

# **The Prevalence of Cerebrospinal Fluid HIV Escape Varies According to Different Definitions and Underlying Comorbidities**

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Ilaria De Benedetto has no financial relationships  
with commercial entities to disclose

# Background

- Despite suppressive combined antiretroviral therapy (cART) in some individuals CSF HIV-RNA is intermittently detected

Canestri, et al. CID, 2010; Eden, et al. JID 2010, 2016;  
Peluso, et al. AIDS 2012; Rawson, et al. J of Inf, 2012

- Recently the Global CSF HIV-1 Escape Consortium has been established in order to understand mechanisms, pathogenesis and clinical implications of cerebrospinal fluid (CSF) HIV-escape (CSF-E)
- Nonetheless cross-site data reconciliation can be difficult since the prevalence of CSF-E varies among studies with reported frequencies between 0 and 28% according to different HIV-RNA cut-offs, to the high variability of HIV measurement especially at low viral loads and to the inclusion of patients presenting central nervous system (CNS) affections

Joseph, et al. J Virus Erad, 2016; Brambilla, et al. AIDS, 1999;  
Swenson, et al. JCM, 2014; Braun, et al. J Clin Virol, 2017

# Prevalence of Asymptomatic CSF-E

Ref	n	Def	Disorder	Prev	Predictors
<i>Yil08</i>	94	CSF>50 p<50	Asympt	2%	HAART use
<i>Ede11</i>	69	CSF>50 p<50	Asympt	10%	longer cART, >blips, TT interruptions
<i>Cus12</i>	87	CSF>40 p<40	Asympt	6.7%	lower CPE (age, high peak VL)
<i>Let10</i>	842	CSF>50 p<50	No severe Neurol	4%	p HIV RNA, White, Non-adher, lower CPE
<i>Raw12</i>	69	CSF>50 p<50	Mixed	23%	lower CPE
<i>Cal14</i>	84	CSF>50 p<50	Mixed	28.6%	Higher IQs and det NRTIs
<i>Pin15</i>	151	det CSF CSF>1 Log <sub>10</sub>	No Neurol Dis	12.5%	Male, higher CD4, ABC/3TC use
<i>Nig16</i>	40	CSF 0.5 Log <sub>10</sub> >p	Asympt	18%	1 or > episodes of detectable pl HIV RNA
	43		Mixed	0%	
<i>DiC18</i>	38	det CSF CSF>0.5 Log <sub>10</sub>	25 HAND, Mixed	5.3%	Detectable plasma HIV RNA and RAMs

Eden A, et al. JID 2011; Letendre S, et al. CROI 2010; Cusini A, et al. JAIDS 2012; Rawson T, et al. J of Inf 2012; Calcagno A, et al. CID 2014; Pinnetti C, et al. CROI 2015; Nightingale S, et al. JNV 2016; DI Carlofelice M, et al. HIV Medicine 2018

# Objectives

To compare the prevalence of CSF-E in cART-treated patients according to different definitions and underlying comorbidities

# Materials and methods

Retrospective observational study conducted from 1993 to 2018

## Inclusion criteria

HIV-positive cART-treated patients with available plasma and CSF HIV-RNA

### CSF-E definitions

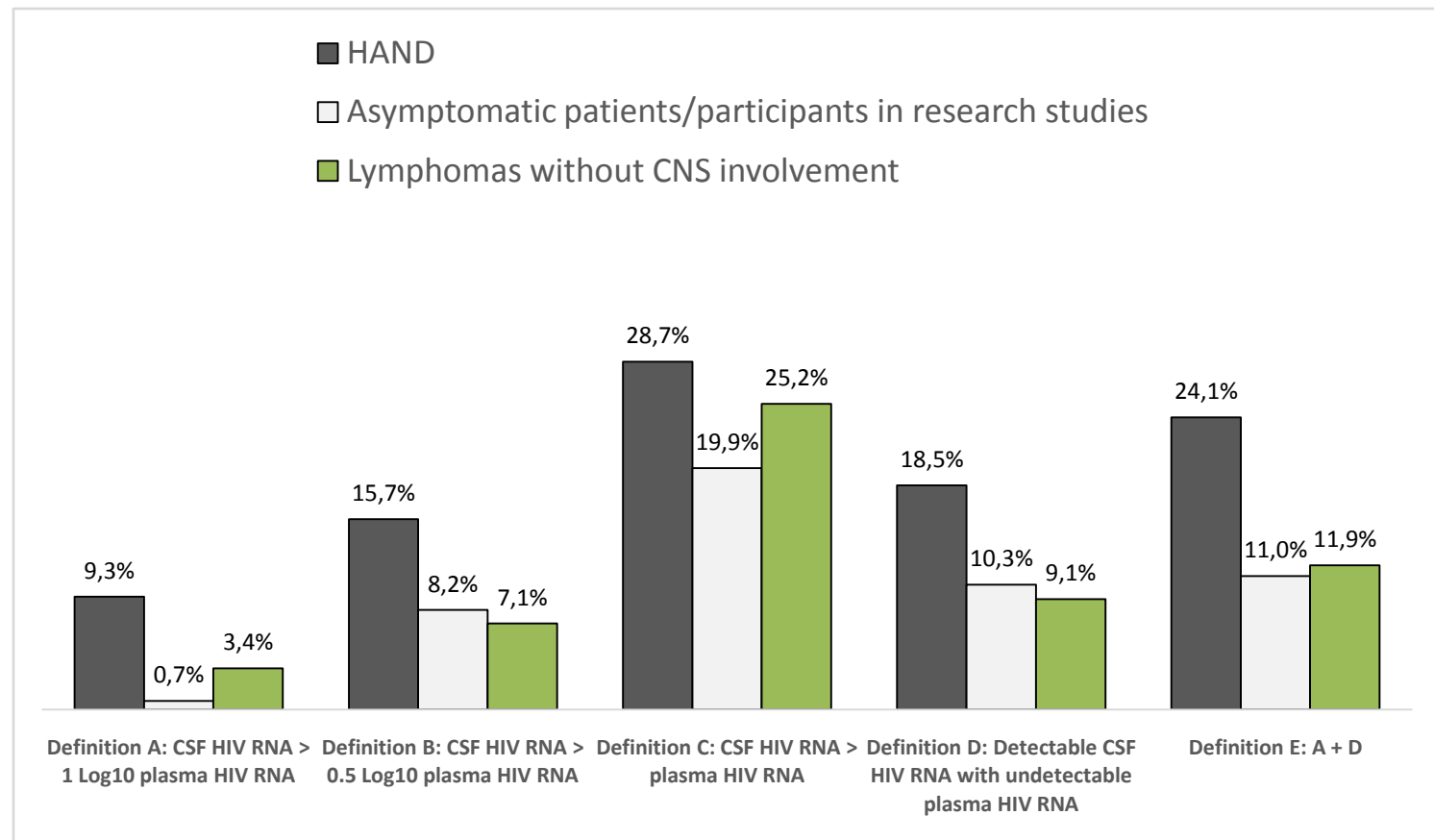
- CSF HIV-RNA 1  $\text{Log}_{10}$  higher than plasma HIV-RNA (**Definition A**)
- CSF HIV-RNA 0.5  $\text{Log}_{10}$  higher than plasma HIV-RNA (**Definition B**)
- CSF HIV-RNA higher than plasma HIV-RNA (**Definition C**)
- CSF detectable with plasma undetectable HIV-RNA (**Definition D**)
- The combined A plus D criteria (**Definition E**)

• Asymptomatic patients/participants in research studies (**A/R pts**) and those with lymphomas without CNS involvement (**LYM pts**) were included for comparisons

# Characteristics of the study population (n=1093)

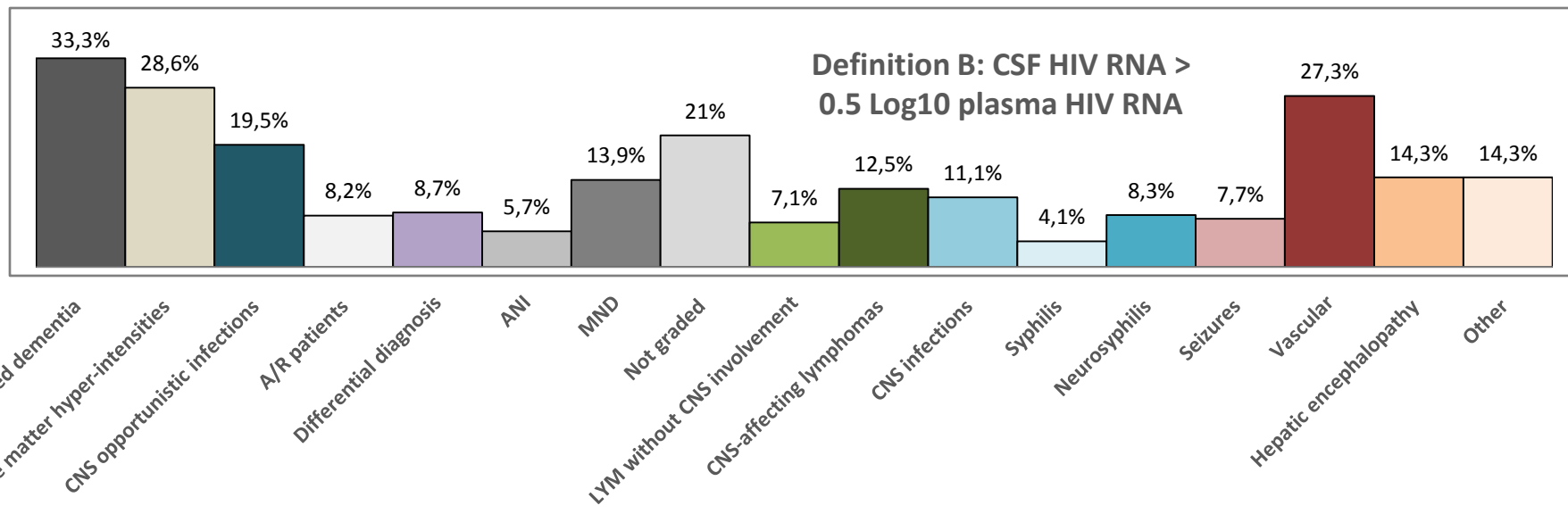
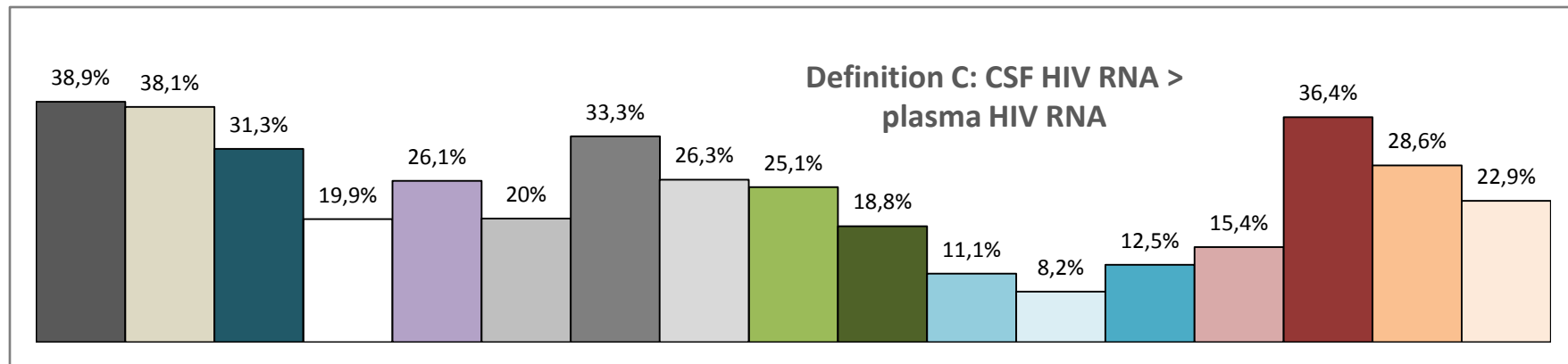
	N (%) or Median (IQR)
Male gender	873 (79.9)
Age, years	47 (40-53)
Plasma HIV-RNA < LOD	496 (45.4)
Plasma HIV-RNA, Log <sub>10</sub> cp/mL	1.69 (1.56-2.60)
CSF HIV-RNA < LOD	508 (46.5)
CSF HIV-RNA, Log <sub>10</sub> cp/mL	1.69 (1.56-2.50)
CSF-E definitions	
A	73 (6.7)
B	132 (12.1)
C	274 (25.1)
D	114 (10.4)
E	169 (15.5)
Underlying comorbidities:	
LYM without CNS involvement	352 (32.2)
CNS opportunistic infections	256 (23.4)
A/R patients	144 (13.2)
Other	341 (31.2)

# Prevalence of CSF escape according to different definitions and underlying conditions





# Prevalence of CSF escape according to definitions C and B and underlying conditions



# Conclusions

- The prevalence of CSF escape in cART treated patients varied according to escape definitions and comorbid conditions
- The “CSF higher than plasma HIV-RNA” criterion, suggested by the EACS guidelines, is associated with the highest rate of escape
- CSF/plasma discordance is associated with the increased expression of host inflammatory mediators in the CSF with similar profiles between patients with high ( $>1\log_{10}$ ) and low level discordance (ie.  $0.5-1\log_{10}$ )

Nightingale, et al. Cytokine, 2016

- The clinical relevance of different definitions needs to be carefully established in prospective studies including the evaluation of the interplay between CSF HIV-escape and immune-activation

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All patients enrolled in the study