Poster: 1018 b

A randomized trial to compare the efficacy and safety of PEG-interferon (PEG) alfa-2b plus ribavirin (RBV) vs PEG alfa-2a plus RBV for treatment of chronic hepatitis C in HIV co-infected patients.

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BACKGROUND

- The gold standard of chronic hepatitis C (HCV) therapy is Peg-interferon (PEG) plus ribavirin (RBV).

- In HIV infected patients, randomized clinical trials have reported a wide range of response to PEG alfa-2b+RBV (27 to 55%)[1-3] and to PEG alfa-2a+RBV (27 to 40%)[4-5]

- Despite two Peg-interferons are available so far no head to head comparisons in HIV patients have been reported.

1:JAMA, 2004; **2**:AIDS, 2004; **3** :J Viral Hep, 2007.
4-5: NEJM, 2004.

OBJECTIVE

- The aim of the present study was to compare, in HIV patients, the efficacy and safety of:

Peg-interferon alfa-2b (**PEG 2b**) + RBV

vs

Peg-interferon alfa-2a (**PEG 2a**) + RBV.

METHODS

- Prospective, randomized, multi-centre, open-label clinical trial
- Inclusion criteria:
  - Detectable HCV-RNA
  - Alanine aminotransferase >1.5-fold upper normal limit
  - Abnormal liver histology
  - CD4 counts >250 cells/mm^3 and HIV-RNA <50000 copies/mL.

- Treatment arms:

  PEG 2b (80-150 µg/wk adjusted to body weight)

  or

  PEG 2a (180µg/wk)

  + RBV (800-1200 mg/d adjusted to body weight) in both arms

- Duration of treatment: 48 weeks.

METHODS

- Primary endpoint:
  - Sustained Virological Response

    (**SVR**= HCV-RNA negative at week 72).

- Sample size was calculated to detect, with 80% power, differences above 20 percentual points if they exist.

METHODS

PEG 2b (80-150 µg/wk) + **RBV** (800-1200 mg/d)

PEG 2a (180µg/wk) + **RBV** (800-1200 mg/d)

BL **4wk** **12wk** **24wk** **48 wk** **72 wk**

vEVR = very Early Virological Response= HCV-RNA negative

EVR = Early Virological Response: HCV-RNA negative or a drop ≥2log of HCV-RNA from baseline

VR = Virological Response: HCV-RNA negative

SVR = Sustained Virological Response: HCV-RNA negative

Demographics and Baseline Characteristics

- Baseline Characteristics of **182** included patients:

		Interferon (nº patients)		All (182)
		PEG 2b (86)	PEG 2a (96)	
Male gender #		68 (79.1)	64 (66.7)	132 (72.5)
Age (years)*		40,7 (5,0)	40,6 (5,4)	40,7 (5,2)
Age at HCV infection time (years) *		23,3 (6,9)	22,2 (6,6)	22,8 (6,8)
Baseline weight (Kg) *		69.4 (12,3)	67.3 (10,8)	68.3 (11,5)
Time with HCV infection (years) *		17.3 (6,4)	18.3 (6,0)	17.8 (6,2)
HCV Genotype #	**1**	32 (39,5)	47 (50,5)	79 (45,4)
	2	3 (3,7)	3(3,2)	6(3,4)
	3	31 (38,3)	28(30,1)	59 (33,9)
	4	15 (18,5)	15 (16,3)	30 (17,2)
Baseline HCV-RNA >600.000 IU/ml #		50 (60,2)	54 (58,1)	104 (59,1)
Baseline HCV-RNA >800.000 IU/ml #		48 (57,8)	50 (53,7)	98 (55,7)
Fibrosis score #	**0-2**	51 (70,8)	64 (71,1)	115 (70,9)
	3-4	21 (29,2)	26 (28,9)	47 (29,1)
Baseline ALT (IU/mL)*		111.2 (75,3)	89.1 (47,4)	99.4 (62,9)
HIV risk group #	**IDU**	69 (81,2)	68 (70,8)	137 (75,7)
	HMX	4 (4,7)	7 (7,3)	11 (6,1)
	HTX	9 (10,6)	20 (20,8)	29 (16)
	Others	3 (3,5)	1 (1)	4 (2,1)
Baseline CD4 cell count (cell/mL) *		592.5 (269,2)	602.3 (279,6)	597.7 (274,0)
Baseline CD4 cell count >300 #		78(91,8)	88 (91,7)	166 (91,7)
HIV viral load < 200copies/mL #		63 (74,1)	70 (72,9)	133 (73,5)

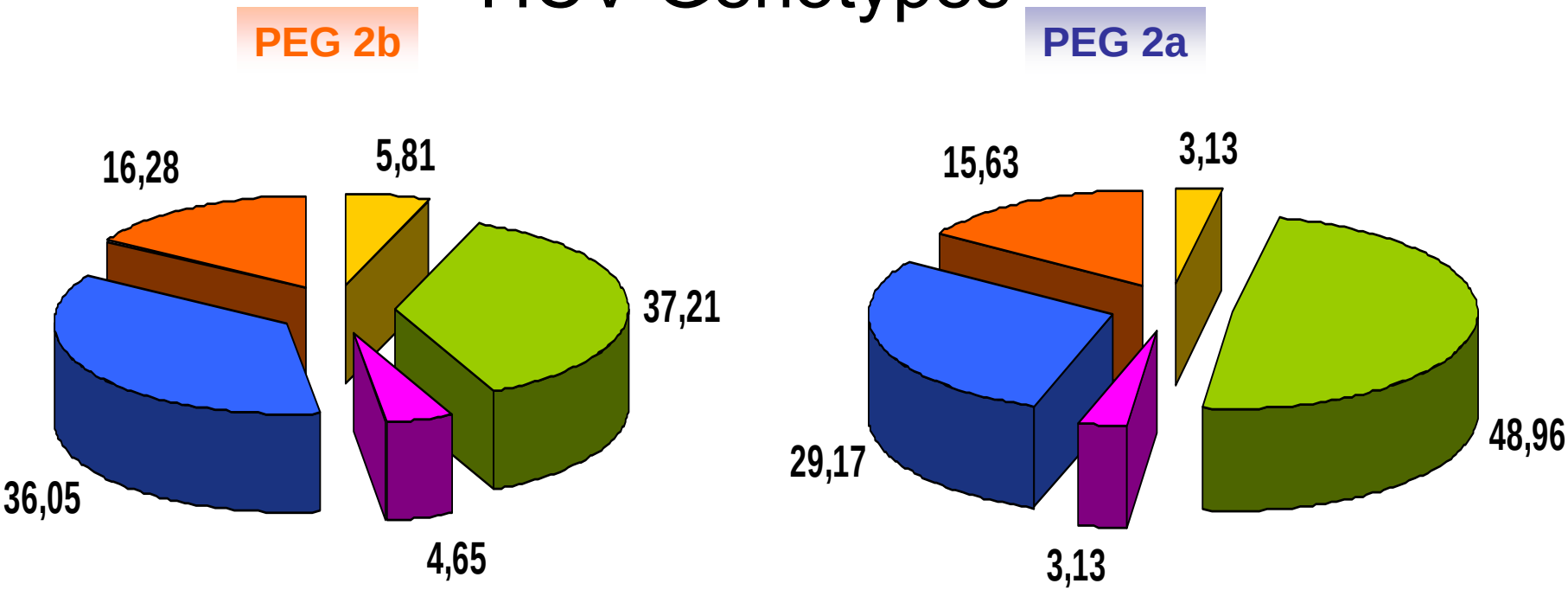
* Mean (Std Desv); # Number (%)

Both groups were well balanced:

- 72,5% males
- 76% former drug users
- 63% HCV genotype 1 or 4
- 29% bridging fibrosis or cirrhosis
- 56% HCV viral load > 800000 IU/mL.

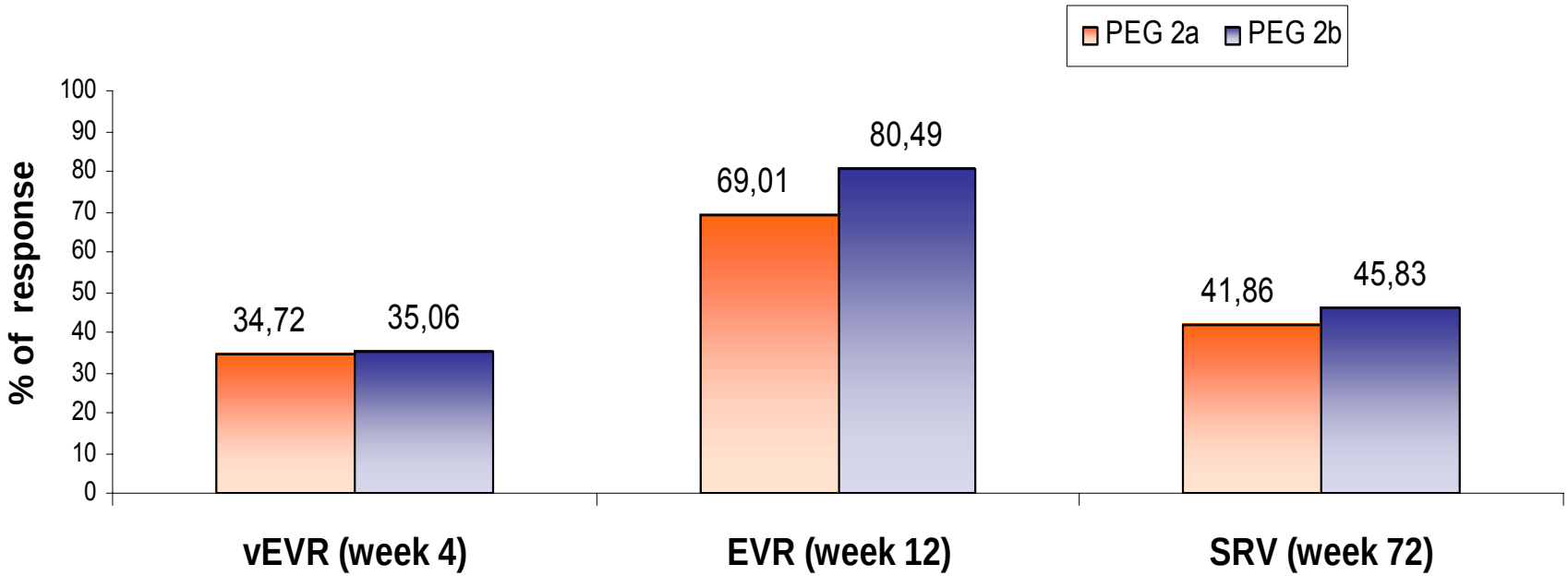
Demographics and Baseline Characteristics

- HCV Genotypes



RESULTS

- Global vEVR, EVR and SVR:



(Primary endpoint)

RESULTS (SVR)

- Overall SVR was achieved in **44%**

  42% PEG 2b vs 46% PEG 2a, (p=0.65)
- Genotype 1 or 4:

  30% (28% vs 32%), (p=0.67)
- Genotypes 2 or 3:

  66% (62% vs 71%), (p=0.6)

RESULTS (EVR)

- EVR was obtained in **75%** of patients

  69% PEG 2b arm vs 80% in PEG 2a (p=0.13)

- PPV*of SVR was 64%

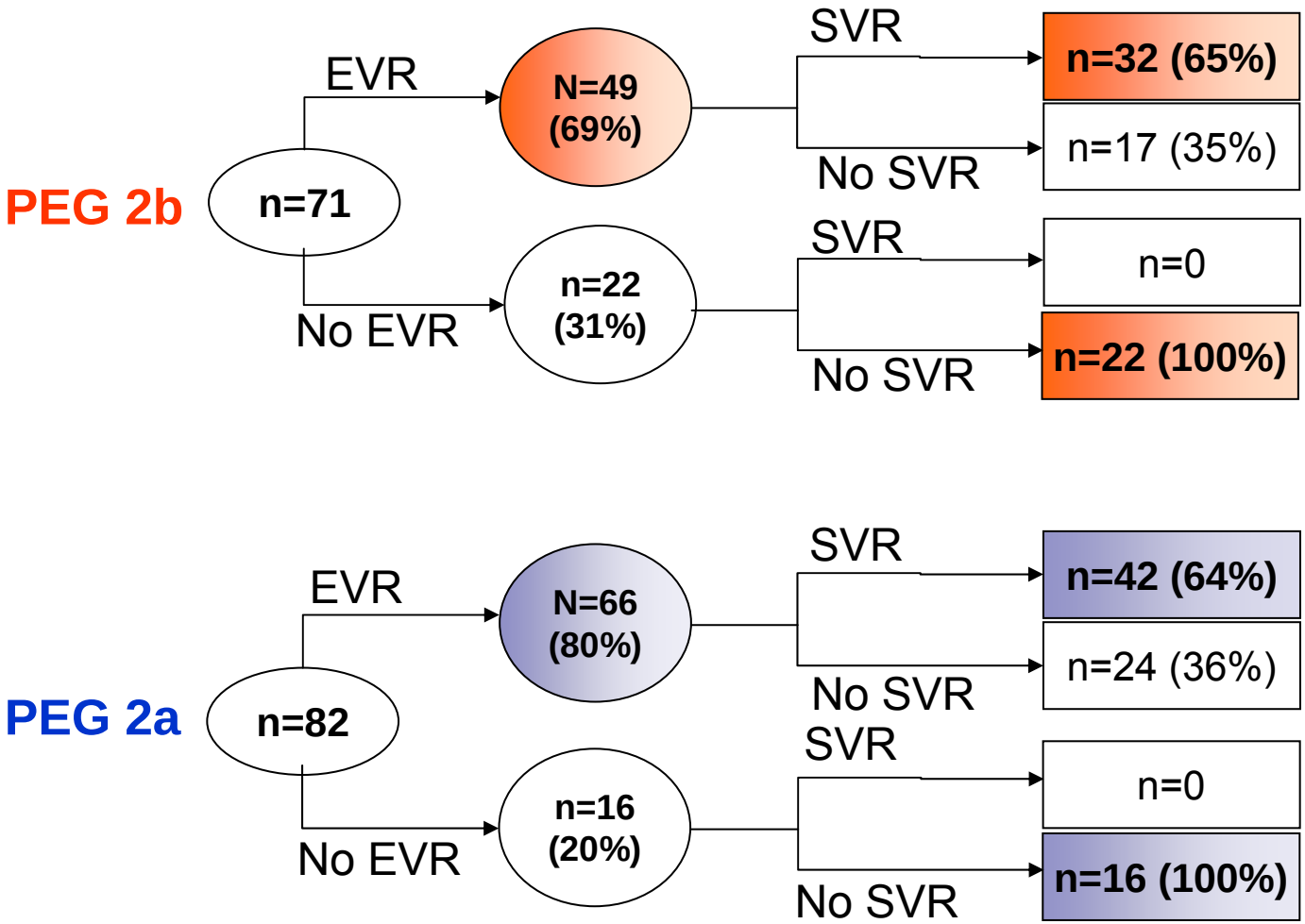
  65% in PEG 2b arm vs 64% in PEG 2a (p=1)

- NPV*of SVR: 100% in both arms.

(* PPV: Positive Predicted value: NPV: Negative Predicted Value)

RESULTS (EVR)

- Global PPV and NPV of EVR:



RESULTS (vEVR)

- vEVR was similar in both arms:

35%

- Overall PPV of SVR: 81%

88% in PEG 2b vs 74% in PEG 2a,(p=0,29)

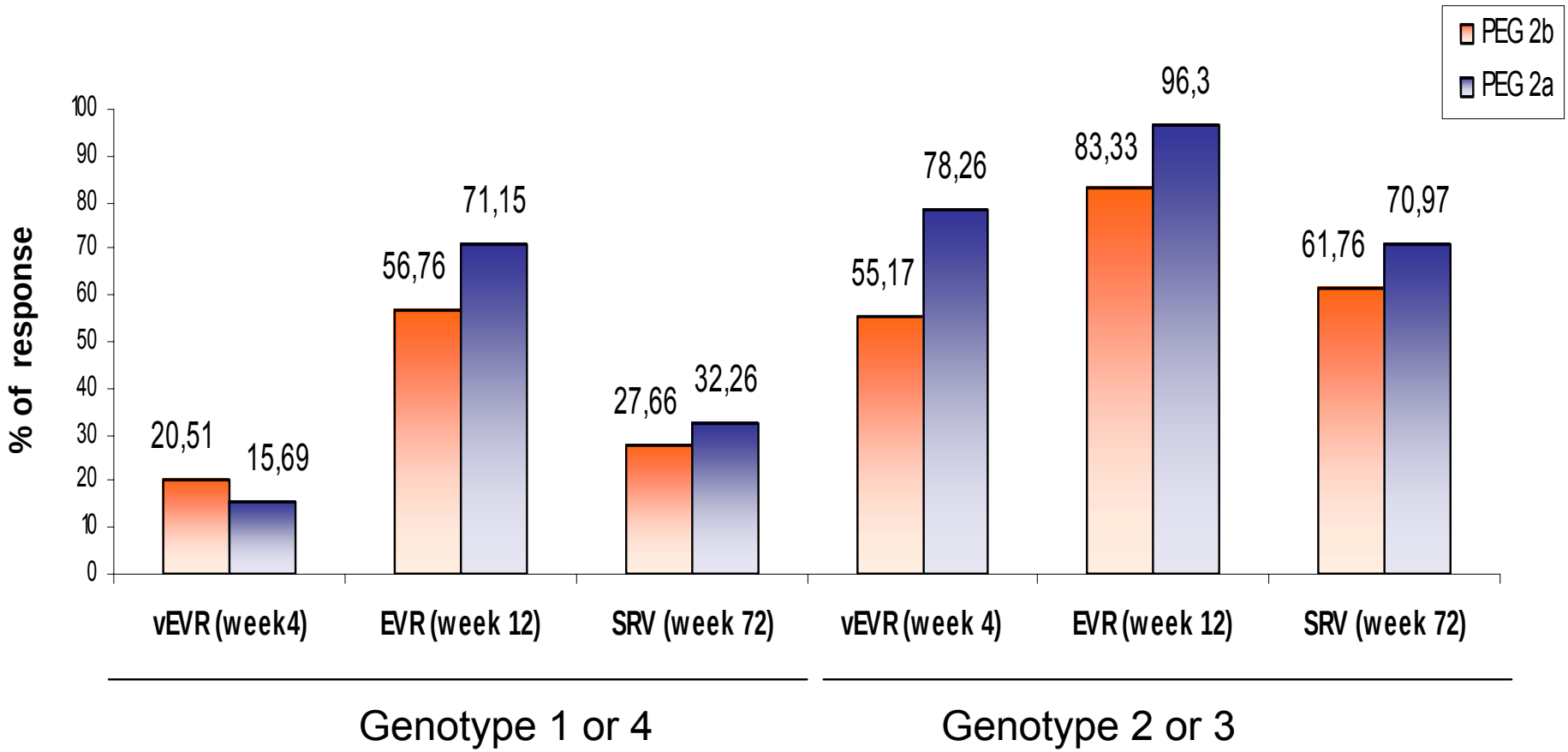
RESULTS

	PEG 2b			PEG 2a			Global		
	1/4	2/3	all	1/4	2/3	all	1/4	2/3	all
vEVR	20	55	35	16	78	35	18	65	35
PPV of SVR	87	87	88	62	78	74	15	82	81
NPV of SVR	87	61	79	72	60	70	78	61	74
EVR	57	83	69	71	96	80	65	89	75
PPV of SVR	50	76	65	51	81	64	51	78	64
NPV of SVR	100	100	100	100	100	100	100	100	100
SVR	28	62	42	32	71	46	30	66	44

All data in percentage. No statistically significant differences

RESULTS

- vEVR, EVR and SVR by genotype:



RESULTS

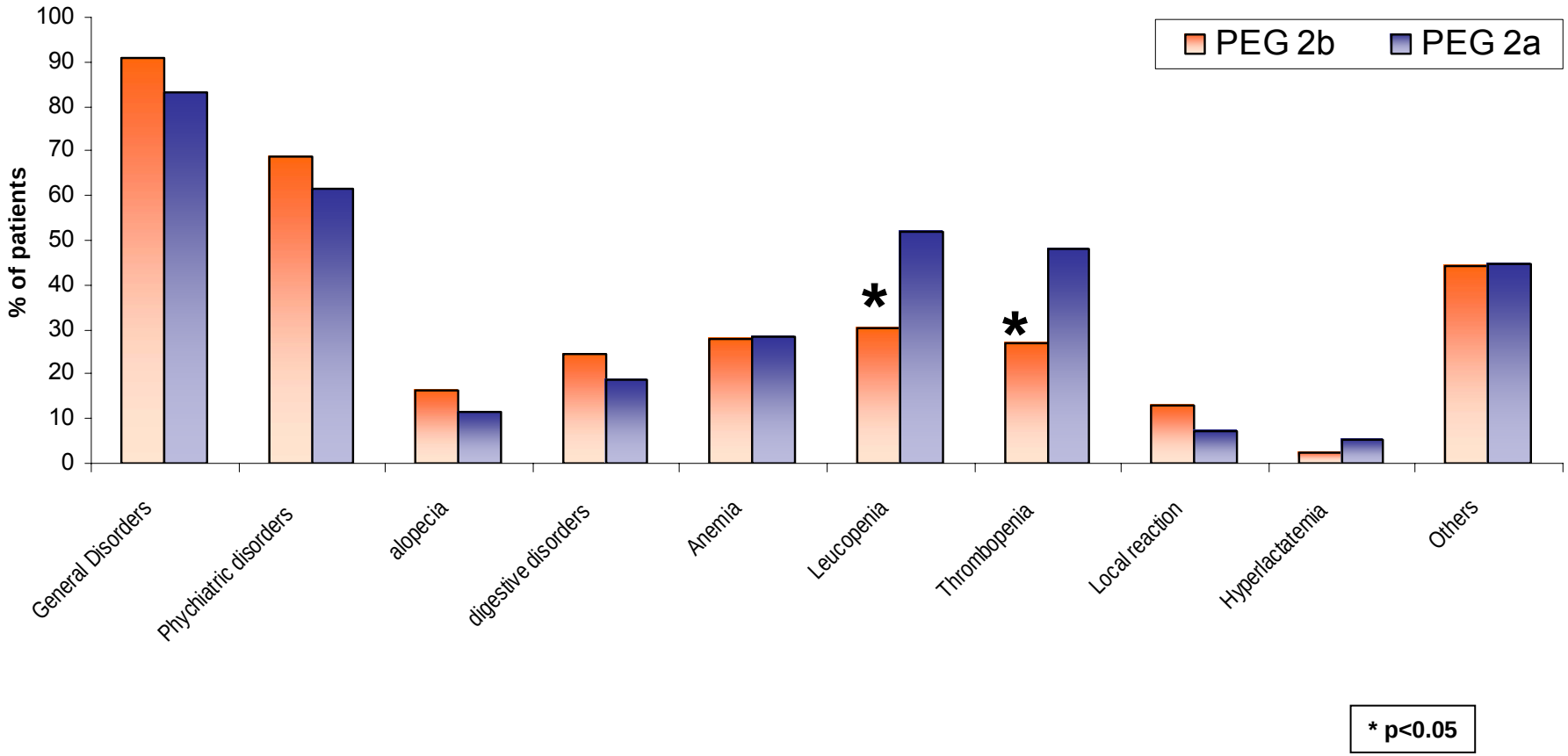
- **The independent factors related with SVR in the multivariate analysis were:**

  - HCV genotype 2 or 3
  - male gender
  - age ≤40 years

Effect	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	variable	Pr > Chi-Square
Age: <= 40 years vs > 40 years	2.637	1.308	5.317	age	0.0067
PEG 2a vs PEG 2b	1.606	0.813	3.171	Interferon	0.1725
Gender: male vs female	2.828	1.241	6.447	gender	0.0134
HCV Genotype: 2+3 vs 1+4	4.618	2.317	9.202	genotype	<.0001

RESULTS (AEs)

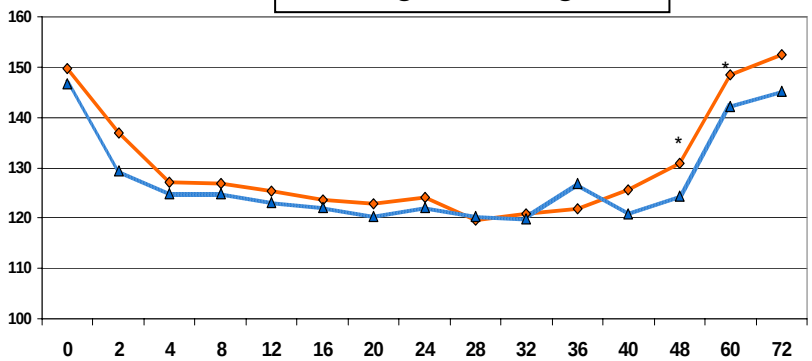
- 96% of patients presented ≥ 1 side effect.



RESULTS (AEs)

- Haematologycal adverse events during the therapy:

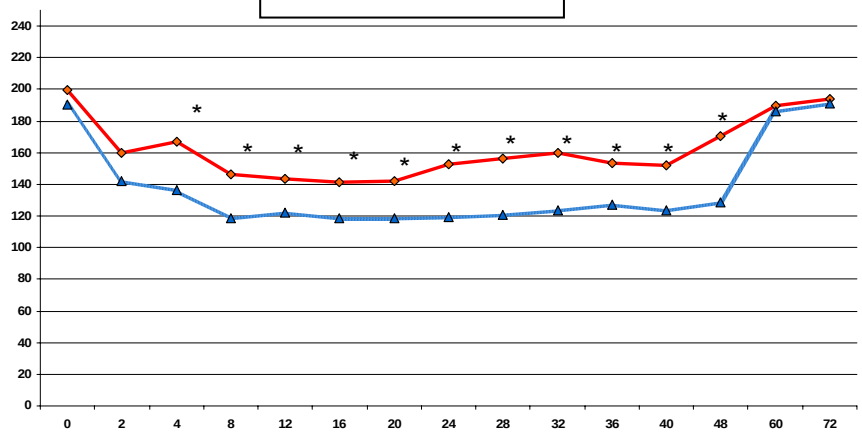
Hemoglobine mg/dL



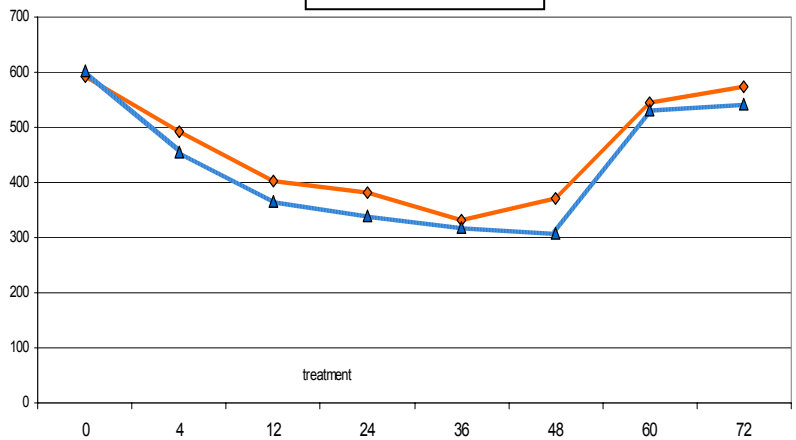
PEG 2b

PEG 2a

Platelets cel/mL



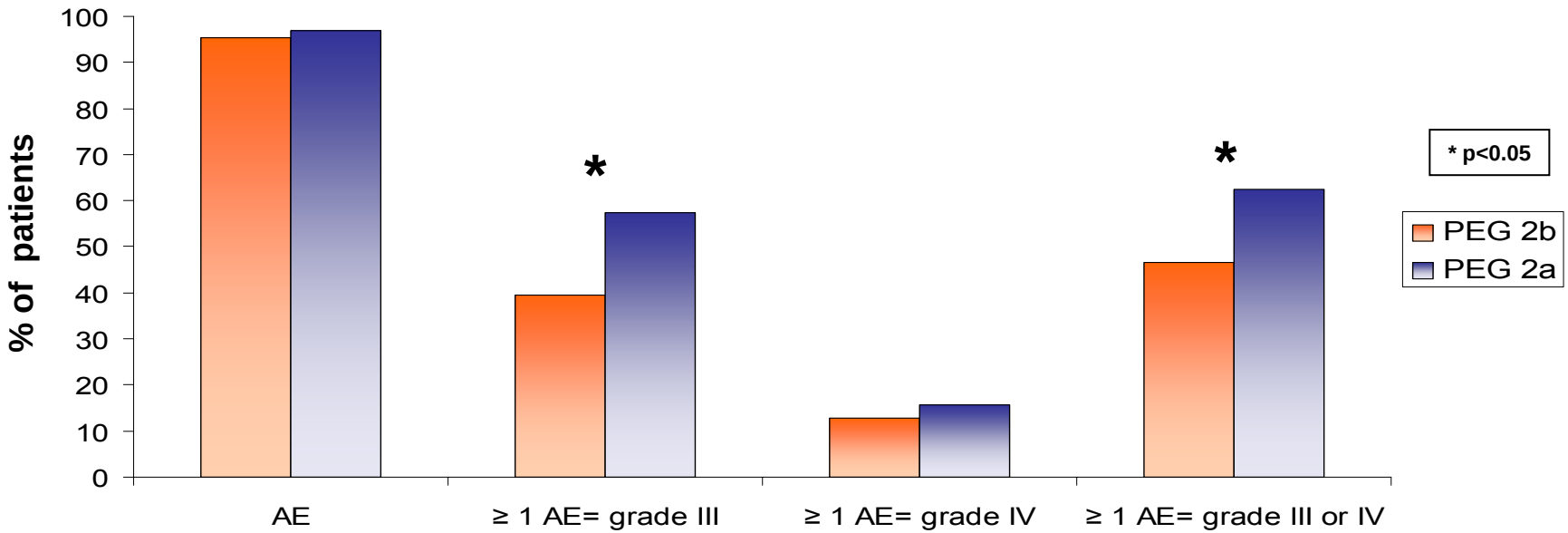
CD4 cel/mL



*p <0,05

RESULTS (AEs)

- Adverse effects Grade III or IV.

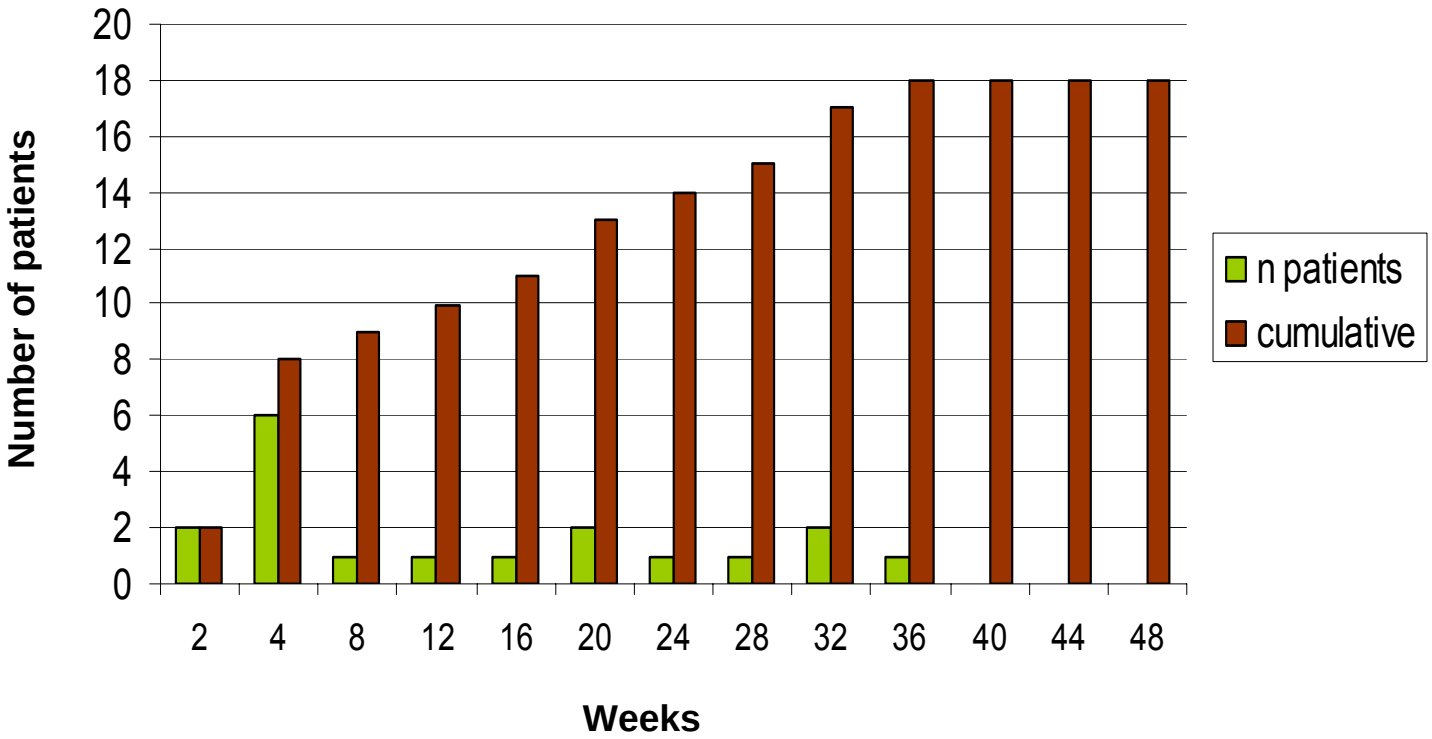


- 10% (n=19) of patients discontinuated the treatment due to adverse effects

  8% (n=7) in PEG 2b and 13% (n=12) in PEG 2a arm, (p=0.56)

RESULTS

- Cumulative and number of patients with adverse events leading to treatment discontinuation.



CONCLUSION

In HIV infected patients, treatment of chronic HCV with RBV plus PEG 2b or PEG 2a had no statistically significant differences in tolerance and efficacy.