Circulating tumor DNA (ctDNA) in advanced non-small cell lung cancer (NSCLC) from HIV-infected patients is associated to shorter overall survival (OS): results from phase II trial (IFCT-1001 CHIVA)


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BACKGROUND
- In 2010, cancer represented 34% of the causes of death in France in HIV-infected population, and lung cancer was the first cause of mortality in this population.
- The prognosis of non-small cell lung cancer (NSCLC) is worse in HIV-positive individuals. Some authors suggest that these poor outcomes may be related to interactions and additive toxicities of the cytotoxic and antiretroviral drugs. A is likely that the disease is particularly aggressive. Recommendations for treatment of advanced NSCLC are lacking in this population, as HIV positiveness is an exclusion criteria from most trials. There is a crucial need to identify new therapeutic targets in this specific population to improve their prognosis.
- We have previously showed in a retrospective cohort of 41 HIV-positive patients that mutation rates were 5.5% for EGFR and 11% for KRAS (Lavolé et al., Rev. Mal. Respir. 2014). However, few data are available on the molecular profile of NSCLC in HIV-positive population.
- Furthermore, circulating tumor DNA (ctDNA) is an approved biomarker to test the presence of EGFR mutations in advanced NSCLC, and it has been shown to be a prognostic marker in HIV-uninfected patients.
- Our goal was to assess its prognosis value and the molecular profile of NSCLC in HIV-positive patients.

METHODS
- 56 HIV-positive patients with advanced NSCLC were included in IFCT-1001 CHIVA phase II trial, evaluating carboplatin AUC5 pre-estimated 500 mg/m2 every 3 weeks, followed by a maintenance with pemetrexed as first line of treatment.
- Baseline blood samples were collected in all patients, and cfDNA was assessed by ultrasensitive NGS using a dedicated variant caller algorithm.
- For OS and PFS, univariate Cox models were applied to select the most promising prognostic variables (threshold p<0.05). A multivariate Cox model was then applied using a backwards procedure to adjust for potential confounders.

RESULTS
- Median OS was 7.5 months (95% CI 5.0-9.0 months).
- Median PFS was 0.7 months (95% CI 0.5-0.9 months).
- The majority of patients (80%) developed detectable ctDNA.
- EGFR mutations were observed in 37% of patients.
- KRAS mutations were observed in 20% of patients.
- 24 patients had received prior chemotherapy.
- 13 patients had received prior radiotherapy.
- 4 patients had received prior biological therapy.

CONCLUSIONS
- This study highlights the potential clinical utility of ctDNA to monitor the evolution of NSCLC in HIV-infected patients.
- The molecular profile of NSCLC in HIV-positive patients is distinct from that in HIV-uninfected patients.
- This study provides a rationale for further investigation of ctDNA in HIV-positive patients with advanced NSCLC.

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