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

Self-assessment Case – Session

Immunotherapy

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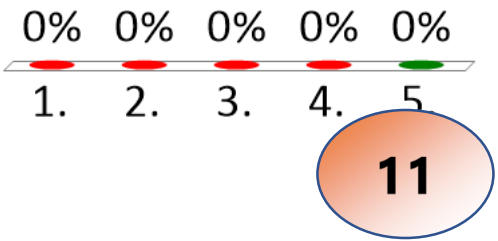
Introduction

- 54y male, DLBCL “double hit” (*MYC*/*BCL2*) IV-A
- BURKIMAB: CR; ASCT
- Relapse +8m post ASCT
- Refractory to high doses of methothrexate
- Palliative cyclophosphamide/prednisone.
- A 10/10 matched unrelated donor available

BURKIMAB:Rituximab, high-dose methotrexate, dexamethasone, VP16, ifosfamide/cyclophosphamide, vincristine, doxorubicin, cytarabine and IT methotrexate × 6

Q1) What is the preferred therapeutic option?

1. Continue on palliative treatment
2. Try intensive chemotherapy
3. Nivolumab
4. Allo-SCT
5. CAR-T cells



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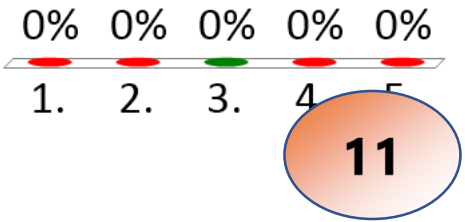
Evolution 1

- He was enrolled in a clinical trial with a 2nd generation (4-1BB) A3B1 anti-CD19 CAR
- 4.5×10^6 CART19/kg day 0 after Cyclo (900 mg/m^2)/Flu (90 mg/m^2)
- 12 hrs later developed 40^0C, tachycardia and mild hypotension

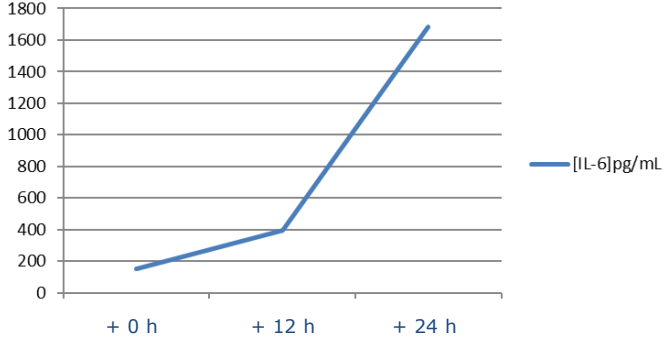
Q2) What is the most likely diagnosis?

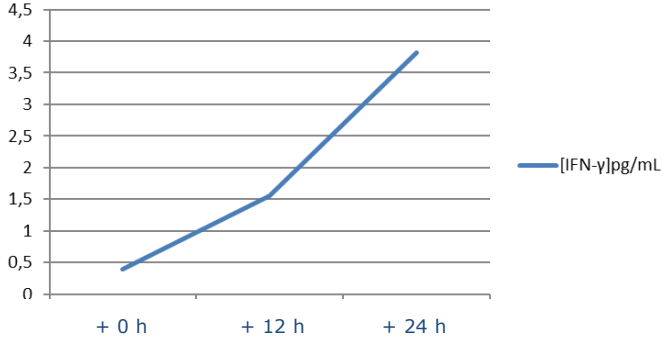
1. Systemic infection. Cytokine release syndrome (CRS) excluded
2. CRS. IL-6 blockade. Infection excluded
3. Mild CRS, infection to be ruled out
4. If high IL-6 levels, it must be CRS: IL-6 blockade
5. Blood transfusion reaction



Evolution 2

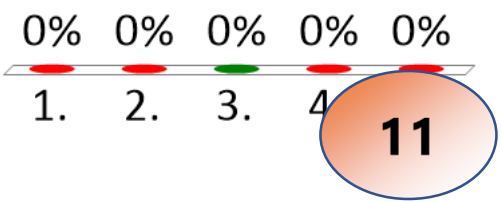
- 12hrs after antibiotics and IV fluids , progressive hypotension, mild renal failure, febrile
- Blood levels of IL-6 and IFNg showed a large peak
- No microbiological findings





Q3) What should you do now?

1. CRS. Vasopressors in the ward
2. CRS. Vasopressors and tocilizumab in the ward
3. CRS. Vasopressors in the intensive care unit (ICU)
4. CRS. Vasoppresors and tocilizumab in the ICU
5. Septic shock. Transfer to the ICU

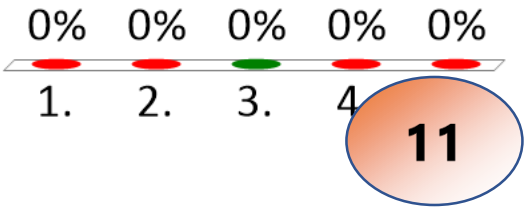


Evolution 3

- Patient was transferred to the ICU
- Antibiotics and IV fluids were escalated and low dose noradrenaline was initiated
- 6hs later, fever, severe hypotension, mild respiratory insuffiency
- Still, with no microbiological findings

Q4) What should you do now?

1. Severe CRS. High dose vasopressors
2. sCRS. High dose vasopressors + corticsteroid
3. sCRS. High dose vasopressors + tocilizumab
4. sCRS. High dose vasopressors + corticosteroid + tociilizumab
5. Uncontrolled sepsis. Escalate antibiotics + antifungals



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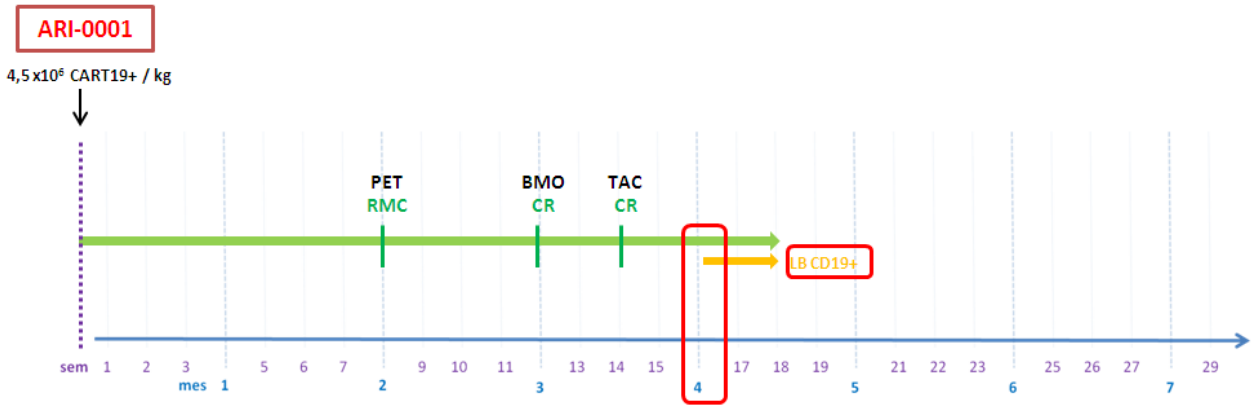
Evolution 4

- 8 mg/kg tocilizumab
- +2h no fever
- +24h vasopressors tappering
- +48h haemodynamic normalization
- +7d ICU discharge
- +21d hospital discharge

Evolution 5

- +2m PET-CT : Complete metabolic response (CMR)
- +3m Bone marrow biopsy :Complete response (CR)
- +3m CART19 non-detectable by flow cytometry
- +4m B cell recovery



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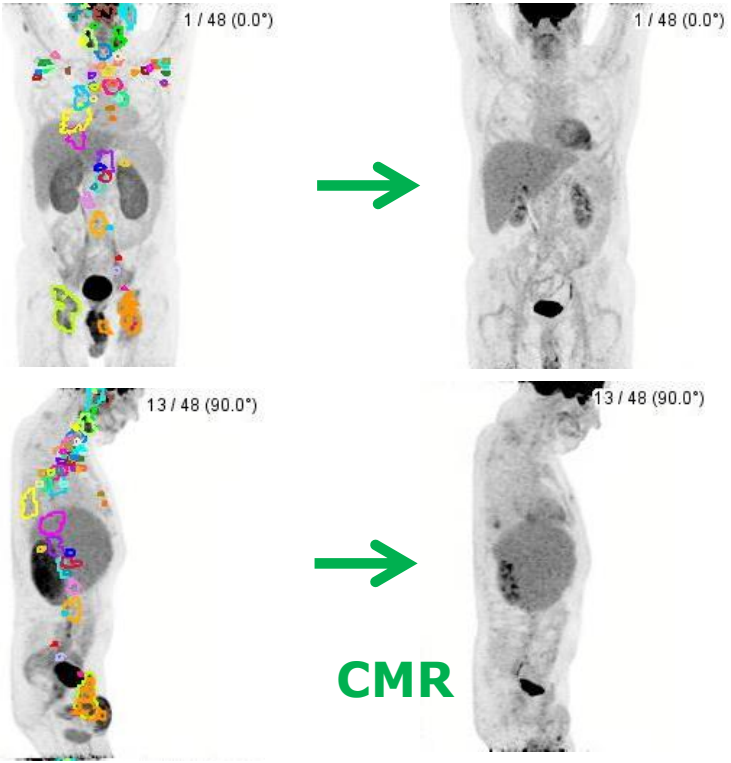
Evolution 5

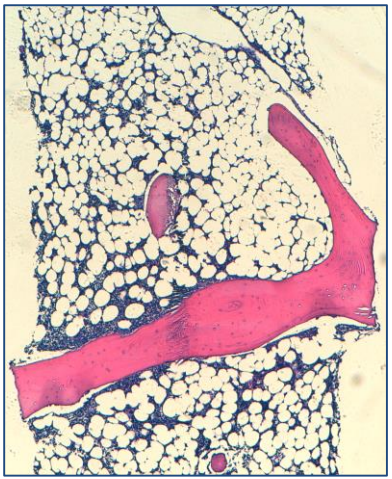
+2 mo

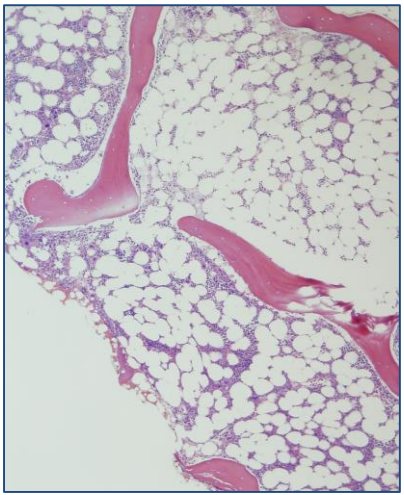


CMR

Evolution 5

+3 mo

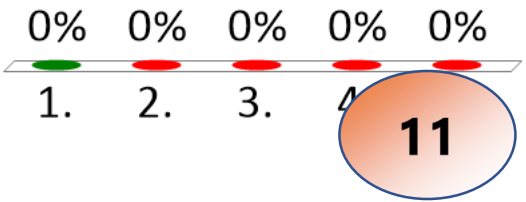




CR

Q5) What should you do now?

1. Watch & wait
2. Try boosting CART19 persistence with nivolumab
3. Consolidate response with AlloSCT
4. Repeat CART19 infusion while in CR
5. Repeat CART19 infusion only if CD19+ relapse



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Discussion

- CART19: 50% CR in DLBCL relapse/refractory
- Severe CRS 23%
- Rapid response to tozilizumab (± steroids)
- No long-term consequences after CRS
- CART19 40% disease free survival (plateau) in DLBCL relapse/refractory

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References

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