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# Outcomes of second line antiretroviral therapy in HIV-infected patients: data from the ICONA cohort

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on behalf of the ICONA Foundation study group

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## Disclosure of potential conflicts of interest

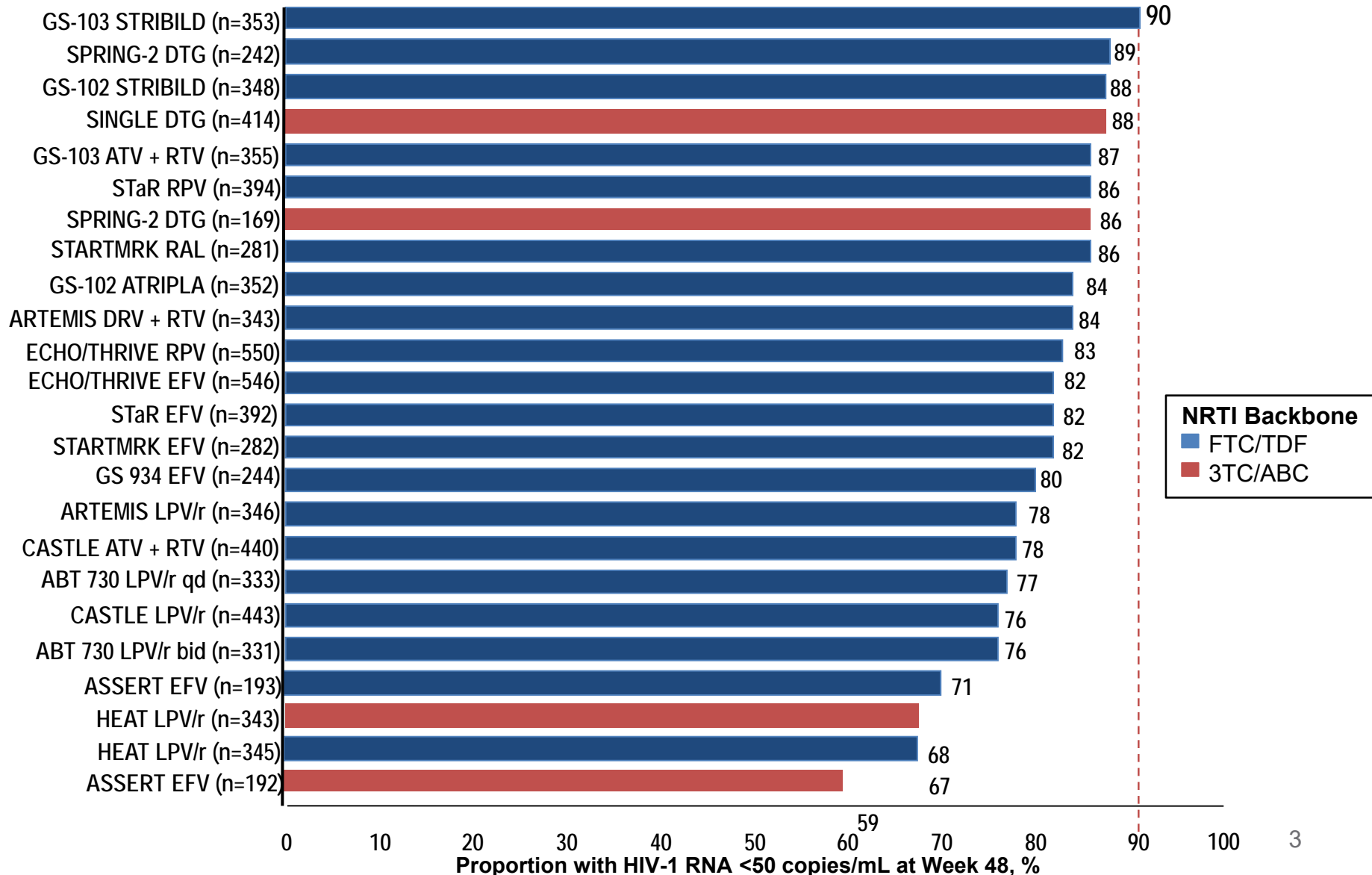
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- Has been advisor for Gilead, AbbVie, BMS, and Janssen-Cilag and MSD
- Had received speakers' honoraria from Gilead, ViiV, BMS, MSD, AbbVie, and Janssen-Cilag
- Had received support for travel meetings from Gilead, BMS, AbbVie, Janssen-Cilag, MSD, and ViiV
- Had received grant for research from Gilead and ViiV

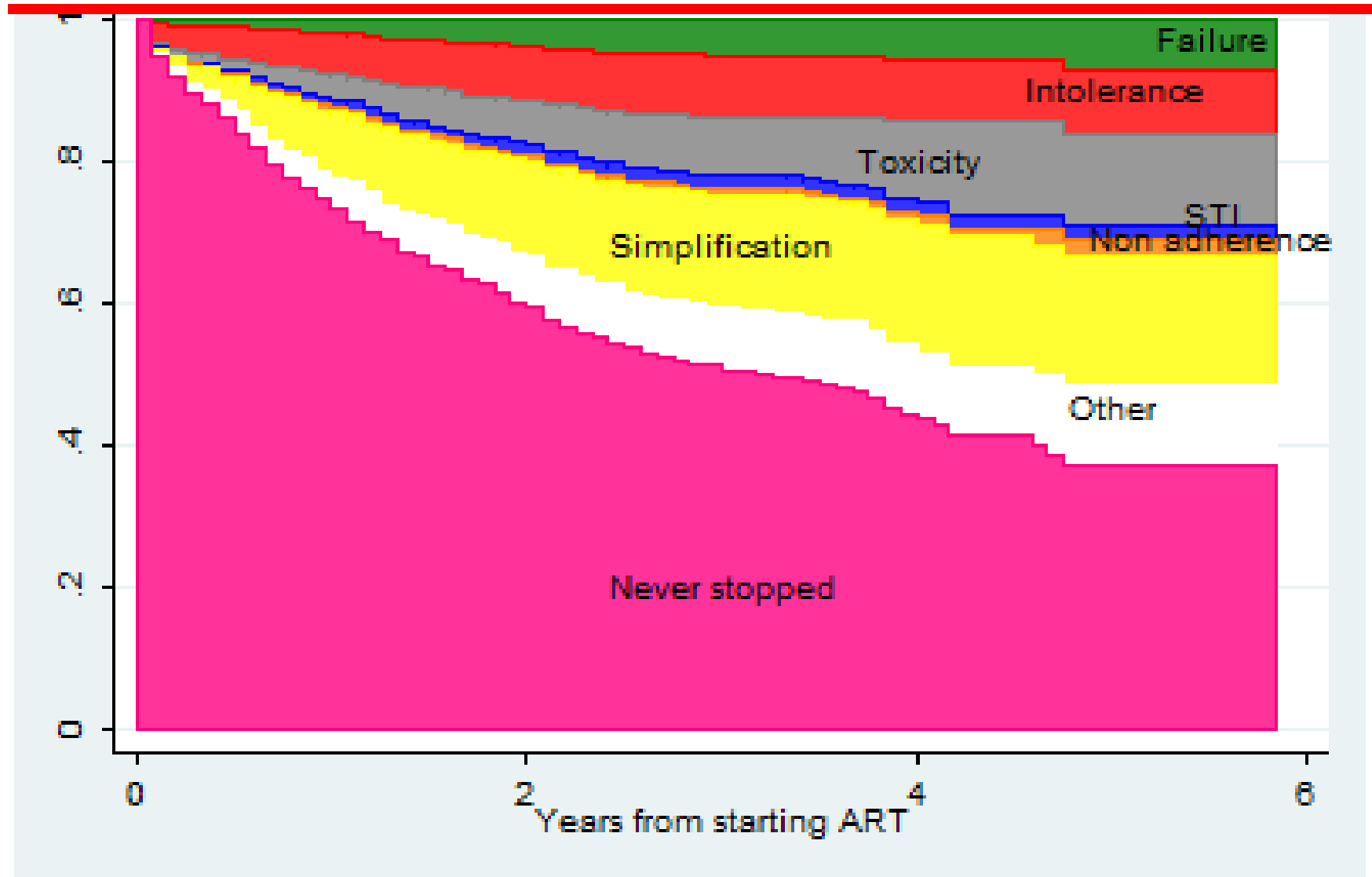
## Treatment-Naive Clinical Trials: Historical Data\*

# <50 c/mL HIV RNA at Week 48

\*This slide depicts data from multiple studies published from 2004-2013. Not all regimens have been compared head-to-head in a clinical trial



# Cause di discontinuazione della prima linea HAART nel periodo 2008-2014



# AIM OF THE STUDY

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## Setting:

**HIV-1 infected patients fully responsive to first-line cART**

## To evaluate:

- **Treatment failure of second line cART**
- **Predictive factors of failure**

# Patients & Methods

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- Start 1st-line cART from Jan 2008 in ICoNA
- Switch to the 2<sup>nd</sup>-line regimen with HIV-RNA <50 copies/mL
- 2nd-line treatment failure was defined
  - The first HIV-RNA  $\geq$  200 copies/mL
  - Discontinuation of any drug
- Factors associated with treatment failure were evaluated with multivariable Cox regression which retained significant factors ( $p < 0.05$ ) at univariable analysis. K-M was used to estimate treatment failure probability.
- Variables analyzed were: gender, age, risk factor for HIV, migrants, CDC stage, CD4 at cART start and at switch, HCV and HBV co-infection, duration of viral suppression at switch, calendar year of switch, type of first-line and second-line regimen, causes of switch.

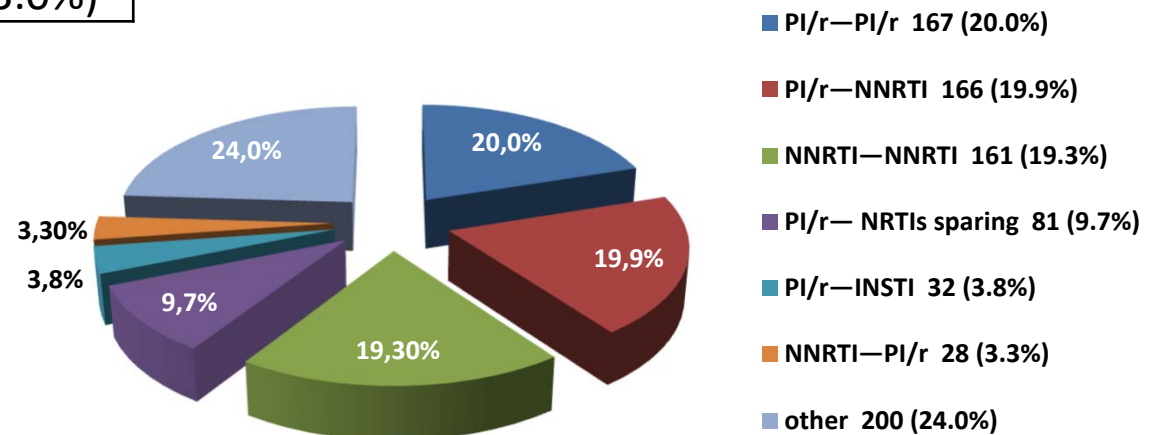
# Characteristics of 835 pts included

Male gender, n(%)	679 (81.3%)
Age, yrs, median (IQR)	41 (34-49)
<b>Mode of HIV transmission, n(%)</b>	
heterosexual	321 (38.4%)
IVDU	52 (6.2%)
homosexual	411 (49.2%)
Other/unknown	51 (6.1%)
CDC stage C at switch., n(%)	91 (10.9%)
<b>CD4 at switch, cell/mmc, n(%)</b>	
0-199	54 (6.5%)
200-349	80 (9.6%)
350-500	164 (19.6%)
500+	449 (53.8%)
missing	88 (10.5%)
<b>HCV Ab, n(%)</b>	
positive	79 (9.5%)
negative	712 (85.3%)
missing	44 (5.3%)
Duration of 1° line, months, median (IQR)	16 (9-26)
Months of viral suppression during first line, median (IQR)	13 (7-24)
<b>Calendar year of switch</b>	
2008-2011	210 (25.1%)
2012-2015	625 (74.9%)
<b>Type of switch</b>	
Change/remove of the backbone	200 (24.0%)
Change of the third drug	530 (63.5%)
Change/remove of the backbone plus change of the third drug	105 (12.6%)

# RESULTS 2

First line: type of regimen, n(%)	
NRTIs+NNRTI	215 (25.8%)
NRTIs+PI/r	479 (57.4%)
NRTIs+INSTI	32 (3.8%)
NRTI-sparing	39 (4.7%)
other	70 (8.3%)
Cause of switch	
toxicity	355 (42.5%)
simplification	274 (32.8%)
other	167 (20.0%)
patient's decision	14 (1.7%)
missing	25 (3.0%)

Second line: type of regimen, n(%)	
NRTIs+NNRTI	368 (44.1%)
NRTIs+PI/r	232 (27.8%)
NRTIs+INSTI	65 (7.8%)
NRTI-sparing	120 (14.4%)
other	50 (5.9%)





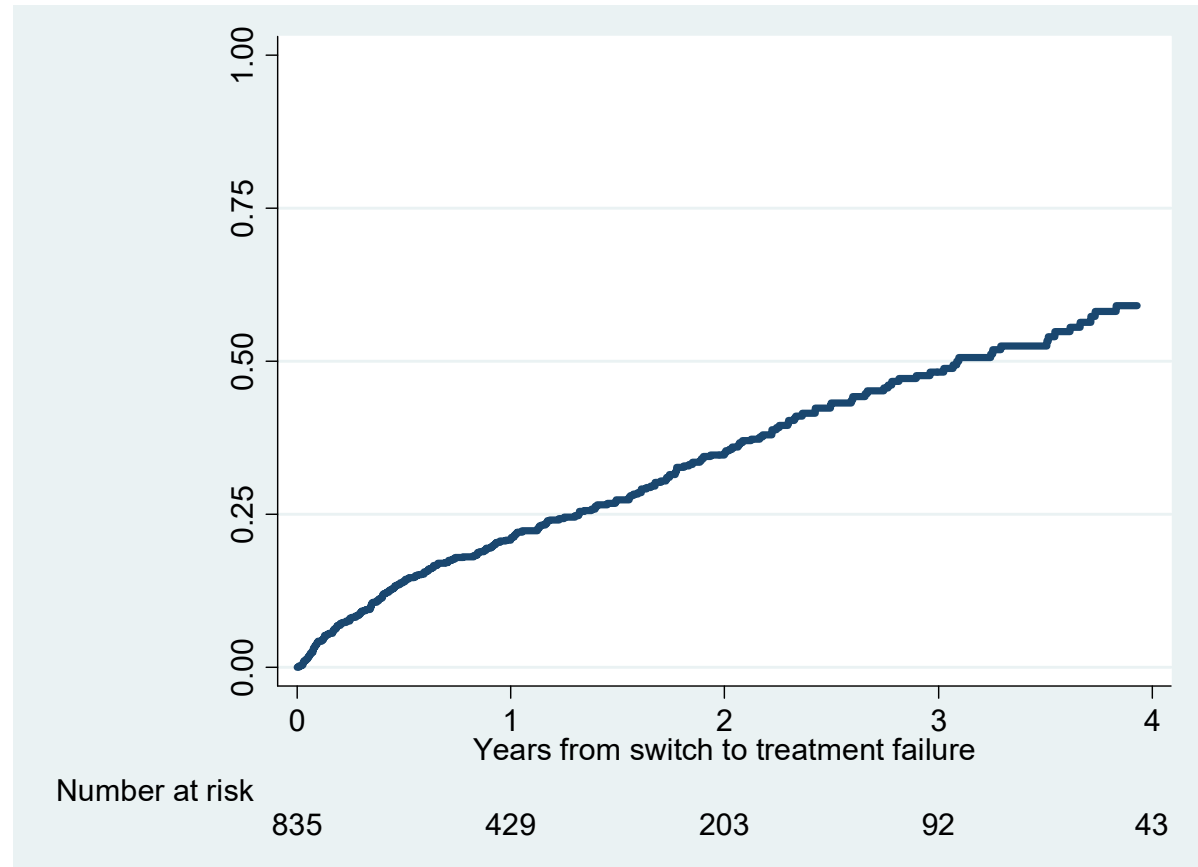
# RESULTS 3

## Kaplan-Meier curve and estimates of the probability of treatment failure

267 subjects experienced treatment failure over a period of 1,144 PYFU

### Treatment failure probability

1-year	21.0% (95%CI 18.1-24.2)
2-years	35.0% (95%CI 31.0-39.3)
3-years	48.2% (95%CI 43.0-53.7)



# RESULTS 4

## Crude and adjusted hazard ratio of treatment failure estimated by Cox regression

	HR	95%CI	P-value	*AHR	95%CI	P-value
<b>Mode of HIV transmission</b>						
heterosexual	1.00			1.00		
IVDU	1.09	0.68 1.73	0.719	0.73	0.41 1.31	0.296
homosexual	0.73	0.57 0.95	0.018	0.69	0.53 0.91	0.009
Other/unknown	0.60	0.33 1.09	0.093	0.46	0.24 0.86	0.016
<b>Type of switch from 1° to 2° line</b>						
nn-nn	1.00			1.00		
pi/r-nn	1.64	1.01 2.66	0.044	1.64	1.00 2.70	0.052
pi/r-pi/r	2.37	1.50 3.75	<0.001	2.18	1.34 3.55	0.002
pi/r-nrti sparing	2.26	1.33 3.83	0.002	2.48	1.38 4.45	0.002
nn-pi/r	2.05	1.05 4.01	0.036	1.93	0.96 3.85	0.064
nn-solo nrti	29.30	8.69 98.78	<0.001	14.64	3.20 66.94	0.001
pi/r-ii	2.14	0.92 4.94	0.076	1.98	0.83 4.71	0.124
other	2.42	1.53 3.83	<0.001	2.37	1.43 3.92	0.001
<b>Cause of switch</b>						
toxicity	1.00			1.00		
patient's decision	3.11	1.45 6.68	0.004	3.35	1.48 7.56	0.004
other	1.04	0.75 1.44	0.803	1.10	0.79 1.53	0.576
simplification	0.99	0.74 1.32	0.941	0.87	0.62 1.22	0.416

\*The model was adjusted also for HCV Ab positivity, CD4 cell count at switch, duration of viral suppression and STR second line.

# CONCLUSIONS

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- **In patients with a previously controlled cART the rate of 2nd-line treatment failure is elevated.**
- **The need for lifelong antiretroviral therapy for HIV infection argues for the use of 2<sup>nd</sup> regimens with the most favourable efficacy and safety profile.**

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