**Background**

- The number of circulating CD4+ T lymphocytes in patients with human immunodeficiency virus is the most robust predictive factor for assessing HIV disease stage, predicting progression to clinical AIDS and AIDS-related death, determining antiretroviral treatment eligibility, and monitoring response to therapy.
- After a variable period of ART, the CD4+ T-cell count can reach a value that ensures protection against opportunistic infections – classically more than 200 × 10^6 cells/l. The kinetic and the magnitude of CD4+ T recovery is extremely variable among ART treated subjects.
- Two particular populations have been described:
  - The ‘CD4-exploders’ (CD4e), defined as people gaining a large amount of cells under a defined time;
  - The ‘CD4 peak achievers’ (CD4a), who reach a very high level of CD4+ T cells.
- The ‘CD4-exploders’ have been shown to display a high amount of virgin T cells and a reduced number of T cells with a phenotype typical of lymphocytes with an increased tendency to undergo cell activation/death (Musini et al. 2000).
- The ‘CD4-exploders’ have been shown to have significantly higher plasma levels of IL-7, a cytokine with a crucial importance for the generation and survival of T cells. In some studies high amount of IL-7 has shown to be related to breast cancer, colon cancer, hematological malignancies, autoimmune diseases (such as multiple sclerosis, rheumatoid arthritis) (Kim et al., 2008).
- Moreover Bonnard described a cluster of patients HIV/HCV coinfected with high CD4 count with a faster fibrosis progression suggesting a potential detrimental role of large CD4 expansion.
- It is important to further characterize these populations and investigate whether such extreme CD4 recoveries might modify persons’ risk of severe non-AIDS (sNAE) or death.

**Aims of the study:**
- Incidence and clinical-demographic features of “CD4 exploder” (CD4e) and “CD4 peak achiever” (CD4a) over suppressive cART in ICONA:
- To evaluate the association between these conditions and the risk of serious non-AIDS events (sNAE) death.

**Study population**

Population: 5,795 Icona HIV+ patients who started cART from naive and achieved/maintained VL<50cp/ml.
- CD4 exploders (CD4e) = gain/maintenance >600 cells/mm3 above pre-cART (n=306);
- CD4 peak achievers (CD4a) = achievement of absolute CD4+1000 followed by at least another consecutive >1000 value (n=249)

**Methods**

- Endpoints: to be a CD4e; to be a CD4a
- Incidence by 3 years of suppressive cART; Kaplan-Meier curves/Cox regression model to identify factors independently associated;
- Endpoint: sNAE (malignancies, cardiovascular, cancer, infection) death
- Survival analysis with T0 3 years from the date of VL suppression comparing the risk of sNAE/death based on the status of CD4e and CD4a.

**Results**

Survival analysis

CD4e and CD4a have been used as covariates in a survival analysis with time 0 years after viral suppression and endpoint time to severe non-AIDS events in people who were still free from non-AIDS cancer at that point. Kaplan Meier curves of time to severe non-AIDS event/death for CD4e and CD4a showed a decreased probability to reach the end point only for CD4e (fig. 3 and 4).

**Conclusions**

Approximately 10% of people have extreme CD4 count recovery by 3 years provided a VL<50 copies/mL. CD4 count response is more likely in those of young age, without HIV infection and who started a PI based therapy. CD4e tended to have a lower risk of sNAE/death independently of CD4a, suggesting that a fast kinetic of immune recovery might be more important than the absolute number achieved.