



Drop in CD4+ counts below 200 cells/ μ L after reaching (or starting from) values higher than 350 cells/ μ L in HIV-infected patients with virological suppression

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Disclosure of potential conflicts of interest

- Nicola Gianotti
 - Has been advisor for Gilead Sciences, AbbVie and Janssen-Cilag and Merck Sharp and Dohme
 - Had received speakers' honoraria from Gilead Sciences, ViiV, Bristol-Myers Squibb, Merck Sharp and Dohme, Roche, AbbVie, Boehringer Ingelheim, and Janssen-Cilag
 - Had received support for travel meetings from Gilead Sciences, Bristol-Myers Squibb, AbbVie, Janssen-Cilag, Merck Sharp and Dohme, Roche, and ViiV.



Background and Aim

- In HIV-infected people receiving ART, CD4+ count tend to increase or remain stable as long as viral load is ≤ 50 copies/mL.
- CD4+ cells drops below 200 cells/ μL appear to occur infrequently while viral load (VL) is suppressed, but robust estimates are lacking.
- **Aim of the study:** to describe the probability of, and factors associated with, a drop in CD4+ counts below 200 cells/ μL after reaching (or starting from) values >350 cells/ μL while VL remained ≤ 50 copies/mL.



Methods

- We included all ART-naïve participants (pts) enrolled in the ICONA Foundation Study cohort who started cART with:
 - a) **>350 CD4+/ μ L and subsequently achieved a VL \leq 50 copies/mL**
 - or
 - b) **\leq 350 CD4+/ μ L and subsequently reached values **>350 cells/ μ L after achieving and maintaining a VL \leq 50 copies/mL****
- **Baseline** was defined as the date of **achieving a VL \leq 50 copies/mL (group a) or of achieving >350 CD4+/ μ L (group b)**
- All patients had >350 CD4+/ μ L at baseline and at least one additional CD4+ count measure after baseline
- **Primary end-point:** the cumulative risk (Kaplan-Meier estimates) of a CD4+ drop below 200 cells/ μ L after baseline
 - FU was censored at the date of VF (defined as a confirmed HIV-RNA >50 copies/mL), death or last clinical visit.
- Factors independently associated with a confirmed CD4+ drop below 200 cells/ μ L were identified by a multivariable **Cox regression model**.



Results

- **5,941 patients** included in the analysis.
- Median (IQR) follow-up: **3.7 (1.7, 7.6) years.**



Main characteristics of patients according to CD4 count at ART start (1)

	CD4+ count at ART start (cells/ μ L)			
	>350 (n = 2309)	\leq 350 (n = 3632)	<i>p-value</i>	Total (n = 5941)
Age, years, median (IQR)	40 (34, 46)	40 (34, 46)	0.649	40 (34, 46)
Females, n(%)	529 (22.9%)	946 (26.0%)	0.006	1475 (24.8%)
Not Italian nationality, n(%)	215 (9.3%)	463 (12.7%)	0.002	678 (11.4%)
AIDS diagnosis, n(%)	98 (4.2%)	656 (18.1%)	<.001	754 (12.7%)
HCVAb, n(%)			0.006	
<i>Negative</i>	1613 (69.9%)	2402 (66.1%)		4015 (67.6%)
<i>Positive</i>	442 (19.1%)	814 (22.4%)		1256 (21.1%)
<i>Not tested</i>	254 (11.0%)	416 (11.5%)		670 (11.3%)
Calendar year of baseline, median (IQR)	2010 (2003, 2013)	2008 (2002, 2012)	<.001	2009 (2002, 2012)

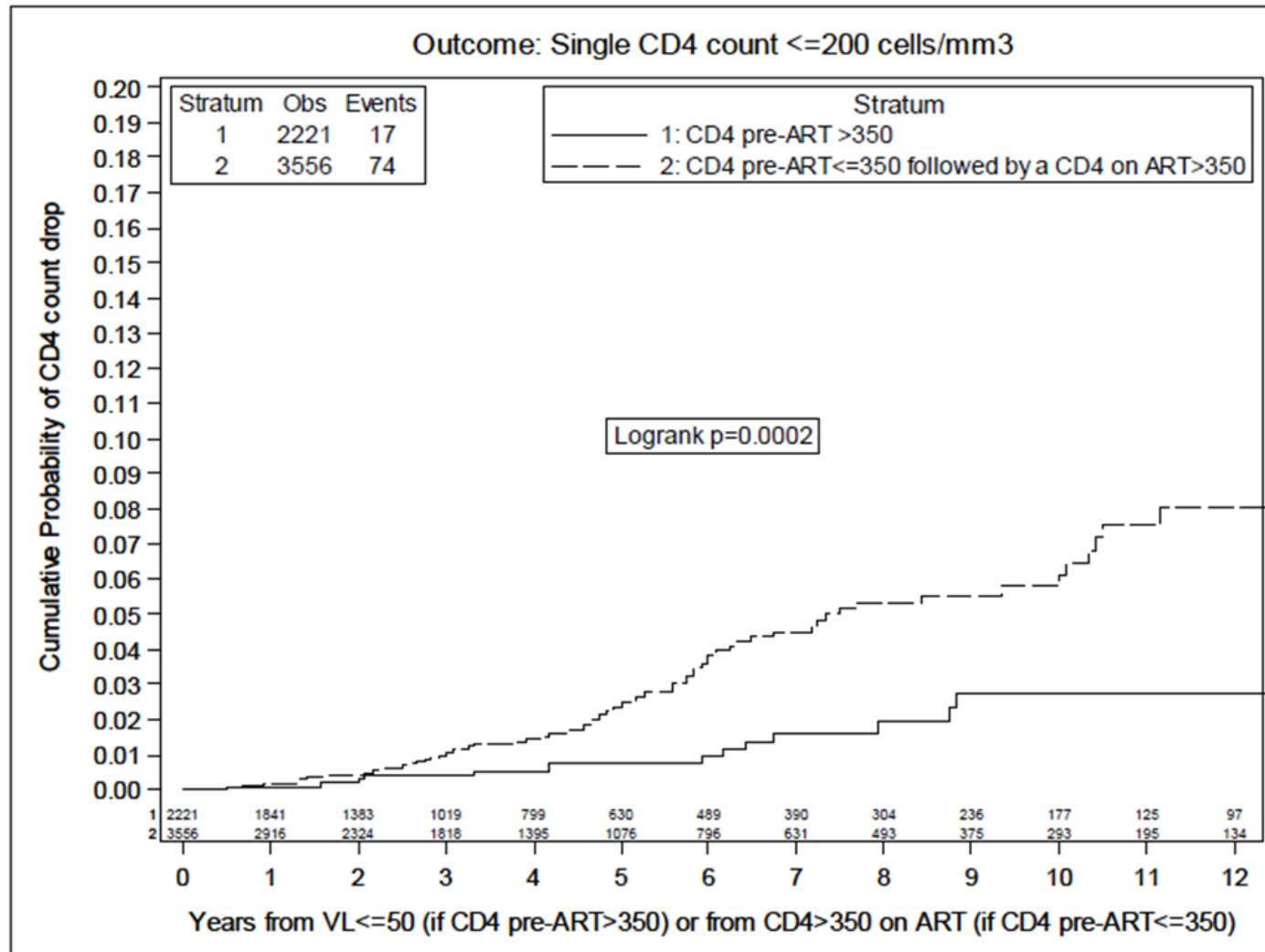


Main characteristics of patients according to CD4 count at ART start (2)

	CD4+ count at ART start (cells/ μ L)			
	>350 (n = 2309)	\leq 350 (n = 3632)	<i>p-value</i>	Total (n = 5941)
CD4+ count, cells/ μ L, median (IQR)	660 (539, 836)	425 (384, 490)	<.001	481 (403, 638)
CD8+ count, cells/ μ L, median (IQR)	943 (695, 1255)	942 (684, 1281)	0.724	942 (687, 1267)
CD4+/CD8+ ratio \leq 0.3	85 (3.8%)	589 (16.9%)	<.001	674 (11.8%)
Viral load, log ₁₀ copies/mL, median (IQR)	1.60 (1.40, 1.70)	1.70 (1.60, 2.51)	<.001	1.70 (1.58, 2.00)
Time from HIV diagnosis to baseline, months, median (IQR)	47 (20, 101)	32 (12, 86)	<.001	38 (15, 93)
Type of ART started			<.001	
2 NRTIs+ NNRTI	1007 (43.6%)	1175 (32.4%)		2182 (36.7%)
2 NRTIs+ PI	448 (19.4%)	933 (25.7%)		1381 (23.2%)
2 NRTIs+ PI/r	460 (19.9%)	779 (21.4%)		1239 (20.9%)
Other	394 (17.1%)	745 (20.5%)		1139 (19.2%)



Cumulative risk of CD4+ drop below 200 cells/ μ L (single value)



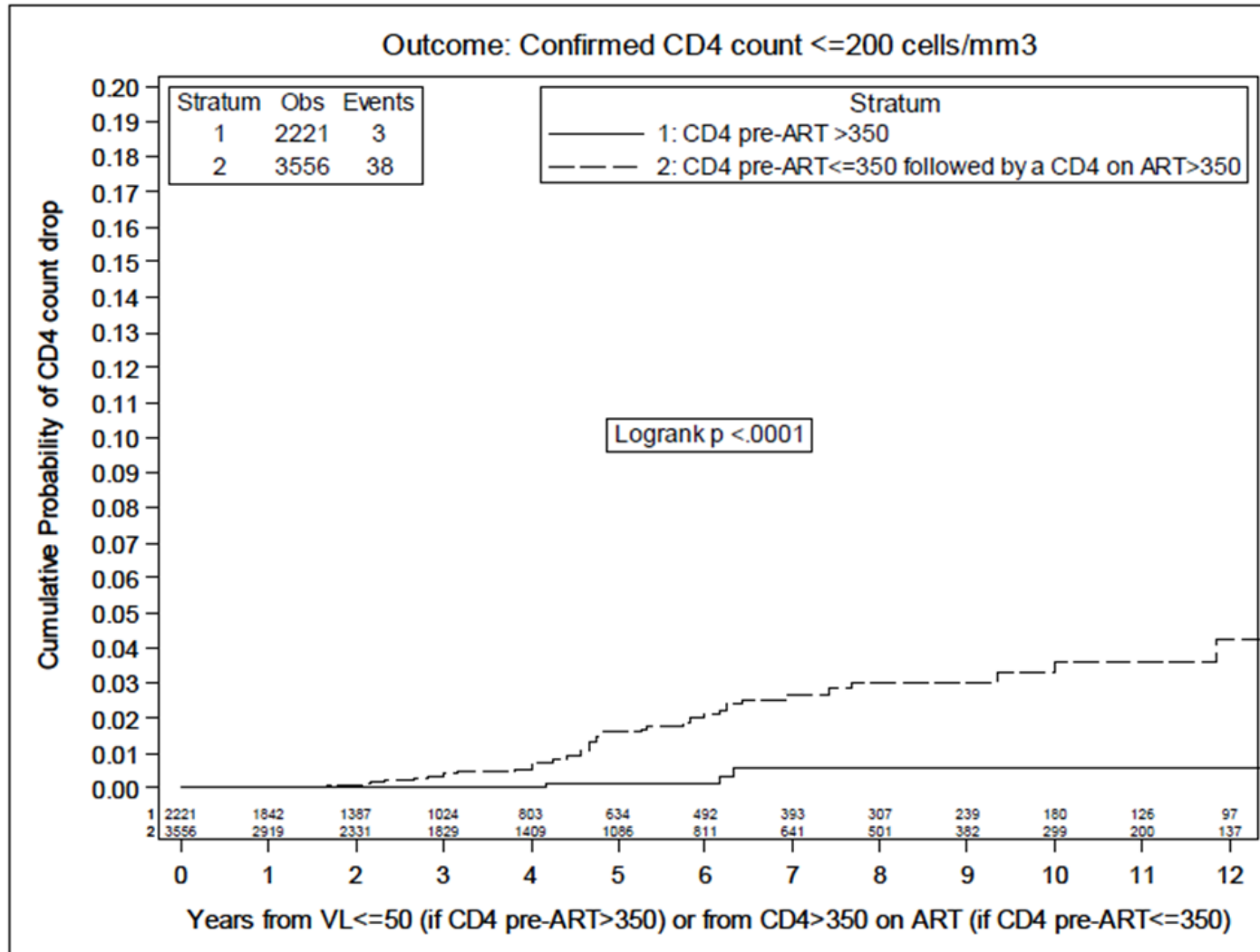


Estimated risk of CD4+ drop below 200 cells/ μ L (two consecutive values) according to CD4+ at starting cART

	KM estimates (95%CI) of confirmed CD4+ drop below 200 cells/ μ L	
	<i>pre-ART CD4+ \leq350 cells/μL</i>	<i>pre-ART CD4+ >350 cells/μL</i>
4-year	0.7% (0.3%, 1.1%)	0.1% (0.0%, 0.4%)
8-year	3.0% (1.9%, 4.1%)	0.6% (0.0%, 1.2%)
12-year	4.3% (2.4%, 6.1%)	0.6% (0.0%, 1.2%)



Cumulative risk of CD4+ drop below 200 cells/ μ L (two consecutive values)





HRs from fitting a multivariable Cox regression model

	HRs of confirmed CD4+ drop below 200 cells/ μ L from fitting a Cox regression model	
	<i>Unadjusted</i>	<i>Adjusted*</i>
Baseline CD4+ count		
per 100 cells/ μ L higher	0.54 (0.37, 0.76)	0.61 (0.40, 0.92)
<i>p-value</i>	<i><.001</i>	<i>0.02</i>
Year of baseline		
per more recent year	0.75 (0.67, 0.83)	0.74 (0.63, 0.86)
<i>p-value</i>	<i><.001</i>	<i><.001</i>

*Adjusted for CD4+ count at ART start (>350 vs. \leq 350 cells/ μ L), gender, years from HIV diagnosis, AIDS at baseline, nadir CD4+ count, CD4+/CD8+ ratio, pre-ART viral load, HCV-Ab test result, type of cART started (NNRTI- vs. PI- or other class- based). None of these were independently associated with the outcome

Results were similar when we defined CD4+ drop below 200 cells/ μ L using a single count.

To be done

- Review concomitant treatments and clinical events occurred around CD4+ drop
 - IFN/RBV?
 - Lymphoma?
 - Chemo/radiotherapy?
 - Immunosuppressive therapy?
 - Other?



Conclusions

In virologically suppressed pts who started ART with >350 CD4+/ μ L, or reached >350 CD4+/ μ L after VS

- A confirmed CD4+ drop below 200 cells/ μ L was very rarely observed over the first two years of FU.
- In the worst scenario (upper 95% limit in people who started cART with ≤ 350 cells/ μ L), the probability of a confirmed CD4+ drop below 200 cells/ μ L at 12 years was 6.1%.
- Pts who started ART in less recent years and those with lower BL CD4+ counts were at higher risk of CD4+ drop below 200 cells/ μ L despite VS.



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