

PART III  
INFLAMMATION

# Background

- Inflammation is a healthy response to infection or injury
- Cardinal signs, first noted by Aulus Cornelius Celsus in the first century
  - Calor (heat)
  - Dolor (pain)
  - Rubor (redness)
  - Tumor (swelling)



# Background

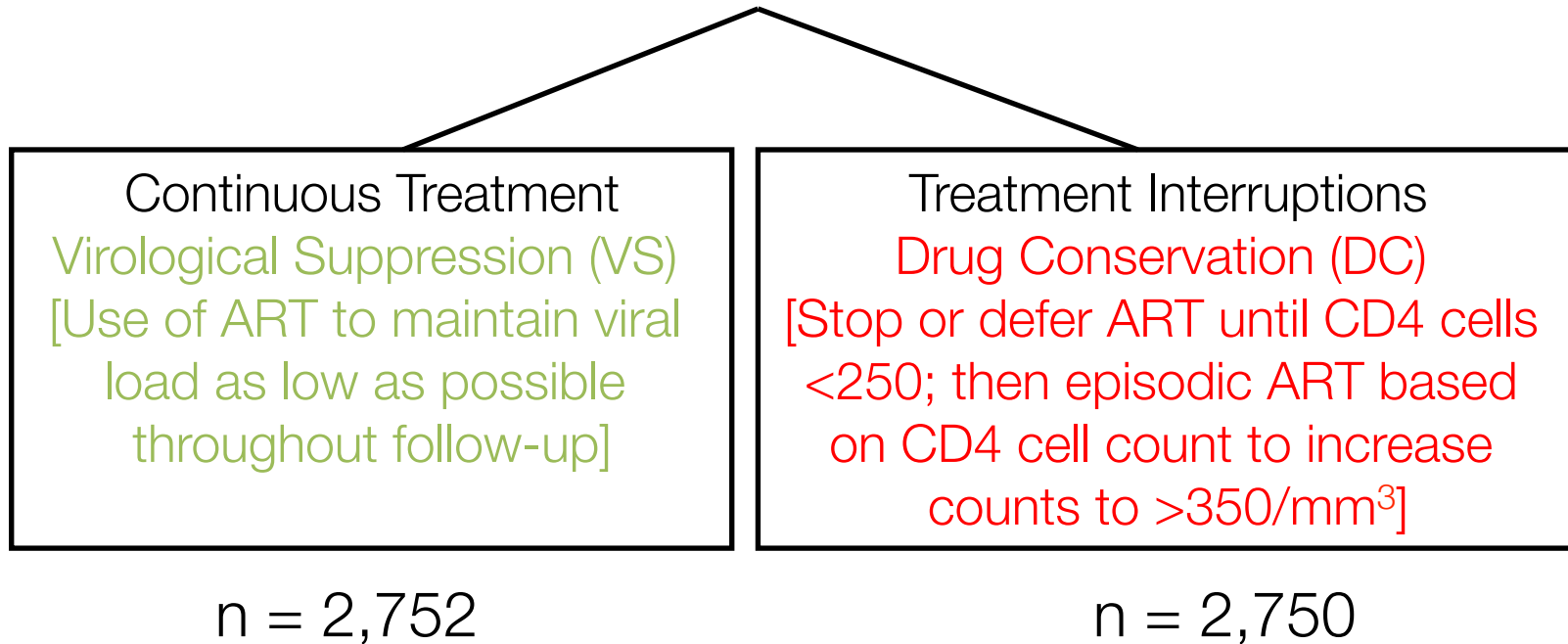
- Inflammation is normally temporary
  - Accompanies immune activation by acute infections, such as rhinovirus (common cold) and influenza (the flu)
  - Intended to deliver fluid, proteins, and cells from the blood to damaged tissues
  - Causes numerous vascular, cellular, and metabolic changes, leading to symptoms
  - Once infection is cleared, immune activation and inflammation subside

# Background

- Inflammation can also be ongoing
- Accompanies continuous immune activation by chronic infections
  - HIV, herpes viruses (e.g., CMV), hepatitis C
- When ARV treatment suppresses HIV, immune activation and inflammation subside, but not completely
  - Also documented in long-term nonprogressors (LTNPs)

# SMART and Inflammation

CD4 cell count  $>350$  cells/mm<sup>3</sup>



Strategies for Management of Antiretroviral Therapy (SMART) trial

- Median ages: 44 in VS group; 43 in DC group
- Median pre-SMART ART: 6 years in both groups

# SMART & Inflammation

- Risk of illness and death doubled in DC group
- Few classic AIDS-related illnesses (~8%)
- Main contributors:
  - Cardiovascular disease
  - Renal (kidney) disease
  - Hepatic (liver) disease

# SMART & Inflammation

- Certain blood markers were predictive of death in SMART:
  - Increased D-dimer (associated with blood coagulation and clots)
  - Increase IL-6 (an inflammatory chemical messenger, or cytokine)
- Treatment interruption was linked to significant increases of both markers
  - Markers also elevated with treated HIV vs. comparable HIV-negative cohort
- Both markers linked to cardiovascular disease in HIV-negative people

# Summary

- SMART, among other studies, demonstrates inflammation predicts poor health in PLWHIV
  - Consistent with HIV-negative findings
- Inflammation and its association with illness and death has been confirmed in younger cohorts of PLWHIV, compared with similar associations usually seen in non-HIV patient populations