis
- Bone marrow cytology/histology
- Peripheral blood assessment
- WHO 2016 classification
- Iron staining/monitoring
- Serum EPO in symptomatic anemia
- Molecular diagnostics/NGS
- TP53 in MDS del(5q)

Risk stratification:
- IPSS/IPSS-R
- Patient-based risk stratification

Follow-up/outcomes:
- Response assessment
- Patient-reported outcomes (PRO)

Domain 2: *Therapy* (n=8)
Supportive care:
- Transfusions of red blood cell concentrates
- Transfusions of platelet concentrates

Lower-risk:
- Erythropoietin stimulating agents
- Lenalidomide in MDS del(5q)

Higher-risk (unfit patients):
- Hypomethylating agents (HMAs)

Higher risk (fit patients):
- Induction before allo HSCT (blasts ≥ 10%)
- Up-front allo HSCT (blasts 5-10%)
- Allo HSCT

Domain 3: *Provider/ infrastructural characteristics* (n=7)
Personnel:
- Multidisciplinary care team

Organization:
- Safe handling of cytotoxic drugs
- Interdisciplinary diagnostic review
- Interdisciplinary treatment board
- Teaching and continuing education
- Emergency services

Cooperation:
- Access to clinical trials

bjh guidelines

British Society for Haematology guidelines for the management of adult myelodysplastic syndromes

Sally B. Killick,[1] Wendy Ingram,[2] Dominic Culligan,[3] Helen Enright,[4] Jonathan Kell,[2] Elspeth M. Payne,[5] Pramila Krishnamurthy,[6] Austin Kulasekararaj,[6] Manoj Raghavan,[7] Simon J. Stanworth,[8] Simone Green,[9] Ghulam Mufti,[6] Lynn Quek,[6] Catherine Cargo,[10] Gail L. Jones,[11] Juliet Mills,[12] Alex Sternberg,[13] Daniel H. Wiseman[14] and David Bowen[10]

- I pazienti a rischio basso/intermedio (IPSS basso o int-1 o IPSS-R molto basso, basso, intermedio = score inferiore a 3.5) e che presentano anemia sintomatica o hemoglobina inferiore a 10 g/dl dovrebbero essere considerati per un tentativo terapeutico con ESA se presentano una intermedia/elevata probabilità di risposta in base allo score nordico (1-A)
- Al fine di massimizzare i benefici degli ESA, il trattamento dovrebbe essere iniziato non appena appropriato e prima che il paziente sviluppi trasfusione-dipendenza (1-B)
- I pazienti dovrebbero proseguire il tentativo terapeutico con ESA per un massimo di 24 settimane (inclusivo di 8 settimane iniziali, 8 settimane ad alte dosi, e, se necessario, 8 settimane di combinazione con G-CSF) prima di definire la refrattarietà al trattamento. (2-B)
- I pazienti che ottengono una risposta parziale o completa agli ESA dovrebbero proseguire il trattamento a lungo termine alla dose minima efficace a mantenere la risposta o finchè la risposta non venga persa (2-B)
- I valori di emoglobina nei pazienti in trattamento con ESA non dovrebbero superare i 12 g/dl (2-C)

- I pazienti con MDS e citopenie sintomatiche dovrebbero ricevere terapia di supporto (1-A)
- Le trasfusioni di emazie concentrate dovrebbero essere somministrate per migliorare l'anemia sintomatica (1-A)
- Le strategie trasfusionali, incluse le soglie di emoglobina, dovrebbero considerare i fattori clinici, inclusi quelli paziente-specifici (1-A)
- Nei pazienti che ricevono emotrasfusioni con regolarità, andrebbero garantiti il match per Rh, k o antigeni addizionali (2-C)
- Tutti i pazienti a rischio basso/intermedio dovrebbero ricevere chelazione marziale dopo aver ricevuto 20 unità di emazie concentrate o quando la ferritinemia risulta superiore a 1000 mcg/l (1-B)
- La chelazione marziale è inoltre raccomandata nei pazienti candidati al trapianto di cell staminali emopoietiche, se la finestra temporale è compatibile
- Il deferasirox è il farmaco di scelta per operare la chelazione marziale nei pazienti con MDS sulla base dei dati di safety e compliance
- La chelazione marziale dovrebbe essere interrotta alla riduzione della ferritinemia sotto i 500 mcg/l (sotto i 1000 mcg/l per la desferoxamina)

bjh guidelines

British Society for Haematology guidelines for the management of adult myelodysplastic syndromes

Sally B. Killick,[1] Wendy Ingram,[2] Dominic Culligan,[3] Helen Enright,[4] Jonathan Kell,[2] Elspeth M. Payne,[5] Pramila Krishnamurthy,[6] Austin Kulasekararaj,[6] Manoj Raghavan,[7] Simon J. Stanworth,[8] Simone Green,[9] Ghulam Mufti,[6] Lynn Quek,[6] Catherine Cargo,[10] Gail L. Jones,[11] Juliet Mills,[12] Alex Sternberg,[13] Daniel H. Wiseman[14] and David Bowen[10]

- I pazienti on MDS 5q- a rischio basso/intermedio (IPSS basso o int-1 o IPSS-R inferiore a 3.5) con anemia sintomatica e una moderata/elevata probabilità di risposta dovrebbero avviare un tentativo terapeutico con ESA (1-B)
- Nei pazienti on MDS 5q- a rischio basso/Int-1 che siano trasfusione-dipendenti e non elegibili o non-responsivi ad ESA (inclusi i pazienti che hanno perso la risposta all'ESA) va considerato il trattamento con lenalidomide 10 mg al giorno per 321 giorni in cicli di 28 giorni, previa attenta verifica dei rischi e dei benefici del trattamento (1-B)
- Solo alcuni pazienti con MDS 5q- a rischio basso/Int-1 (o IPSS R inferiore a 3.5) sono candidabili al trapianto di cellule staminali emopoietiche allogeniche: i pazienti trasfusione-dipendenti che falliscono (o non sono elegibili a) il trattamento con lenalidomide.
- La lenalidomide non è raccomandata per i pazienti con eccesso di blasti midollari (sup a 5%) o anomalie cariotipiche complesse o rischio IPSS intermedio-2/alto
- I pazienti anziani fit e senza un cariotipo sfavorevole dovrebbero ricevere chemioterapia intensiva con regimi AML-like oppure terapia demetilante. I pazienti devono tuttavia essere informati della durata inferiore della sopravvivenza mediana riportata dagli studi di real-life rispetto allo studio pivotal (12.4 vs 18.9 mesi)
- La terapia demetilante preferita in prima linea è l'azacitidina 75 mg/m2 al giorno per 7 giorni consecutivi oppure con pause di 2 giorni week-end (5-2-2) e dovrebbe essere proseguita finchè viene mantenuta la risposta. La decisione di interrompere la terapia con azacitidina nei pazienti che non ottengono la risposta dopo 6 cicli ma hanno una malattia stabile è a discrezione delle preferenze del medico e del paziente
- I pazienti con MDS elegibili al trapianto di cellule staminali emopoietiche allogeniche devono essere discusse con il centro trapianti già alla diagnosi ed eventualmente nuovamente alla progressione. L'eligibilità al trapianto dovrebbe essere guidata dagli score di rischio HCT-CI e EBMT - Il performance status e l'età dovrebbero essere utilizzati per scegliere l'intensità del condizionamento
- Nel considerare il timing ottimale del trapianto nei pazienti a basso rischio vanno considerati vari elementi clinici quali il carico trasfusionale, la profondità delle citopenie, la fibrosi midollare
- Può essere preso in considerazione il trapianto up-front nei pazienti con una quota blastica midollare 5-10% e una malattia lentamente progressiva, nei pazienti con MDS ipocellulare , e nei pazienti con fibrosi midollare.
- Non si raccomanda il trapianto nei pazienti con mutazione TP53 in associazione a cariotipo monosomico complesso in ragione degli esiti clinici sfavorevoli

P I C O

- PICO 1.1.a – Is Luspatercept[6] (I) recommended in transfusion-dependent[5] low/intermediate risk[1] MDS-RS[2] patients refractory (or not eligible) to ESA (P) (*versus red blood cell transfusions) (C*) in order to induce transfusion-independence[7] and improve their quality of life (O)?
- PICO 1.1.b – Is Luspatercept[6] (I) recommended in transfusion-dependent[5] low/intermediate risk[1] MDS (non RS)[3] patients refractory (or not eligible) to ESA (P) (*versus red blood cell transfusions) (C*) in order to induce transfusion-independence[7] and improve their quality of life (O)?
- PICO 1.2.a – Is Luspatercept[6] (I) recommended in transfusion-dependent[5] low/intermediate risk[1] MDS-RS[2] patients eligible[4] but never exposed to ESA (P) (*versus ESA) (C*) in order to induce transfusion-independence[7] and improve their quality of life (O)?
- PICO 1.2.b – Is Luspatercept[6] (I) recommended in transfusion-dependent[5] low/intermediate risk[1] MDS (non RS)[3] patients eligible[4] but never exposed to ESA (P) (*versus ESA) (C*) in order to induce transfusion-independence[7] and improve their quality of life (O)?
- PICO 2-a – Is Eltrombopag (I) recommended *versus best available therapy (included transfusional therapy)* in low/intermediate risk MDS with severe symptomatic (bleeding) thrombocytopenia (transfusion-dependent) in order to minimize clinically relevant major bleedings and avoid the need for transfusional support (O)?
- PICO 2-b – Is Eltrombopag (I) recommended *versus best available therapy* in low/intermediate risk MDS with moderate thrombocytopenia (PLT <30.000/mcl) in order to minimize clinically relevant major bleedings and avoid the need for transfusional support (O)?
- PICO 3.1.a – Is Lenalidomide (I) recommended in transfusion-dependent[5] low/intermediate risk[1] 5q- MDS patients refractory (or not eligible) to ESA (P) (*versus red blood cell transfusions) (C*) in order to induce transfusion-independence[7] and improve their quality of life (O)?
- PICO 3.1.b – Is Lenalidomide (I) recommended in transfusion-dependent[5] low/intermediate risk[1] 5q- MDS patients eligible[4] but never exposed to ESA (P) (*versus ESA) (C*) in order to induce transfusion-independence[7] and improve their quality of life (O)?
- PICO 3.2.a – Is Lenalidomide (I) recommended in not transfusion-dependent[5] low/intermediate risk[1] 5q- MDS patients refractory (or not eligible) to ESA (P) (*versus red blood cell transfusions) (C*) in order to delay start of transfusion-dependence and improve their quality of life (O)?
- PICO 3.2.b – Is Lenalidomide (I) recommended in not transfusion-dependent[5] low/intermediate risk[1] 5q- MDS patients eligible[4] but never exposed to ESA (P) (*versus ESA) (C*) in order to delay start of transfusion-dependence and improve their quality of life (O)?
- PICO 7 – Is Imetelstat (I) recommended in ESA refractory (or not eligible) low/intermediate risk MDS patients (P) (*versus best available therapy) (C*) in order to in order to induce transfusion-independence[7] and improve their quality of life (O)?

guideline production according to GRADE: STEPS of the process

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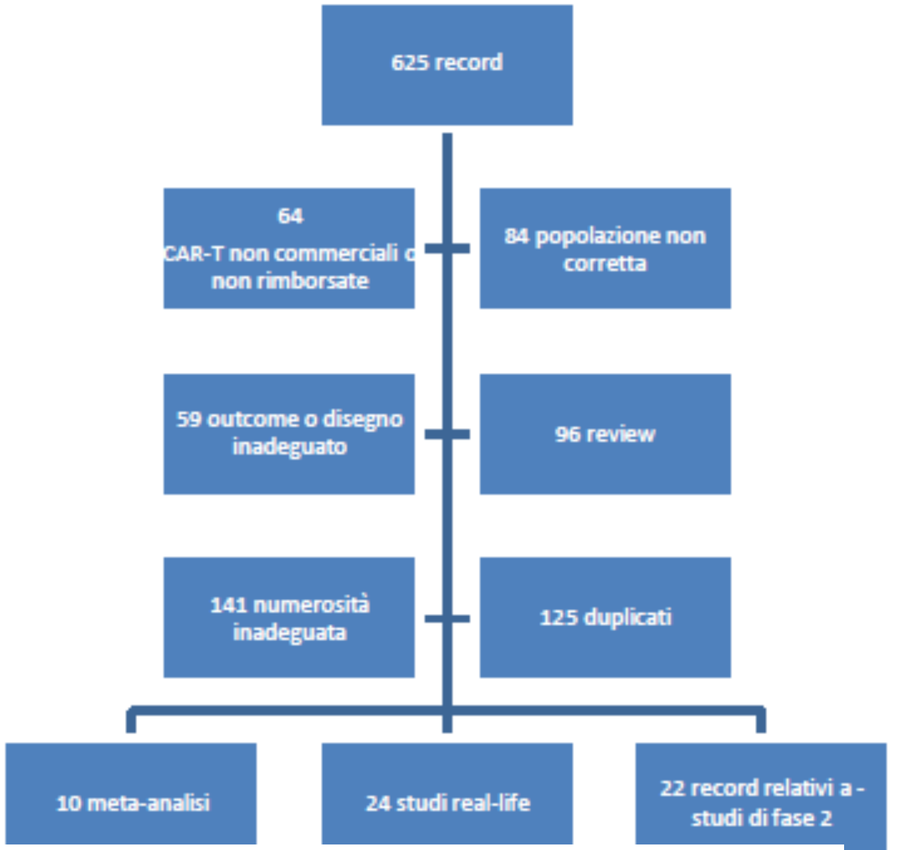
2a- Is the CPG robust = SYSTEMATIC?

Grading of Recommendations,

Assessment, Development,

and Evaluation

PRISMA Diagram PICO 1.1.A e 1.1.B

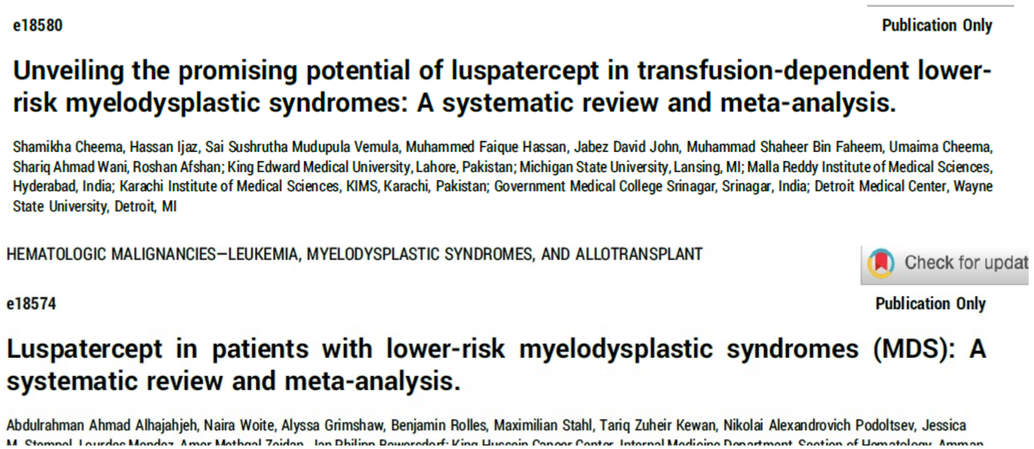


QUERY EMBASE

- 'diffuse large b cell lymphoma' OR 'mantle cell lymphoma'
- AND
- 'chimeric antigen receptor immunotherapy'/exp OR 'chimeric antigen receptor immunotherapy' OR 'chimeric antigen receptor t-cell'/exp OR 'chimeric antigen receptor t-cell' OR 'axicabtagene ciloleucel' OR 'tisagenlecleucel t' OR 'brexucabtagene autoleucel')
- AND
- 'clinical trial'/de OR 'cohort analysis'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'meta-analysis'/de OR 'observational study'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'prospective study'/de OR 'randomized controlled trial'/de OR 'retrospective study'/de

Standard search for evidence

- SLNG richiede interrogazione di almeno 2 database bibliografici
- EMBASE è il piu ampio
- TRIP è free e puo supportare ricerca di evdenza grigia (es. sull'impatto economico)



e18580 Publication Only

Unveiling the promising potential of luspatercept in transfusion-dependent lower-risk myelodysplastic syndromes: A systematic review and meta-analysis.

Shamikha Cheema, Hassan Ijaz, Sai Sushrutha Mudupula Vemula, Muhammed Faique Hassan, Jabez David John, Muhammad Shaheer Bin Faheem, Umaima Cheema, Shariq Ahmad Wani, Roshan Afshan; King Edward Medical University, Lahore, Pakistan; Michigan State University, Lansing, MI; Malla Reddy Institute of Medical Sciences, Hyderabad, India; Karachi Institute of Medical Sciences, KIMS, Karachi, Pakistan; Government Medical College Srinagar, Srinagar, India; Detroit Medical Center, Wayne State University, Detroit, MI

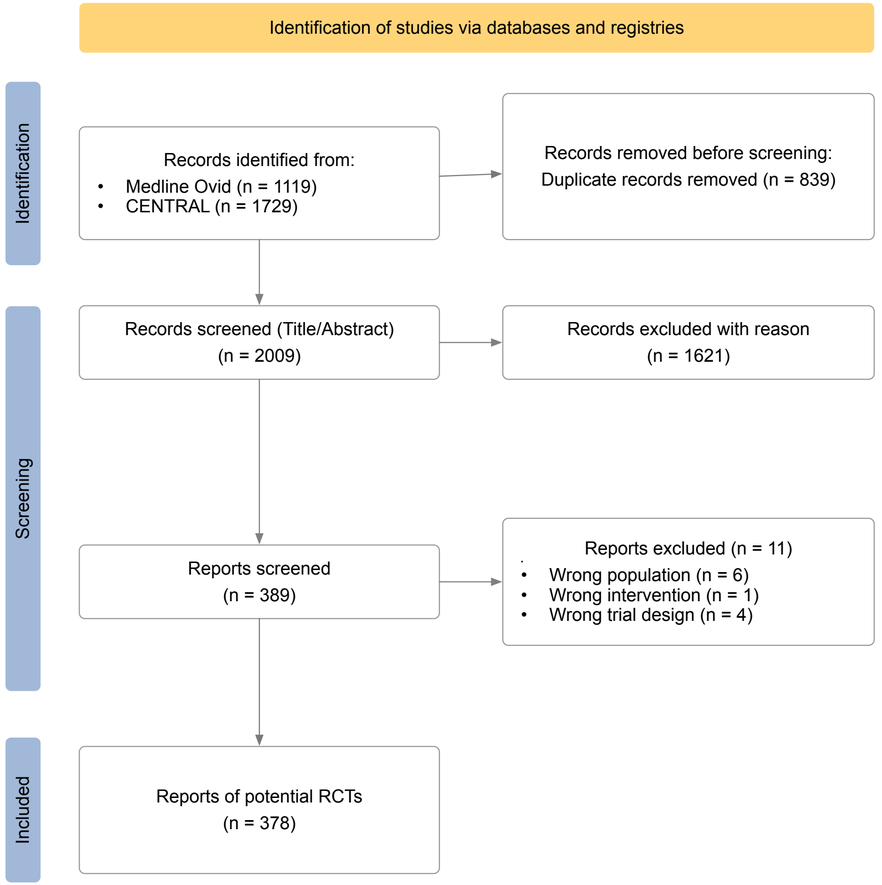
HEMATOLOGIC MALIGNANCIES—LEUKEMIA, MYELODYSPLASTIC SYNDROMES, AND ALLOTRANSPLANT

Check for updat

e18574 Publication Only

Luspatercept in patients with lower-risk myelodysplastic syndromes (MDS): A systematic review and meta-analysis.

Abdulrahman Ahmad Alhajahjeh, Naira Woite, Alyssa Grimshaw, Benjamin Rolles, Maximilian Stahl, Tariq Zuheir Kewan, Nikolai Alexandrovich Podoltsev, Jessica



Methodological Tips

- MSR25 To Merge Randomized Controlled Trials and Real-World Evidence With Bayesian Network Meta-Regression: A Case Study in Patients With Myelodysplastic Syndromes
  Jiu L., Wang J., Mantel-Teeuwisse A.K., Goettsch W.G.
  Value in Health 2022 25:12 *Supplement* (S354-)

- A Meta-analysis was conducted in MDS patients receiving RIC vs MAC : Bayesian NMA algorithms integrating RCT and real-world data differed in the results

BODY of EVIDENCE

1. CRITICAL Outcomes
2. Relative EFFECT size
3. INDIRECT evidence

Summary of findings – PICO 1A

OUTCOME	END POINT	STUDY (N pts, design)	PTCY (& IS)	COMPARATOR	RELATIVE EFFECT	QUALITY
aGVHD	Gr 2-4 d100	Ayala 2023 (matched pair retrospective analysis 100 vs 100)[1]	57%	CysA-based 23%	P<0.001	MODERATE
	Gr 2-4 Gr 3-4	Greco 2021 [48 pts]	25% 9%			LOW
	Gr 3-4 d100	Holtan 2022 ASH (randomized study BMT CTN - 128 matched related donors)[2]	&Tac+MMF 6.3%	Tac/MMF 14.7%	P=0.001	NA
	Gr 2-4 Gr 3-4 d100	Iqbal 2023[3] [8 vs 28]	&Sirolimus 17.2% 7%	MTX+Tac 34.5% 11.5%	Ns But shorter time to IS discontinuation (138 vs 232 days, p<0.001)	VERY LOW (indirectness: most MUD)
	Gr 2-4 Gr 3-4	Kwon 2019 (#57 vs 50 pts, retrospective)[4]	22.6% 8.8%	CysA+MTX 52.2% 24.4%	P=0.0015 (p=0.006 at MV analys) P=0.016	LOW
	Gr 2-4 Gr 3-4	Lazzari 2022 [77 pts, siroliums]	18% 6%			LOW
	Gr 2-4 d180 Gr 3-4	Mehta 2022 (140 vs 271)	44% 8%	37% 11%	ns	LOW
	Gr 2-4 Gr 3-4	Mehta 2022 bis [242 vs 144; MUD & MSD]	&Tac 38% 8%	Tac/MMF 67% 10%	HR 2.1 (1.6-2.8) Ns Lower rate of grade 1-2 GI and skin	LOW (mixed MRD & MUD)

Outcome-specific Body of Evidence

Limiti delle evidenze PICO 1.1.B

ESITO	Disegno degli studi	Numerosità e caretteristiche dei pazienti	Effetto relativo e incertezza	Consistenza degli studi
SOPRAVVIVENZA LIBERA DA PROGRESSIONE	Uno studio di fase 2; alcuni studi real-life	*Numerosità moderata; popolazione selezionata*	*Effetto relativo non valutabile.* *Incertezza moderata*	*Buona*
SOPRAVVIVENZA GLOBALE	Uno studio di fase 2; alcuni studi real-life; uno studio di confronto indiretto matched	*Numerosità moderata*	*Effetto relativo grande (confronto indiretto)* *Incertezza moderata*	*Buona*
QUALITA' della VITA	Uno studio di fase 2	*Limitata numerosità dei pazienti, selezionati..*	*Manca*	*Non valutabile*
CRS grado 3-4	Uno studio di fase 2; alcuni studi real-life	*Buona numerosità degli studi real-life.*	*Manca (evento avverso CART specifico).* *Discreta omogeneità nel grading della CRS*	*Buona*
ICANS	Uno studio di fase 2; alcuni studi real-life	*Buona numerosità degli studi real-life.*	*Manca (evento avverso CART specifico).* *Discreta omogeneità nel grading dell'ICANS*	*Buona*

ESITI DESIDERABILI	Studi	CAR-T	Comparatore & Effetto Relativo	Qualità del corpo dell'evidenza
SOPRAVVIVENZA LIBERA DA PROGRESSIONE	1 studio di fase 2. Alcuni studi retrospettivi.	52.9% a 24 mesi Mediana 25.8 mesi	*RBAC: 10.1 mesi* *HR: NA*	*BASSA*
SOPRAVVIVENZA GLOBALE	1 studio di fase 2. Alcuni studi retrospettivi.	60.3% a 30 mesi Mediana 46.6 mesi	*Mediana 9.7 mesi* *HR 0.32-0.49*	*MODERATA*
QUALITA' della VITA	1 studio di fase 2	Transitoria riduzione	*NA*	*BASSA*
ESITI NON DESIDERABILI				
CRS grado 3-4	1 studio di fase 2. Alcuni studi retrospettivi.	15%	*Evento avverso specifico*	*MODERATA*
ICANS grado 3-4	1 studio di fase 2. Alcuni studi retrospettivi.	31%	*Evento avverso specifico*	*MODERATA*

Author(s): Shannon Bates, Bram Rochwerg, John Riva, Meha Bhatt, Nicole Schwab
Date:
Question: Anticoagulant prophylaxis compared to no anticoagulant prophylaxis to prevent VTE in women undergoing assisted reproduction
Setting: Inpatient or outpatient setting
Bibliography: American Society of Hematology 2018 Guidelines for Management of Venous Thromboembolism: Venous Thromboembolism in the Context of Pregnancy

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	anticoagulant prophylaxis	no anticoagulant prophylaxis	Relative (95% CI)	Absolute (95% CI)		
PE: LMWH alone or LMWH combined with aspirin from day of embryo transfer to delivery or fetal demise												
1 [1,a]	observational studies	serious [b]	not serious	not serious	serious [c]	none	0/23 (0.0%)	1/211 (0.5%)	**OR 2.99** (0.12 to 75.40)	**9 more per 1,000** (from 4 fewer to 259 more)	⨁◯◯◯ VERY LOW	CRITICAL
DVT: LMWH alone or LMWH combined with aspirin from day of embryo transfer to delivery or fetal demise												
1 [1,a]	observational studies	serious [b]	not serious	not serious	serious [c]	none	0/23 (0.0%)	1/211 (0.5%)	**OR 2.99** (0.12 to 75.40)	**9 more per 1,000** (from 4 fewer to 259 more)	⨁◯◯◯ VERY LOW	CRITICAL
Pregnancy Rate (LMWH - dalteparin 2500 units/d or enoxaparin 40mg/d or 1mg/kg/d)												
3 [2,3,d,e]	randomised trials	not serious	serious [f]	not serious	serious [g]	none	66/190 (34.7%)	49/196 (25.0%)	**RR 1.66** (0.94 to 2.90)	**165 more per 1,000** (from 15 fewer to 475 more)	⨁⨁◯◯ LOW	CRITICAL
Implantation Rate (cohort >= 3 failures) with LMWH (dalteparin 2500 units/d or enoxaparin 40mg/d or 1mg/kg/d)												
3 [4,h]	randomised trials	serious [i]	not serious	not serious	serious [j]	none	75/344 (21.8%)	42/330 (12.7%)	**RR 1.73** (0.98 to 3.03)	**93 more per 1,000** (from 3 fewer to 258 more)	⨁⨁◯◯ LOW	CRITICAL
Thrombocytopenia (enoxaparin 40mg/d) from day of embryo transfer to delivery or fetal demise												
1 [5,k]	randomised trials	not serious	not serious	serious [l]	very serious [c]	none	2/42 (4.8%)	0/41 (0.0%)	**RR 4.89** (0.24 to 98.70)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	CRITICAL
Vaginal Bleeding (100mg aspirin from day of embryo transfer to delivery or fetal demise) during pregnancy												
1 [6,m]	randomised trials	not serious	not serious	not serious	very serious [c]	none	2/52 (3.8%)	2/55 (3.6%)	**RR 1.02** (0.15 to 6.97)	**1 more per 1,000** (from 31 fewer to 217 more)	⨁⨁◯◯ LOW	CRITICAL
Pregnancy Rate with Low-dose Aspirin (<150mg/d)												
10 [3]	randomised trials	serious [n]	not serious	not serious	serious [c,o]	none	341/1071 (31.8%)	330/1071 (30.8%)	**OR 1.19** (1.01 to 1.39)	**38 more per 1,000** (from 2 more to 74 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; **OR**: Odds ratio; **RR**: Risk ratio

Explanations

a. [Villani 2015] This was either LMWH alone or LMWH combined with aspirin from day of embryo transfer to delivery or fetal demise.
b. The panel felt that the observational nature of these studies would lead to potential bias and uncertainty.
c. The 95% confidence interval crosses null value, there is a small sample size and/or a low event rate which leads to uncertainty.
d. Anticoagulation in included trials was started at either oocyte retrieval or embyro transfer and continued for various durations.
e. [Akhtar 2015] (LMWH - dalteparin 2500 units/d or enoxaparin 40mg/d or 1mg/kg/d) [Dentali 2012, random effects model]
f. There was a mix of prophylactic dose (2 studies) and intermediate dose.
g. The findings were sensitive to choice of statistical model approach.
h. [Potdar 2013] (cohort >= 3 failures) with LMWH (dalteparin 2500 units/d or enoxaparin 40mg/d or 1mg/kg/d)

3- Tradeoffs & uncertainty appropriately managed?

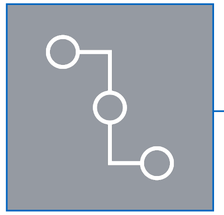
CPGs

Effetti desiderabili	Grandi	Il miglioramento della sopravvivenza globale (del tutto sovrapponibile al miglioramento della sopravvivenza libera da progressione) associato alla terapia con CAR-T rispetto alla BAT è stato giudicato clinicamente rilevante e molto ampio rispetto alla sopravvivenza media di questa popolazione.
Effetti indesiderabili	Moderati	La frequenza con cui si presentano eventi avversi severi e potenzialmente fatali quali la CRS e ICANS è stata giudicata rilevante. Tuttavia, un'adeguata gestione clinica di questi eventi avversi fa sì che siano reversibili nella maggioranza dei casi e le complicanze fatali associate alla terapia si realizzano in meno del 5% dei pazienti trattati.
Qualità delle prove	Bassa	
		abile alla progressione della malattia di base.
Risorse necessarie	Costi elevate	
Qualità delle prove (risorse)	Bassa	

Raccomandazione FORTE nonostante qualità del corpo dell'evidenza per gli outcome critici fosse BASSA:

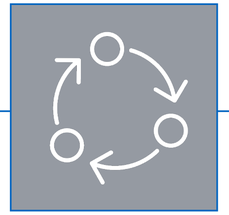
dettagliata e trasparente argomentazione (es. delta benefit)

EVIDENCE-to-DECISION



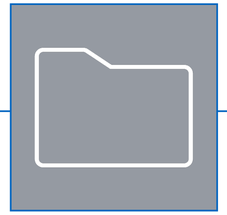
DESIRABLE OUTCOMES

Size of effect & certainty of the evidence



UNDESIRABLE OUTCOMES

Size of effect & certainty of the evidence

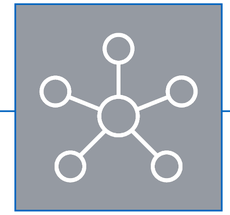


BALANCE

Discussion on desirable vs undesirable

OTHER OUTCOMES

Costs, equity, acceptability, applicability



SUBGROUPS

Specific issues

Raccomandazione forte contro l'intervento	Raccomandazione condizionata contro l'intervento	Raccomandazione condizionata di non differenza fra l'intervento e il confronto	Raccomandazione condizionata a favore dell'intervento	Raccomandazione forte a favore dell'intervento
○	○	○	○	●

Explicit grading

Cost-Effectiveness of Reduced-Intensity Allogeneic Hematopoietic Cell Transplantation for Older Patients With High-Risk Myelodysplastic Syndrome: Analysis of BMT CTN 1102

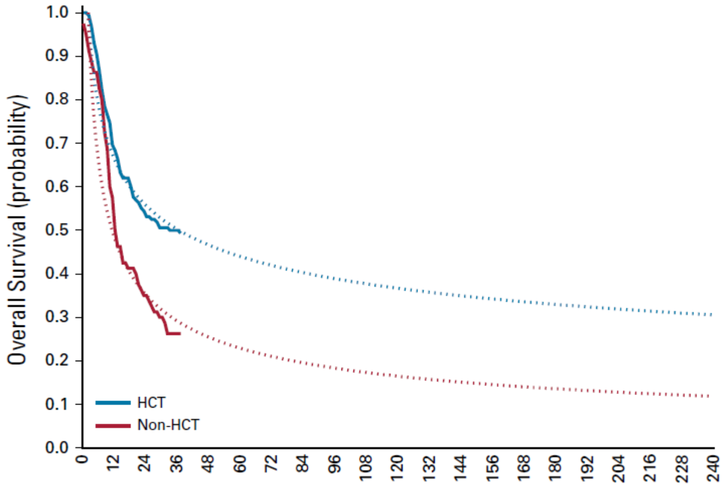
Wael Saber, MD, MS[1]; Aasthaa Bansal, PhD[2,3]; Lily Li, MPA[2]; Bart L. Scott, MD[2]; Lindsey R. Sangaralingham, MPH[4,5];

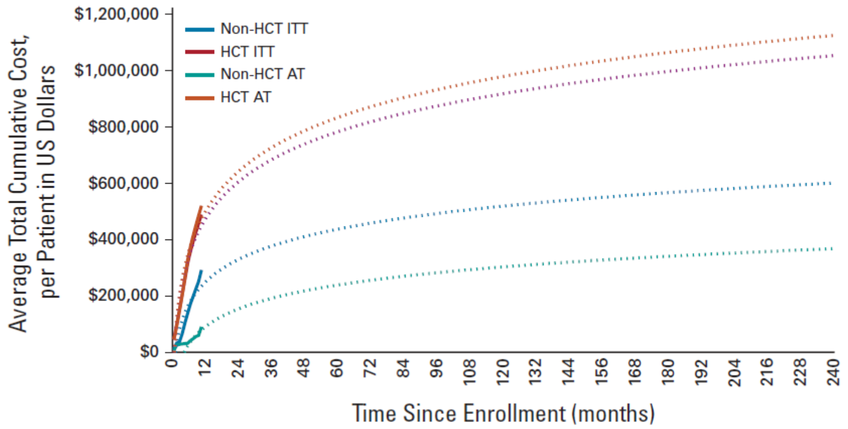
A Input ranges for persons <65 years

One-Way Sensitivity Analysis Input Range	LYs	QALYs	Costs
HCT	7.32 to 8.58	3.02 to 6.53	$1,029,024 to $1,076,578
Non-HCT	3.69 to 5.27	3.03 to 4.20	$586,138 to $614,979

B Input ranges for persons ≥65 years

One-Way Sensitivity Analysis Input Range	LYs	QALYs	Costs
HCT	7.49 to 8.73	5.98 to 6.99	$775,195 to $817,220
Non-HCT	3.51 to 5.12	2.95 to 4.31	$547,141 to $578,847





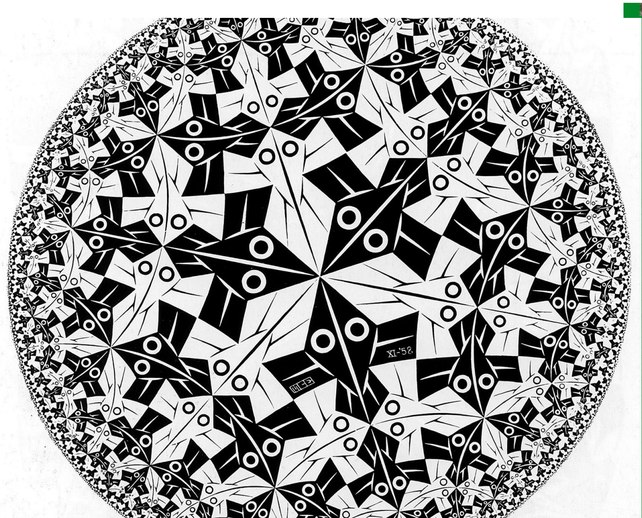
Hemonc methodologist view

Cochrane Library

Cochrane Database of Systematic Reviews

Healthcare outcomes assessed with observational study designs compared with those assessed in randomized trials: a meta-epidemiological study (Review)

Toews I, Anglemyer A, Nyirenda JLZ, Alsaid D, Balduzzi S, Grummich K, Schwingshackl L, Bero L



THRESHOLDS

Clinically relevant differences

Journal of Cancer Policy 34 (2022) 100364

Contents lists available at ScienceDirect

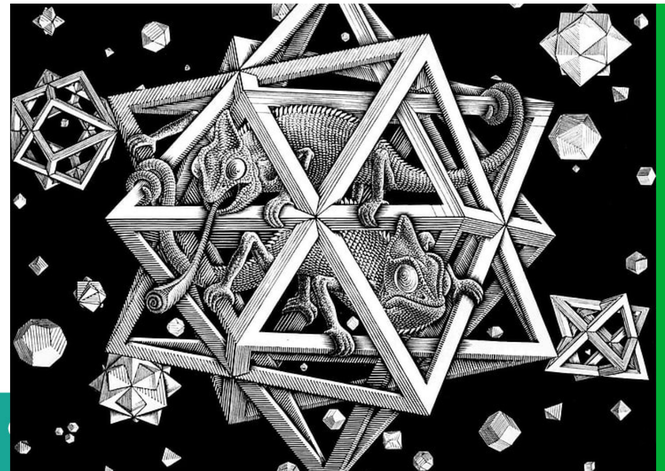
Journal of Cancer Policy

journal homepage: www.elsevier.com/locate/jcpo

ELSEVIER

FDA validation of surrogate endpoints in oncology: 2005–2022

Anushka Walia [a], Alyson Haslam [b,*], Vinay Prasad [b]



UNCERTAINTY

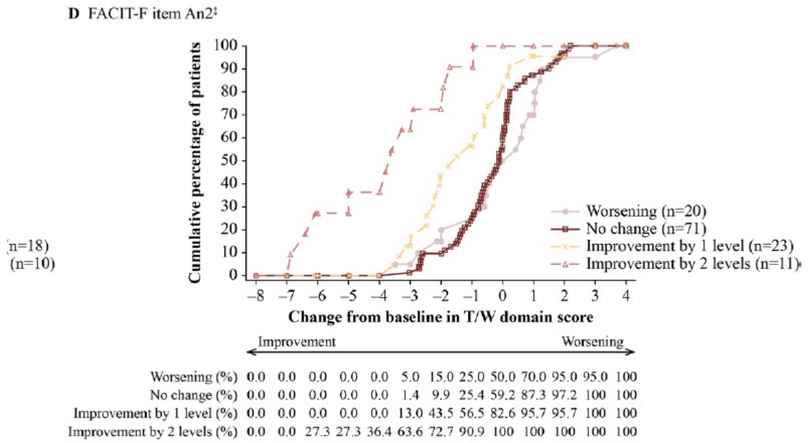
Surrogate outcomes & false cause-effect paradigms

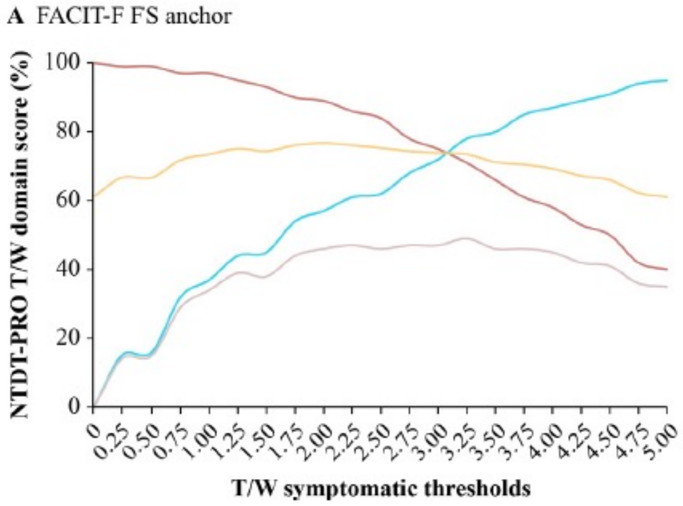
Open access Original research

BMJ Open

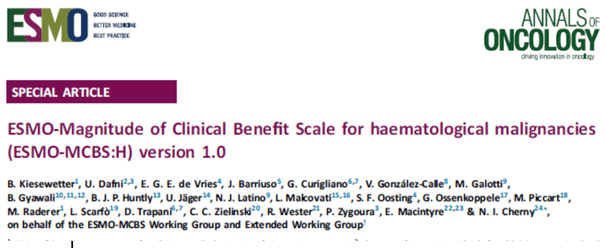
Identifying thresholds for meaningful improvements in NTDT-PRO scores to support conclusions about treatment benefit in clinical studies of patients with non-transfusion-dependent beta-thalassaemia: analysis of pooled data from a phase 2, double-blind, placebo-controlled, randomised trial

Ali T Taher ,[1] Khaled M Musallam,[2,3] Vip Viprakasit,[4] Antonis Kattamis,[5] Jennifer Lord-Bessen,[6] Aylin Yucel,[6] Shien Guo,[7] Christopher G Pelligra ,[8] Alan L Shields,[9] Jeevan K Shetty,[10] Mrudula B Glassberg,[11] Luciana Moro Bueno,[10] Maria Domenica Cappellini[12]





MINIMAL IMPORTANT DIFFERENCE of OUTCOMES



ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ANNALS OF ONCOLOGY driving innovation in oncology

SPECIAL ARTICLE

ESMO-Magnitude of Clinical Benefit Scale for haematological malignancies (ESMO-MCBS:H) version 1.0

B. Kiesewetter[1], U. Dafni[2,3], E. G. E. de Vries[4], J. Barriuso[5], G. Curigliano[6,7], V. González-Calle[8], M. Galotti[9], B. Gyawali[10,11,12], B. J. P. Huntly[13], U. Jäger[14], N. J. Latino[3], L. Makovati[15,16], S. F. Oosting[4], G. Ossenkoppele[17], M. Piccart[18], M. Raderer[1], L. Scarfò[19], D. Trapani[6,7], C. C. Zielinski[20], R. Wester[21], P. Zygoura[3], E. Macintyre[22,23] & N. I. Cherny[24]*, on behalf of the ESMO-MCBS Working Group and Extended Working Group†

	GVHD ORR	GRFS	REL	NRM
TRIVIAL	<5%	<5%	<3%	<3%
SMALL	5-10%	5-10%	3-5%	3-5%
MOD	10-20%	10-15%	5-10%	5-10%
LARGE	>20%	>15%	>10%	>10%

Quanto sono sostanziali gli effetti DESIDERABILI attesi?

- Irrilevanti
- Piccoli
- Moderati
- Grandi
- Variano
- Non so

Non solo RACCOMANDAZIONI

Remarks

- Supports interpr etation of evidence or consensus-based recommendation in framing PICO subdomains
- Not actionable in isolation

Implementation considerations

- Describe the how , who, wher e, when and what r elated to implementing a r ecommendation
- Are actionable but not separate from related recommendation
- e.g. drug dosing, description of complex intervention

Recommendation ◀ Subgroup consideration ▶ **Remark**

Institut für Öffentliches Gesundheitswesen | Institute of Public Health
Cochrane Haematology

METHODOLOGIC SUPPORT FOR EHA | ERCI ITP GUIDELINE PROJECT

Cochrane Haematology

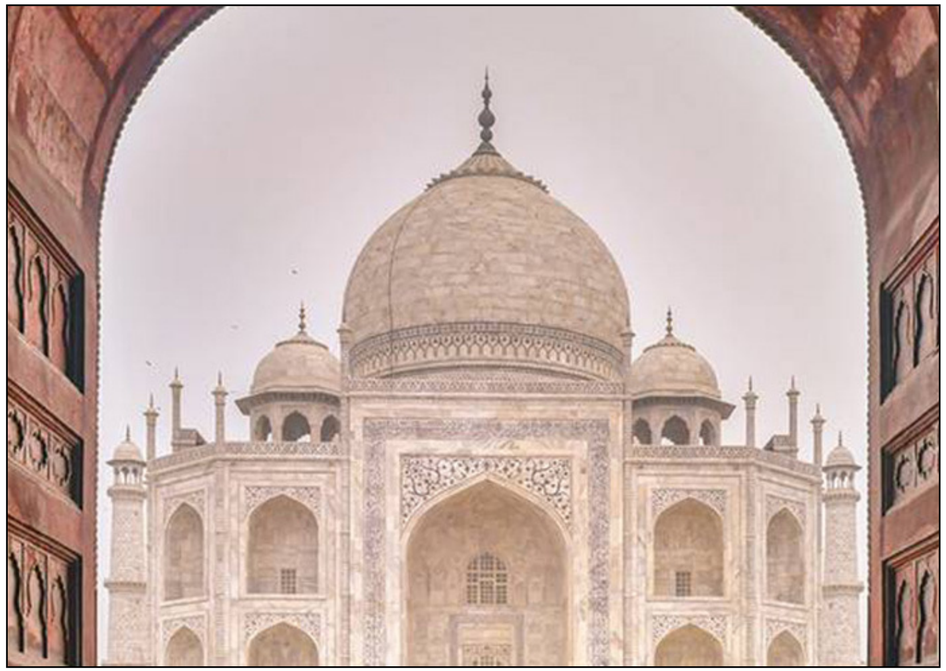
Consensus-based Recommendations and Good Practice Statements

INSTRUCTIONS

What are they, and what are they not?

	Consensus-based / GPS	Evidence-based
Systematic search for aggregate evidence or primary studies	✗	✓
Risk of bias assessment of included studies	✗	✓
Clear attribution of systematically researched and evaluated evidence base to the recommendation (i.e. including reference to certainty assessment and citations)	✗	✓
Assigned a certainty of evidence GRADE-ing (high, moderate, low, very low)	✗	✓
Assigned a recommendation strength (i.e. strong or weak/conditional recommendation for or against)	✗	✓
Consider implications of the recommendation	✓	✓
Structured approach to consensus-finding	✓	✓

Write good practice statement	
Are the population and intervention components clear?	☐ Yes ☐ No
If you answered **NO** → Check whether you are developing an implementation consideration (addresses the *who*, *where*, *when* or *what* related to implementing a recommendation, e.g. drug dosage)	
All the following criteria must be fulfilled to consider the statement a GPS	
(1) Message is truly necessary regarding actual health care practice	This criterion has been addressed: ☐ Yes ☐ No
(2) Implementing the GPS results in a large net positive consequence after consideration of all relevant outcomes and potential downstream consequences	This criterion has been addressed: ☐ Yes ☐ No GRADE summary factors: • Balance of desired & undesired outcomes ☐ • Best estimate of values/preferences and the importance of outcomes (to patients) ☐ • Resource considerations ☐
(3) There is a well-documented clear and explicit rationale connecting the indirect evidence	This criterion has been addressed: ☐ Yes ☐ No
(4) Clear and actionable	This criterion has been addressed: ☐ Yes ☐ No
Final judgement	
Did you answer **YES** to all of the above?	☐ Yes → Development as GPS is appropriate ☐ No → Development as GPS is <u>not</u> appropriate ↓ Revisit the PICO question and the importance of addressing it: ↓ Is the problem a priority? ☐ Yes → Implication for research ☐ No → No recommendation



1 EVIDENCE-BASED REC.

Inclusi statement per i SOTTOGRUPPI

BACKGROUND st.

Statement descrittivi (not actionable) o parte della pratica clinica universale

2

RESEARCH st.

Laddove l'evidenza è giudicata insufficiente per sostenere una GP (per incertezza o margine di beneficio netto) ma il quesito è meritevole

4

GOOD PRACTICE r.

Quando evidenza è prevalentemente indiretta, parzialmente non consensusale

3

REMARK

Suggerisce azioni pratiche di implementazione di una EBR o GPR (es. schedula terapia farmacologica)

5

Indicazioni di Buona Pratica Clinica

Sempre Systemstic Review

Tabella 5. Revisione sistematica dell'età massima nei pazienti sottoposti a CAR-T

Studio (primo autore, paese)	N	Età superiore	Referenza
Jacobson, US	1297	91	*Transplantation and Cellular Therapy* 2022 28:9 (581.e1-581.e8)
Bastos-Oreiro, Spagna	226	77	Front Immunol 2022 Jul 12; 13:855730
Kuhnl, UK	300	78	*Br J Haematol*. 2022; 198:492–502.
Batchy, Francia	729	81	Nature Medicine | VOL 28 | October 2022 | 2145–2154
Spaniaart, Olanda	129	79	HemaSphere 2022 6 Supplement 3 (2564-2565

QUESITO 1.2.C

Nei pazienti con linfomi B aggressivi potenzialmente candidati a CAR-T e una documentata sindrome mielodisplastica è raccomandata la terapia con CAR-T rispetto alla terapia standard al fine di ottimizzare il rapporto tra esiti non desiderati (CRS, neurotssicità) ed esiti desiderati (sopravvivenza, PFS, qualità di vita)?

INDICAZIONE 1.2.C

In caso di documentata sindrome mielodisplastica la terapia con CAR-T va valutata caso per caso, in base al rischio di tossicità e di evolutività, in quanto la patologia mieloide non viene eradicata dai linfociti CAR.

Remark

Tutti i pazienti con citopenie non spiegate prima della linfocitoaferesi necessitano di uno studio midollare (aspirato e biopsia): nel caso in cui venga riscontrata morfologicamente displasia, vanno avviati ad uno studio cariotipico e molecolare con pannello NGS mieloide.

4- Easy to use?

FULL PAPERS?

ITALIAN LANGUAGE?

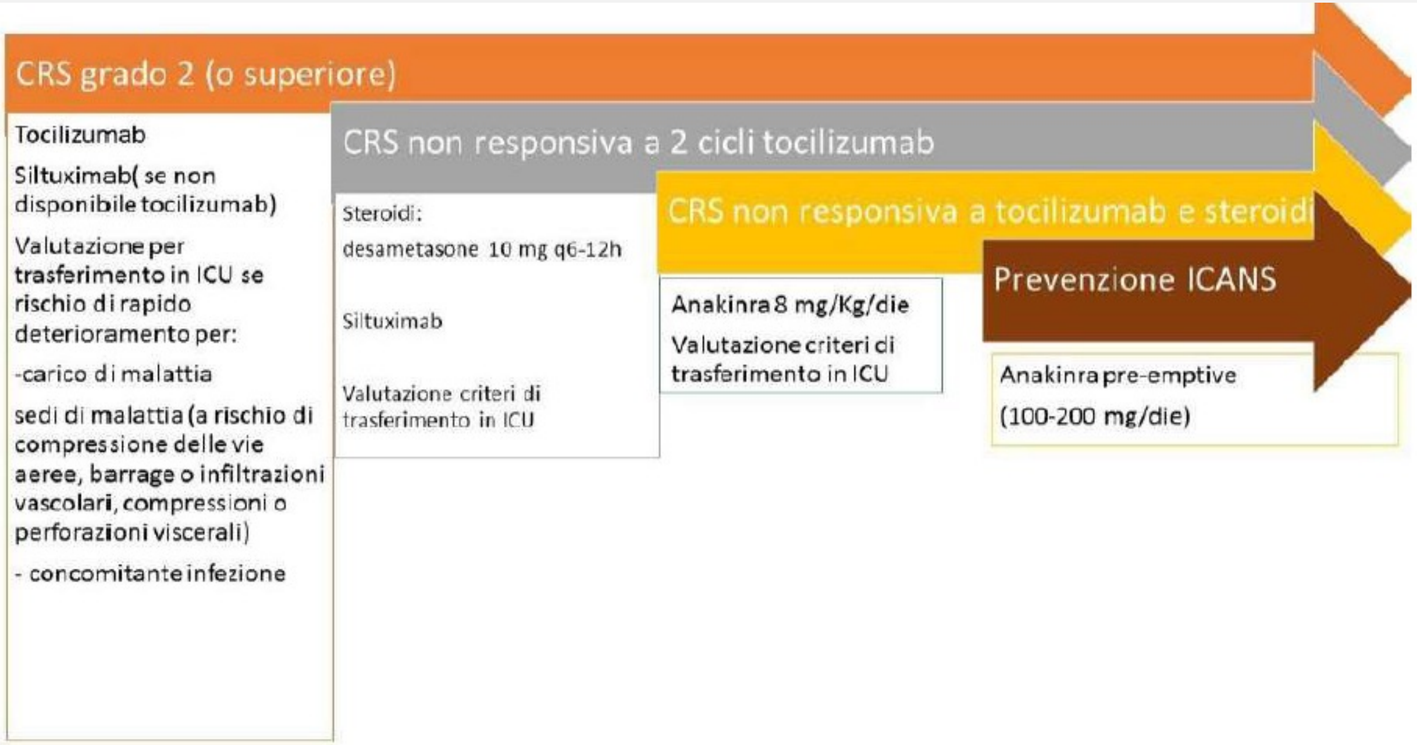
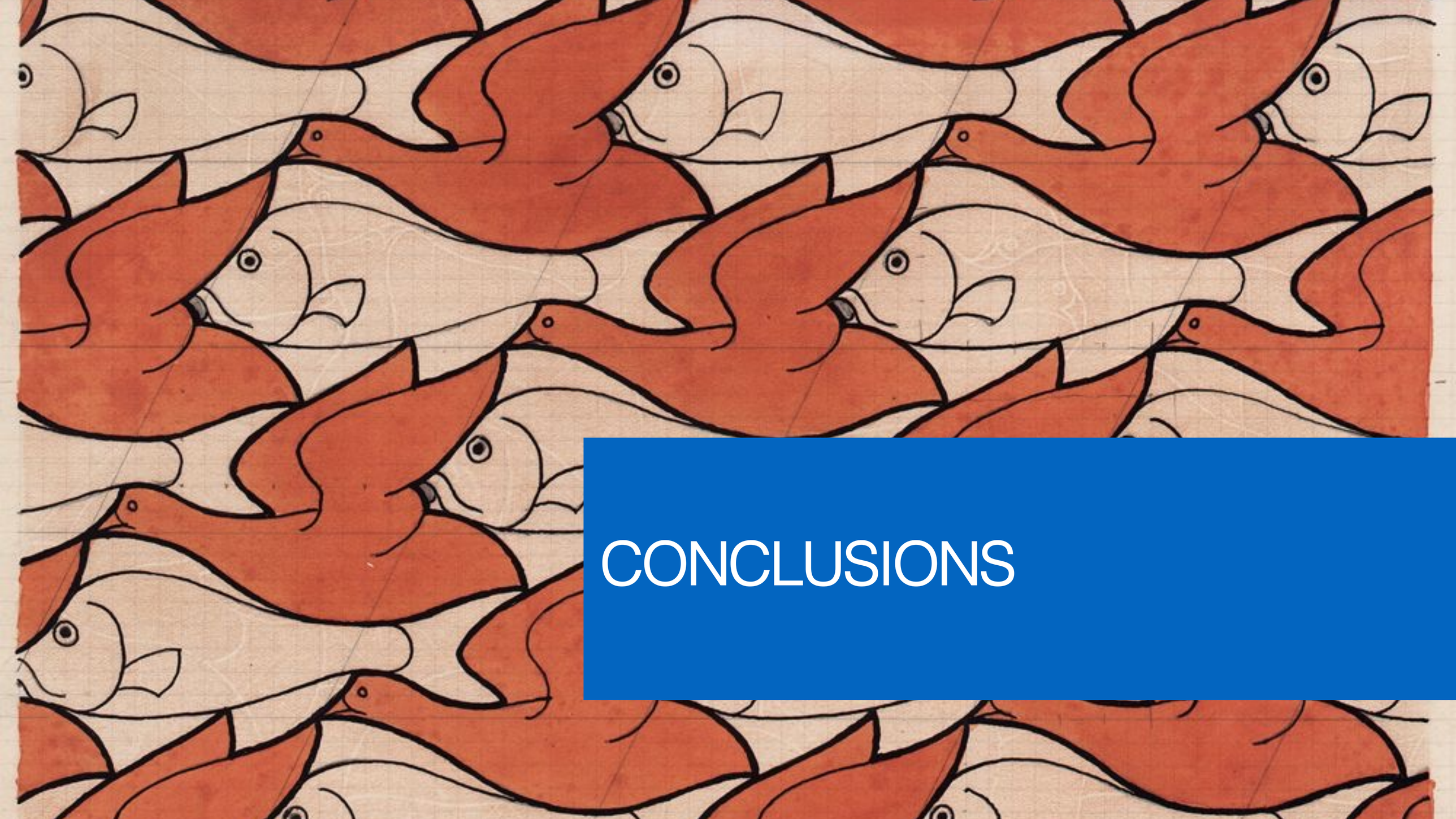


Figura 4. Gestione della CRS



CONCLUSIONS

1

Narrative Reviews

2

Systematic reviews

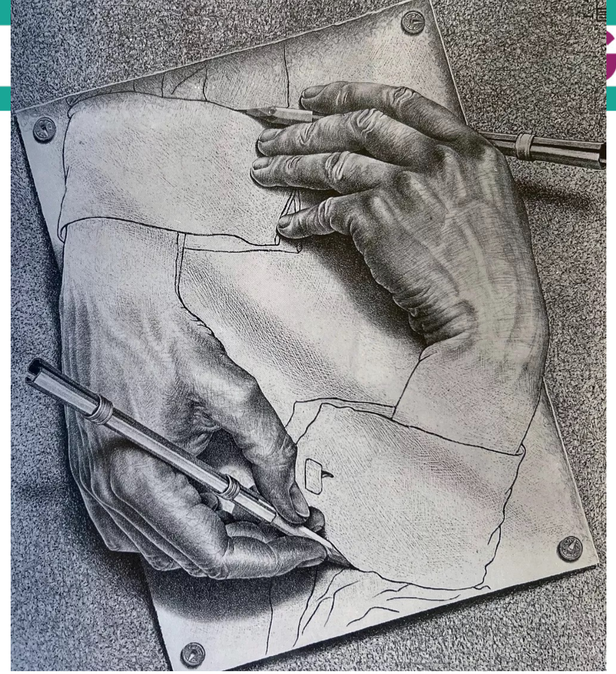
Position papers

3

Consensus Recommendations

4

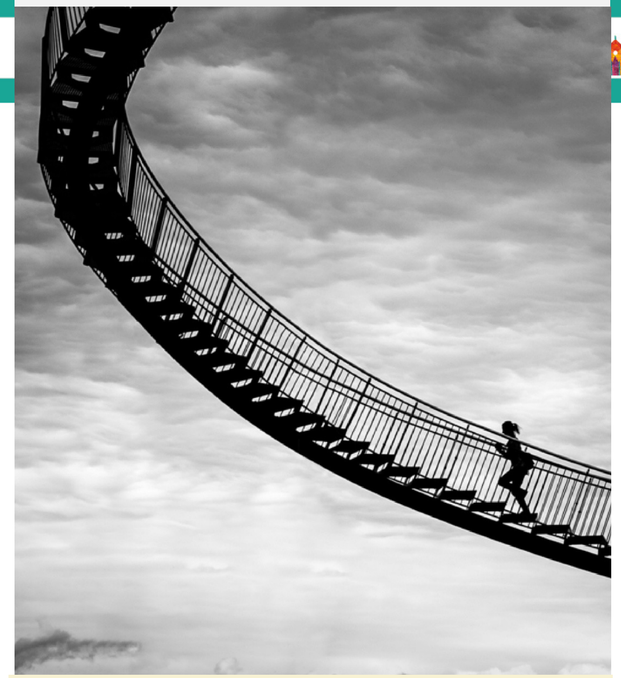
GUIDELINES EVOLUTION



Vanno umilmente distinti gli STATEMENT in base alla QUALITA' del CORPO di EVIDENZA

Strong vs conditioned

Ev-based recc vs good practice recc



L'EBM dovrebbe entrare nel programma delle Scuole di Medicina e delle Scuole di Specializzazione

La ricerca SISTEMATICA dell'evidenza è necessaria pur con shortcuts (rapid SR):

SR già disponibili vs no evidence available

Inconsistent pieces of ev

Gli outcome (e i comparator) vanno ESPLICITATI

La maggior parte dell'eminence-based medicine non esplicita, analizza solo una parte dell'evidenza e giudica su outcome surrogati

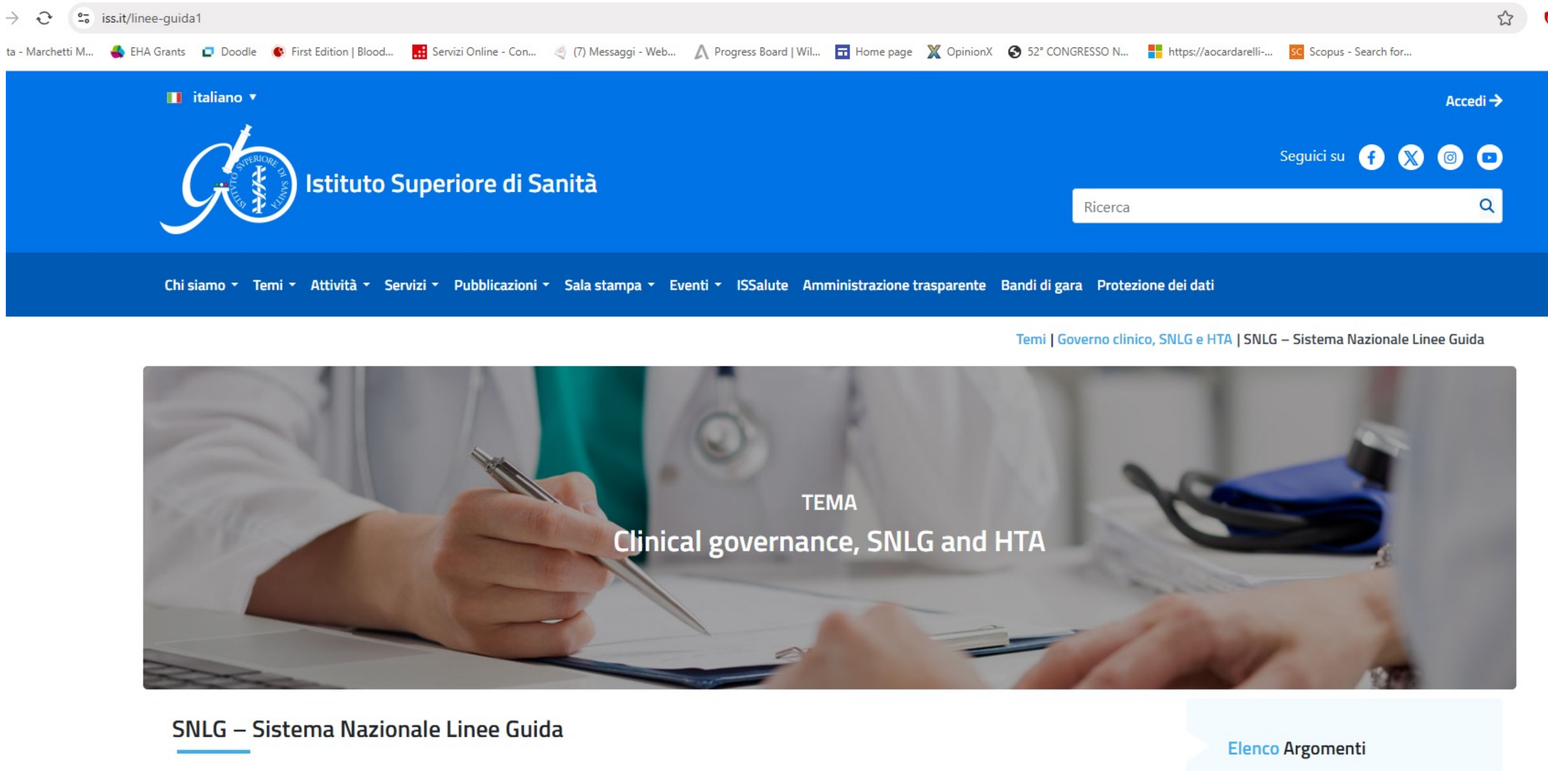
La DIGNITA' e il VALORE di una linea-guida dipende dalla robustezza del metodo con cui è stata sviluppata

LEA , SOP e PDTA dovrebbero essere basati su

Call for FISiM project

MINIMALLY CLINICALLY RELEVANT DIFFERENCE of MDS OUTCOMES

CALL for YOUNG HEMATOLOGISTS collaboration to National & European CPGs



GRAZIE

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