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Emicuzimab – front line treatment for (all) patients with haemophilia and inhibitors; the case for NO!

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AGENDA – why Emicuzimab should not be used upfront for ALL patients with inhibitors

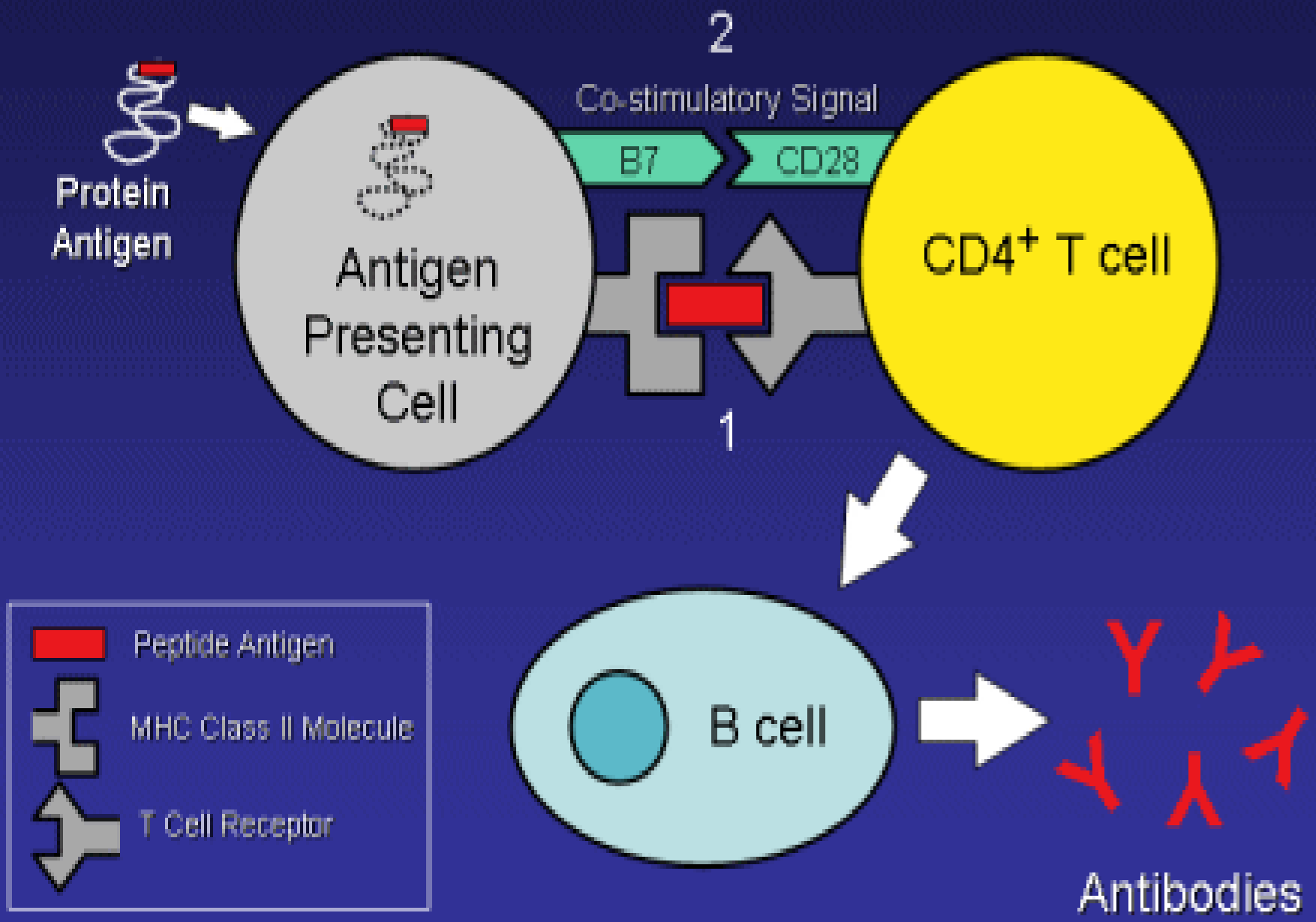
- Not all patients with inhibitors are the same
- Not all inhibitors are the same
- What about the role of new clotting factor agents?
- Peaks and troughs in factor VIII?

Inhibitor in haemophilia

- Development of inhibitors in patients with severe **haemophilia A is relatively common** (up to 33% of patients with severe haemophilia and 13% of patients with non severe haemophilia)

- Development of inhibitors is associated with significant morbidity
  - Reduced quality of life, financial stress, need for central line access, strained familial relationships and greater mortality

- Management of patients is **problematic and expensive**


2
Co-stimulatory Signal
B7
CD28
Protein Antigen
Antigen Presenting Cell
CD4+ T cell
1
B cell
Antibodies
Peptide Antigen
MHC Class II Molecule
T Cell Receptor

Treatment and prevention of bleeds in patients with inhibitors

- Majority of morbidity of patients with inhibitors is related to an increased bleeding frequency but **therapy (and prevention) is available**

- Bypassing agents are available and effective for the treatment of bleeds with **> 80% efficacy rate**

- Prophylaxis with FEIBA and rVIIa has been extensively investigated
  - PROFieba – reduction from 10.8 to 4.2 bleed (6 month period)
  - rVIIa – reduction in bleeds from 5.6 to 3.0 bleeds per month (90 ug/kg group)

Immune tolerance therapy

- Frequent, prolonged exposure to clotting factor
  - Inhibition of B cell memory
  - Induction of T cell anergy
  - Development of anti-idotypic antibodies
  - Development of suppressor T cells

- Success rates of immune therapy vary (from 50 – 80%)

- *When successful patients can return to routine prophylaxis with factor VIII*

- Prolonged expected treatment – often referring to years of therapy

Immune tolerance therap
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Low titre inhibitors – mar nt with high dose fa

- Not all inh
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- W ro VIII

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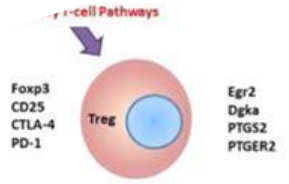

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Factor VIII and the stress response (good or bad?)

- Early 20th century
  - Blood hypercoagulability documented during fight or flight response
  - Evolutionary interpretation of these observations was that "*rapid coagulation may reasonably be considered as an instance of adaptive reaction serviceable to the organism in the injury which may follow the struggle that fear or rage may occasion*"
- Role of ability for factor VIII increases in
  - Physical activity (sports)
  - Emergency surgery
  - Trauma

Emicuzimab – mechanism of action (baseline level of factor [illegible] 5% compared to "[illegible] (physic[illegible]

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Conclusion

- Emicuzimab – front line treatment for (all) patients with haemophilia and inhibitors
  - Not all inhibitor patients are the same
  - Not all inhibitors are the same
  - Role of the newer factor VIII products
  - Role of factor VIII peaks and troughs

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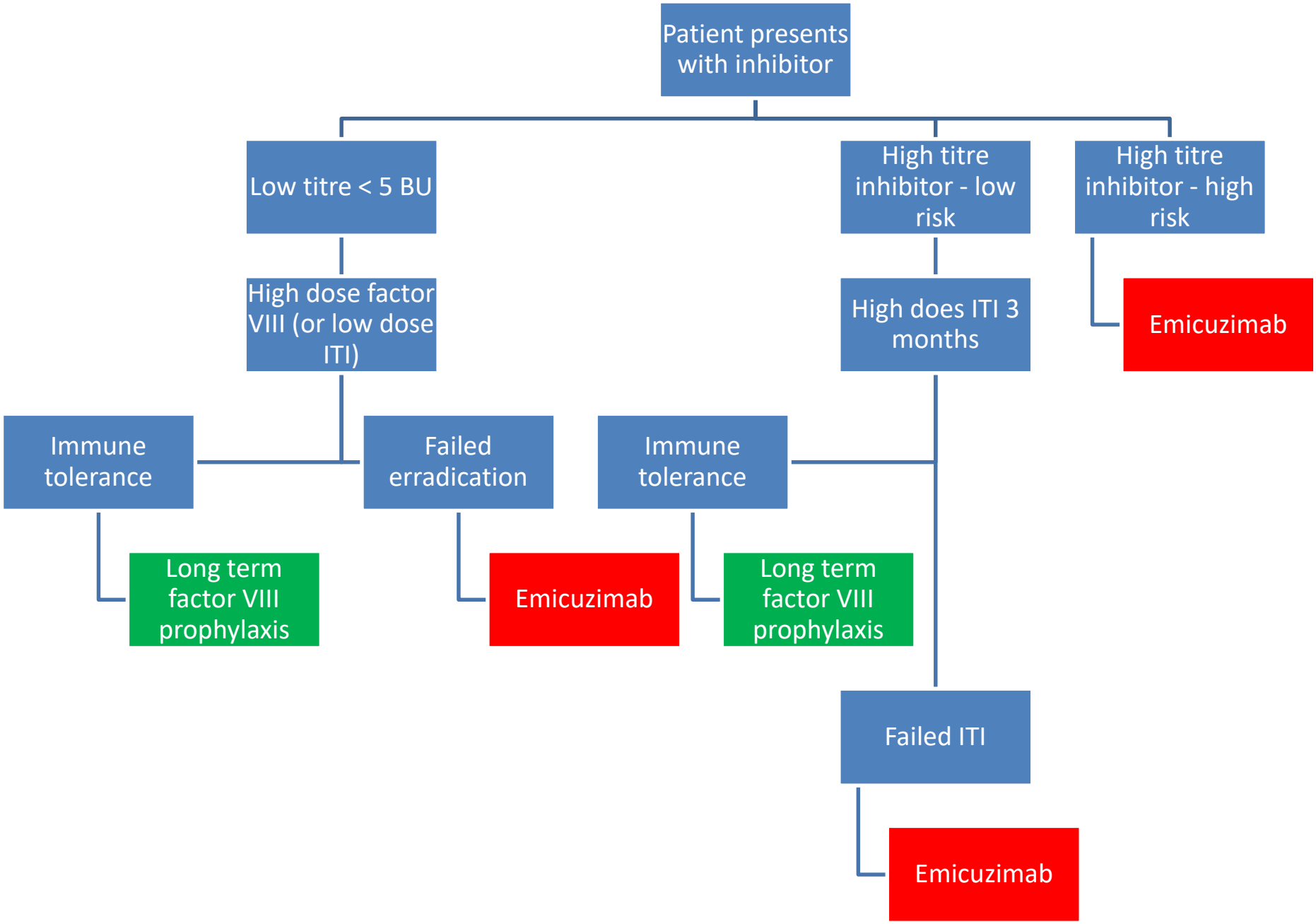
Patient presents with inhibitor
Low titre < 5 BU
High titre inhibitor - low risk
High titre inhibitor - high risk
High dose factor VIII (or low dose ITI)
High does ITI 3 months
Emicuzimab
Immune tolerance
Failed erradication
Immune tolerance
Long term factor VIII prophylaxis
Emicuzimab
Long term factor VIII prophylaxis
Failed ITI
Emicuzimab


MY OPPONENT IS WRONG!
BUT I AGREE WITH EVERYTHING SHE IS SAYING.