EUROPEAN HEMATOLOGY ASSOCIATION

ROHS Российское профессиональное общество онкогематологов

RSH

EHA-ROHS-NHS Tutorial on "Real world challenges and opportunities in diagnostics and management of onco-haematological patients today"

Self-assessment Case – Session

Immunotherapy

Speaker: A Urbano Ispizua

Case 2

Moscow, Russia

April 12-13, 2019

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Introduction

- 19yrs male, B-ALL. Induction chemo with high risk protocol. CR MRD-
- Relapse at the end of consolidation
- FLAG-Ida. CR MRD-. MyMR Allo-SCT
- Relapse at +5m post allo. 20,000 blast cells/mm3 PB (CD19+/CD22+)

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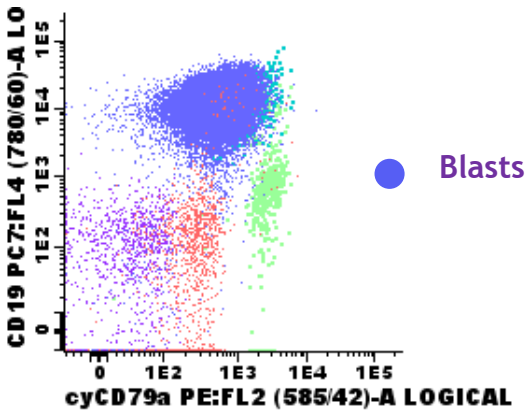
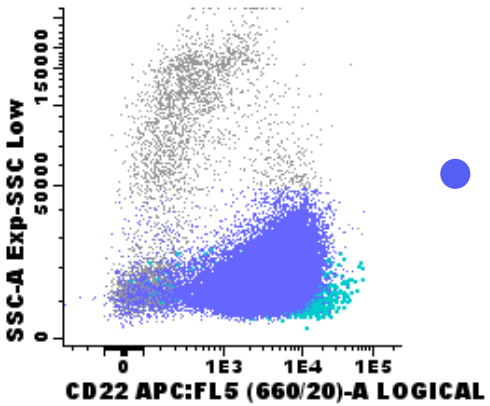
Introduction



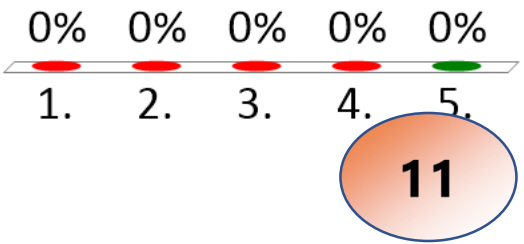
Blasts



Blasts

Q1) What is the preferred option?

1. Withdraw immunosuppression
2. Donor lymphocyte infusion
3. Inotuzumab-ozogamicin +/- second Allo-SCT
4. Blinatumomab +/- second Allo-SCT
5. CAR-T19 cells



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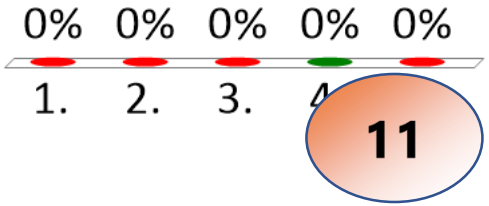
Evolution 1

- Transferred to receive CAR-T19 treatment (ARI-0001 cells)
- ECOG 1, and 13,000 blasts/mm3 PB
- BMA 95% blasts (B-II)
- CD3+ cell count in PB 1200/μl

Q2) What is the preferred option?

1. PBMC harvest and CART administration
2. Cytoreductive treatment and PBMC harvest
3. PBMC harvest, and then lymphodeplection regimen pre CAR-T
4. PBMC harvest, cytoreductive treatment, lymphodeplection regimen, and CAR-T administration
5. Excluded from the CAR-T programme



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Evolution 2

- PBMCs were collected and introduced in a CliniMACS Prodigy
- Methylprednisolone 1.5mg/kg + cyclophosphamide 300 mg/day x5
- Grade 4 neutropenia and thrombo-cytopenia. No blasts in PB/bone marrow aspirate (BMA)

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Evolution 3

- 1× 10^6 CART19+/kg after conditioning with cyclophosphamide + fludarabine
- 72hs later:38^0C, rise in CRP and ferritin, and a generalized skin rash
- CAR-T cell peak in peripheral blood

Evolution 3

- Skin biopsy revealed discrete spongiotic dermatitis, with no interface injury, and a slight perivascular lymphocytic infiltration, with some CD3+/CD8+ lymphocytes of activated appearance (negative for CD19)
- No GI symptoms or liver inflammation

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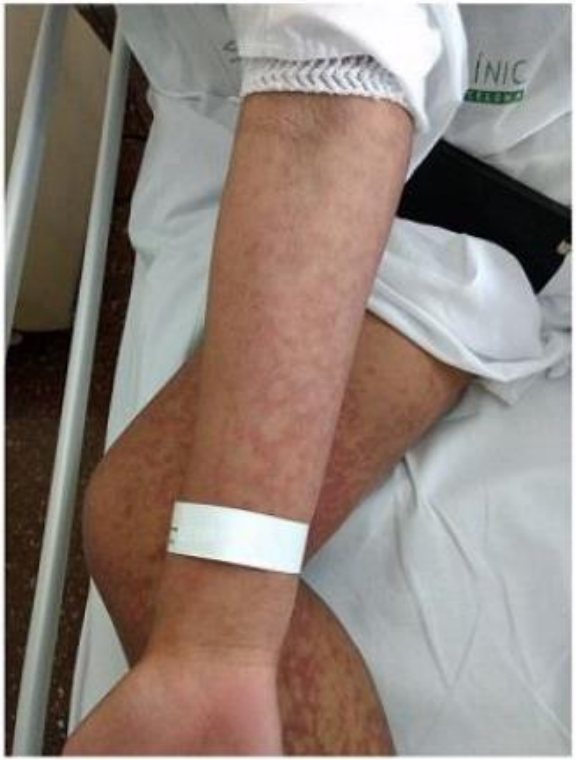
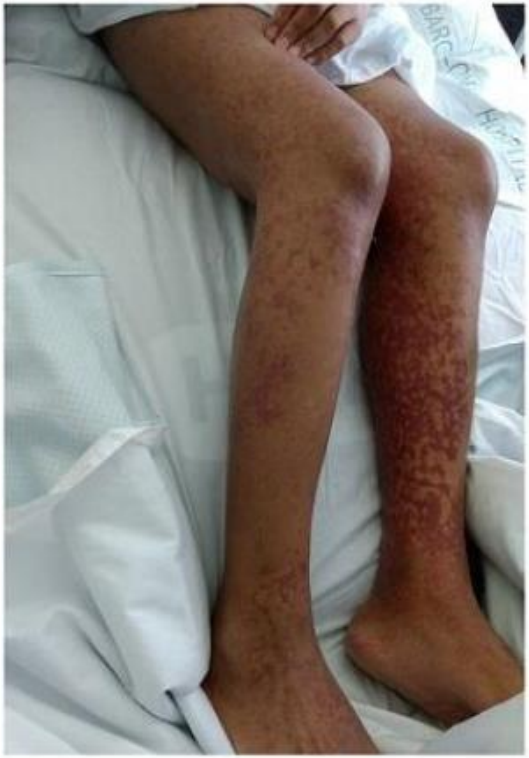
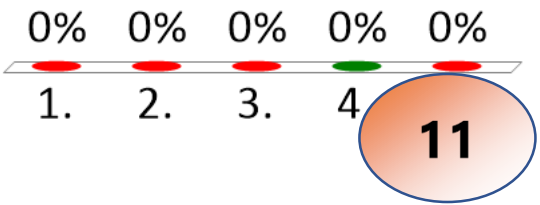
Evolution 3





Q3) What is the cause of the skin rash and how should it be treated?

1. GvHD, steroids
2. CAR-T cell expansion, tocilizumab
3. CAR-T cell expansion, systemic steroids
4. CAR-T cell expansion, topical steroids
5. Rash may be related to thrombocytopenia



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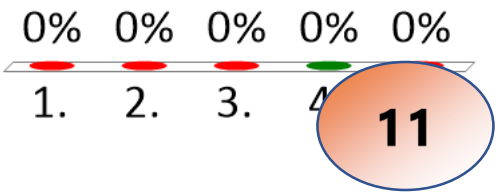
Evolution 4

- Topical steroids were initiated and the skin rash improved rapidly
- Both neutropenia and thrombocytopenia grade 4 at +30
- Bone marrow biopsy was compatible with aplastic anemia

Q4) What should you do now?

1. Second Allo-SCT
2. Boost of donor CD34+
3. Eltrombopag
4. G-CSF and transfusion support
5. Transfusion support. No G-CSF



Evolution 5

- G-CSF: good response
- Platelet transfusion every 5 days
- No need for red cell transfusions
- +4m, no CAR-T cell detection: B-cell recovery. CR, MRD- by both flow cytometry and NGS
- +6m, extensive cutaneous GvHD, systemic steroids and photopheresis

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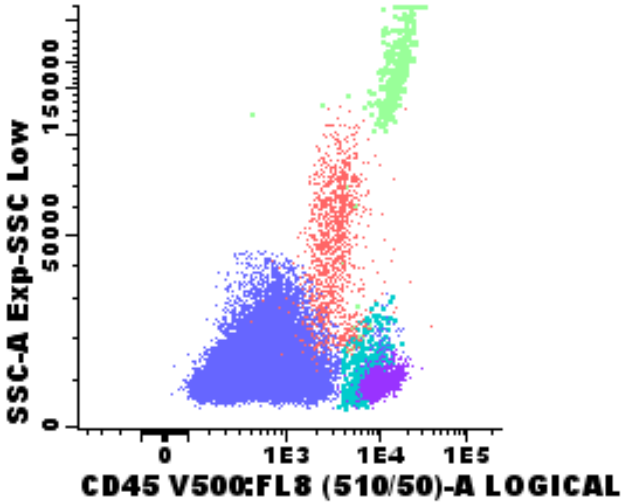
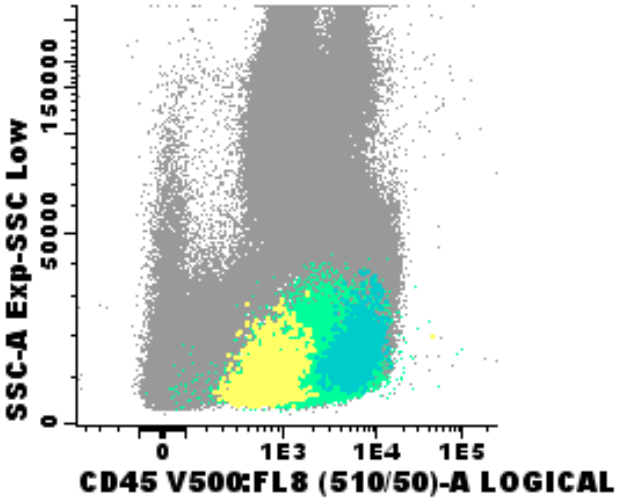
Evolution 5



Before CAR-T19



+4 mths after CAR-T19

● Blasts

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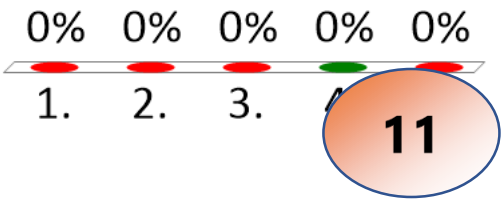
Evolution 6

- +12m BMA CR MRD- by flow cytometry (FC)
- +16m, bilateral tibial pain. PET-TC positive. Biopsy: CD19+/CD22+ blasts. (BMA: CR MRD- by FC)
- Prior Allo-SCT was performed 2 years before. ECOG 0

Q5) What should you do now?

1. Palliative treatment
2. CART19 cells (same CAR-T product)
3. CART19 cells (change CAR-T product)
4. Blinatumomab + Allo-SCT
5. Inotuzumab-ozogamicin + Allo-SCT



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Evolution 7

- Patient has started treatment with blinatumomab with good clinical response (pain), to be followed by a second Allo-SCT (from a different donor)

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Many thanks