Abstract #1305

Different Immunologic and Virologic Contexts for HIV-Associated Lymphoma in the CNICS Cohort

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BACKGROUND

- Pathobiology of HIV-associated lymphoma may be changing in the era of effective antiretroviral therapy (ART)
- Lymphoma incidence is increased soon after ART, perhaps due to the immune reconstitution inflammatory syndrome (IRIS)[1-3]

OBJECTIVE

- To describe varying immunologic and virologic contexts for HIV-associated lymphoma in a large multicenter cohort

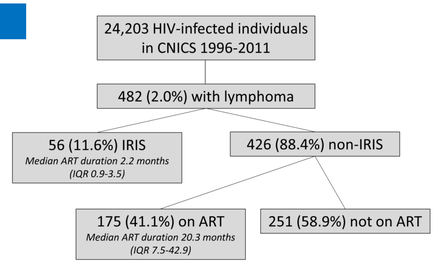
METHODS

- CNICS includes 8 observational HIV cohorts in the US
- Data are collected from patient medical charts and electronic medical records
- Cancer diagnoses are verified via a standardized verification procedure at all sites
- We included all individuals with non-Hodgkin lymphoma (NHL) or Hodgkin lymphoma (HL) between January 1, 1996 and December 31, 2011, and categorized them at lymphoma diagnosis as:
  - Unmasking lymphoma IRIS (on ART ≤6 months with ≥0.5 $\log_{10}$copies/mL reduction in HIV RNA)
  - On ART without IRIS (ART >6 months OR ≤6 months without HIV RNA response)
  - Off ART
- CD4/HIV RNA during the 12 months before and after lymphoma diagnosis were assessed using individual patient-level CD4/HIV RNA curves
- Summative curves were derived by plotting median and interquartile values at each monthly time point across all patients within each group

CNICS SITES



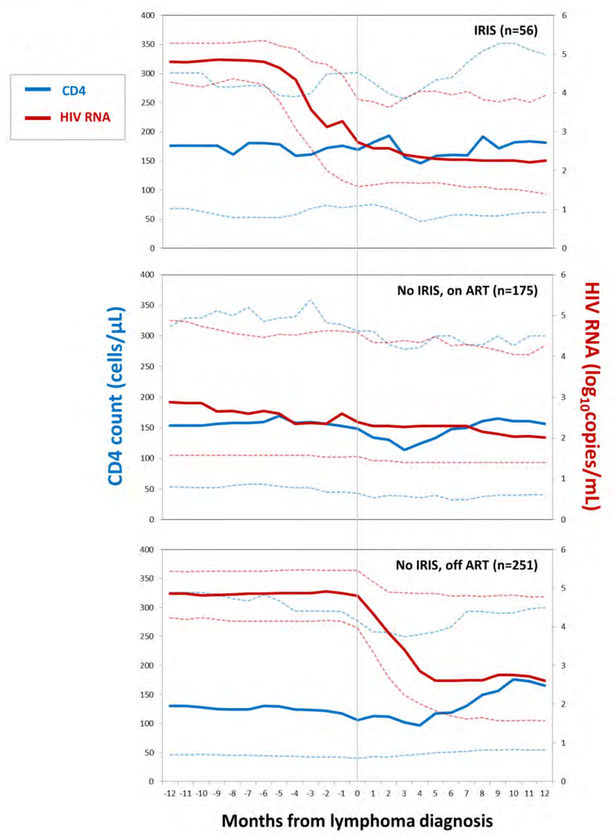
PATIENTS



OTHER RESULTS

- IRIS cases were on ART for a median 2.2 months (IQR 0.9-3.5), and 48% had HIV RNA <400 copies/mL
- Non-IRIS cases on ART were on ART for a median 20.3 months (IQR 7.5-42.9), and 58% had HIV RNA <400 copies/mL
- During the 12 months before and after lymphoma diagnosis, 3439 CD4 measures [median 8 (IQR 5-10) per patient] and 3266 HIV RNA measures [median 7 (IQR 5-10) per patient] were available, with roughly equal distribution before and after lymphoma diagnosis
- IRIS cases demonstrated marked reductions in HIV RNA after ART in the months before lymphoma diagnosis without significant CD4 increases, and modest CD4 increases in the 12 months after lymphoma diagnosis
- Non-IRIS cases on ART demonstrated limited CD4 increases and modest reductions in HIV RNA after lymphoma diagnosis

CD4 & HIV RNA



OTHER RESULTS CONT'D.

- Non-IRIS cases off ART demonstrated robust CD4 increases and reductions in HIV RNA after lymphoma diagnosis, resulting from ART initiation by six months in 79% of patients

LIMITATIONS

- Could not exclude subclinical lymphoma leading to care seeking and ART initiation before lymphoma diagnosis
- Data did not allow reliable characterization of paradoxical lymphoma IRIS

STRENGTHS

- Results from a large and diverse HIV-infected population in routine care, with extensively verified lymphoma diagnoses
- Specific attention to lymphoma IRIS using a uniformly applied case definition, an entity which has not been previously described in detail

CONCLUSIONS

- In the ART era, HIV-associated lymphoma develops in different immunologic and virologic contexts
- These differing contexts may influence histology, biology, and clinical outcomes
- Our previous work has suggested:
  - Lymphoma developing on ART may be associated with worse outcomes even after adjustment for histology and other covariates, suggesting possible biologic differences from lymphoma occurring without ART exposure[4-5]
  - Lymphoma IRIS has similar long-term survival to non-IRIS, but possibly increased early mortality followed by reduced late mortality[6]
- Attenuated CD4 increases soon after ART initiation, despite HIV RNA suppression, might suggest developing lymphoma

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References: 1. Lanoy et al, Blood 2011; 2. Jaffe et al, AIDS 2011; 3. Yanik et al, CID 2013; 4. Gopal et al, JNCI 2013; 5. Gopal et al, AIDS 2013; 6. Gopal et al, ASH Annual Meeting 2013.