1333P - Prognostic value of circulating nucleosomes during treatment with or without immunotherapy in Non-Small Cell Lung Cancer: results from Nucleo-Lung study

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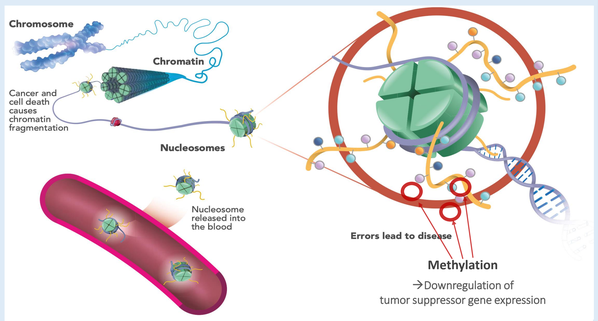
CONTEXT

Epigenetic modifications of **nucleosomes** (DNA wound around histone proteins released into the blood stream after cell death) are involved in gene expression and are dysregulated in tumors *(Scheme 1)*.



Scheme 1: Nucleosomes released by cancer cells carry methylated histones that can be detected in patients' plasma (figure from Volition®)

Aberrant levels of methylated nucleosomes have been reported in **lung cancer** *(Grolleau et al., 2023)* and the diagnostic and prognostic values regarding overall survival (OS) of baseline titers in metastatic NSCLC was previously presented *(Couraud et al. ELCC 2024)*.

OBJECTIVE OF THIS STUDY :

To explore the **prognostic values of nucleosomes titers** regarding overall survival (OS) and progression-free survival (PFS) according to the first-line treatment **with/without immune checkpoint inhibitor (ICI)**

MATERIALS & METHODS

• K2EDTA plasma samples from **45 patients with stage IV NSCLC** were collected at diagnosis and throughout disease management (at each treatment cycle) from the prospective **ONCOPRO** study (NCT03787056) led in the University Hospital of Lyon.

Patients were grouped according to first-line treatment: cohort **05PM = with immunotherapy** (n=21) and cohort **06PM = without immunotherapy** (n=24).

• **H3K27Me3-nucleosome** concentrations were measured by the immunoassay Nu.Q® assays (Volition SRL, Belgium) on IDS i10 automated immunoanalyzer (Immunodiagnostic Systems Ltd, UK).

• Statistics were performed on R software (version 4.2.1). Association with survivals and relapses were quantified by Hazard ratios (HR). The ability to predict events was quantified by the area under the ROC curve.

RESULTS

1 H3K27Me3-nucleosome titers are prognostic for OS at baseline and 3rd cure, regardless of ICI

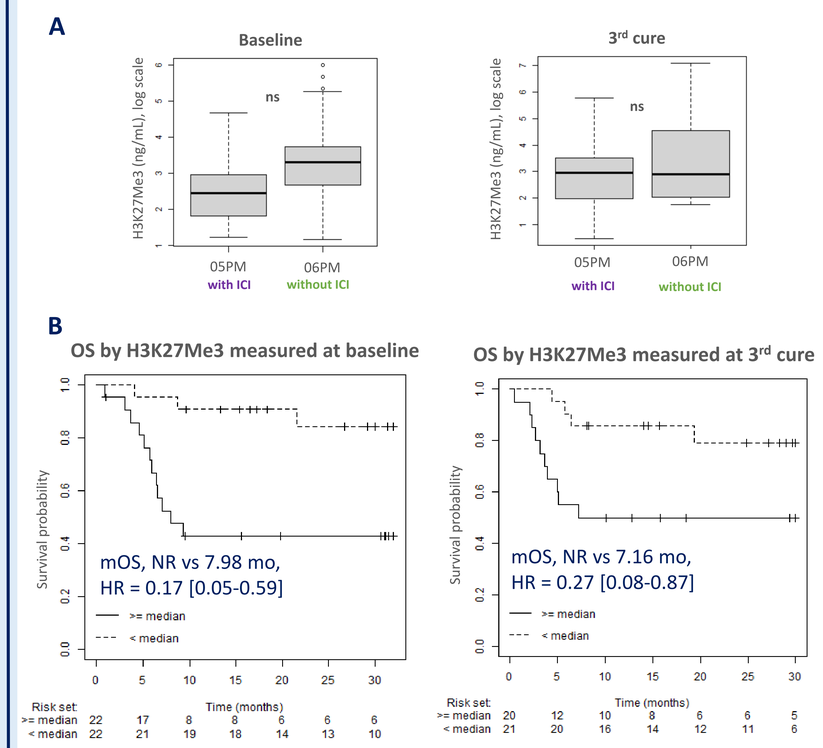


Figure 1

(A) H3K27Me3-nucleosome titers in patients treated in first-line with immunotherapy (05PM) and without immunotherapy (06PM) at baseline (left) (Wilcoxon test, p = 0,051) and after 2 cycles of treatment (right) (Wilcoxon test, p = 0,397). Median H3K27Me3 baseline in 05PM = 11.86 ng/mL; Median H3K27Me3 baseline in 06PM = 27.07 ng/mL;Median H3K27Me3 at 3rd cure in 05PM = 11.56 ng/mL; Median H3K27Me3 at 3rd cure in 06PM = 29.71 ng/mL

(B) Survival analyses according to H3K27Me3-nucleosome titers at diagnosis (left) and after the 3rd cure (right) in patients with metastatic lung cancer independently of treatment.

2 H3K27Me3-nucleosome titers tends to predict PFS in patients without ICI, particularly at baseline

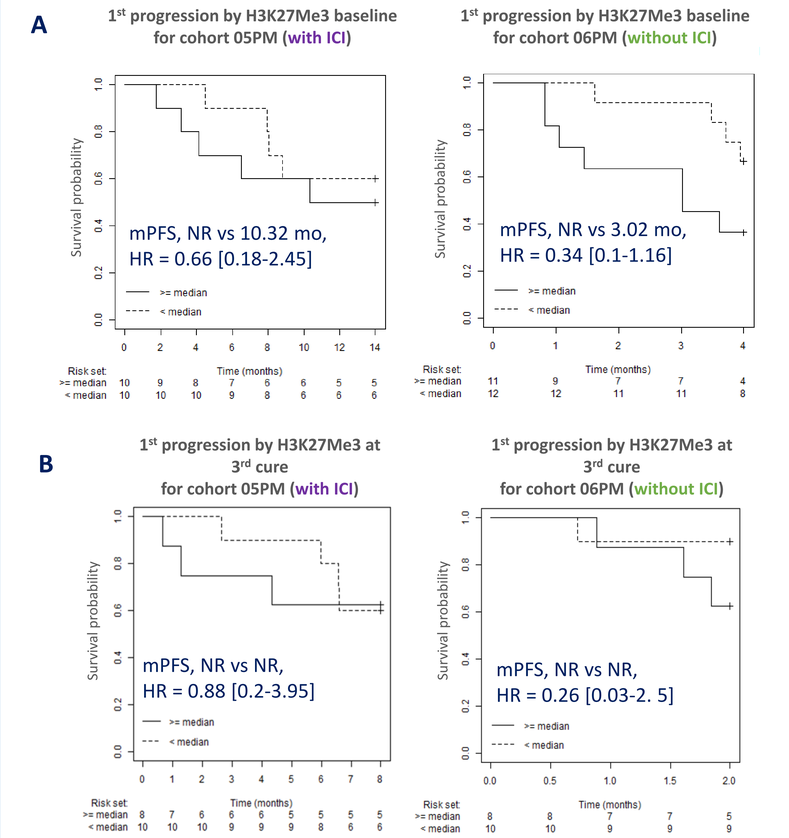


Figure 2

Progression-free survival analyses according to H3K27Me3-nucleosome blood titers at diagnosis (A) and at 3rd cure (B) in the palliative cohorts treated with immunotherapy (05PM, left) and without immunotherapy (06PM, right).

3 H3K27Me3-nucleosome titers and ctDNA mutational status were not related

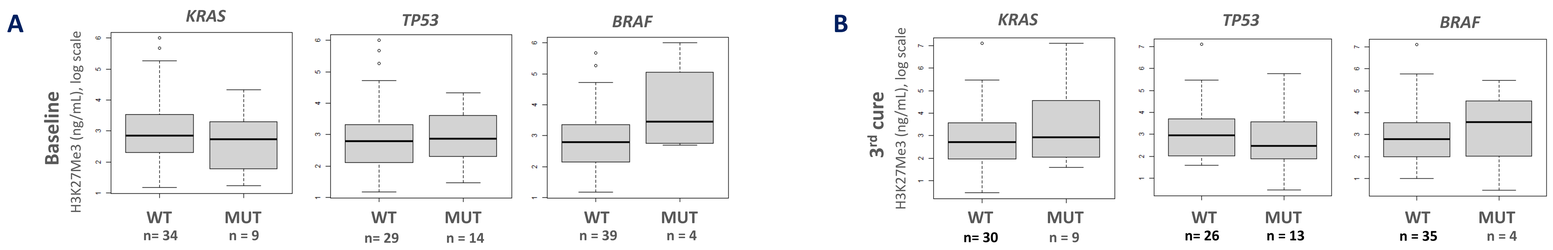


Figure 3

H3K27Me3 concentrations according to circulating tumor DNA mutational status (MUT = mutant, WT = wild-type) at baseline (A) and after 2 cycles of treatment (B).

CONCLUSION

Measurements of H3K27Me3-nucleosome titers:

- **is a non-invasive biomarker potentially relevant in lung cancer monitoring**
- **predictive of survival independently of treatment and mutational status**
- **alerts on the risk of early progression without immunotherapy**

PERSPECTIVES

As a reflect of circulating tumor burden, methylated nucleosomes concentrations could be of interest in the context of **other solid tumors** and will be investigated in other plasma samples collected in the ONCOPRO study (420 patients with 16 types of newly diagnosed cancers).

The association between nucleosomes titers and **molecular profiling** on circulating DNA will be pursued considering the small effective studied herein.

Study sponsored by:

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