Case 4

Dr Marina Karakantza

Case 4

Female-19years old

Ph positive B ALL- transplanted at 1st CR1

Conditioning: Etoposide/TBI

Graft MUD , total dose 6.44x10^6/Kg

Recipient A RhD pos: Donor O RhD pos (minor incompatibility)

Neutrophil engraftment D +20

Platelet engraftment D+35

GvHD prophylaxis: tacrolimus

Case 4–post transplant course

Complications:

- D+40 tacrolimus induced MAHA resolved after switch to mycophenolate mofetil (MMF)
- Recurrent CMV reactivations
- No evidence of acute or chronic Graft v Host Disease (GvHD)

Case 5–post transplant course

Day +241 (10 month post transplant)

Admission with symptoms of acute anaemia . Bleeding excluded

Laboratory findings

Hb **64** g/L, WBC 4.4x10^9/L, neutrophils 2.57x10^9/L, platelets 154x10^9/L

bilirubin 82 (ref range 2-21) , LDH 1917 (ref range 160-430) , serum haptoglobin 0.07 (ref range 0.40-1.60)

DCT 5+ (IgG 5+, IgM 4+, C3c2+, C3d 3+)

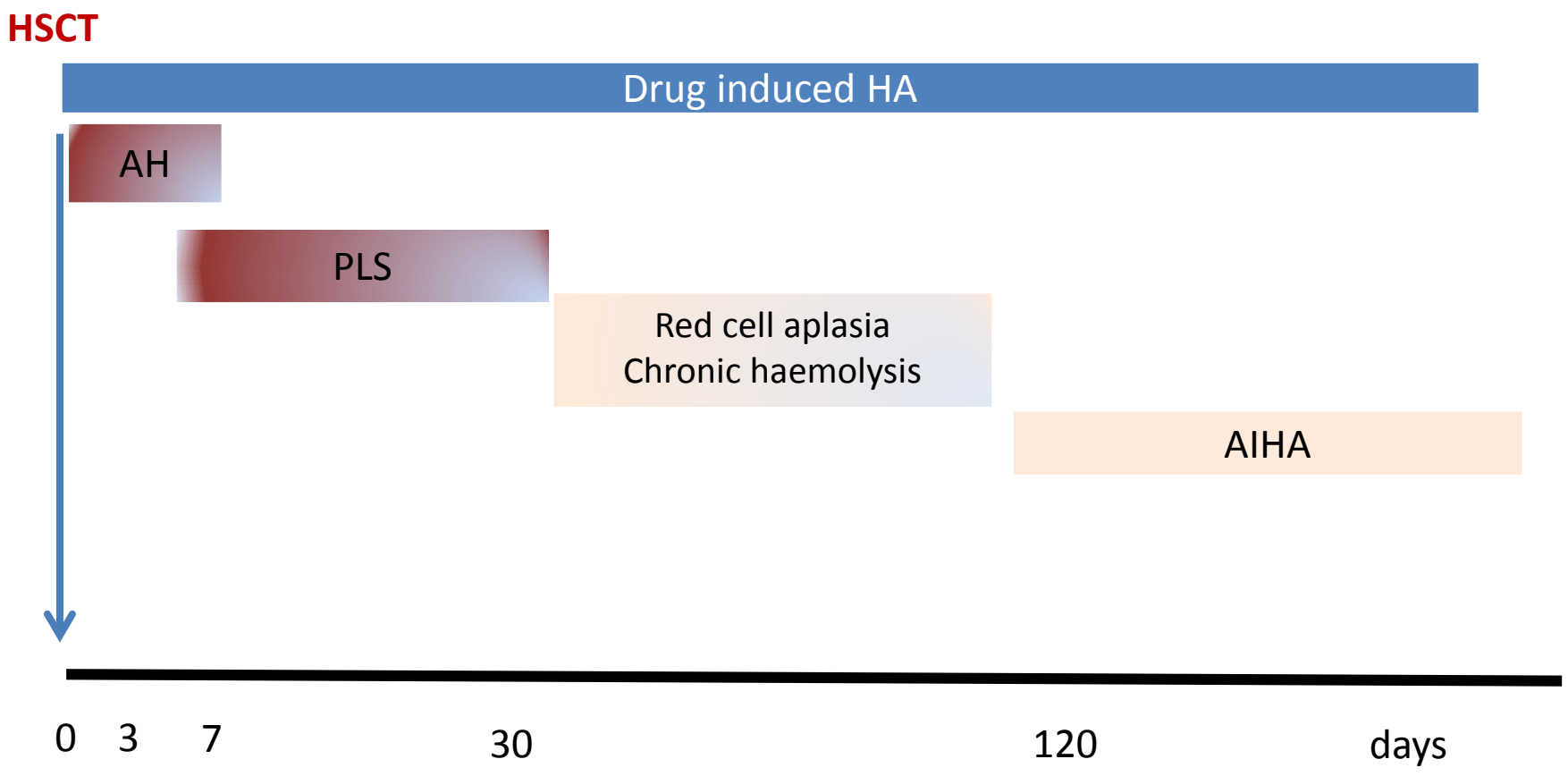
- ongoing CR, no evidence of disease, BCR-ABL negative
- full donor chimerism

Case 4- Question 1

Which of the following is the most likely cause of late onset (> 180 days), DCT positive, acute haemolysis post BM transplant?

A. Persistent formation of anti-A/B by recipient's lymphocytes in major ABO incompatibility
B. Formation of anti-A/B by donor lymphocytes in minor ABO incompatibility.
C. Autoimmune haemolytic anaemia
D. All of the above

Timing matters!!



AH Acute haemolysis
PLS Passenger Lymphocyte Syndrome

Autoimmune Haemolytic Anaemia (AIHA) post HSCT

AIHA post HSCT is due to antibodies produced by the donor's immune system against donor red cell antigens ("donor to donor")

The underlying pathogenetic mechanisms are complex leading to uncontrolled expansion of autoreactive lymphocyte clones

Median time of onset is 5-12 months after HSCT

- early onset group 2-8 months –cold AHIA

Dysregulation of reconstitution of T and early B lymphocytes

- late onset group 6-12 months- warm AHIA

Dysregulation of reconstitution of mature B lymphocytes

Incidence 2-5%

Laboratory findings-AIHA post HSCT Leeds Teaching Hospitals

Patient	Month Post HSCT	IgM	IgG	IgA	C3d	C3c
1	7	2	5	ND	4	ND
2	7	0	5	0	3	0
3	5	1	4	0	4	1
4	14	3	5	1	4	2
5	5	0	3	0	0	0
6	4	0	5	0	1	3
7	9	4	5	0	3	4

Case 4- Question 2

Which one of the following has NOT been shown to be a risk factor for development of autoimmune haemolytic anaemia post BM transplant?

A. Graft versus Host Disease (GvHD)
B. GvHD prophylaxis with cyclosporin
C. Ex vivo T cell depletion
D. Graft from a matched unrelated donor
E. Transplants for non-malignant diseases

Risk factors

Depth of conditioning induced lymphopenia

- Ex vivo T cell depletion
- In vivo T cell depletion i.e ATG , alemtuzumab
- Non malignant haematological disorders i.e aplastic anaemia, CVID
- Cord grafts
- Matched unrelated donors

Factors activating the immune system

- Chronic GvHD
- Viral infections

Case 4
Risk factors

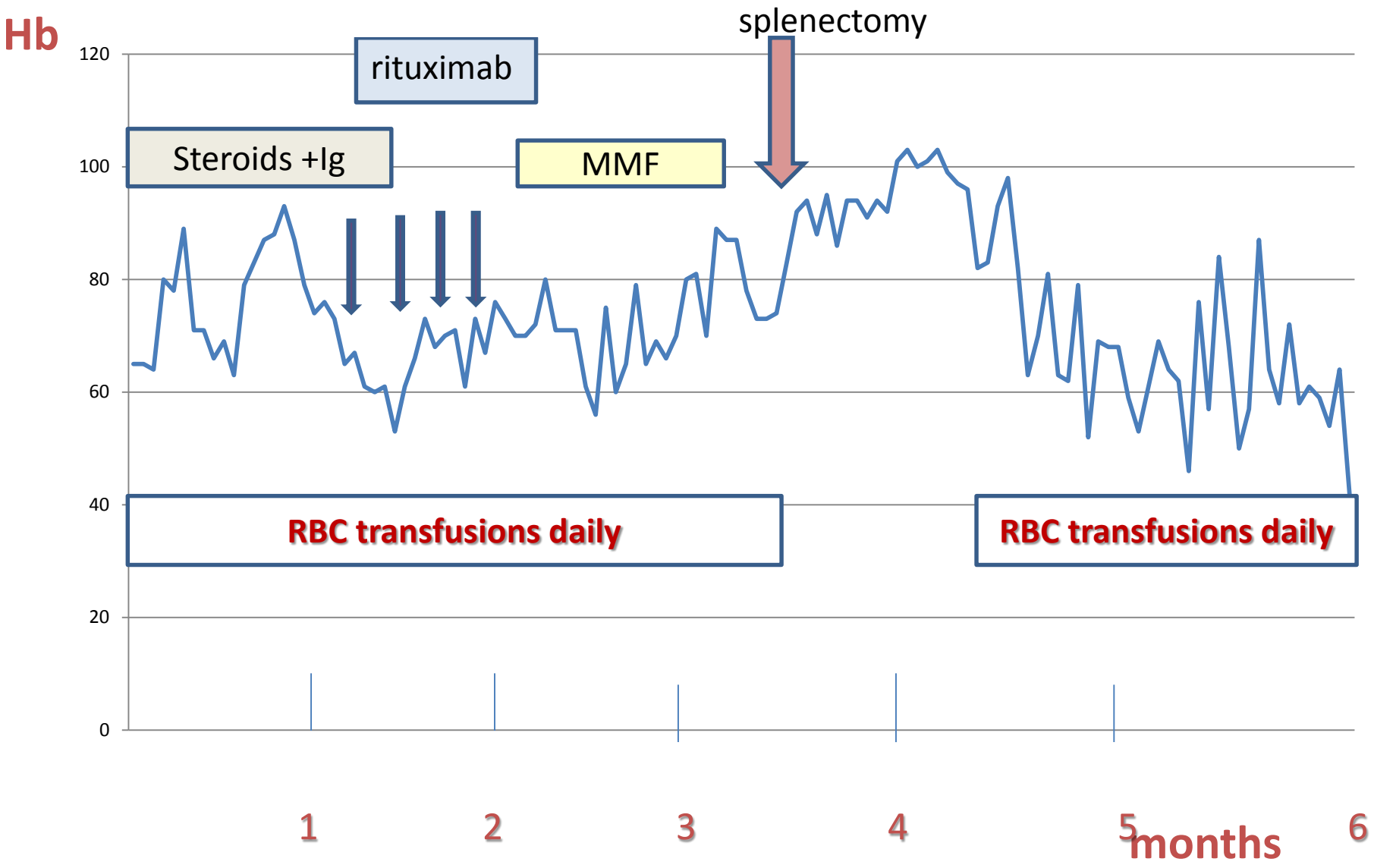
- Matched unrelated donor
- Recurrent reactivations of CMV

Case 4- Question3

Which of the following treatments is recommended as 2nd line therapy for AHIA post BM transplant?

A. Rituximab
B. Cyclosporin or mycophenolate mofetil (MMF)
C. Splenectomy
D. Donor lymphocyte infusions
E. All the above

Case 4


Hb
120
100
80
60
40
20
0
rituximab
splenectomy
Steroids +Ig
MMF
RBC transfusions daily
RBC transfusions daily
1
2
3
4
5
6
months

Management of AIHA post HSCT

AIHA that develops after HSCT is more refractory to treatment than primary AIHA

1st line treatment : steroids ± IV Ig

10%

2nd line treatment : rituximab

46% for adults

83% for children

1st line: a combined regimen of steroids and rituximab

M. Wang et al. / Biol Blood Marrow Transplant 21 (2015) 60-66

Management of AIHA post HSCT

In the presence of severe lymphopenia due to

- Ex vivo T depletion
- In vivo T depletion
- Primary non malignant haematological disorder accompanied with lymphopenia

Early consideration of DLI

In the presence of chronic GvHD

intensification of GvHD treatment

Splenectomy:

can be recommended for warm AIHA to patients without contraindications

Case 4

Short, partial response to splenectomy
Died from AIHA in remission from her leukaemia and without GvHD

Adults

<50% complete response

36% mortality directly attributable to AIHA

Children

87% complete response

Thank you