What are Myelodysplastic Syndromes and what are current treatment options?

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Content

• What is MDS?
• What are the goals for treatment?
• How do we treat MDS in the UK in 2019?
What is MDS? (Myelodysplastic syndromes)

Summary introduction

• It *is* a blood cancer
  • Biologically correct
  • But often behaves very differently from other cancers
• It is *not* leukaemia

• Affects an older age group
  • average age is 74yrs
Normal bone marrow cells → Healthy blood production

MDS cell (Internal damage) → More cells die

External damaging proteins

Low blood counts =
Low-risk MDS
Healthy blood production

MDS cell (Internal damage) → Blast cells increase

Healthy bone marrow cells

Some normal cells die naturally

Cells don’t die naturally: “blasts”

Higher-risk MDS
Bone marrow in MDS: too many cells

Healthy bone marrow

MDS
Bone marrow in MDS: abnormal cells
Diagnosis of MDS

- Abnormal bone marrow cells – dysplasia
- Sometimes increased (‘excess of’) leukaemia-like ‘blasts’
- Chromosome / gene changes
- Genetic mutations
MDS is not one, but many diseases

Classifying MDS

– Examining bone marrow under microscope

– Also use genetic information

= WHO classification system
(latest is 2016/17)
## WHO classification 2016/17

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<th>WHO 2017</th>
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<td>MDS with single lineage dysplasia (MDS-SLD)</td>
<td>Refractory Cytopenia with Unilineage Dysplasia</td>
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<td>MDS-SLD with ring sideroblasts</td>
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<td>MDS, unclassifiable (MDS-U)</td>
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Who gets MDS?

• Average age = 74 years

• Males more than females
What causes MDS?

- Largely unknown
  - Rare complication of previous chemotherapy / radiotherapy

- Not normally an inherited condition
  - Small numbers of families have relatives with MDS/AML
Clinical features of MDS
what patients feel

• Fatigue & breathless on exertion – anaemia
  • Most common symptoms

• Infection
  • Various

• Bleeding
  • Uncommon but increases as disease progresses
What matters to MDS patients?

• Quality of life
  • Manage my fatigue (and other complications)

• Quantity of life
  • Manage my shortened life expectancy
    • Modify the natural history of MDS where possible
How long is life expectancy with MDS?

Estimating prognosis

• Scoring systems like IPSS-R
  • ‘Low-risk’ MDS
  • ‘High-risk’ MDS

• *Experience* - to bring the ‘score’ into context
How do we assess patients’ prognosis?

Revised International Prognostic Scoring System (IPSS-R)

- Values of blood cells
  - haemoglobin,
  - neutrophils,
  - platelets
- Percentage of blast cells in bone marrow
- Nature of chromosome change in bone marrow
Approach to treatment discussions

Question 1

• Is there a realistic prospect of cure, with an acceptable level of risk?
  • Unfortunately this is relatively infrequent.
Approach to treatment discussions

Question 2

• Are there symptoms?
  • If so, treat these e.g. fatigue, breathlessness due to anaemia, to improve **quality of life**
    – This is the goal for the majority of patients
Approach to treatment discussions

Question 3

• Can we expect to prolong life expectancy with an acceptable improvement in quality life?
  • For example, without most of the time gained spent in hospital.
Approach to treatment discussions

Question 4

• What are the goals of the patient
  • patient preferences
  • Attitude to risk?
How do we decide how MDS should be treated?

Evidence
- From clinical trials

Expert opinion
- From experience
- From registries

Expert consensus guideline
- European
- British
Guidelines – friend or foe?
Guidelines – friend or foe?

Lower-risk MDS recommendations for “standard” allogeneic SCT

(Very) Low Risk
Intermediate Risk
IPSS-R

Poor performance
Nonfit®

Nontransplant strategies*

Good performance
Fit®

No poor risk features**

Nontransplant strategies*

Failure &

Transplant strategies#

Available donor^

Poor risk features**

Transplant strategies#
‘Low-risk’ MDS: 75% MDS patients

Low IPSS risk

- Asymptomatic cytopenia
  - Watchful waiting
  - sEpo <500 mU/mL and/or RBC units <2/month
    - rHuEpo +/- G-CSF
    - Lenalidomide (within prospective registry)

- Symptomatic anemia
  - MDS del(5q)
  - RBC transfusion and iron chelation therapy
  - Age <60 years, BM blasts <5%, normal cytogenetics, transfusion-dependency (hypocellular bone marrow)
    - rHuEpo +/- G-CSF
    - Immunosuppressive therapy with ATG plus CSA

Figure 1. Therapeutic algorithm for adult patients with primary MDS and low IPSS score. BM, bone marrow; sEpo, serum erythropoietin.
How do we treat MDS in the UK now?

- Most patients receive **supportive care**
  - Blood and/or platelet transfusions
  - Antibiotics for infections

- This is a reasonable approach for most, because there are few treatments that work reliably without severe side effects
How do we treat low-risk MDS in the UK now?

• There are drugs approved in the NHS for the active treatment of MDS patients
  • Eprex (EPO)
  • Iron removal – desferrioxamine, Exjade
  • Lenalidomide
Iron removal (chelation)

• Still not clear who should be treated with iron chelation
  – Certainly not everybody on blood transfusions
  – Only when we think that iron chelation will help to improve length of survival

• Currently we remove iron by infusions of Desferal under the skin

• Exjade
  – is a tablet
  – Seems as effective as Desferal
  – Shorter time in use so long term effects not known
How do we treat MDS in the UK now?

Actively treating low blood counts

- EPO (Erythropoietin)
  - Once weekly injections
  - Most effective in patients with few blood transfusions or before the need for blood transfusions
Lenalidomide for MDS with del(5q)
(rare form; 5% MDS patients)

• ~2/3 patients respond well and become free of blood transfusions
• Responses last for at least on average 2 years
High-risk MDS

**Intermediate-2 or high IPSS risk**

- **Age ≥65-70 years or poor performance status**
  - Supportive care
  - Azacitidine

- **Age <65-70 years and good performance status**
  - No suitable stem cell donor
    - Poor risk cytogenetics
    - ≥10% BM blasts, no poor risk cytogenetics
      - Azacitidine
      - AML-like CT OR Azacitidine
    - <10% BM blasts
      - Allogeneic SCT
    - ≥10% BM blasts
      - AML-like CT OR Azacitidine (within clinical trial or prospective registry)
  - Available stem cell donor
    - Allogeneic SCT

*Figure 3. Therapeutic algorithm for adult patients with primary MDS and intermediate-2 or high IPSS score. CT, chemotherapy.*
Azacitidine (Vidaza)

- Azacitidine kills cells as they divide
- Given under the skin daily for 7 days
- Large volume injection
Azacitidine

- 45% patients in the original study who were receiving red cell transfusions stopped needing these.
- Vidaza improved the short term quality of life
- Responses last for about one year
Aiming for cure

Stem cell transplant

– Considered for younger patients (<60-65 years) with all but the lowest risk MDS type
– Mostly uses blood cells now, not bone marrow
  – Preferably from matched brother / sister (only 1 in 3 chance of match)
– Results improving for transplants

Newly published guidelines for stem cell transplant in MDS: 2017
New service for patients: online video consultations with an MDS specialist

Research FOR Patients - For an informed and empowered opinion - Have you made your clinical paper accessible yet? Professor David Bowen and Leeds Teaching Hospitals are pleased to announce the start of a new service for patients who would like a specialist MDS consultation but who are unable to, or prefer not to travel to Leeds for [...]