

HUMAN HERPES VIRUS 8 IS STRICTLY ASSOCIATED WITH THE ONSET, CLINICAL STATUS AND DISEASE PROGRESSION IN PATIENTS AFFECTED BY AIDS-ASSOCIATED KAPOSI' SARCOMA

INTRODUCTION



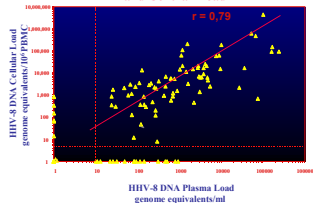
Although several reports have demonstrated a direct linkage between MCD progression and HHV-8 replication, compelling evidences of the direct involvement of HHV-8 in KS onset, development and progression are still missing.

OBJECTIVE: To assess the role that active HHV-8 replication exerts on the onset, development and progression of AIDS-KS

DESIGN: Cross-sectional (60 patients) and longitudinal analysis (50 patients) of HHV-8 plasma viremia and cellular load in AIDS-KS patients with different clinical status.

METHODS: Patients were stratified according to KS status. The amount of HHV-8 DNA in plasma and in PBMCs was determined by calibrated quantitative Real-Time PCR

Correlation between HHV-8 Plasma Viremia and Cellular Load



Characteristics of the patients

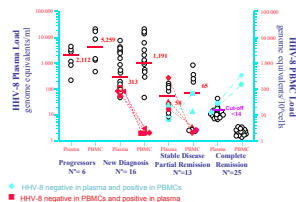
- 1) New diagnosis (NWD, 16 patients), onset of KS lesions in a HIV-seropositive individual.
- 2) Stable disease (STD; 8 patients) or Partial Remission (PR; 5 patients): flattening of at least 50% of nodular lesions or decrease in the number and/or size of the previous lesions by 50% lasting greater than 4 weeks, with no new lesions appearing and no worsening of tumor-associated edema following either the introduction of HAART and/
- 3) Progressive disease (PD, 6 patients) either new lesions or sites of disease, enlargement of previously existing lesions (at least 25% larger), lesions-associated edema, worsening under chemotherapy and an HIV-controlling HAART treatment.
- 4) Complete remission (CR, 25 patients) absence of detectable residual disease lasting at least 8 weeks before the

HHV-8 loads are significantly associated with the clinical status of AIDS-KS patients

Patient Features ^a	KS Clinical Status				
	NWD N=16	PD N=6	CR N=25	PR/STD N=13	P ^b
Age (years)	38 (25-51)	33 (18-50)	43 (31-50)	41 (29-56)	0.15
CD4 cells (x10 ⁶ /l)	176 (5-600)	276 (5-600)	460 (147-726)	503 (8-1061)	0.52
Plasma HIV RNA	4.73 (1.90-6.13)	2.89 (1.90-4.90)	2.94 (1.90-5.04)	4.08 (1.90-5.74)	0.99
Anti-HHV-8 Abs (Istcr)	1200 (40-1200)	1200	1200 (40-1200)	1200 (40-1200)	0.34
HH-8 load (PBMCs)	4.17 (0-4.77)	3.54 (0-6.64)	2.31 (0-2.51)	3.51 (0-4.13)	<0.0001
HHV-8 load (plasma)	2.30 (1.68-4.56)	2.95 (2.36-3.61)	<1.02	1.94 (1.11-1.94)	<0.0001

^aThe median value and range of each variable is given.
^b ANOVA test.

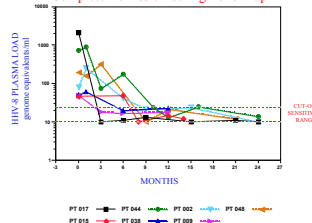
Plasma Viremia and Cellular Load In AIDS-KS Patients



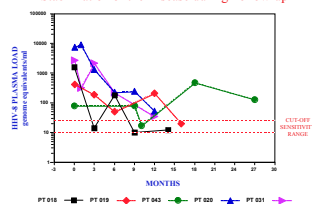
HHV-8 Viremia is strongly associated with the Clinical Status and the Onset of Kaposi' Sarcoma

HHV-8 PLASMA LOAD			
Progressors	Stable	Complete Remission	New Diagnosis
/	p<0,0001	p<0,0001	p=0,2361
Stable	p<0,0001	p=0,0447	p=0,0001
Complete Remission	p<0,0001	p=0,0447	p<0,0001
New Diagnosis	p=0,2361	p<0,0001	/

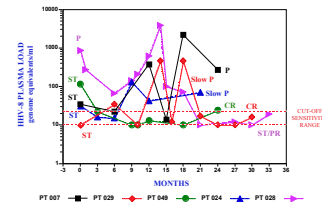
Newly Diagnosed KS Patients that Achieved Complete Remission during Follow-up



Newly Diagnosed KS Patients that Achieved Stabilization of the Disease during Follow-up



Patients with major modifications of their KS status during Follow-up



CONCLUSIONS

Conclusions

A strong association exists between the presence of active HHV-8 infection and clinical course of the disease and between extent of HHV-8 replication and progression of KS.

Taken together, these findings strongly support the hypothesis of a direct involvement of HHV-8 in KS pathogenesis and lesions dissemination

Sensitive, accurate and high-throughput diagnostic tests are useful to monitor HHV-8 infection in KS patients.

FUTURE PERSPECTIVE

These results suggest that antiviral drugs directed against HHV8 could, alongside with conventional therapies for KS, slow down the progression of KS, by containing replication of the virus.

Anecdotal reports support this hypothesis, but further clinical investigation is requested to assess this possible therapeutic option.