The Leeds Teaching Hospitals NHS
NHS Trust

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?

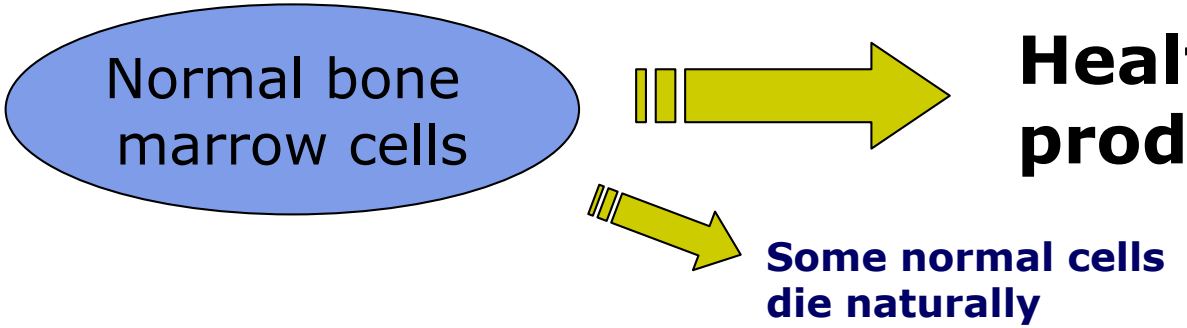
What is MDS?
(Myelodysplastic syndromes)

Summary introduction

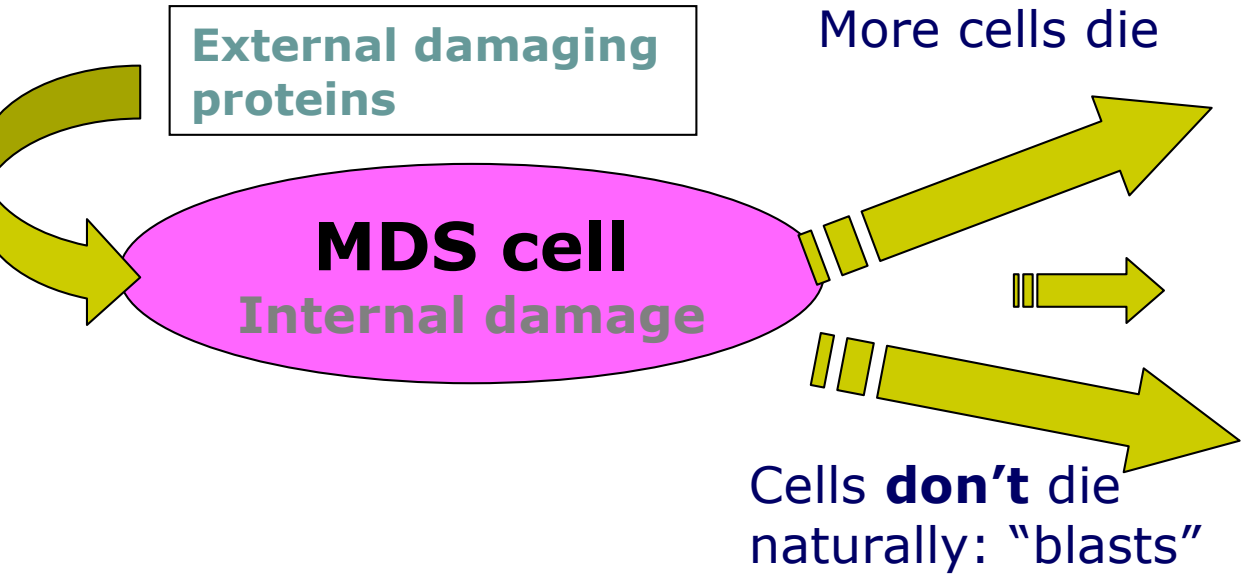
- It *is* a blood cancer
  - Biologically correct
  - But often behaves very differently from other cancers
- It is *not* leukaemia

- Affects an older age group
  - average age is 74yrs

NORMAL

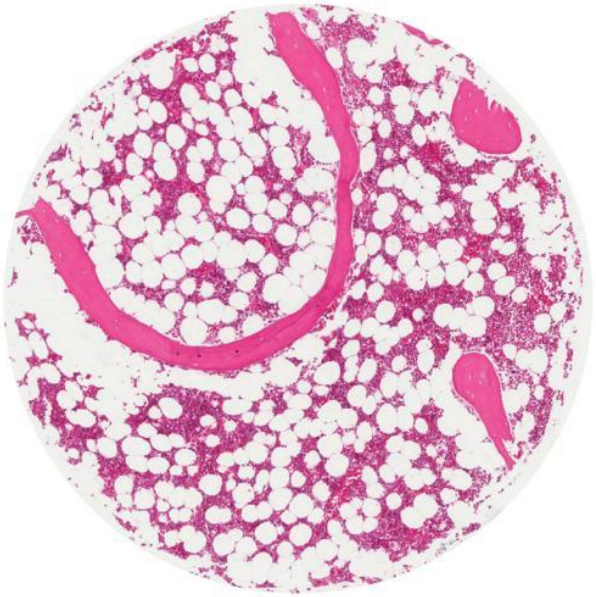

Normal bone marrow cells
Healthy blood production
Some normal cells die naturally

MDS

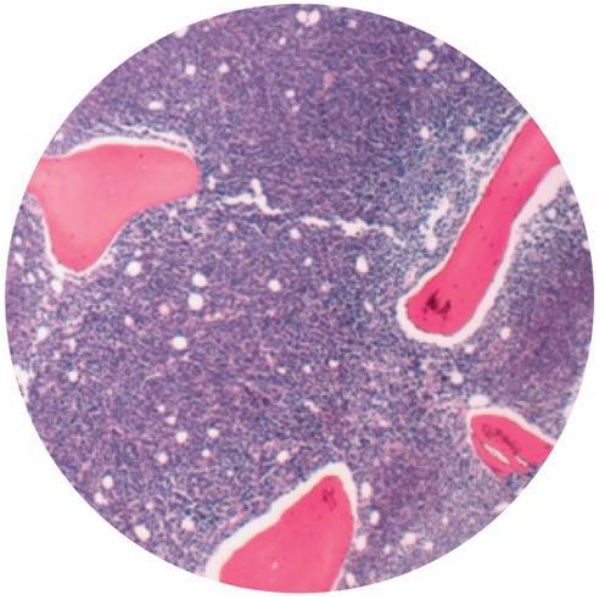

External damaging proteins
MDS cell
Internal damage
More cells die
Low blood counts = Low-risk MDS
Healthy blood production
Blast cells increase = High-risk MDS
Cells don't die naturally: "blasts"

Bone marrow in MDS: too many cells

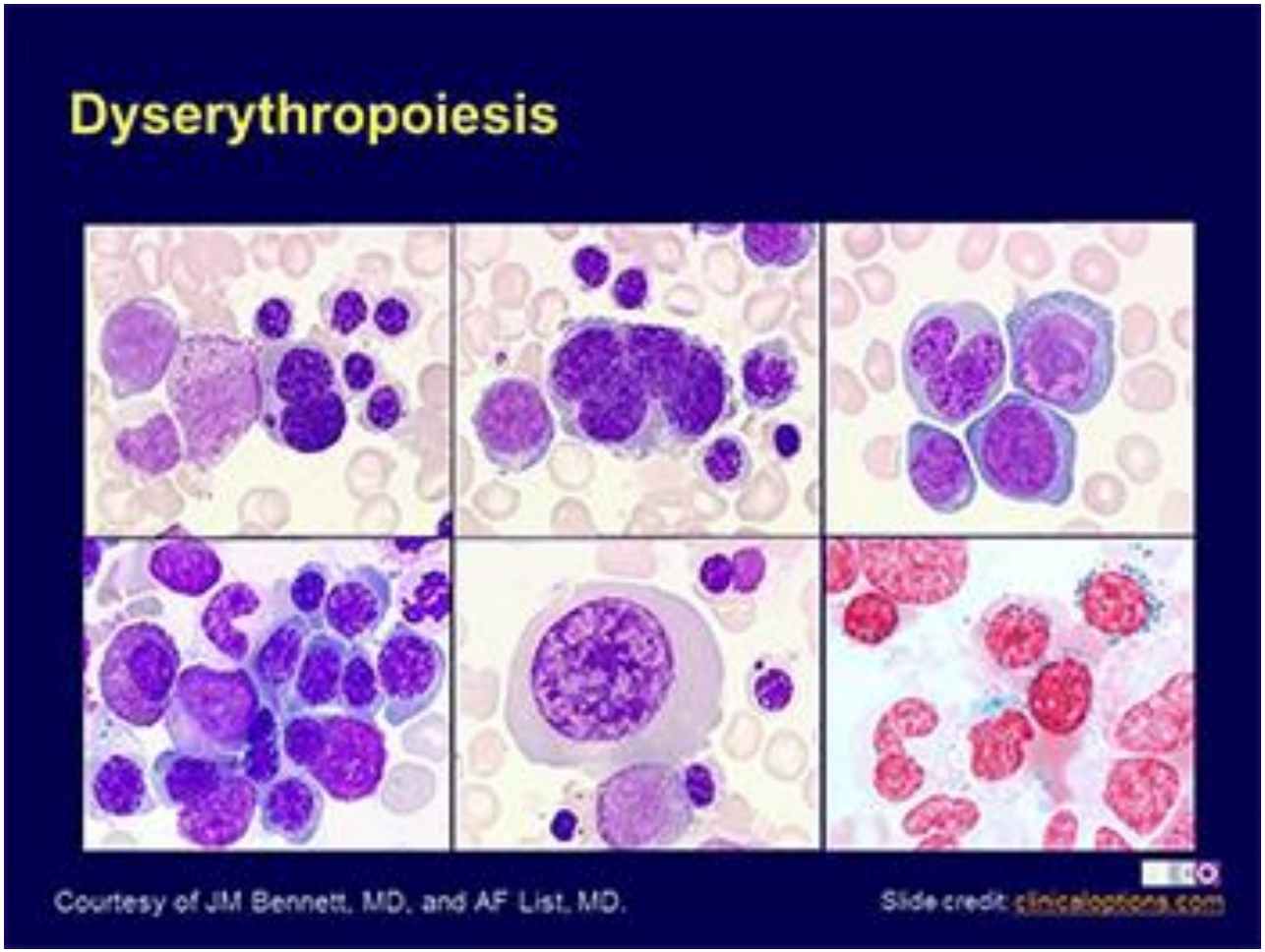
Healthy bone marrow

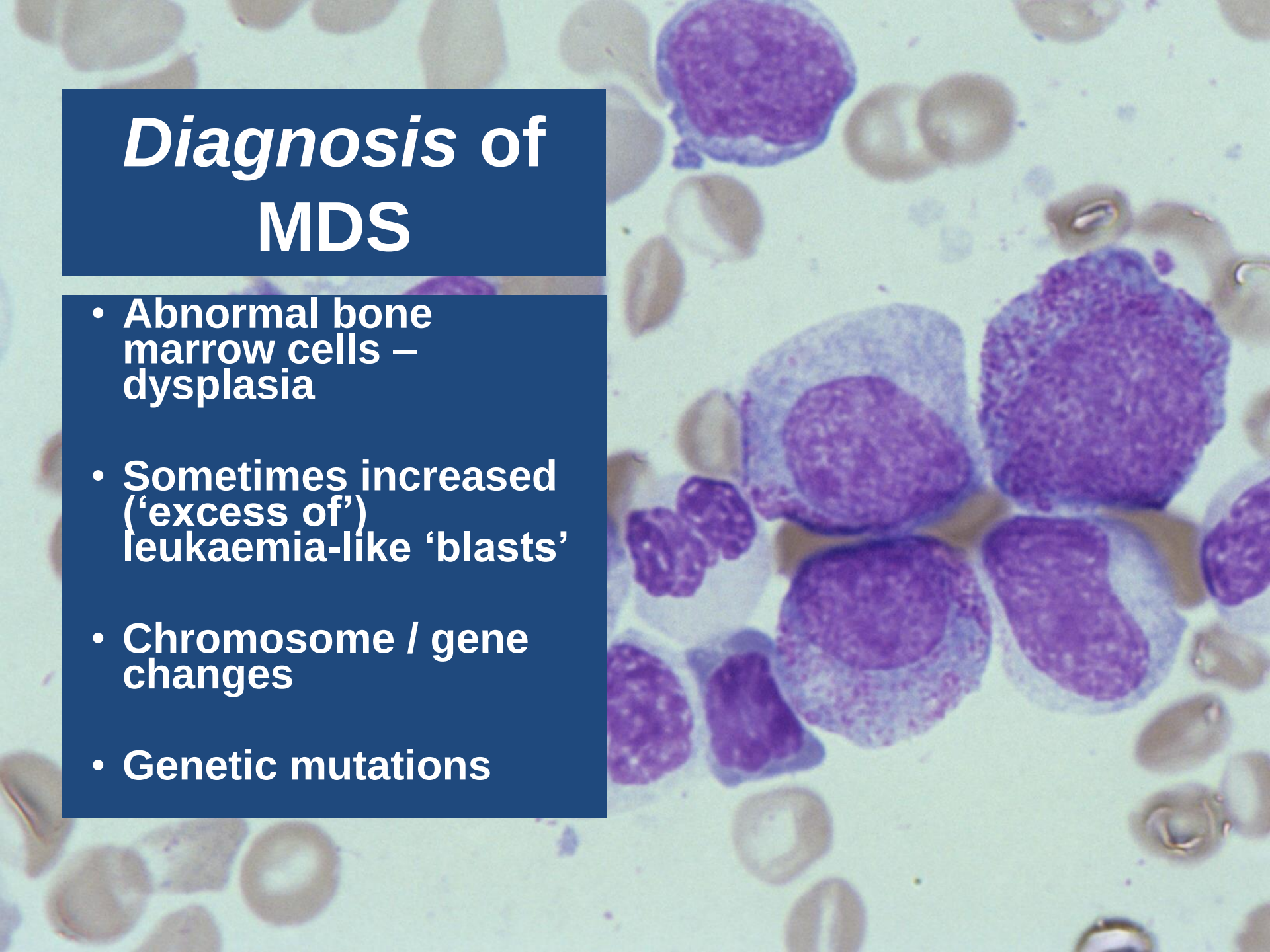


MDS



Bone marrow in MDS: abnormal cells





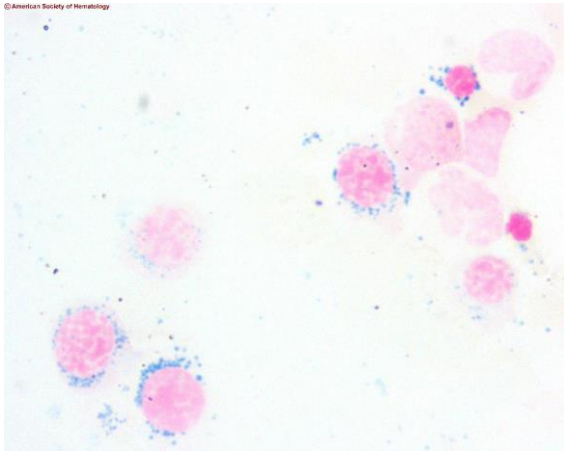
Diagnosis of MDS

- 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

WHO 2017	WHO 2008
MDS with single lineage dysplasia (MDS-SLD)	Refractory Cytopenia with Unilineage Dysplasia
MDS-SLD with ring sideroblasts	Refractory Anaemia with Ringed Sideroblasts
MDS with multilineage dysplasia	Refractory Cytopenia with Multilineage Dysplasia (RCMD)
MDS-MLD with ring sideroblasts	RCMD-RS
MDS with isolated del(5q)	
MDS with excess blasts-1	Refractory Aanaemia with Excess Blasts-1
MDS with excess blasts-2	RAEB-2
MDS, unclassifiable (MDS-U)	

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

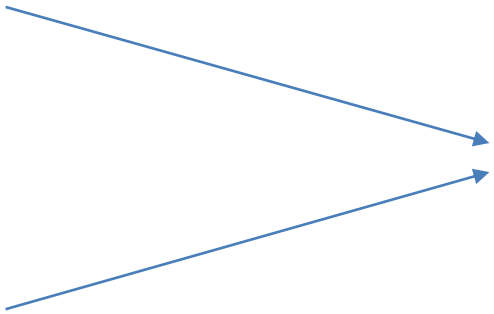
Question 4

- 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

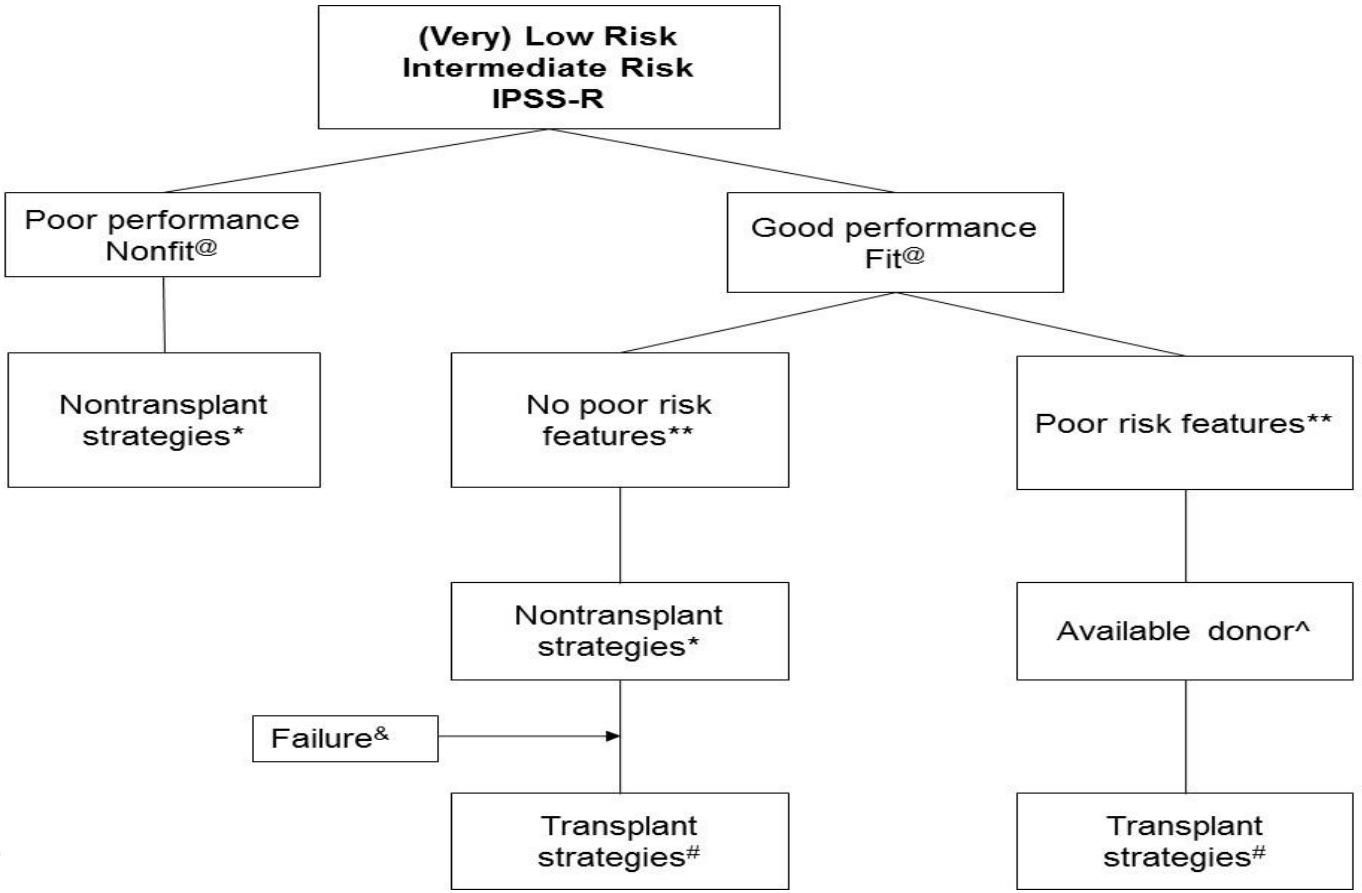


Expert consensus guideline
- **European**
- **British**

Guidelines – friend or foe?

Guidelines – friend or foe?

Lower-risk MDS recommendations for "standard" allogeneic SCT



‘Low-risk’ MDS: 75% MDS patients

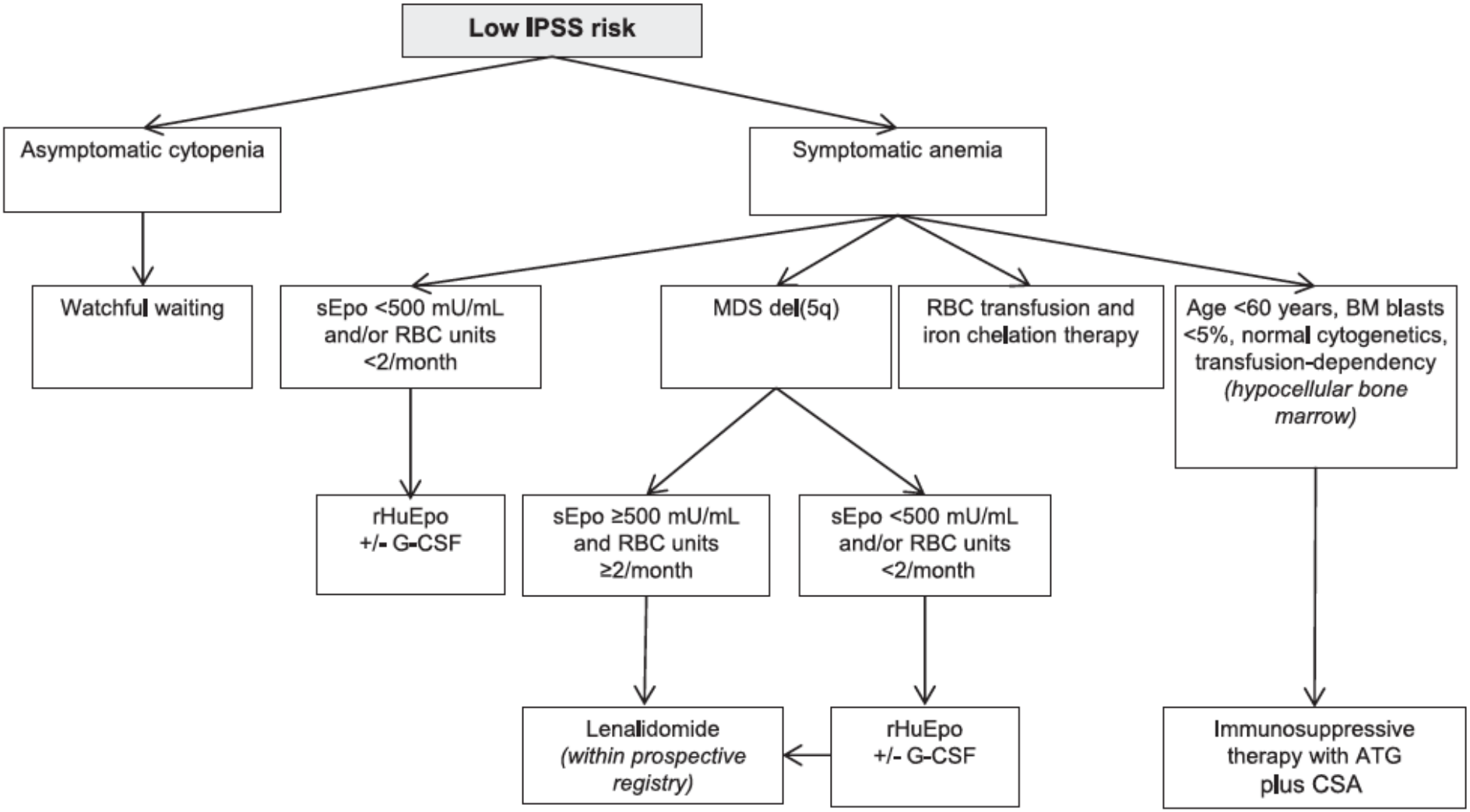
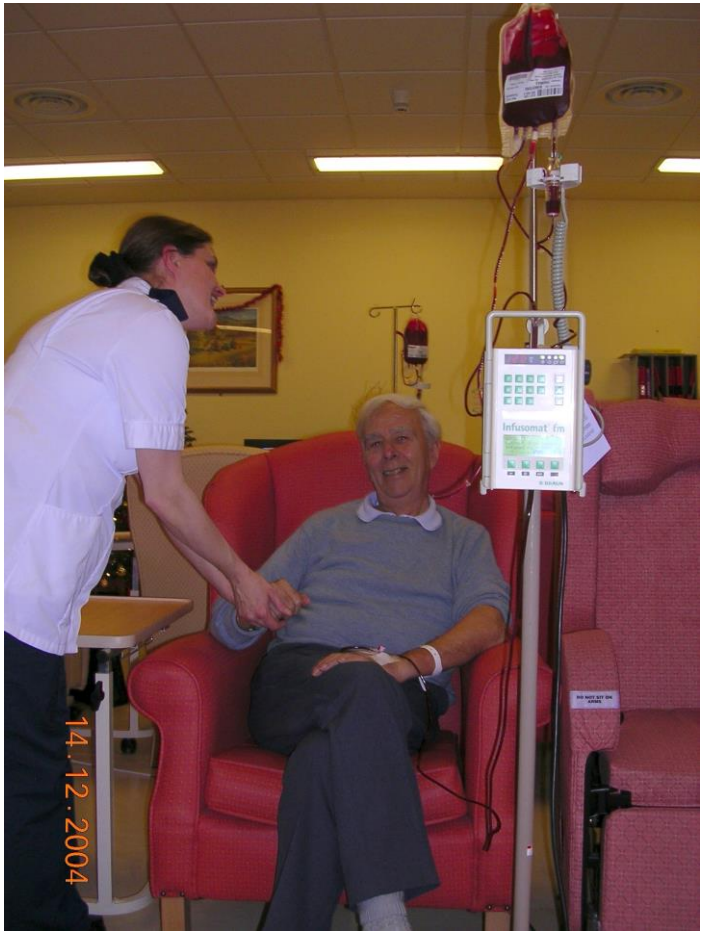


Figure 1. Therapeutic algorithm for adult patients with primary MDS and low IPSS score. BM, bone marrow; sEpo, serum erythropoietin.

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

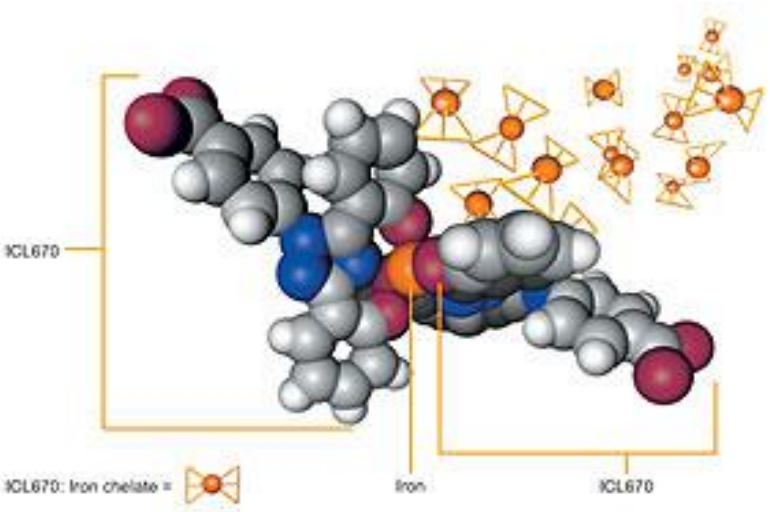


How do we treat low-risk MDS in the UK now?

- 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

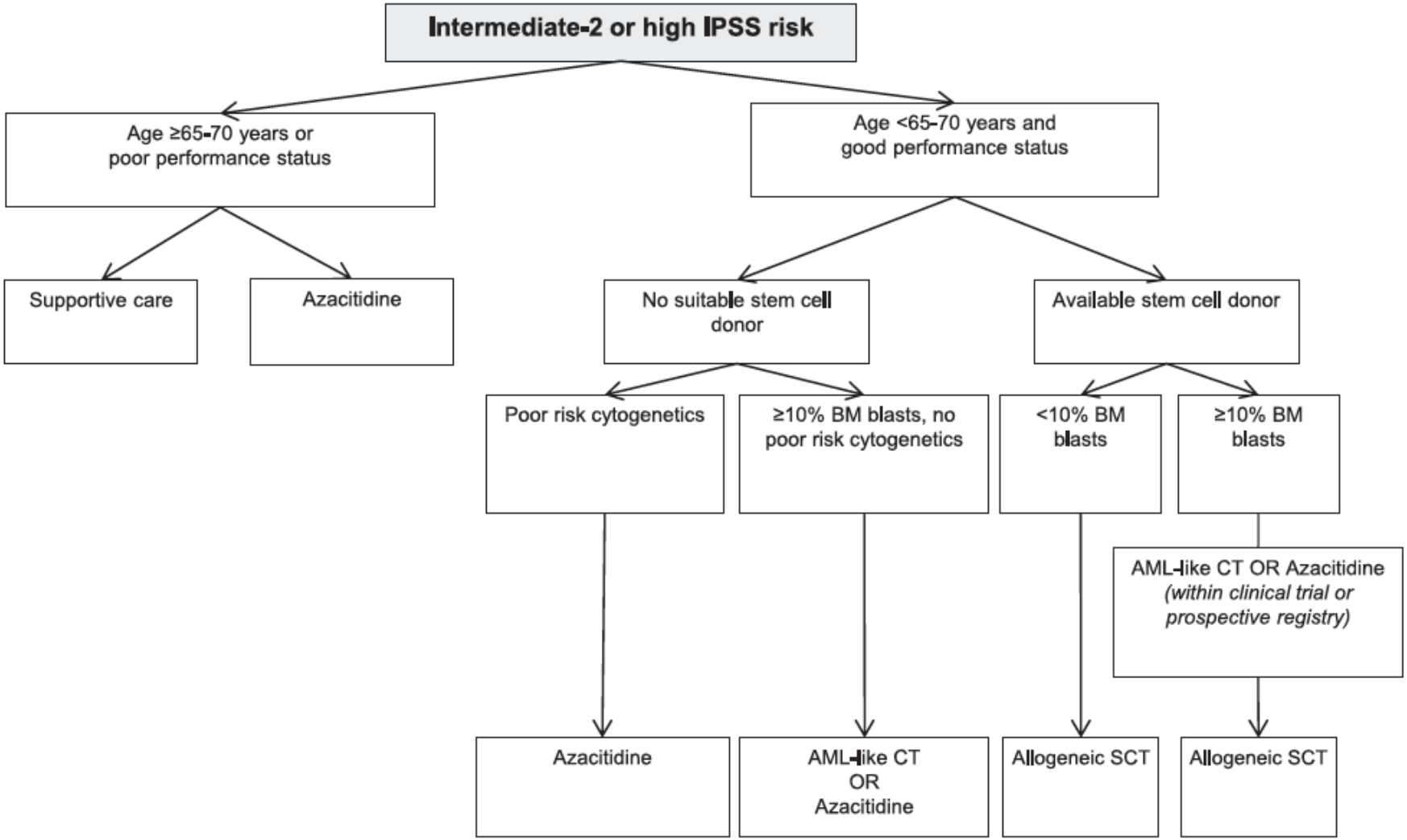


Figure 3. Therapeutic algorithm for adult patients with primary MDS and intermediate-2 or high IPSS score. CT, chemotherapy.

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

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https://mdspatientsupport.org.uk/latest-news

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14 MAR 2019

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 [...]

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https://mdspatientsupport.org.uk/new-service-for-patients-online-video-consultations-with-an-mds-specialist

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Discussion articles

MDS EUROPE

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Can MDS specialists review (and help) more MDS patients please?

Professor David Bowen, Leeds Teaching Hospitals NHS Trust, UK

21 March 2017

St James's Institute of Oncology