SISTEMA SANITARIO NAZIONALE
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CURE PALLIATIVE PRECOCI NELLE SINDROMI MIELODISPLASTICHE

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AIL
AIOM
SICP Società Italiana di Cure Palliative
SIE Società Italiana di Ematologia

LE CURE PALLIATIVE PRECOCI IN EMATO-ONCOLOGIA:

la nuova risposta ai bisogni di pazienti e caregivers

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MDS: A NEW SCENARIO….

Myelodysplastic syndromes (MDS; renamed recently by the World Health Organization [WHO] "MYELODYSPLASTIC NEOPLASMS") include a biologically and clinically diverse group of hematopoietic malignancies (HM) that affect mainly older adults.

Patients are generally grouped into 2 main risk categories (lower- and higher-risk) by risk stratification tools (IPSS, IPSS-R , and most recently, IPSS-M).

Wide heterogeneity in clinical outcomes: a personalized, patient-centered approach to treatment.

Amer M. Zeidan et al. Blood 2023

Myelodysplastic syndromes, thy name is heterogeneity

- **Classification of the heterogeneous spectrum MDS requires both morphologic and molecular analysis to effectively subgroup patients.**

- **Positive impact of combining the International Consensus Consortium (ICC) morphologic approach with prior clinical (IPSS-R) and mutational (IPSS-M) categorization to provide useful clinical evaluation of MDS patients.**

Greenberg PL. Br J Haematol. 2023 May;201(3):381-382.

Distinguishing AML from MDS: a fixed blast percentage may no longer be optimal

Diagnosing AML = Blast count + genetic/cytogenetic abnormalities

1976 — FAB System

>30% blasts to diagnose AML

1999 — WHO 1999

>20% blasts to diagnose AML

- Patients with 20-30% blasts had similar outcomes as patients with >30% blasts
- AML diagnosis regardless of blast % in patients with certain cytogenetic abnormalities

2008 — WHO 2008

>20% blasts to diagnose AML; inclusion of additional recurrent genetic abnormalities

2016 — WHO 2016

>20% blasts to diagnose AML; in patient with <20% blasts, diagnosis of AML with specific recurrent cytogenetic abnormalities

2022 — WHO 2022

- Eliminated blast cutoffs for most AML types with defining genetic alterations but retained a 20% blast cutoff to delineate MDS from AML

2022 — ICC 2022

- ≥10% blasts to diagnose AML in patients with certain defining genetic abnormalities
- Introduced a new category of MDS/AML in association with defined genomic abnormalities to include cases with 10-19% blasts

AML=Acute Myeloid Leukemia. MDS=Myelodysplastic Syndrome.

1.Arber DA, et Al. Blood. 2022 Sep 15;140(11):1200-1228. doi: 10.1182/blood.2022015850. 2.Khoury JD. et Al. Leukemia. 2022 Jul;36(7):1703-1719. doi: 10.1038/s41375-022-01613-1.3.Döhner H. et Al. Blood. 2022 Sep 22;140(12):1345-1377. doi: 10.1182/blood.2022016867.

IPSS-R Risk Group	Points	% of Patients	Median survival, years	Time to 25% with AML, years
Very low	≤1.5	19%	8.8	Not reached
Low	>1.5 - 3	38%	5.3	10.8
Intermediate	>3 - 4.5	20%	3	3.2
High	>4.5 - 6	13%	1.6	1.4
Very High	>6	10%	0.8	0.73

Greenberg PL, Blood. 2012

Treatment of higher risk MDS

Objectives:

- **Survival prolonging.**
- **AML progression delay.**
- **Cure (HSCT only).**

Hypomethylating Agents

Inhibitors of DNA methyl transferases:

Azacitidine. **Decitabine.**

ICT, selected patients.

Allogenic SCT, selected patients.

Time to referral to EPC: at the diagnosis!

As for patients with AML.

Treatment of lower- risk MDS

Objectives:

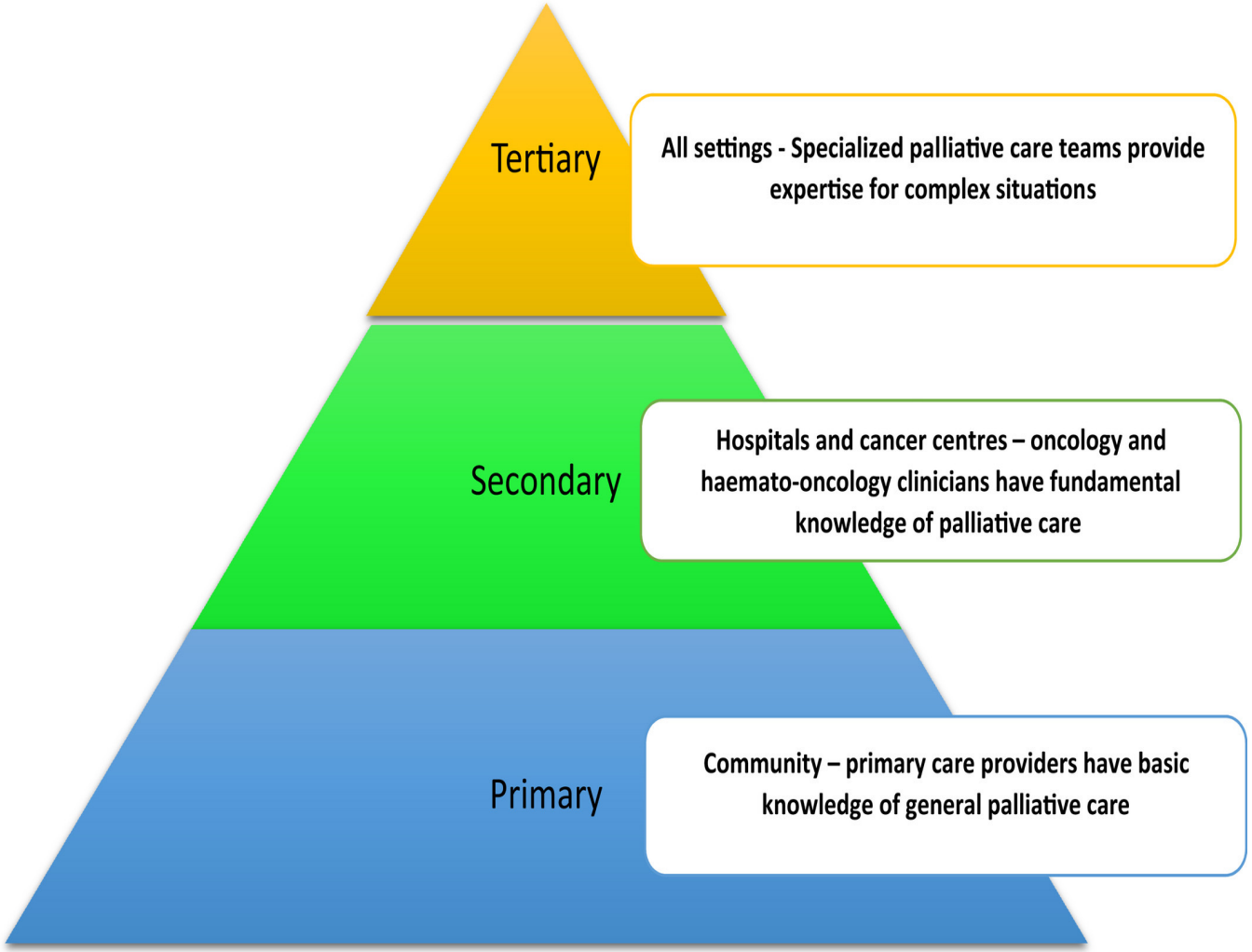
- Quality of life
- Cytopenias control.
- Survival prolonging (progression). Cure (HSCT only).

- Clinical observation.
- Comorbidities management.
- RBC transfusions.
- Growth factors (ESAs).
- Thrombomimetics (eltrombopag).
- TGF-beta inhibitors.
- Hypomethylants .

???Time to PC referral: symptomatic cytopenias?

Disease progression (i.e. Epo-failure)?

Early integration of PC for patients with HM: a conceptual model of PC delivery based on setting and provider.



Br J Haematol, Volume: 199, Issue: 1, Pages: 14-30, First published: 07 June 2022, DOI: (10.1111/bjh.18286)

ANEMIA AND RED BLOOD CELL TRANSFUSION

Anemia is often present in mostly elderly MDS patients. Although RBC transfusions are the most immediate treatment, waiting for the response to disease-specific therapy, or in case of non-response, the choice of the optimal transfusion regimen (threshold: liberal vs restrictive?). is still controversial (Finelli C. et al, 2022).

A patient-oriented RBC transfusion therapy in MDS patients must take into account several factors (Hb, clinical, age, comorbidities, psychological, family and social factors, HRQoL). Many questions remain to be clarified (Finelli C et al 2022).

Transfusion dependency is an indicator of inferior PFS. The negative effect already occurs at transfusion densities below 3 units/16 weeks (de Swart et al. 2019).

Transfusions at home in MDS patients

- **HC program, throughout a 5-years period (2006-2010).**
- **Reliability and the safety of transfusions at home in 211 MDS patients.**
- **Specifically dedicated HC service.**
- **Transfusions at home may represent a valuable option to maintain a good quality of life and avoid the possible discomfort due to hospital admissions and outpatient visits (author's considerations).**

Transfusions are not a therapy, being a supportive measure like others, however revealing the need for treatment in the MDS course.

Transfusions in PC setting for advanced MDS patients?

Niscola et al. 2012

Hemorrhagic complications in patients with advanced HM in HC: an Italian experience

- Out of 469 HM patients 123 (26%) experienced major bleeding.
- Prophylactic tranexamic acid prednisone low doses (unproven efficacy, empirical choice).
- Hemorrhagic episodes was 232 (49%); 2 episodes per patient.

- Local hemostatic measures.
- Platelet units were transfused at home in 188 (81%) cases; RBC as required.

- Resolution of bleeding at home: 206 (88%) of the 232 episodes.
- Bleeding was the cause of hospitalisation in four cases.
- Out of 447 deceased patients, 26 (6%) died because of bleeding.

- Home bleeding management proved to be a safe and effective choice.

Cartoni et al. 2009

Management of infective complications in patients with advanced HM in HC.

151 patients in HC, 70 (46%) developed a total of 109 febrile episodes.

FUO in 51% of cases; microbiologically (26%) and clinically documented (23%) infections were recorded.

Oral ciprofloxacin in patients not neutropenic; IV ceftriaxone plus amikacin in neutropenic patients for empiric home antibacterial treatment.

65% of febrile episodes responded to the initial antibacterial therapy with a further 16% after modification; overall, 19.3% of the infective episodes were fatal.

The prognosis appearing to be similar to that usually observed in the same category of patients in an inpatient setting.

HC could be the option of choice for advanced HM patients with infective complications.

Girmenia et al, 1997

How to enter palliative care?
The barriers of the Healthcare System

- **Uncertainties in the prognosis.**
- **Vision of palliative care as reserved for the end of life and excluding therapies to prolong survival.**
- **Lack of time to discuss all topics..**
- **Fear of taking away hope from the patient.**
- **Lack of feedback and documentation (i.e. advance treatment directives).**
- **Lack of in-depth knowledge of the patient and family (i.e. potential problems in the transition phase)**
- **Difficulty of the patient and/or family to understand and accept the information received (potential conflicts, recriminations as well as problems in the necessary caring alliance).**

Tavares et al. ERJ, 2017

Palliative care for patients with hematologic malignancies : are we meeting patients' needs early enough?

- **Patients with HM have a high need for palliation, with patients reporting high physical and psychological symptom burden associated with their disease.**

- **PC is a specialty focused on improving QoL of patients with serious illnesses.**

- **Two trials (AML, HSCT) specifically demonstrated benefits of integrated PC (alongside curative-intent) early in the disease course.**

- **Despite the evidence for benefit, HM patients are more likely than those with cancer to access PC and hospice services late in their disease course, resulting in many adverse outcomes including aggressive care at the ELC.**

- **The PC needs of HM patients are unique and vary by disease type (targeted PC interventions based on HM type) as a path forward, but more research is needed.**

Kayastha N et al. 2022

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