

Late diagnosis of HIV-infection

B. Salzberger

Topics

- Definition
- Epidemiology
- Management
 - acute complications
 - initiation of antiretroviral therapy
 - immune reconstitution inflammatory syndrome (IRIS)
- Prevention

Late diagnosis of HIV-infection

- diagnosis of HIV-infection
 - concomitant or close in time with opportunistic complication or
 - with a low CD4-cell count
- how close in time to clinical event?
- CD4-cells how low?

Late diagnosis of HIV-infection

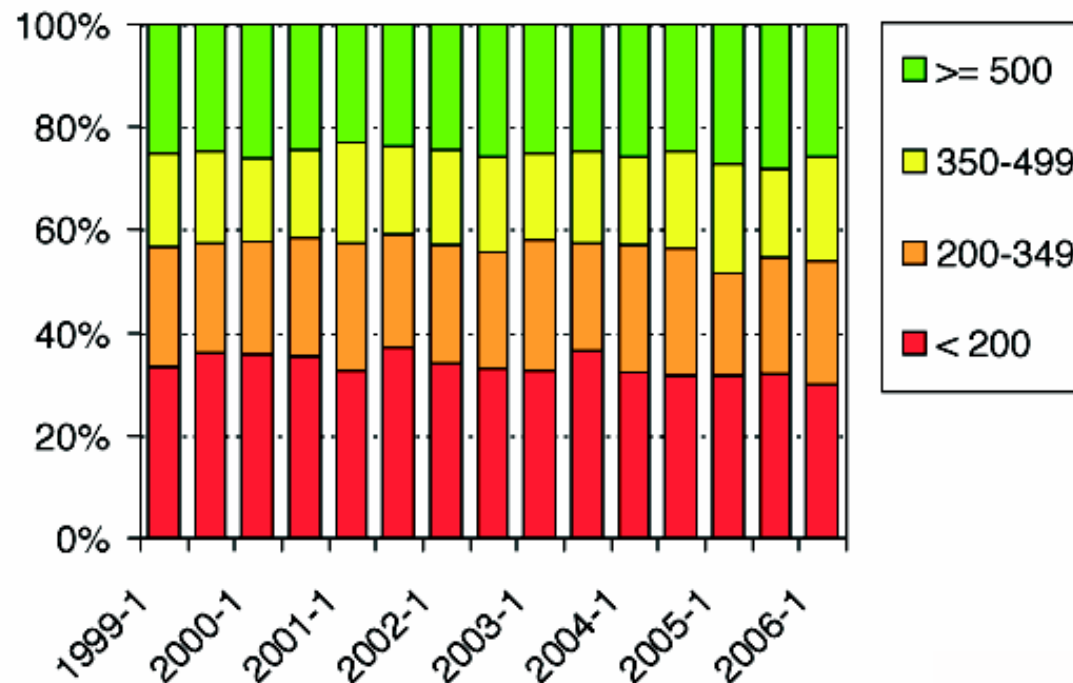
- diagnosis of HIV-infection
 - concomitant or close in time with opportunistic complication or
 - with a low CD4-cell count
- how close in time to clinical event? 3, 6, 12months?
- CD4-cells how low? below 200

How frequent is late diagnosis of HIV?

- different cohorts from Italy, France, UK, Germany
- rate of late HIV-diagnosis relatively uniform 25-40%
 - risk factors
 - migrants
 - women
 - age < 30 or age >50
 - unknown or not reported risk of transmission
 - heterosexual men, living in long-term relationships

Late diagnosis in Germany

- 682 AIDS cases 2003-4
 - >50% no ART before AIDS diagnosis
- CD4 cell count at diagnosis of HIV 1999-2006



ClinSurv-Cohort, RKI 2006; Epid. Bull, April 2005

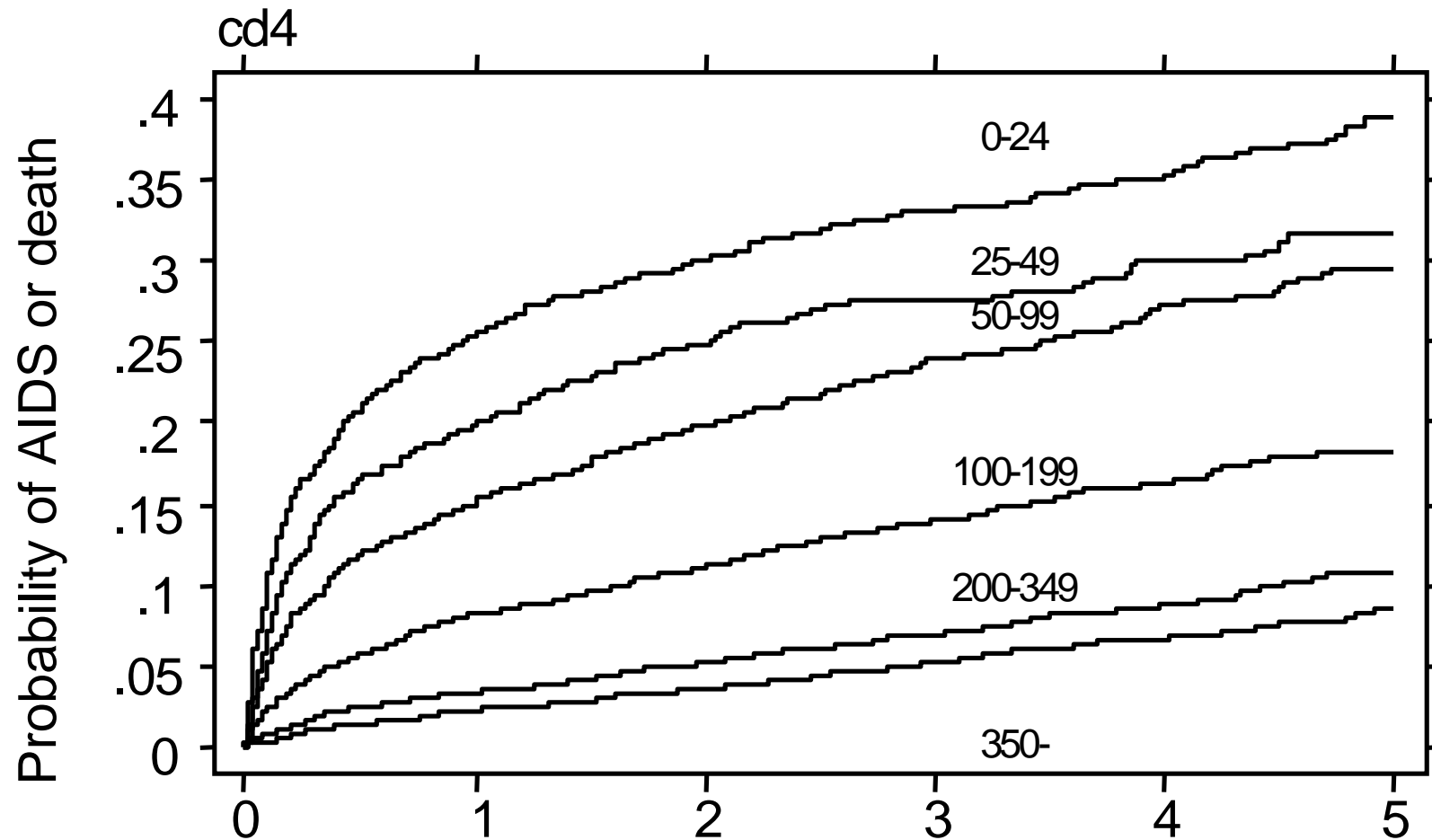
Late diagnosis in UK

- In GB 14000 cases of newly diagnosed HIV-infection between 1993 and 2002 analyzed
 - 31% below 200 CD4/mcl, positive trend to 25% 2002
 - late diagnoses mainly outside London, higher age, non caucasian origin
 - one year mortality with late diagnosis 14 vs. 1%, down to 9,9 vs. 0,5% 2001

Are there consequences of late HIV-diagnosis?

- lower rate of viral suppression if ART is started late
- higher rate of opportunistic infections until immune reconstitution is sufficient
- higher rate of adverse effects of ART, especially when initiated with concurrent OI-therapy
- higher rate of immune reconstitution syndrome
- higher mortality

Clinical events after starting HAART by initial CD4-cell count



Case 1

- 28yo male



Case 1

- Patient with multiple cutaneous nodules, biopsy reveals Kaposi´s-sarcoma, HIV-test positive
- CD4-cell count 230/mcl, Viral load 260.000 copies/ml
- history of repeated deep vein thrombosis and pulmonary embolism - on long-term cumarin-therapy
- Late diagnosis?
- How to treat?

Case 1

- Chance of remission with antiretroviral therapy, so no initial anti-Kaposi therapy
- started on LPV/r + ZDV + 3TC, because of case reports of remission of KS in patients treated with PI-based HAART
- Viral load suppressed, lesions blanching
- effective anticoagulation not possible, even with 4 tbls Cumarin/d
- what to do?

Case 1

- Switched to EFV+ZDV+3TC
- good response in CD4-cell-count, good progress with remission of KS
- now for 3 years below limit of detection, complete remission of KS

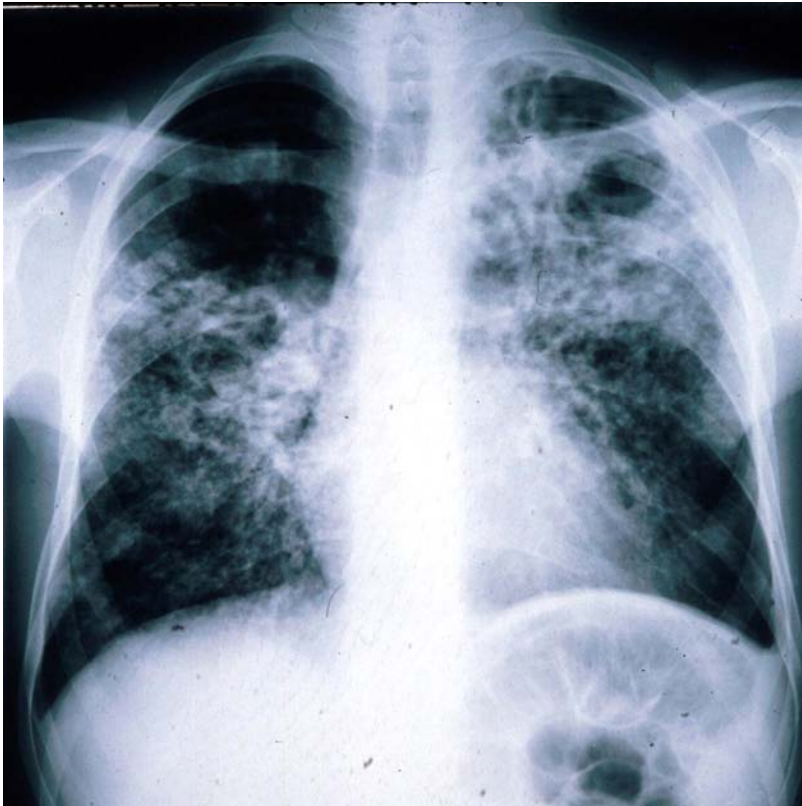
Case 2

- 43yo male, interstitial pneumonia not responding to empiric therapy with fluorquinolones
- in bronchoscopy *Pneumocystis jirovecii*, HIV-positive
- rapidly deteriorating respiratory function
- initiate ART concomitant to OI-therapy?

Case 2

- No data if concurrent ART is helpful in acute OIs
- potential for adverse drug reactions, complication clinical management
- therefore rather withhold ART in acute OI?

Case 3



- 28yo female, recently immigrated from Ukraine
- fever, generalized lymphadenopathy and pulmonary infiltrates
- smear positive for AFB
- culture growing *M. tuberculosis*

Case 3

- HIV+, HCV+
- Viral load 120.000 copies/ml, CD4-cell count 80/mcl
- How to treat?

Key questions in HIV- TBC

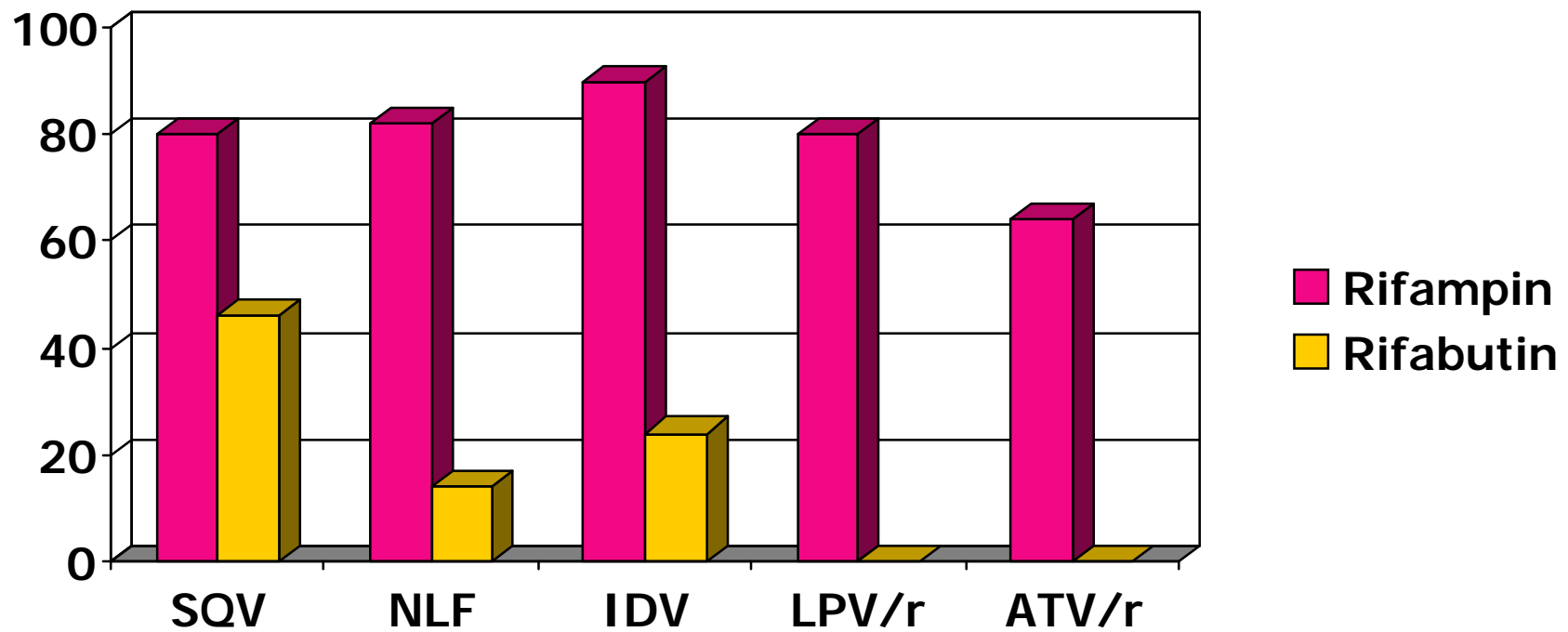
- how to treat TBC?
- when to start highly active antiretroviral therapy (HAART)?
- which HAART?
 - adverse effects
 - interactions with TB treatment

Which TBC treatment?

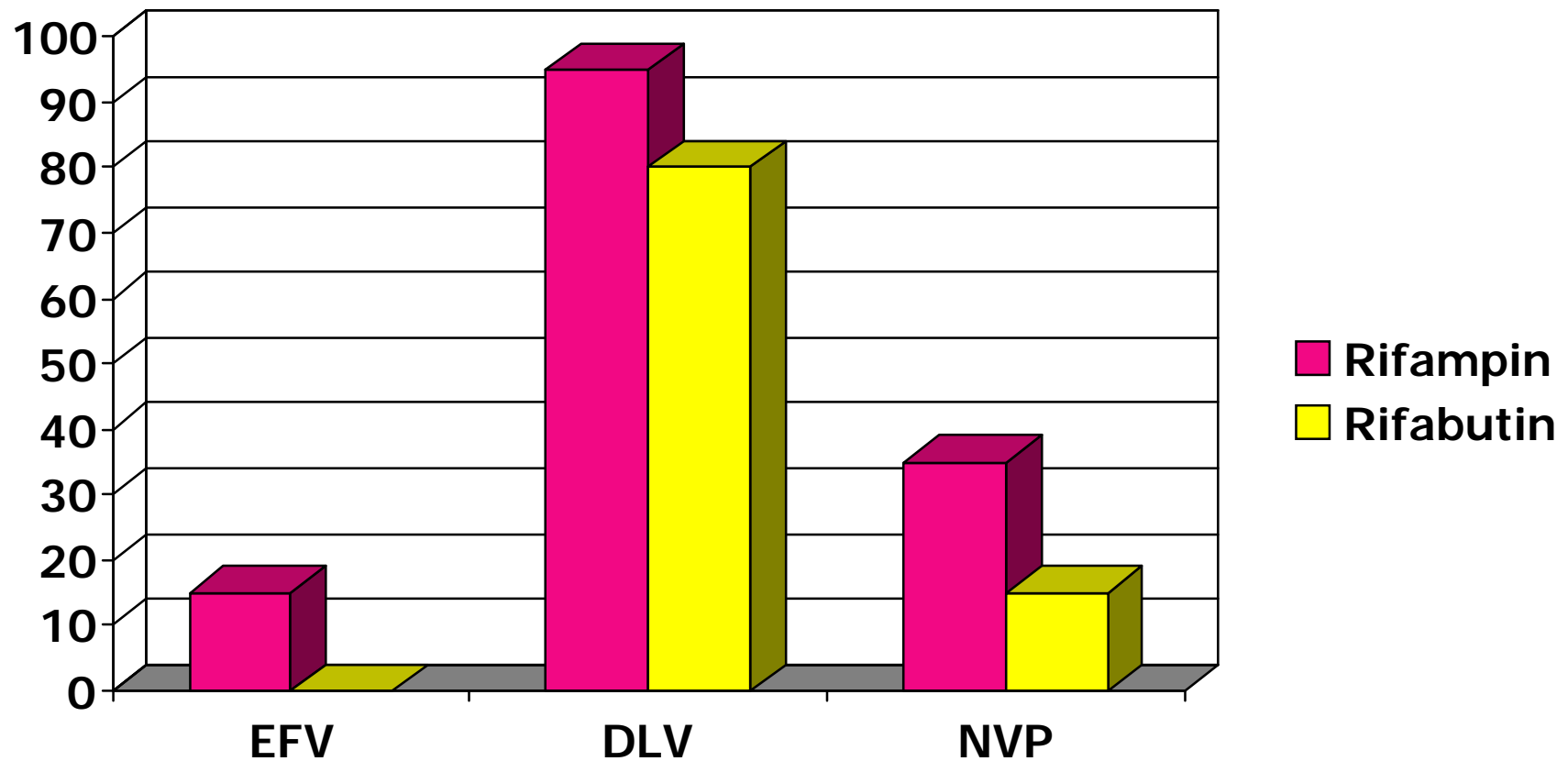
- standard regimen
 - 2 months: INH, RIF, EMB, PZA
 - 4 months: INH, RIF
 - directly observed therapy (DOT)
- rifamycins crucial for success of short- term TBC treatment (6 months)
- which rifamycin?
 - rifampicin
 - rifabutin

Rifampin, Rifabutin and PIs

Decrease in Serum-AUC of PIs



Rifampin, Rifabutin and NNRTIS



**What is the best time to start HAART
in a patient with HIV/ TBC?**

Use of antiretroviral therapy during Tb-infection

- CD4-cell count at diagnosis of Tb
 - <200 start during Tb-therapy
 - 200-350 monitor, start if CD4 declines rapidly
 - >350 monitor,

TB/HIV Co-Infection: Treatment Considerations

- In patients on ARV therapy, evaluate ARV regimen for interactions with TB drugs
- In ARV-naive patients, avoid simultaneous initiation of treatment for TB and HIV
 - consider delay of ARVs for 4-8 weeks after initiation of TB treatment to avoid overlapping of adverse reactions and paradoxical reactions

Case 4

- 44yo male, husband of case 4
- Pleural tuberculosis 2 months after diagnosis of tb in spouse
- HIV+, CD4+cell count 440/mcl, VL 80.000 copies/ml
- How to treat?

Case 5



- 37yo male patient with fever and enlarging lymph nodes after 2 months of HAART and TBC treatment
- Is this clinical deterioration
- what are the likely causes?
- how to manage?

Case 4

- Likely causes for deterioration
 - resistance (HIV/Tb)
 - non- adherence (HIV/Tb)
 - superinfection
 - **immune reconstitution syndrome (IRS)**
- How to manage IRS in TB/HIV-coinfection?
 - continuation of TBC treatment
 - consider stop of ART
 - consider cortisone

IRIS

- worsening of preexisting clinical condition after starting ART
- pathogenesis?
- broad spectrum of conditions with IRIS
 - mykobacterial infections
 - PCP, PML
 - infections with Herpesviruses (CMV, VZV, genitale HSV, Kaposi Sarkome)
 - hepatitis B flare
 - cryptococcosis, Histoplasmosis
 - Parvo B19, Graves´ disease, lung cancer..

IRIS

- with anti-tuberculosis therapy reported
 - paradoxical reaction with initial or delayed worsening after starting therapy
 - absceding and growing lymphadenopathy
 - enhanced inflammation with tuberculos meningitis, CNS-tuberculomas with focal neurologic deficits treated successfully with steroids
- reversion of specific immunosuppression with initial imbalance?

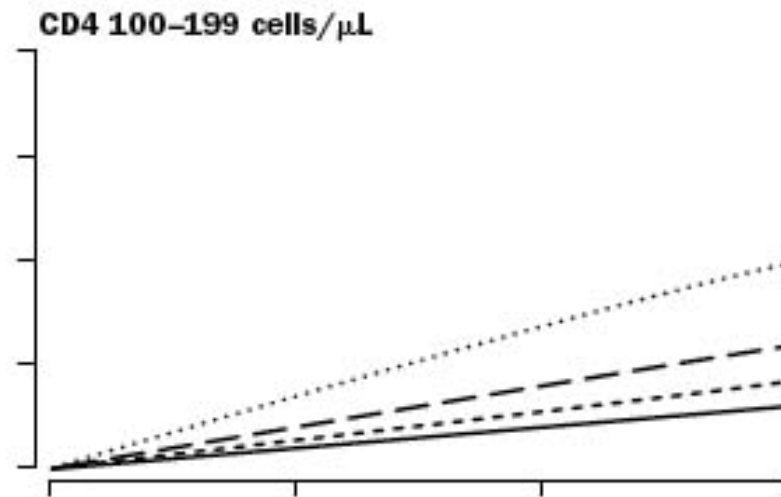
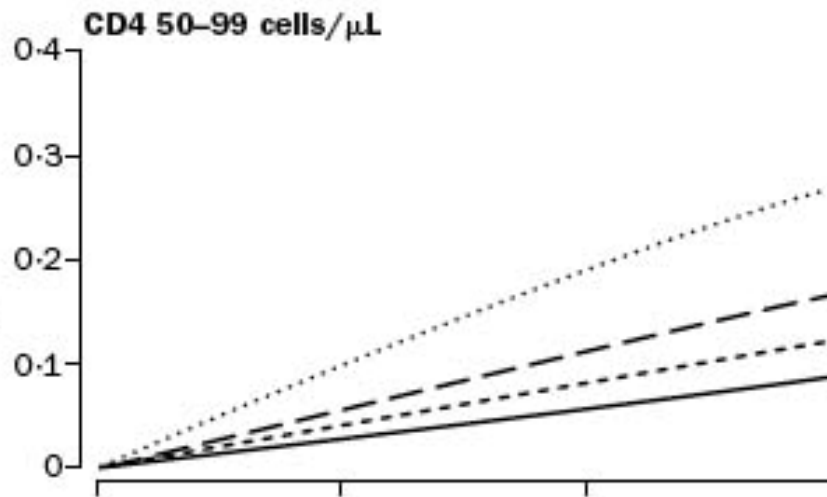
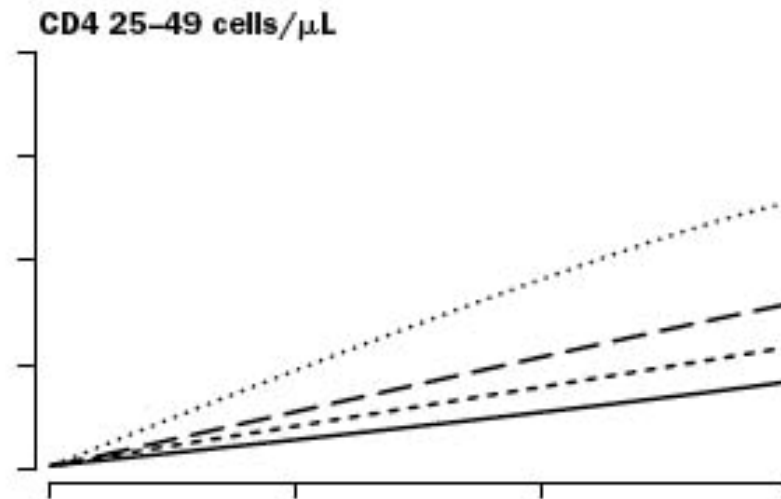
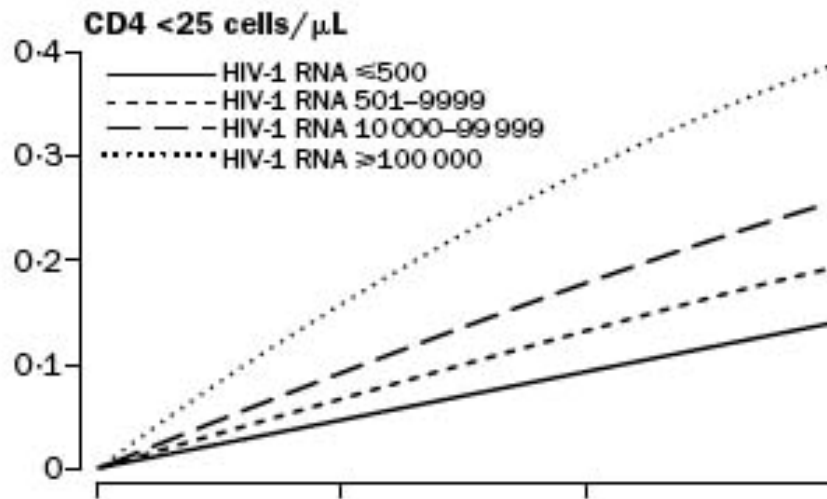
IRIS-Epidemiology

- Frequency
 - 10-25%
 - in a small London cohort 23%
 - depending on
 - prevalence of infections
 - CD4-cell-nadir?
- risk factors
 - younger age
 - low CD4-cell count

Pathogenesis IRIS

- pathogenesis largely unknown
- antigen-specific immune responses enhanced or diminished ?

the good news.... all is forgotten after 6 months of therapy



ART-CC, LANCET 2005

the bad news - prevention

- population at risk is difficult to target
 - not a group with „one denominator“: e.g. gay men, drug users
 - risk of infection not acknowledged

Conclusion

- late diagnosis of HIV is common, risk factors are known
- patient populations difficult to target for prevention
- clinical problems in late HIV-diagnosis
 - time to immune reconstitution crucial
 - concurrent management of acute opportunistic infections and ART
 - immune reconstitution syndrome