19-21 GIUGNO ROMA
UNIVERSITA' CATTOLICA DEL SACRO CUORE CENTRO CONGRESSI EUROPA
RESEARCH and CARE: FROM BENCH, TO BEDSIDE, TO COMMUNITY
Promosso da SIMIT
16° CONGRESSO NAZIONALE ICAR
Italian Conference on AIDS and Antiviral Research
P 94
POSTER 4 YOU ICAR 2024

NK cell profile in the anal mucosa of MSM living with HIV: results from a single center clinical trial

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Introduction

- HPV infection is recognized as the most prevalent sexually transmitted disease, affecting over 80% of sexually active individuals, and is linked to both malignant and benign lesions in cervical, anal, oropharyngeal, penile, vulvar, and vaginal epithelia.
- People living with HIV (PLWH) had a significantly higher prevalence of HPV infection and the risk of anal cancer development in men who have sex with men (MSM) living with HIV (MSMLWH) is 5 times greater than HIV negative individuals (1).
- HIV infection leads to functional alterations in NK and T cells, favoring HPV persistence and neoplastic transformations in several districts, especially in the anogenital area (2).
- Although the impairment of NK cell activity during HPV infection in women is well documented, there is a paucity of data on the profile of NK cells in anal HPV-infected tissues in the context of HIV-HPV co-infection in MSM.

Methods

MSM living with HIV
n=52

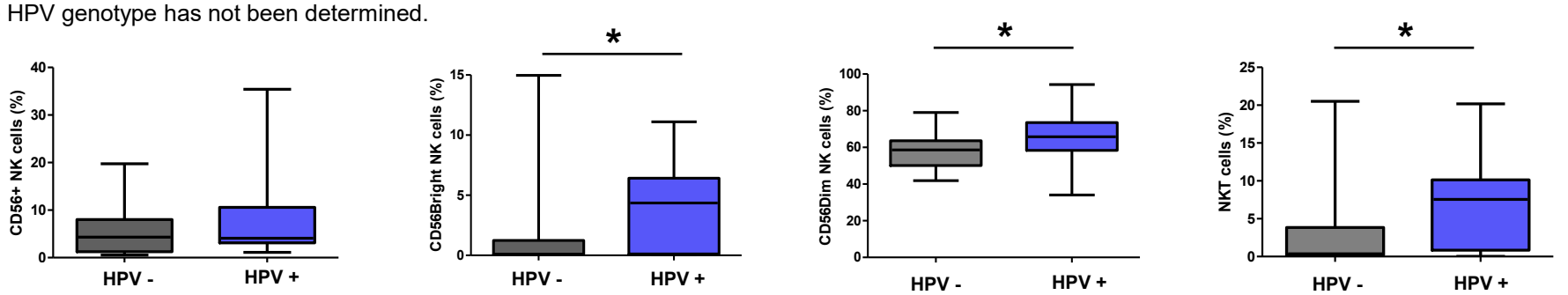
Inclusion criteria:
- age ≥ 18 years old
- being on stable and effective cART for at least 12 months.

Exclusion criteria:
- abnormal anal cytology
- a history of AIN
- being already diagnosed or treated for HPV/anal condyloma.

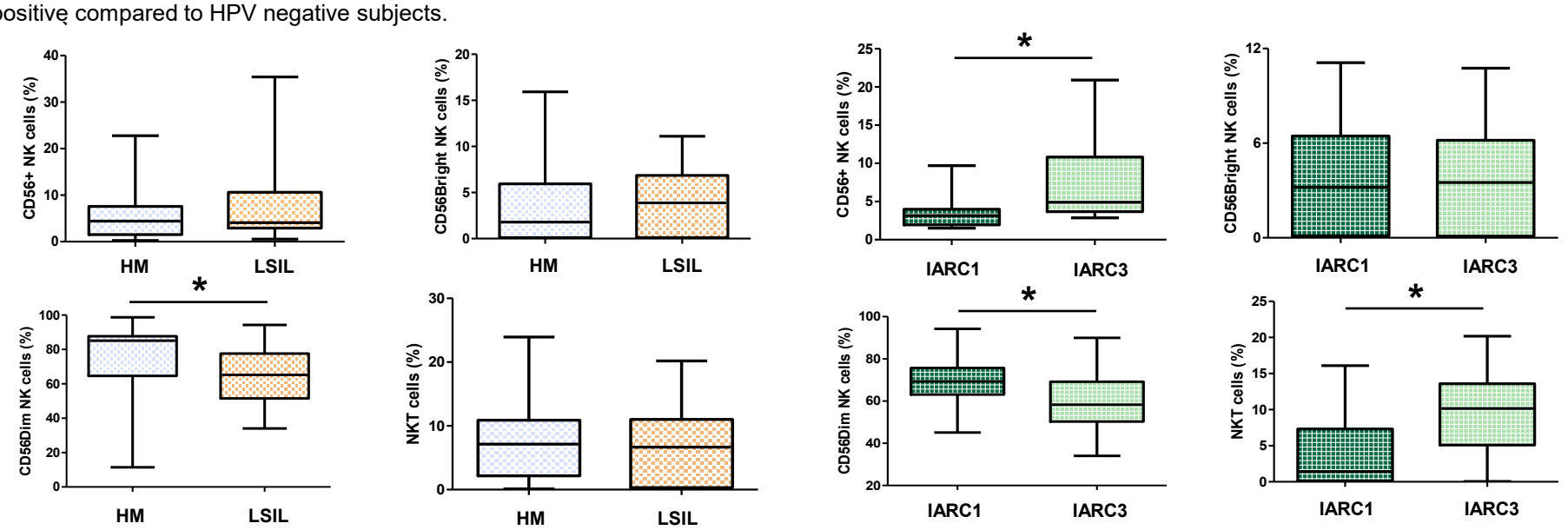
- Anal HPV DNA detection and genotyping
- High Resolution Anoscopy → Anal biopsies → Healthy mucosa-HM / Dysplastic mucosa-LSIL → Frequencies of NK cell subsets: -CD56^{+}CD16^{+} -CD56^{bright}CD16+ -CD56^{bright}CD16+ -NKT

Results

- Among 52 MSMLWH enrolled, HPV DNA was detected in 82.7% (43/52) of anal samples, 2.3% of which showed infection with multiple HPV genotypes. According to IARC HPV classification, 17/43 MSMLWH (39.5%) displayed an HPV infection with a Group 1 genotype, 3/43 (7%) with one belonging to the Group 2, while Group 3 HPV infection was detected in 55.8% (n=24) of HPV positive MSMLWH participants. In 9.3% (4/43) of the positive anal samples the HPV genotype has not been determined.



- Differences in the frequencies of CD56^{bright}CD16^{+} (p=0.009), CD56^{dim}CD16^{+} (p=0.004) NK cells and NKT (p=0.01) were observed in the LSIL of HPV positive compared to HPV negative subjects.



- The frequencies of CD56^{dim}CD16^{+} NK cells were impaired in LSIL of HPV positive MSMLWH as compared to those found in the healthy mucosa (p=0.007);
- The distribution of total CD56^{+}CD16^{+} (p=0.005), CD56^{dim}CD16^{+} NK cells (p=0.04) and NKT (p=0.02) in the LSIL of MSMLWH with IARC Group 1 (high risk) HPV genotype differed from those of IARC Group 3 (low risk).

Conclusion

These results emphasize the importance of mucosal NK-mediated innate immune effector responses during HPV-HIV co-infection and suggest that the impairment of NK cell frequencies may significantly contribute to the progression of HPV-related anal lesions in MSMLWH.

References

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