#712 Dynamic evolution of blood immune-inflammatory descriptors in advanced Non Small Cell Lung Cancer undergoing first line immunotherapy-based regimens

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BACKGROUND

The groundbreaking results of Immune Checkpoint Inhibitors (ICIs) in NSCLC still involve a limited subset of cases, thus imposing an optimization of patient selection.

METHODS

Peripheral blood was prospectively collected at baseline (T0) and at first radiological disease assessment (T1) from 47 consecutive NSCLC patients undergoing first line ICI-based therapy. We performed a flow-cytometric analysis of circulating CD3+, CD8+, CD4+, NK, NKT and Tregs as their expression of functional molecules (PD-1, Granzyme B [GnzB], Perforin [Perf]) and proliferative index (Ki67). Soluble PD-L1 (sPD-L1) was determined by immunoassay together with Lung Immune Prognostic Index (LIPI: LDH + derived Neutrophil-to-Lymphocyte Ratio). All these parameters were correlated to objective response rate (ORR) according to RECIST v1.1 criteria.

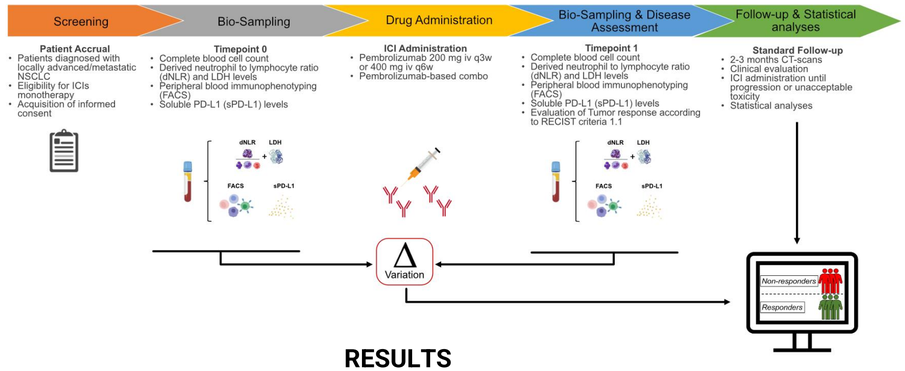
Table 1. Study Population

Age, years (Median, range)		68 (41-82)
		n (%)
Histotype	**SCC**	5 (11)
	ADC	38 (81)
	NSCLC NOS	4 (8)
Sex	**Male**	31 (66)
	Female	16 (34)
Smoking status	**Smokers**	22 (46)
	Ex-Smokers	21 (45)
	Non Smokers	4 (9)
ECOG PS	**0-1**	45 (96)
	2	2 (4)
Stage	**IV**	47 (100)
Number of metastatic sites	**< 3**	14 (30)
	≥ 3	33 (70)
Metastatic Involvement	**Lymph nodes**	44 (94)
	Liver	2 (4)
	Bone	17 (36)
	Adrenal	8 (17)
	Brain	13 (28)
	Contralateral lung	29 (62)
	Pleura	10 (21)
PD-L1 status, % *	**< 1**	8 (17)
	1-49	22 (47)
	≥ 50	13 (28)
Mutational status	**KRAS mutated**	22 (47)
	EGFR mutated $	2 (4)
	BRAF mutated	1 (2)
First-line ICI-based regimen	**Platinum-based ChT + pembrolizumab**	38 (81)
	Pembrolizumab	9 (19)

AIM

To non-invasively intercept tumor-host events implicated in cancer immune surveillance and response to immunotherapy, we explored the dynamic of blood immune-inflammatory markers in a cohort of advanced NSCLC treated with first line ICIs.

STUDY DESIGN



RESULTS

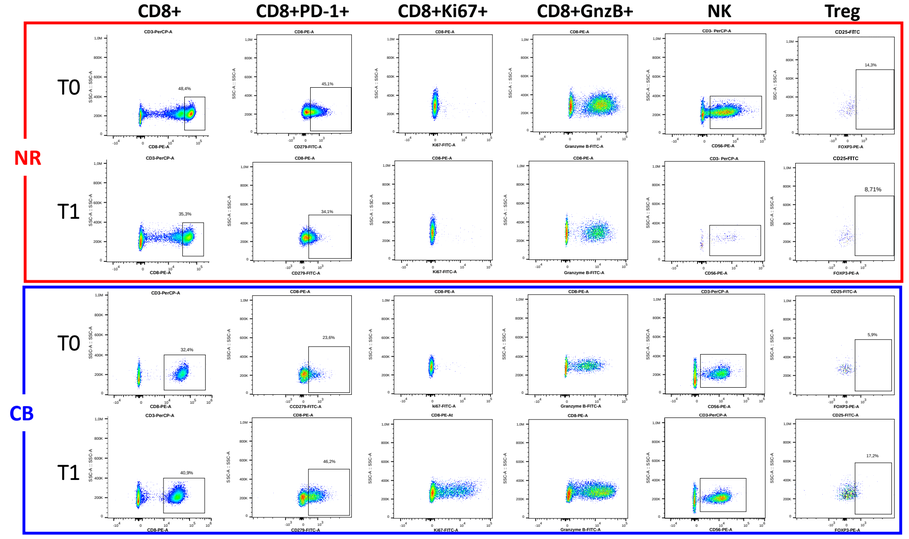


Figure 1. Representative pseudolocolor scatter plots of FACS analysis performed at baseline (T0) and first disease assessment (T1) on peripheral blood from NSCLC patients displaying no response (NR, red) or clinical benefit (CB, blue) to treatment. For NK (CD3-CD56+CD16+) and Treg (CD4+CD25+FOXP3+) only the end product of the gating strategy is shown.

Immune cell dynamics following ICI-based treatment (T0 = baseline; T1 = first radiologic assessment)

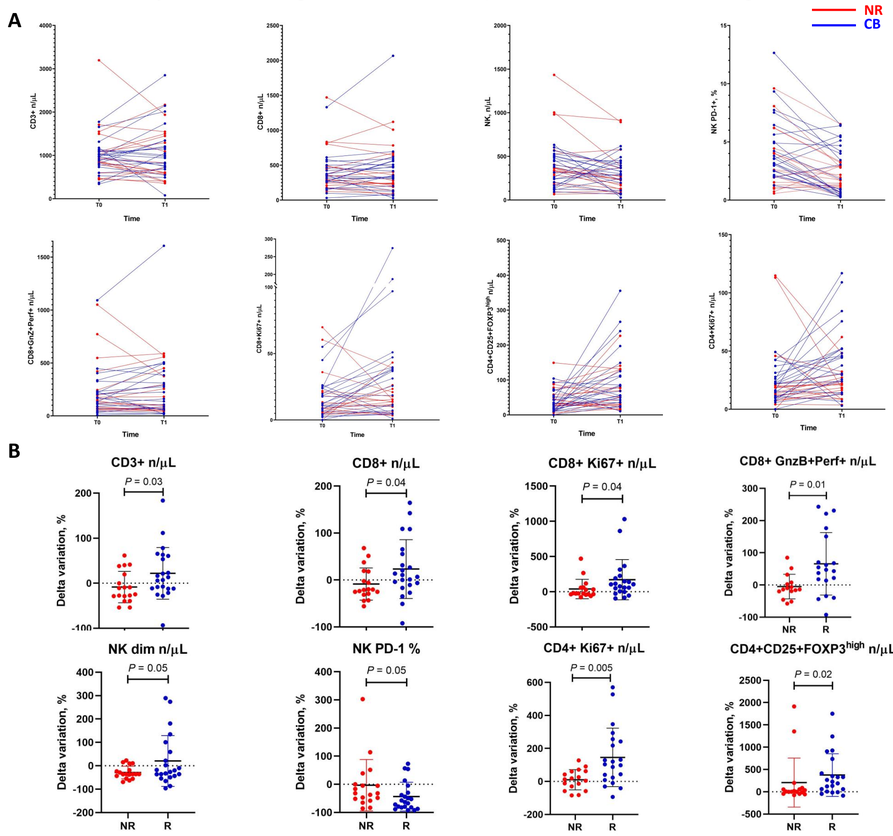


Figure 1. A: Spaghetti plots illustrating the quantitative changes in the absolute number of circulating phenotypes at the two time points in NSCLC patients displaying no response (NR, red) or clinical benefit (CB, blue) to treatment. **B**: Whisker plots of percentage **Δ** variation from T0 and T1 of the indicated blood phenotypes.

CONCLUSION

Our results suggest that tracking the evolution of blood immune-inflammatory profiles may provide valuable predictors of ICI efficacy in NSCLC patients.

The present study is part of a 5-years project funded by Associazione Italiana di Ricerca sul Cancro (AIRC) gathering radiologists, pathologists, molecular biologists and oncologists to test multiomic approaches able to assess the response to immunotherapy in NSCLC.

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