

Abstract 401

Circulating tumor DNA (ctDNA) as predictive biomarker in NSCLC patients treated with Nivolumab

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Authors: [E. Passiglia](#)¹, [A. Perez](#)¹, [A. Listi](#)¹, [M. Castiglia](#)¹, [E. Musso](#)¹, [C. Ancona](#)¹, [S. Rizzo](#)¹, [M. Alù](#)², [L. Blasi](#)², [A. Russo](#)¹; ¹Medical Oncology Unit, Department of Surgical, Oncological and Oral Sciences, University of Palermo, Palermo, Italy, Azienda Ospedaliera Universitaria Policlinico "Paolo Giaccone", Palermo, IT, ²Medical Oncology Unit, Ospedale Civico (A.R.N.A.S.), Palermo, IT

Background

Nivolumab is a programmed death-1 (PD-1) inhibitor recently approved for the treatment of NSCLC patients who failed prior chemotherapy. Searching for predictive biomarkers of immunotherapy efficacy is an area of intensive investigation for translational research. Monitoring circulating tumor DNA (ctDNA) during nivolumab treatment could help clinicians to predict the immunotherapy efficacy and ultimately improve the management of patients.

Methods

From August 2015 to January 2017, 25 NSCLC patients receiving intravenous nivolumab 3 mg/kg every two weeks were included within a translational study. All the patients underwent CT-scan every 6 cycles and responses were evaluated by Response Evaluation Criteria in Solid Tumors (RECIST). Peripheral blood samples were obtained from the patients at baseline and after 4 cycles of therapy and the quantification of ctDNA (ng/ μ L plasma) was performed by qubit dsDNA HS assay and confirmed by qPCR evaluating a 115 bp fragment of ALU repeat. The Mann Whitney test was used for intergroup comparisons of two independent samples. A p-value <0.05 was used as a threshold for statistical significance. Survival analysis was performed using Kaplan-Meier method, providing median and p-value.

Results

Among the 20 patients included, 13 experienced progression disease (PD) at the first CT-scan, 3 partial response (PR), 4 stable disease (SD); 7 patients are still alive at the time of analysis. In 20 patients evaluable for ctDNA analysis at baseline, median ctDNA was significantly higher in patients with time to progression (TTP) < 3 months as compared to TTP > 3 months (p: 0.03). Similarly in 17 patients evaluable for ctDNA analysis after 4 cycles, median ctDNA was significantly higher in patients with time to progression (TTP) < 3 months as compared to TTP > 3 months (p: 0.042). A not significant trend toward a TTP benefit was observed in patients with baseline ctDNA < 0.49 ng/ μ L as compared to ctDNA > 0.49 ng/ μ L (5 vs 3 months; p: 0.06); however ctDNA after 4 cycles < 0.56 ng/ μ L was significantly associated with an improved TTP as compared to ctDNA > 0.56 ng/ μ L (p: 0.05). No significant differences in overall survival (OS) have been observed between these subgroups of patients.

Conclusions

The preliminary results of this study showed that high ctDNA plasma levels are associated with early PD in NSCLC treated with nivolumab, suggesting a potential role of ctDNA as early predictor of response to immunotherapy. These preliminary data need to be explored and confirmed by prospective studies including larger cohorts of patients.

Clinical trial identification

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