



Centre universitaire
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CONFERENCE
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Kaposi sarcoma in ART-treated PLWH and uninfected people: differences in viral and immunological determinants



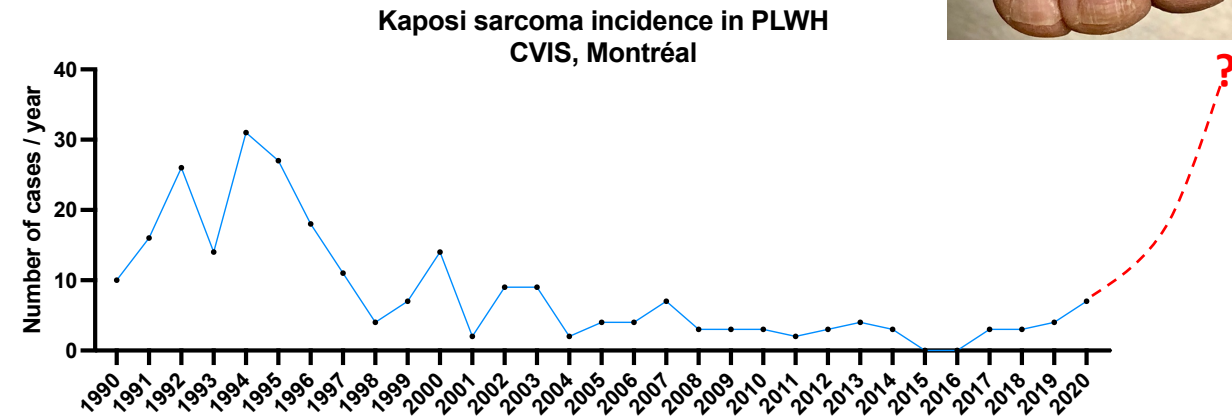
Dr Léna Royston, MD, PhD

Postdoctoral fellow
Dr Jean-Pierre Routy's lab
Montréal, Canada

Background & Methods



- Incidence of HHV8-induced Kaposi sarcoma (KS): decreased in PLWH with ART
- Reemergence of cases in ART-treated PLWH with restored CD4 T-cells and HIV control
- Mostly middle-age men, with cutaneous lesions similar to classic KS lesions arising in elderly men¹



Hypothesis: HIV-induced immunosenescence is associated with a progressive decrease in HHV-8 immune control.

Objective of the study:

- Compare virological and immunological determinants of KS in ART-treated PLWH and in HIV-uninfected people (classic KS)

Prospective cohort study including:

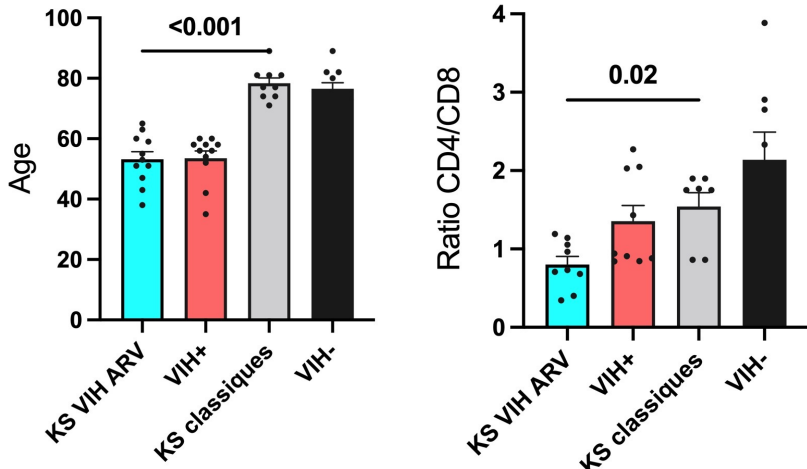
- ART-treated PLWH with undetectable HIV viral load who develop KS (n=10)
 - Age-matched ART-treated PLWH without KS (n=10)
- HIV-uninfected people with classical KS (n=10)
 - Age-matched HIV-uninfected controls without KS (n=10)

Collection of blood (PBMC/plasma) +/- skin samples

¹ Royston et al., *AIDS*

1. Clinical results

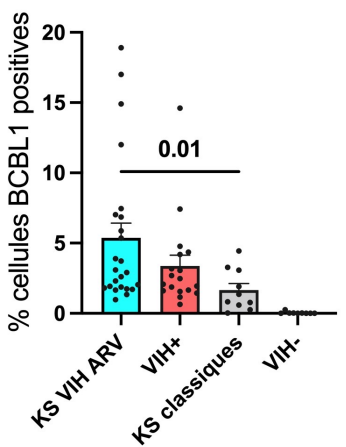
Characteristics	KS ART (n=11)	HIV+ controls (n=11)	Classic KS (n=10)	HIV- controls (n=10)
Age, years (range)	53.0 (38-65)	53.5 (35-60)	78.3 (71-89)	76.5 (70-89)
Sex, % males	100%	100%	80%	80%
CD4 T-cells/ μ L (range)	579 (234, 1099)	509 (346, 1172)	437 (46-730)	929 (517, 1271)
CD8 T-cells/ μ L (range)	608 (357, 1919)	473 (224, 1488)	394 (200, 582)	373 (186-948)
CD4:CD8 ratio (range)	0.73 (0.3, 1.2)	0.91 (0.4, 2.3)	1.31 (0.2-1.9)	2.33 (1.1, 6.1)
HIV VL, log10 copies/mL	<1.7	<1.7	N/A	N/A



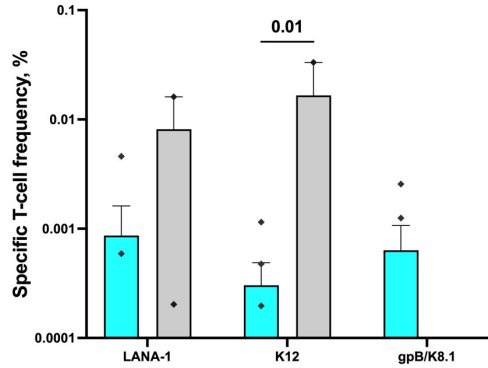
Results: ART-treated PLWH with KS compared to classic KS : \searrow age, \searrow CD4/CD8 ratio

2. Immunological results

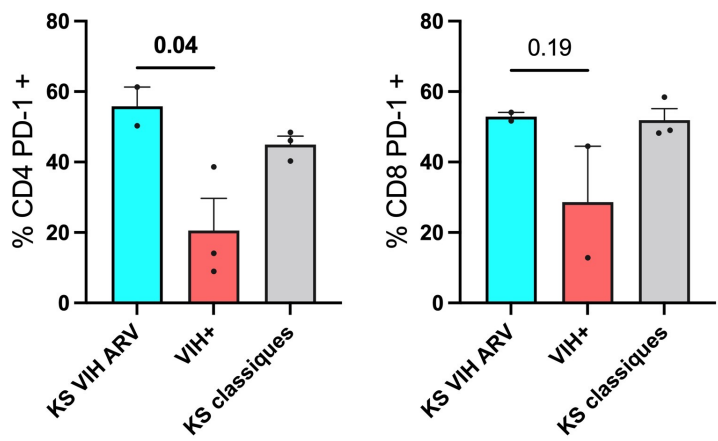
A. Anti-HHV-8 IgGs



B. Anti-HHV8 specific T-cell response



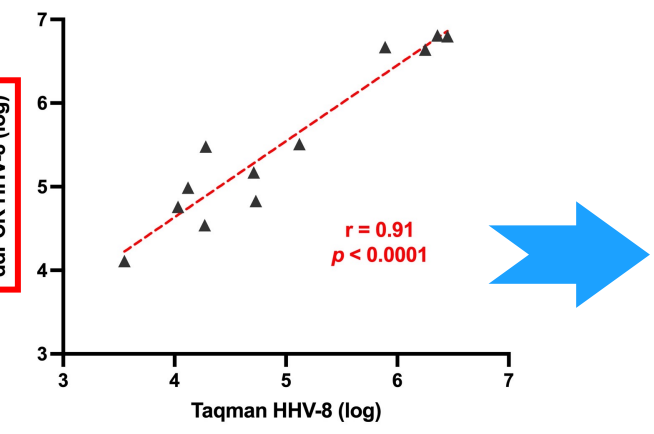
C. T-cell phenotype in skin biopsies



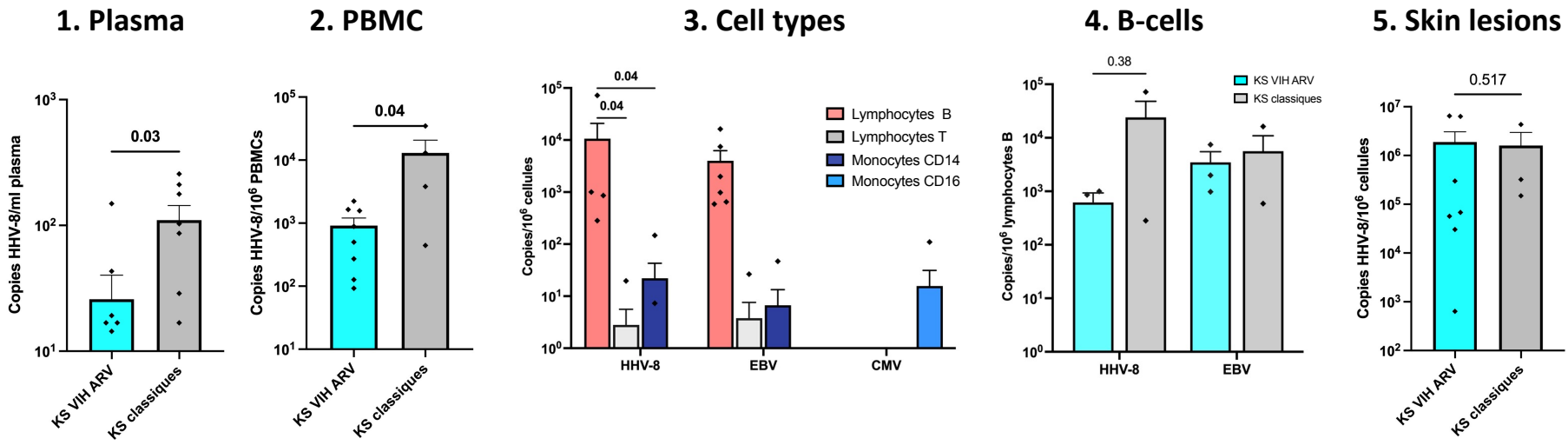
Results: ART-treated PLWH with KS compared to classic KS : \nearrow anti-HHV-8 IgG, \searrow anti-HHV-8 T-cell response, \nearrow PD-1 on CD4 T-cells in skin biopsies in both KS groups

3. Virological results

A. HHV-8 ddPCR assay development

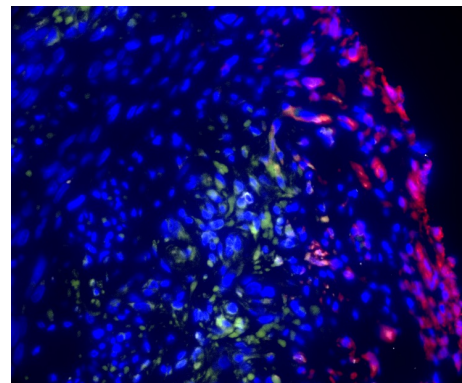


B. HHV-8 quantification in samples



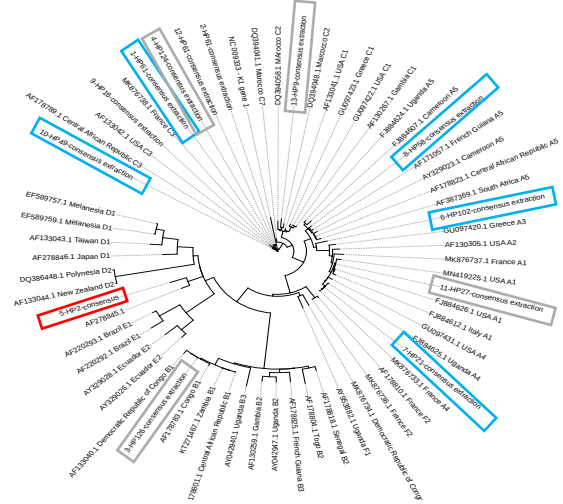
C. HHV-8 detection in tissues by IF

Biopsy of a KS lesion in a ART-treated PLWH



Green: HHV-8 Pink: CD3 Red: CD8

D. HHV-8 whole-genome sequencing



Results:

- ddPCR HHV-8: sensitive and accurate
- ART KS vs classic: \searrow HHV-8 VL in plasma/PBMC
- Genotypes A and C + 1 new subtype !!

KS ART: genotypes A (2) & C (2)
Classic KS: genotypes A (2) & C (2) + 1 new subtype (inuit patient)

Conclusions:

- KS in ART-treated PLWH compared to classic KS: **younger age, lower CD4/CD8 ratio**
- HHV-8 viral control differs between KS in ART-treated PLWH and classic KS:
 - ART KS vs classic: \searrow HHV-8 VL in plasma/PBMC, \searrow anti-HHV-8 T-cell response but \nearrow anti-HHV-8 IgG
 - Genotypes of HHV-8 strains: subtypes A and C + 1 new subtype

Next steps:

- Assessing the phenotype of circulating T-cells, analysis of inflammatory/angiogenic circulating cytokines
- Continue genotyping of HHV-8 strains \rightarrow confirmation of a new subtype/variant?

Acknowledgments



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Dr Jean-Pierre Routy

Dr Stéphane Isnard

Dre Carolina Berini

Josée Girouard

Angie Massicotte

Tsoarello Mabanga

Simeng Bu

All study participants !

lena.royston@mail.mcgill.ca

Sorbonne, Paris

Dre A Jary

Dr V Leducq

Dr V Calvez

Dre AG Marcelin

Université

Montpellier

Dre M Pastore

Dre C Reynes

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