

INTRODUCTION

Kaposi sarcoma (KS) is an enigmatic disease with an unpredictable evolution, it can range from an indolent disease to a life threatening presentation with fatal consequences. Adverse prognosis factors are disseminated disease, lung involvement and immune reconstitution inflammatory syndrome (IRIS). Over 50% of patients with SK diagnosis have concomitant infections. Although the role of cytokines in SK has been studied, it has not been described their behavior in presence of concomitant infections.

OBJECTIVE

To measure plasma cytokines levels (IL-6, IL-10, IL-1 β and IFN- γ) from patients with disseminated KS at baseline, at 4 and 12 weeks of follow-up and compare their behavior in patients with and without syphilis and/or concomitant infectious AIDS (Acquired Immune Deficiency Syndrome) defining events (IADE).

MATERIALS AND METHODS:

A prospective and observational study was conducted from October 2015 to November 2017. A complete clinical evaluation with active search of co-infections: laboratory exams, thorax and abdominal CT-scan, gastrointestinal endoscopy, syphilis and viral hepatitis serology, blood marrow culture and tissue biopsy if needed was performed. All patients with syphilis were treated within the first four-weeks; by 12th week all were on combined antiretroviral therapy as well as on treatment of the diagnosed co-infection. Disseminated KS was defined with ≥ 30 skin lesions and/or digestive, lymphadenopathic and lung affection. IADE included were *Mycobacterium Avium* Complex disease, disseminated histoplasmosis and *Penicillium* lung infection. Plasma cytokines levels were measured by ELISA assay.

STATISTICAL ANALYSIS

Descriptive analysis of the variables of interest was done. Groups were compared using Mann-Whitney test considering $p < 0.05$ as statistically significant.

RESULTS

Twenty patients were included in this report, all were men who had sex with men with a mean age of 31 years (IQR 11.7), CD4 total count median was 52.5 cell/mm³ (IQR 145.5), viral load median was 206,240 copies/mL (IQR 441,041). 35% (n=5) had syphilis, six (30%) had infectious AIDS defining events, 3 (15%) with disseminated *Mycobacterium Avium* Complex, 2 (10%) with disseminated histoplasmosis and one with *Penicillium* lung infection.

IL-1 β was lower to 2 pg/mL in all samples. The median levels of IL-6, IL-10 and IFN- γ at baseline and at week 12, in patients with and without syphilis, without any co-infection and with infectious AIDS defining events are shown in Table 1

Table 1. Plasma cytokine levels in patients with and without syphilis and IADE at baseline, 4 weeks and after 12 weeks follow-up.

Plasma cytokine levels (pg/mL)	Syphilis + (n=7)	Syphilis - (n=13)	p value	IADE - (n=13)	IADE +(n=7)	p value
IL-6 baseline	12.4	20.7	0.02	16.1	35.8	0.03
IL-6 4 weeks	13.7	22.6	NS	22.4	31.4	NS
IL-6 12 weeks	10.1	13.9	NS	11.8	16.6	NS
IL-10 baseline	12.8	18.6	NS	11.3	20.6	NS
IL-10 4 weeks	7.2	9.5	NS	19.1	8.7	NS
IL-10 12 weeks	7.6	9.9	NS	8.9	17.4	NS
IFN- γ baseline	8.06	8.4	NS	10.1	9.3	NS
IFN- γ 4 weeks	5.6	8.27	NS	5.6	17.6	0.033
IFN- γ 12 weeks	5.6	5.56	NS	5.6	14.5	0.018

NS: non-significant; IADE: Infectious AIDS defining events.

DISCUSSION

IL-6 in patients with KS and syphilis were significantly lower at baseline. In patients with IADE IL-6 was significantly higher at baseline, decreasing parallel to treatment; contrary IFN- γ was significantly increased suggesting that IFN- γ is up-regulated once patients start anti-infectious therapy no related to syphilis infection (Figures 1 and 2). Meanwhile IL-10 was decreasing in patients with or without syphilis; and in patients with IADE there is not a direct relation with treatment.

CONCLUSION

Plasma cytokines levels are diverse in patients with different co-infections and are modified when treatment is given for syphilis and when infectious AIDS defining events begin to be treated, IFN- γ increases and IL-6 decreases. Cytokines play an important role in KS and other factors like concomitant infections may influence its behavior. Because some of the IADE require prolonged treatments it would be important to follow-up patients for a longer time.

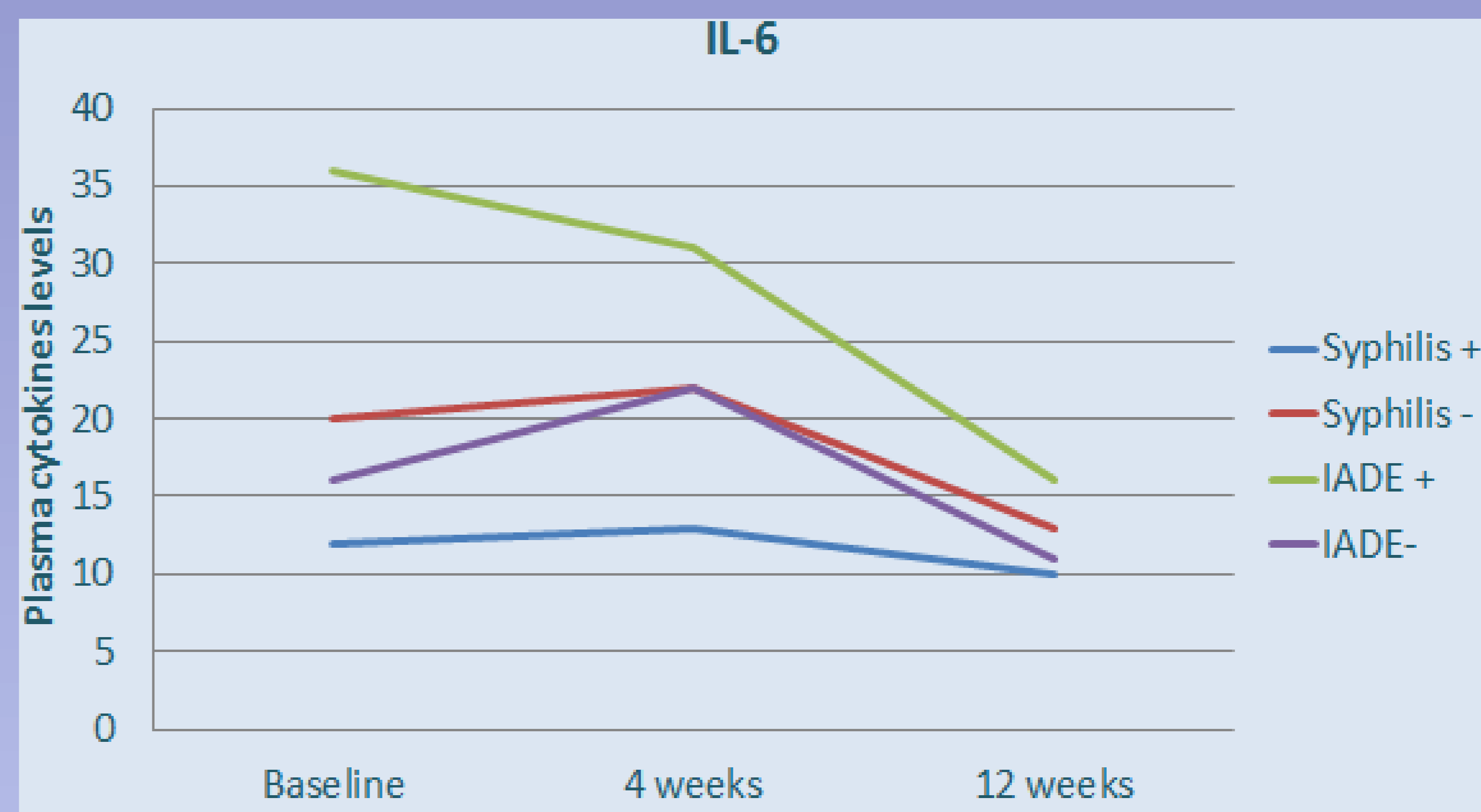


FIGURE 1. IL-6 plasmatic levels at baseline, 4 and 12 weeks in patients with and without syphilis and IADE. IADE: Infectious AIDS defining events.

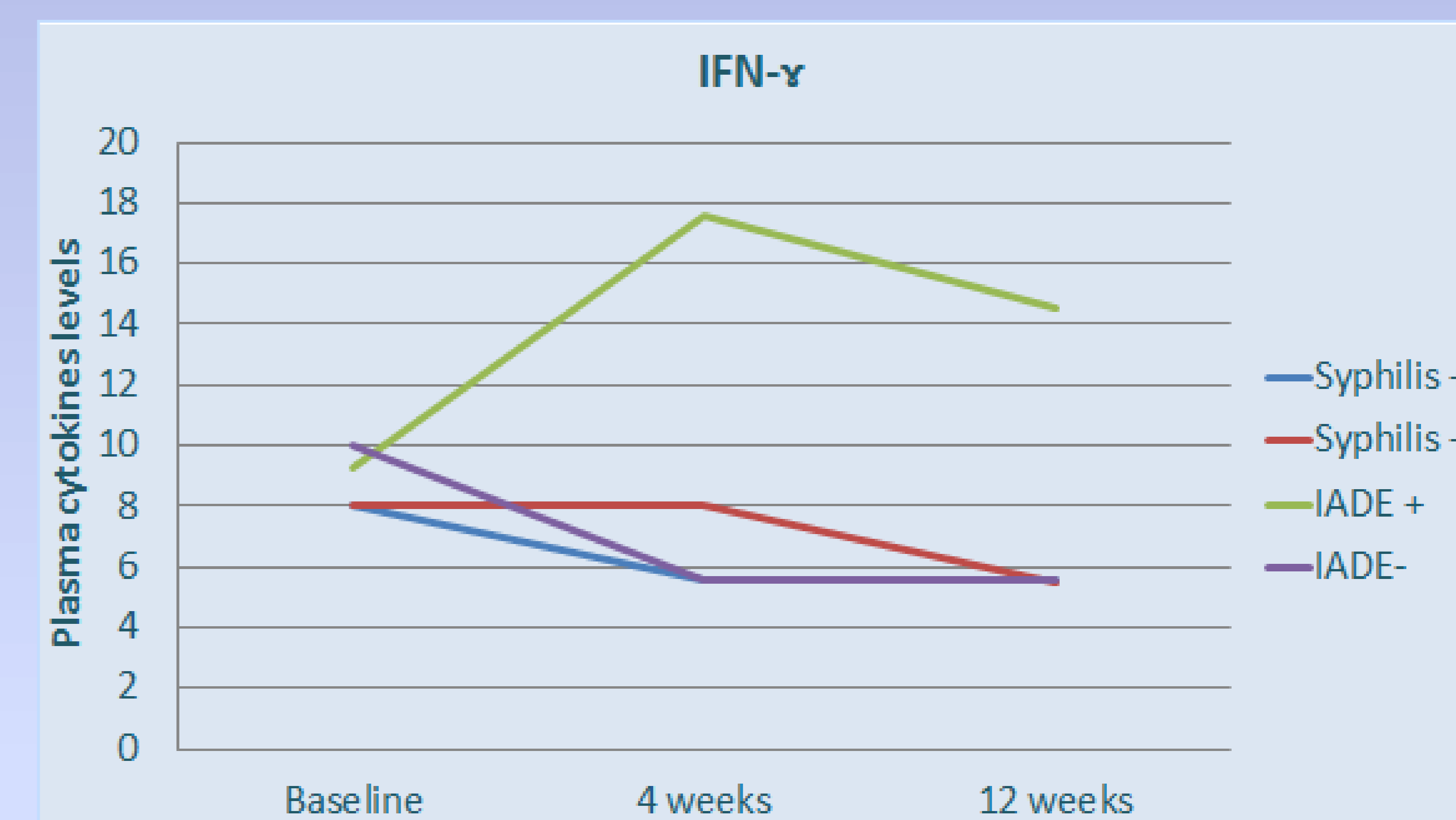


FIGURE 2. IFN- γ plasmatic levels at baseline, 4 and 12 weeks in patients with and without syphilis and IADE. IADE: Infectious AIDS defining events.