DISCONTINUATIONS & VIROLOGIC RESPONSE IN LATE PRESENTERS WITH INSTI- OR PI-BASED ART

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Background

- The optimal antiretroviral (ART) regimen for treatment naive patients with advanced HIV is unknown[1]
- Active opportunistic infections and/or low CD4+T-cell count are exclusion criteria in most clinical trials
- Protease inhibitors (PI) are commonly used in advanced disease, however there are few data on outcomes associated with integrase inhibitors (INSTI) in this population [2,3]

[1] Manzardo et al. JAIDS 2007, [2] Landay at al, JID 2003, [3] Samri at al Antivir Ther 2007

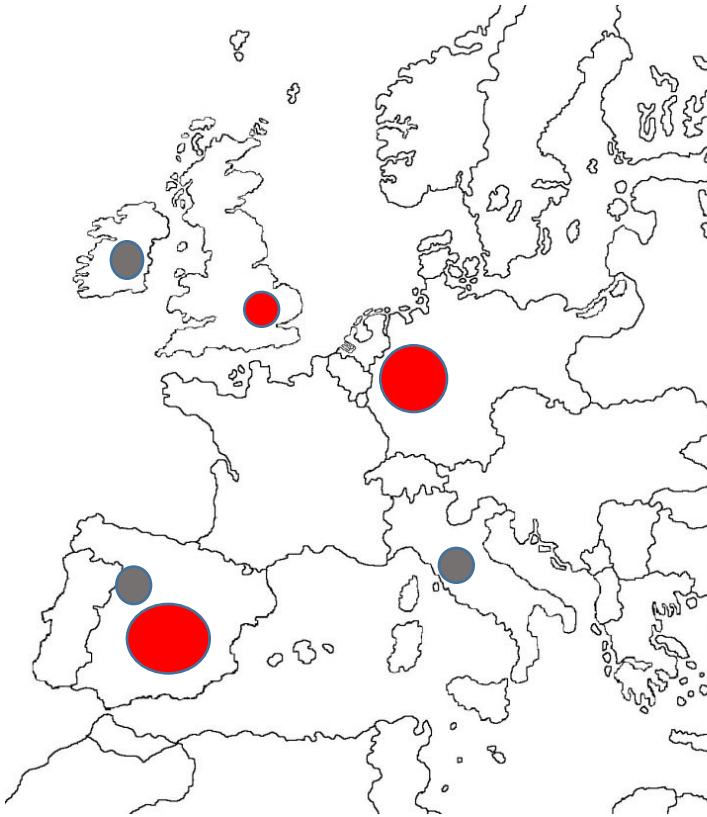
Aims

- To compare the tolerability of PI-based vs INSTI-based regimens in those with advanced HIV

- To compare the efficacy of PI-based vs INSTI-based regimens in those with advanced HIV at 12 and 48 weeks after treatment initiation

Methods

- Retrospective multicentre European cohort
- Inclusion criteria:
  - CD4+T-cell count <200 cells/µL and/or AIDS defining disease at the time of starting ART
  - Treatment naive starting either PI or INSTI based ART (any backbone)
  - >18 years old
  - Commenced ART between January 2014- December 2016
- Primary endpoint:
  - ART discontinuation at 12 and 48 weeks following start of therapy



Methods

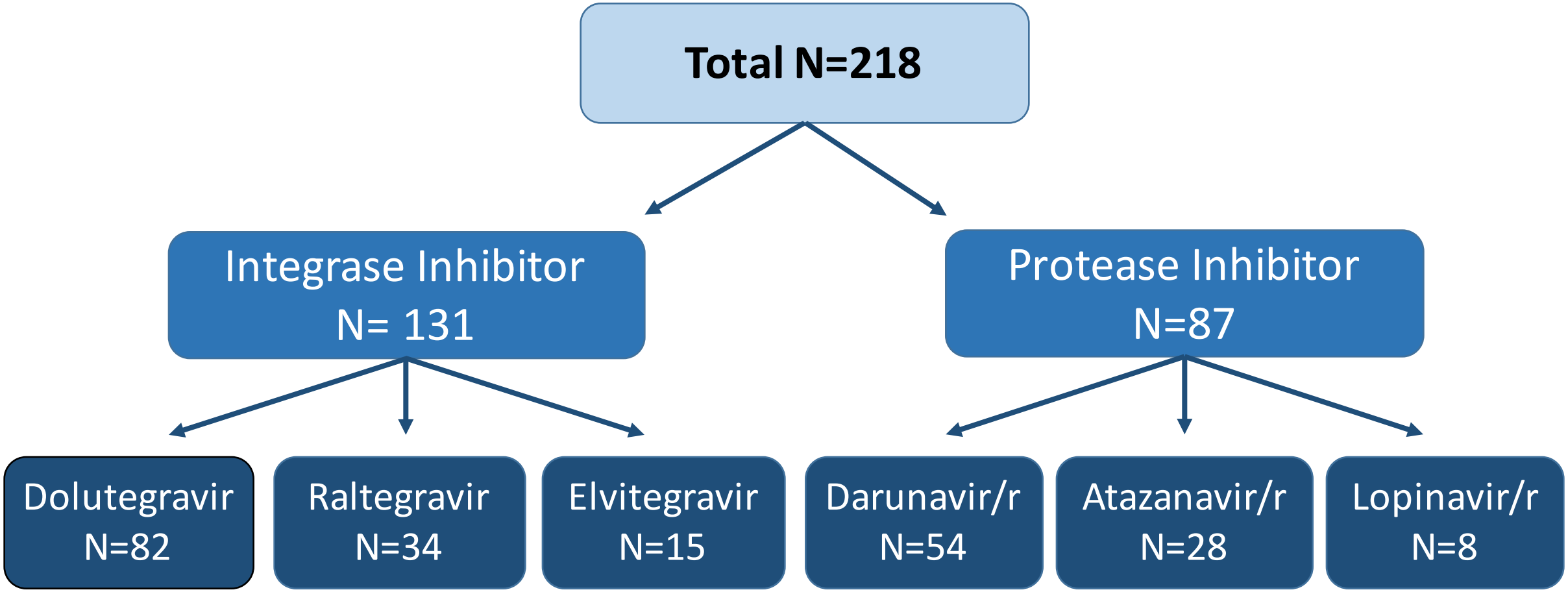
- Secondary endpoints measured at 12 and 48 weeks
  - HIV viral load<50 copies/ml
  - Mortality
  - AIDS defining illness
  - Adverse events
  - CD4 cell count

- Statistics
  - Differences between PI and INSTI groups will be assessed using Mann-Whitney tests, Chi-squared tests or Fisher's exact tests, as appropriate

Baseline Characteristics

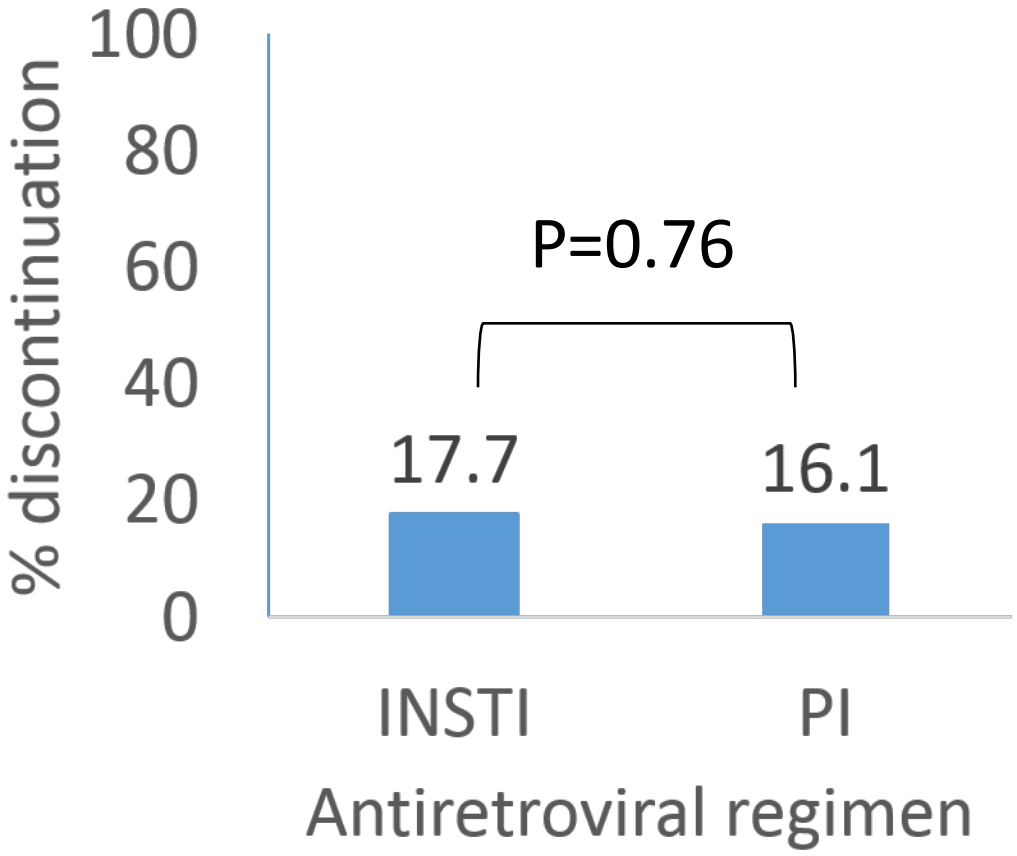
	INSTI (N=131)	PI (N=87)
Age in years, median (SD)	42 (33, 42)	44.9 (36, 44.8)
Male, N %	111 (84.7)	77 (88.5)
European ethnicity, N %	105 (80.2)	61 (70.1)
AIDS defining illness, N %	75 (57.3)	46 (52.9)
CD4 cell count (cells/µl), median (IQR)	103.5 (42, 180)	90 (33, 144)
CD4:CD8 ratio, median (IQR)	0.12 (0.08, 0.2)	0.10 (0.06, 0.2)
HIV viral load $\log_{10}$ (cps/ml), mean (SD)	5.8 (1.2)	5.7 (1.2)

Antiretroviral regimens at baseline



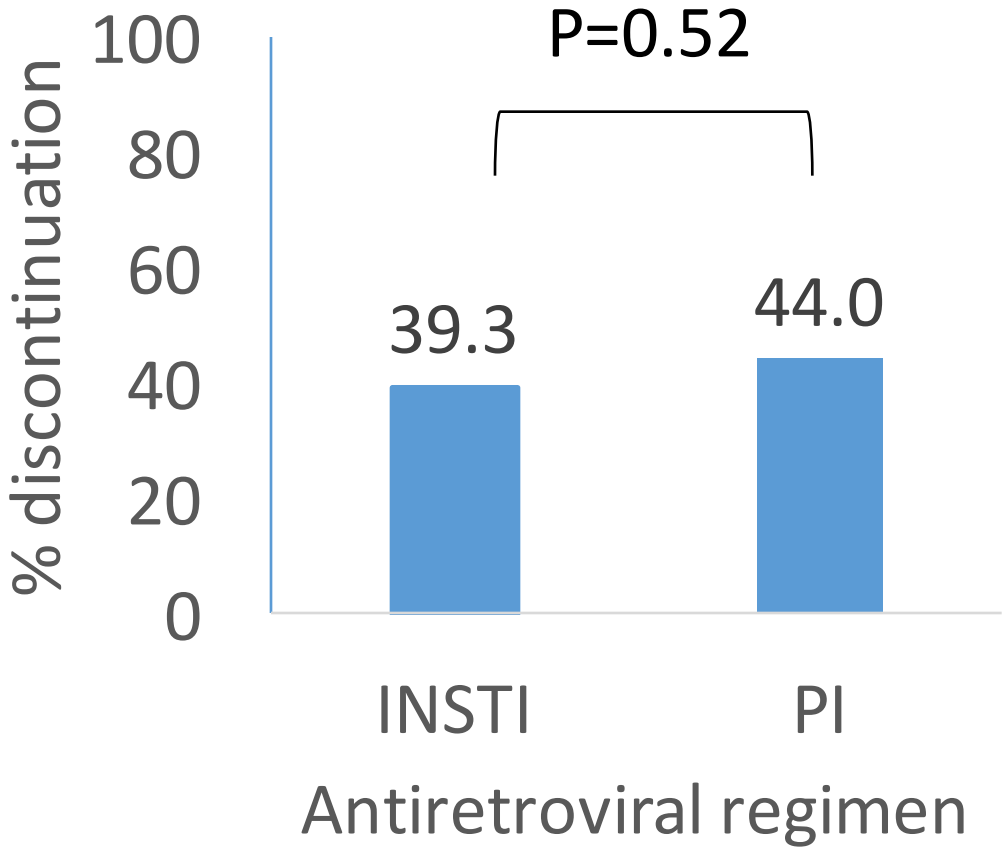
- **Backbone**: 78% tenofovir disosproxil fumarate/emtricitabine

% discontinuation of first line ART by week 12



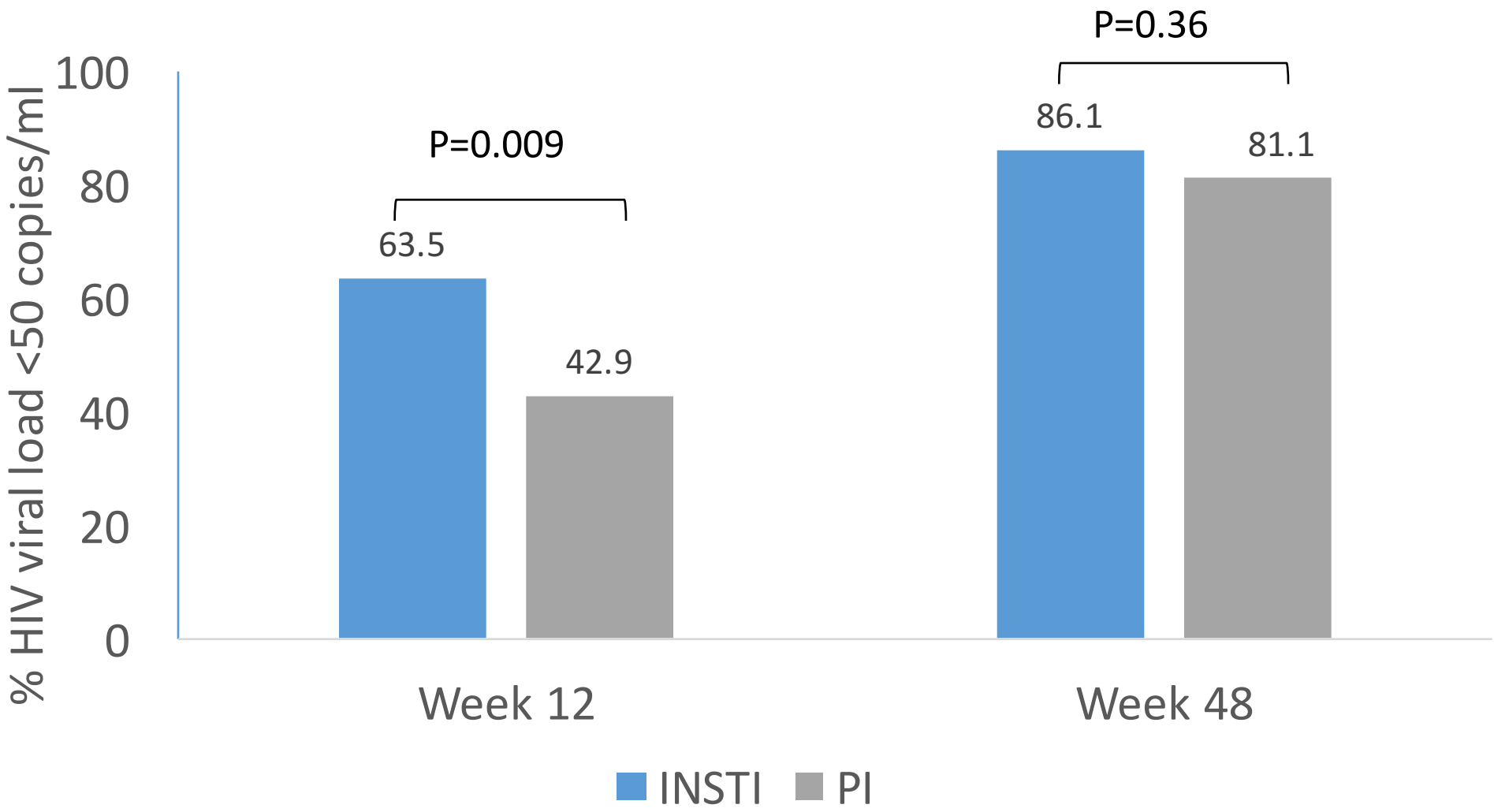
Reason for discontinuation	INSTI (N=23)	PI (N=14)
Side effects N (%)	5 (21.7)	4 (28.6)
Patient wishes N (%)	0 (0)	1 (7.1)
Non-compliance N (%)	1 (4.4)	1 (7.1)
Other N (%)	0 (0)	2 (14.3)
Not documented N (%)	17 (73.9)	6 (42.9)

% discontinuation of first line ART by week 48



Reason for discontinuation	INSTI (N=42)	PI (N=33)
Side effects N (%)	3 (7.1)	6 (18.2)
Patient wishes N (%)	3 (7.1)	3 (9.1)
Non-compliance N (%)	2 (4.8)	1 (3.0)
Comorbidity N (%)	7 (16.7)	1 (3.0)
Treatment failure N (%)	4 (9.5)	3 (9.1)
Drug interactions N (%)	0 (0)	2 (6.1)
Other N (%)	1 (2.4)	1 (3.0)
Not documented N (%)	22 (52.4)	16 (48.5)

Virological outcomes at week 48

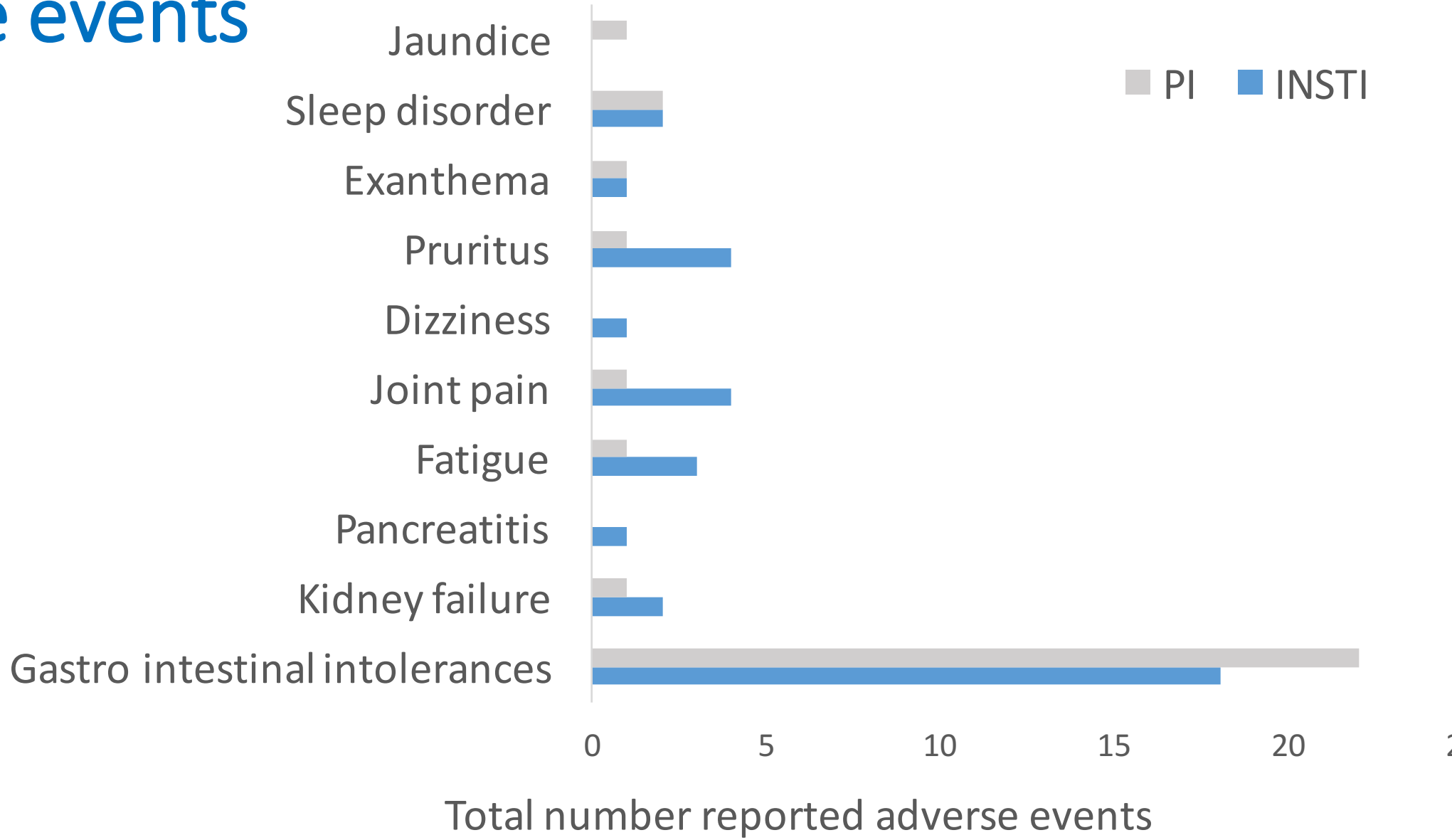


Clinical outcomes at week 48

Outcome at 48 weeks	INSTI	PI	P
CD4 cell count, median (IQR)	360 (243.5, 461)	315 (234, 461)	0.41
CD4:CD8 ratio, median (IQR)	0.33 (0.24, 0.43)	0.31 (0.2, 0.47)	0.68
HIV VL<50 cps/ml*, N (%)	93 (86.1)	60 (81.1)	0.36
Adverse events, N (%)	30 (24.8)	27 (32.9)	0.21
Category B diagnosis, N (%)	11 (8.6)	3 (3.5)	0.17
Category C diagnosis, N (%)	12 (9.4)	6 (6.9)	0.52
Mortality, N (%)	3[1] (2.2)	3[2] (3.5)	0.45

[1] Multifocal leukoencephalopathy, non-AIDS defining cause of death (1 cause death not reported)
[2] PCP + Kaposi's sarcoma, PCP + Kaposi's sarcoma + CMV, Kaposi + primary effusion lymphoma
*N=167

Adverse events



Limitations

- Many limitations of retrospective studies
  - Reliant on documentation
  - Loss to follow up
  - Confounders
- No information on factors that led to choice of 3rd agent (for example drug interactions, resistance testing, need for immediate treatment)
- No data specifically looking at IRIS

Conclusion

- No significant differences in discontinuation rates and virological response at week 48
- Choice between INSTI and PI can be made on an individual basis
- Future research will focus on the identifying factors associated with regimen selection in this cohort

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