Immunological Non Responders to HAART in Botswana: Characteristics & Risk factors

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Background

High global burden of HIV/AIDS

- 34 million people living with HIV/AIDS worldwide
- 23 million in Sub-Saharan Africa

  ↑ prevalence Southern Africa (UNAIDS,2012)

Botswana prevalence rate 25% adults

- 316 000 adults living with HIV
- 15 000 children under 14 years (National AIDS Council, 2010)

Background

Usually untreated infection →immunological deterioration

- CD4 T-helper cell decay, ↑ viral load (McMichael *et al*., 2010; Moir, Tae-Wook & Fauci, 2011)

Immune activation

- Cytokine activation (inflammatory)
- GALT damage →microbial translocation
- AICD → immune exhaustion

(Douek *et al*., 2009; McMichael *et al*., 2010)

Background

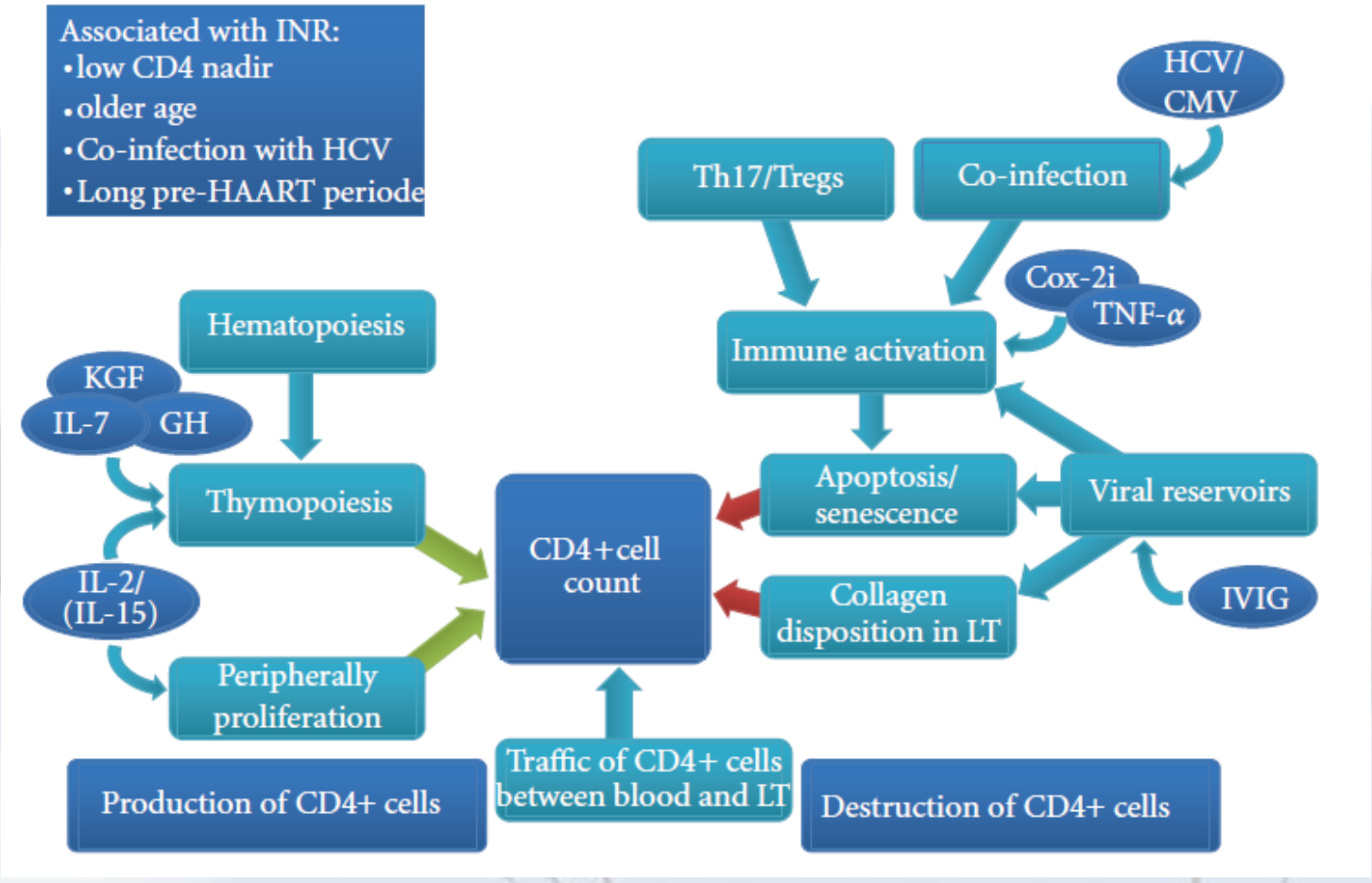
HAART

- ↓morbidity & mortality, ↑CD4 count, ↓viral load (Bofill *et al*., 2006, Bussmann *et al.*, 2008)
- >500 cells/µl = non HIV positive morbidity & mortality (Gaardbo *et al*., 2012; Nixon & Landay, 2010).

Response heterogeneity

- Poor immunologic response despite virologic control
- 15-30% <200 cell/µl by 12 months treatment
- clinical risk (Casotti *et al*., 2011; Gaardbo *et al*., 2012; Nakanjako *et al*., 2011)

Background



Gaardbo *et al*., 2012

Justification

Conflicting data over INR & OI/death risk association

(Nakanjako et al., 2008; Gazolla *et al*., 2009; Hermans *et al.,* 2010)

- HR AIDS/death (<200 vs. >350) 10 and CD4 <200 vs. 200-350 at 8.5 (Casotti et al., 2011)

Late treatment initiation (Bussmann *et al*., 2008; Wester *et al.,* 2009; Esposito *et al*., 2011)

- 48% VCT diagnosis <200 cells/µl (UNAIDS, 2012)
- ↓CD4 in HIV –ve in Botswana (Bussmann *et al*., 2004)

Treatment strategies

- IL-2, IL-7 (Gaardbo *et al*., 2012; Gazolla *et al*., 2009)

Hypothesis

Immunological non response to HAART is associated with increased risk for the development of opportunistic infections and or death

Main Objective

Main objective

- To characterise patient factors associated with immunological non response to HAART in Botswana and its association with the risk of developing opportunistic infection and or death

Specific Objectives

Specific objectives

- Determine frequency of INR at 12 months ART
- Characterise polyfunctionality of activated PBMC
- Determine plasma levels of LPS, sCD14
- Determine systemic cytokine profiles of participants
- Associate baseline characteristics, immunological response, PBMC responses, microbial translocation and cytokine profiles with frequency of OI and or death

Methods

Population

- >18 yrs, consented, ART outcome studies
- Botswana MOH clearance, HSPH

Inclusion Criteria

- <200 cells/µl CD4 initiation, VL <400 copies/ml by 6 months, clinical data

Exclusion criteria

- 2 consecutive VL >400 copies/ml post 6 months

Methods

Definition: <200 cells/µl by 12 months ART

Data abstraction

- CD4 counts, Viral load, OI frequencies

Determine frequency INR

Laboratory analysis

- ELISPOT for PBMC responses
- ELISA (LPS,sCD14, cytokine profiles)

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