7.12.5. Myelodysplasie

1. Classificatie

1.1. FAB-classificatie (1982)

TABLE 1. FAB CLASSIFICATION OF MYELODYSPLASTIC SYNDROMES.*

Refractory anemia

Cytopenia of at least one lineage in the peripheral blood (usually anemia)
Normal or hypercellular bone marrow with dysplastic changes
Less than 1 percent blasts in the peripheral blood and less than 5 percent blasts in the bone marrow

Refractory anemia with ringed sideroblasts

Cytopenia (almost always anemia), dysplastic changes, and the same percentages of blood and bone marrow blasts as in refractory anemia
Ringed sideroblasts accounting for more than 15 percent of all nucleated cells in the bone marrow

Refractory anemia with excess blasts

Cytopenia of two or more lineages in the peripheral blood
Dysplastic changes in all three lineages
Less than 5 percent blasts in the peripheral blood and between 5 and 20 percent blasts in the bone marrow

Chronic myelomonocytic leukemia

Peripheral-blood monocytosis (monocyte count, $>1\times10^9$ per liter)
Less than 5 percent blasts in the peripheral blood and up to 20 percent blasts in the bone marrow

Refractory anemia with excess blasts in transformation

Hematologic features similar to those of refractory anemia with excess blasts
More than 5 percent blasts in the peripheral blood or between 21 and 30 percent blasts in the bone marrow or the presence of Auer rods in the blasts

*The descriptions of the syndromes are from Bennett et al.[30] FAB denotes French–American–British.

1.2. WHO-classificatie (1999)

WHO Classification and Criteria for the Myelodysplastic Syndromes.*

Disease	Blood Findings	Bone Marrow Findings
Refractory anemia	Anemia, no or rare blasts	Erythroid dysplasia alone, <5% blasts, <15% ringed sideroblasts
Refractory anemia with ringed sideroblasts	Anemia, no blasts	Erythroid dysplasia alone, <5% blasts, ≥15% ringed sideroblasts
Refractory cytopenia with multilineage dysplasia	Cytopenias (bicytopenia or pancytopenia), no or rare blasts, no Auer rods, <1 billion monocytes per liter	Dysplasia in ≥10% of cells in ≥2 myeloid cell lines, <5% blasts, no Auer rods, <15% ringed sideroblasts
Refractory cytopenia with multilineage dysplasia and ringed sideroblasts	Cytopenias (bicytopenia or pancytopenia), no or rare blasts, no Auer rods, <1 billion monocytes per liter	Dysplasia in ≥10% of cells in ≥2 myeloid cell lines, <5% blasts, no Auer rods, ≥15% ringed sideroblasts
Refractory anemia with excess blasts, type 1	Cytopenias, <5% blasts, no Auer rods, <1 billion monocytes per liter	Unilineage or multilineage dysplasia, 5–9% blasts, no Auer rods
Refractory anemia with excess blasts, type 2	Cytopenias, 5–19% blasts, occasional Auer rods, <1 billion monocytes per liter	Unilineage or multilineage dysplasia, 10–19% blasts, occasional Auer rods
Myelodysplastic syndrome, unclassified	Cytopenias, no or rare blasts, no Auer rods	Unilineage dysplasia in granulocytes or megakaryocytes, <5% blasts, no Auer rods
Myelodysplastic syndrome associated with isolated del(5q)	Anemia, <5% blasts, platelet count normal to increased	Normal-to-increased megakaryocytes with hypolobated nuclei, <5% blasts, no Auer rods, isolated del(5q)

* Information is from Vardiman et al.[2]

1.3. International Prognostic Scoring System (IPSS) for MDS (1997)

	Score				
score	0	0.5	1.0	1.5	2.0
BM blastose (%)	<5	5-10	----	11-20	21-30
karyotype*	Goed	intermediair	slecht		
cytopenies	0/1	2/3			

* goed = normaal, -Y, del(5q), del(20q);
slecht = complex (≥ 3 afwijkingen) of chromosoom 7 afwijkingen
intermediair = andere afwijkingen

Risico groep:	Score	Mediane overleving < 60 jaar	Mediane overleving > 60 jaar
Laag	0	11.8 jaar	4.8 jaar
Laag-intermediair	0.5-1.0	5.2 jaar	2.7 jaar
Hoog-intermediair	1.5-2.0	1.8 jaar	1.1 jaar
Hoog	2.5	0.3 jaar	0.5 jaar

2. Onderzoekingen

- anamnese
- klinisch onderzoek
- complet - formule - reticulocyten
- routinebiochemie (stolling, ionogram, nier-en leverfunctie)
- Fe, TIBC, Ferritine, Vit B12, Foliumzuur serum en RBC
- EPO dosage op indicatie (wordt doorgestuurd naar Luik)
- opsporen PNH clonus
- kwantificeren van CD4+, CD8+ cellen, CD40+ (indicatie)
- dosage immuunglobulines
- beenmergonderzoek:
    - morfologie
    - immunofenotypering
    - karyotypering
    - op indicatie:
        - X-chromosoom-inactivatie (Labo Exp. Hemato.)
        - moleculair onderzoek
- botbiopsie
- RX thorax F/P
- echo abdomen
- donorsearch op indicatie

3. Therapie

3.1. Supportief (alle categorieën)

Transfusie van packed cells

- steeds gedeleucocyteerd
- streefwaarde Hb: 8 g/dl doch in functie van cardiopulm. status
- maandelijks controle van ijzerstatus (Fe, Transferr. Sat., Ferr.)
- ijzerchelatie:Exjade (deferasirox): 10-30 mg/kg/d voor transfusie-dependente patiënten (IPSS ≤ 1.5 en onvoldoende daling ferritine na proeftherapie van 6 maanden Deferoxamine

Transfusie van bloedplaatjes

- profylactische plaatjestransfusies zo BP < 10 – 15 x 109/l

Preventie en behandeling van infecties

- selectieve darmdecontaminatie zo ANC chronisch < 0.5 x 109/l
- bij voorkeur Tavanic: 250 mg/d en Diflucan: 2 x 200 mg/d
- vaccinaties tegen pneumokokken, hemophilus.
- bij neutropene koorts: direct breedspectrum antibiotica starten

Vitamine-supplementen

- Folavit: 4mg/d

3.2. Specifieke therapie

3.2.1. Laag en laag-intermediair risico MDS

- Groeifactoren: EPO + G-CSF
    - indien endogene EPO spiegel < 500 U/l en ≤ 2 transfusies/m
    - via compassionate use programma Amgen (Aranesp -/+Neupogen)
- Immunosuppressieve therapie:
    - cyclosporine A: 5 mg/kg/d po in 2 giften
    - ATG + cyclosporine A: zie hoofdstuk aplastische anemie
- Immunomodulerende therapie:
    - Thalidomide: 50-200 mg/d
    - Lenalidomide (Revlimid): 5-10 mg/d 3w/m (nog niet terugbetaald)
- laaggedoseerde chemotherapie (zie infra)
- Histone deacetylase inhibitie: valproaat tot therapeutische plasmaspiegel
- toekomst: DNA hypomethylatoren (BHS studie decitabine bij laag-/laag-intermediair risico MDS)
- allogene transplantatie: op indicatie (bv jonge patient met hoge transfusienood/multilijnen cytopenie)

3.2.2. Hoog-intermediair en hoog-risico MDS

- AML type chemotherapie (Dauno-AraC inductie en AraC consolidatie)
- Allogene stamceltransplantatie (op indicatie)
- Studieprotocol: Serono, Chroma
- Indien geen kandidaat voor intensieve chemotherapie/studie:
    - Decitabine/Azacytidine: voorlopig via Bijzonder Solidariteitsfonds
    - Lage-dosis chemotherapie: bv.
        - Lage-dosis AraC: 20 mg/m2/d d1-14/maand
        - Purinethol: 50-100 mg/d
        - Vepesid: 100 mg/d bv 5d/w/maand
        - Hydrea: 1-6 x 500 mg/d
        - Lanvis: 1-3 x 40 mg/d
        - Alkeran: 2 mg/d
        - Zavedos (idarubicine): 15 mg/m2/d ged 3d