



*Reimagined*  
**2020**   
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Society for Immunotherapy of Cancer



## Dynamic change of PD-L1 expression on extracellular vesicles predicts response to immune-checkpoint inhibitors in non-small cell lung cancer patients

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**I do not have any relevant financial relationship to disclose**



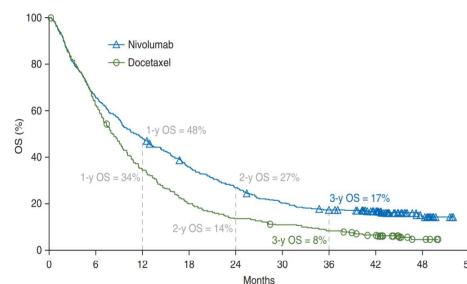
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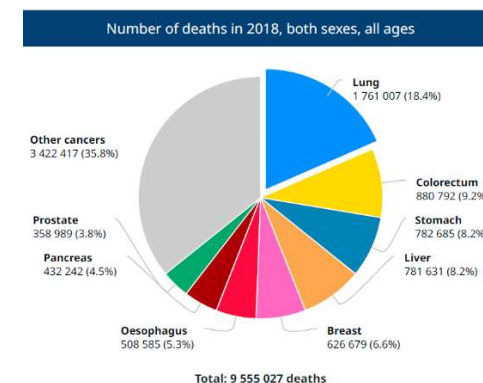
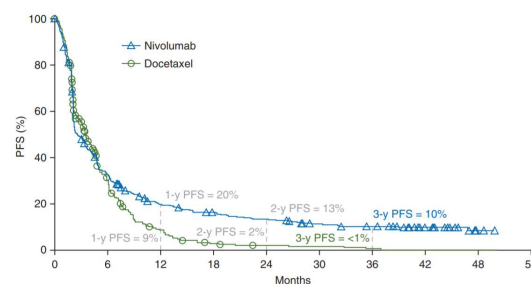
# Introduction

- **Lung cancer and immunotherapy**

- Most frequent and deadliest carcinoma, diagnosed mostly at advanced stages
- Non-small cell lung cancer treatment with immune-checkpoint inhibitors (ICIs)
- Second line therapy



Vokes E.E, et al. *Annals of Oncology* 2018



Ferlay J, et al. *Int J Cancer*. 2019

❖ Only a small subset of patient derive clinical benefit – Suboptimal patient stratification

## Introduction

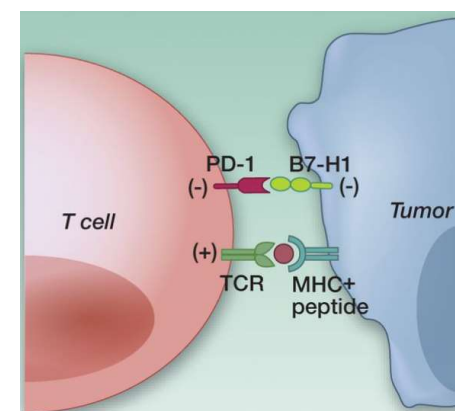
- **Predictive biomarker for ICIs**

**No approved predictive biomarker**

- PD-L1 Immunohistochemistry is the current clinical standard
- Associated to several technical and biological limitations

### PD-L1

- Ligand of PD-1 receptor that can be expressed in tumor cells
- Causes inhibition of T cell and tumor immune evasion



Sznol M, et al. *Clinical Cancer Research* 2013

**Urgent need for accurate predictive biomarkers**



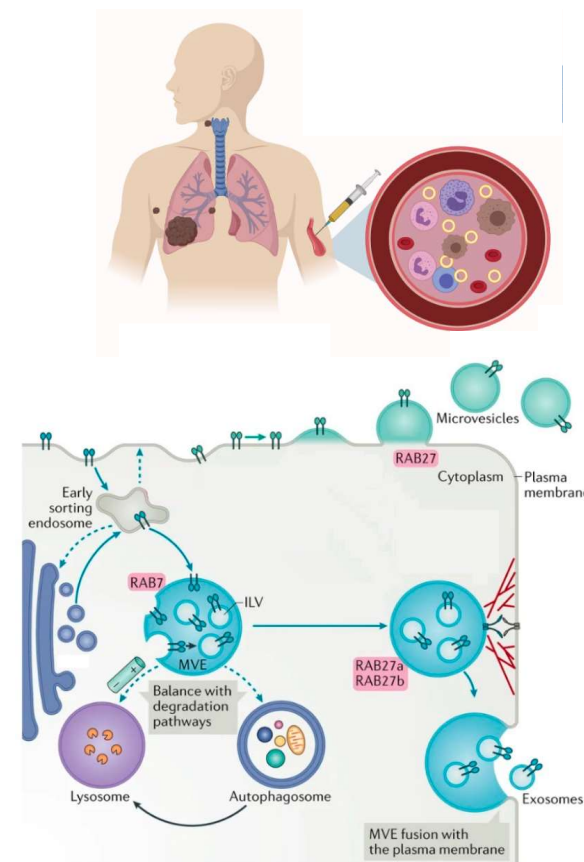
## Introduction

- **Liquid biopsy and extracellular vesicles**

- ✓ Real-time, non-invasive, and repeatable analysis of biomarkers in body fluids.
- ✓ Potential tool for patient stratification and monitoring.

## Extracellular vesicles

- ✓ EVs also play an important role in tumor dissemination
- ✓ Intercellular communication
- ✓ EVs reflect the molecular characteristics of the cell of origin
- ✓ **Present PD-L1: Inhibition of the anti-tumor immune response**



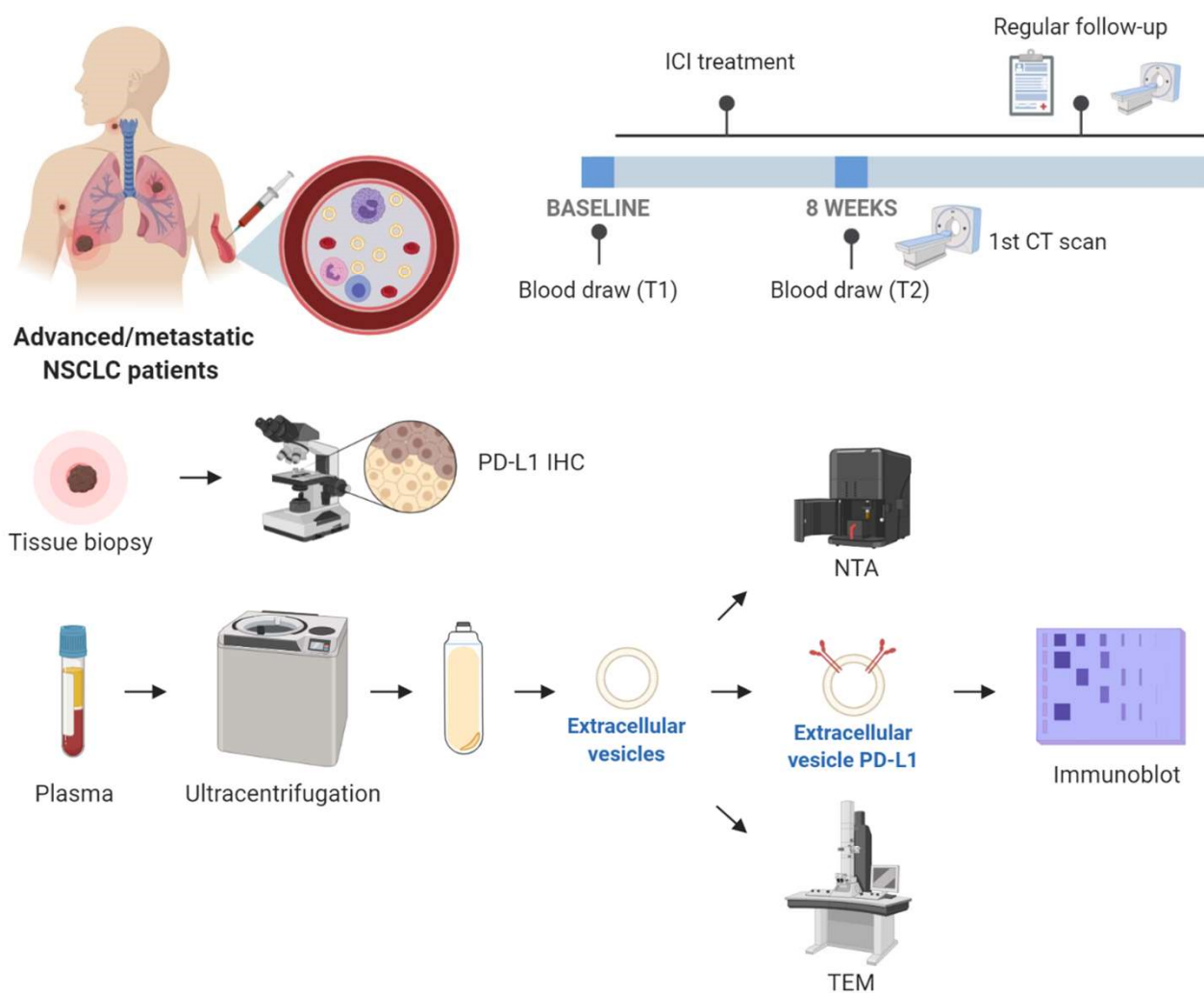
Van Niel G, et al. *Nat Rev Mol Cell Biol.* 2018

## Aims

- ✓ Few only few studies have shown insights about EV PD-L1 role in immunotherapy
- ✓ Suggesting a potential predictive role in melanoma and NSCLC.

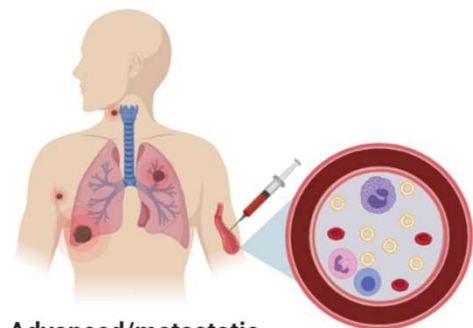
**Evaluate the role of PD-L1 expression in EVs as a predictive biomarker during immunotherapy in NSCLC patients**

# Methods

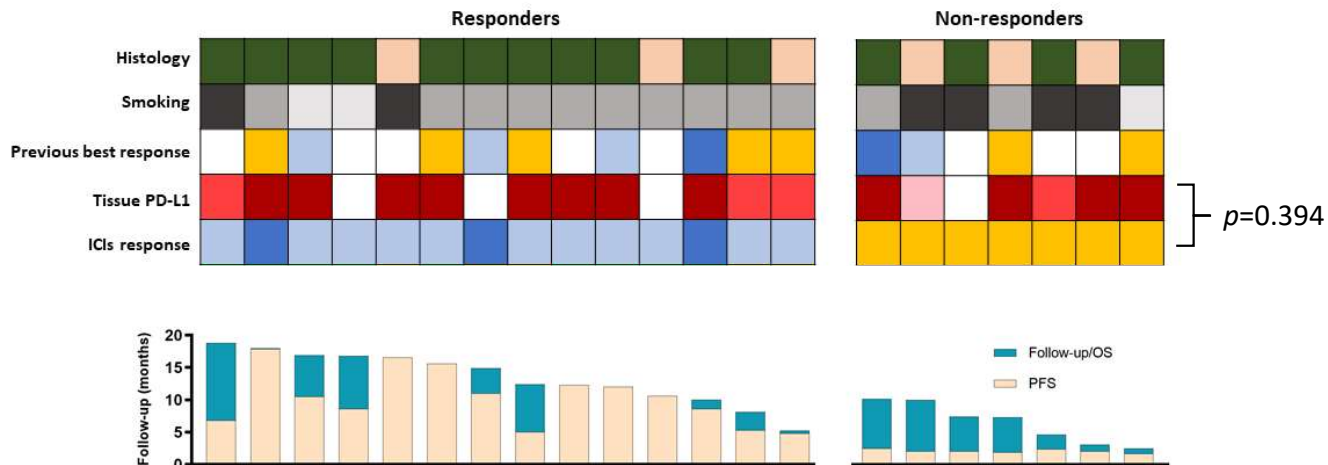
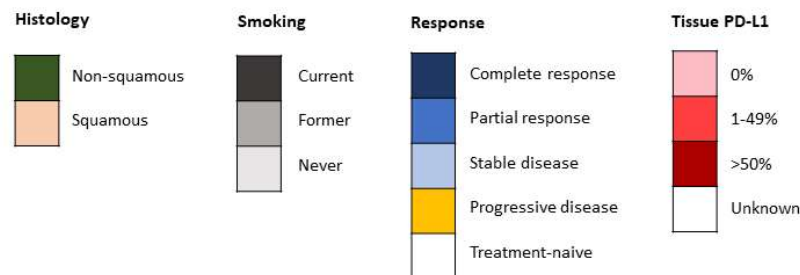
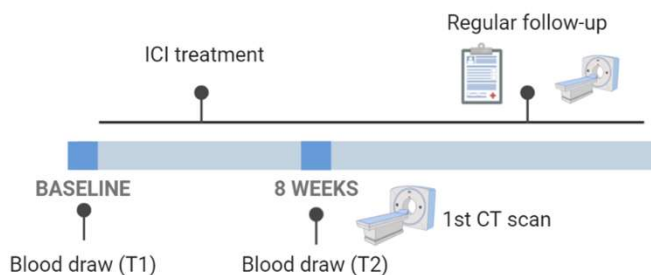




# Results



Advanced/metastatic NSCLC patients

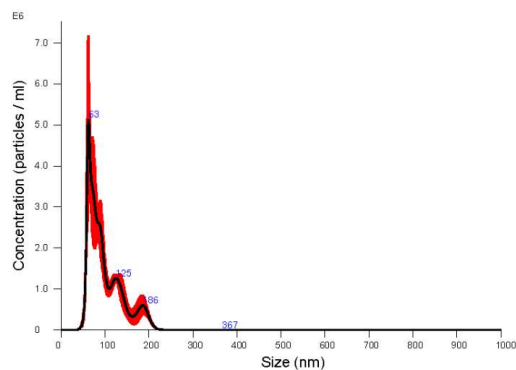


# Results

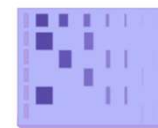
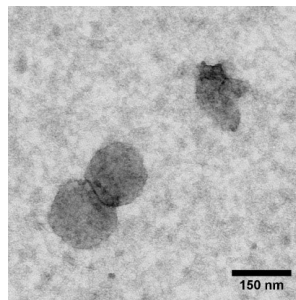
- Extracellular vesicle characterization:



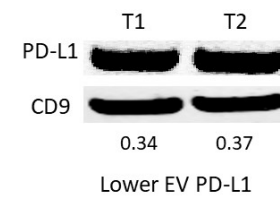
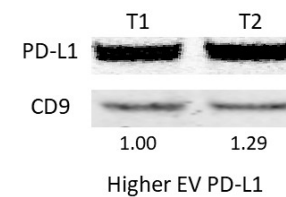
Nanoparticle tracking analysis



Transmission-electron microscopy

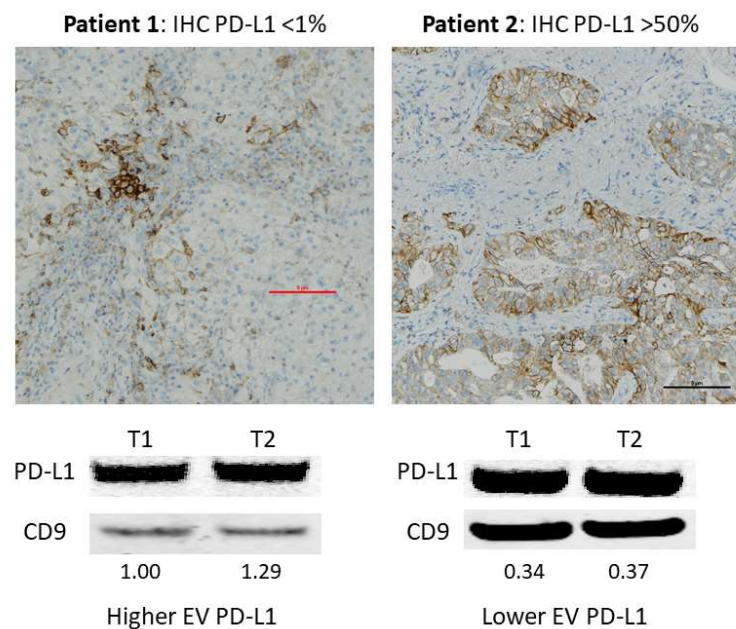


Western blot

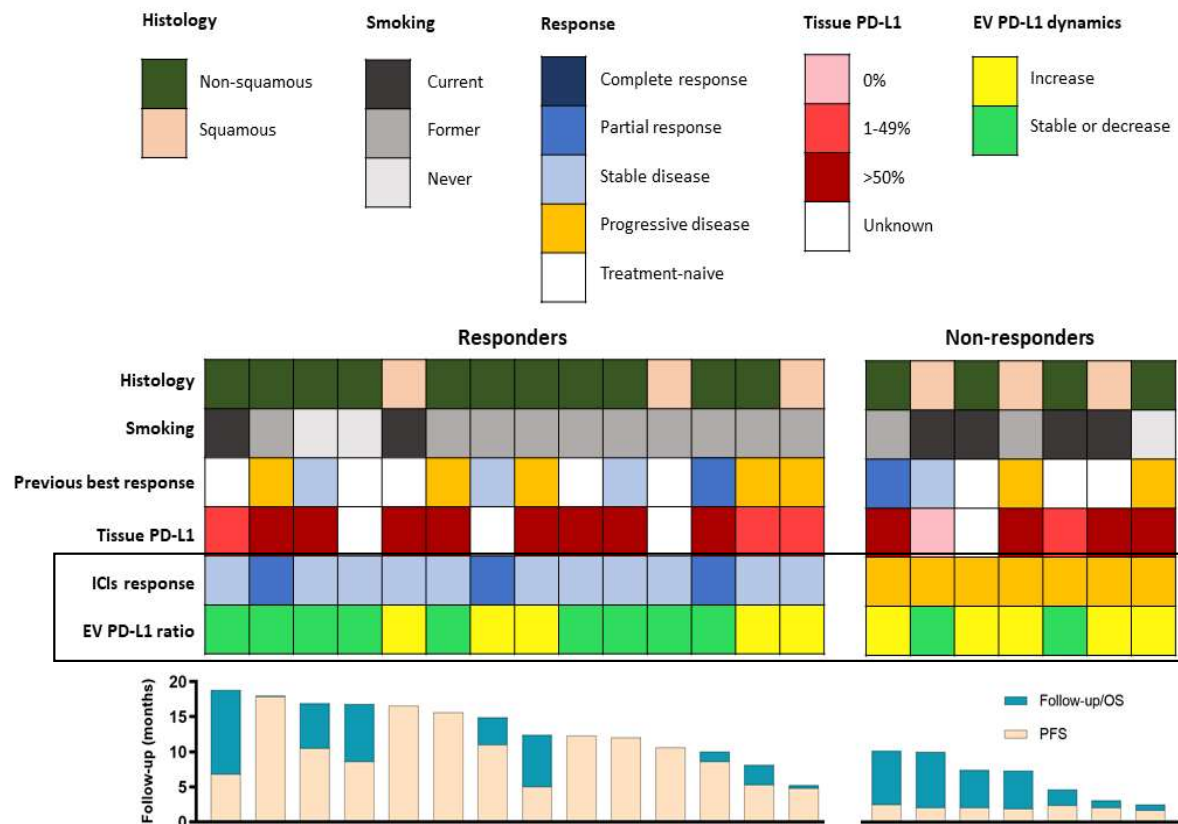
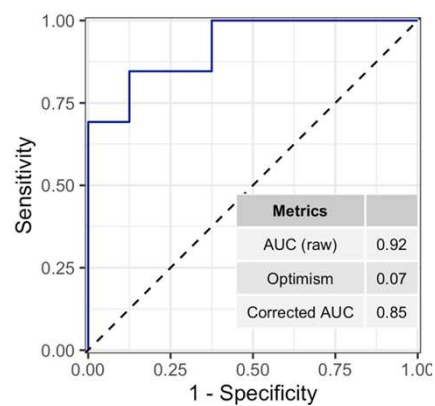
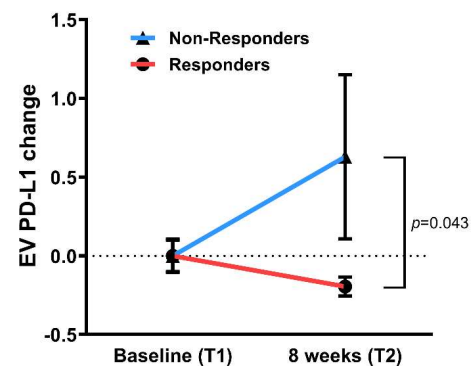


## Results

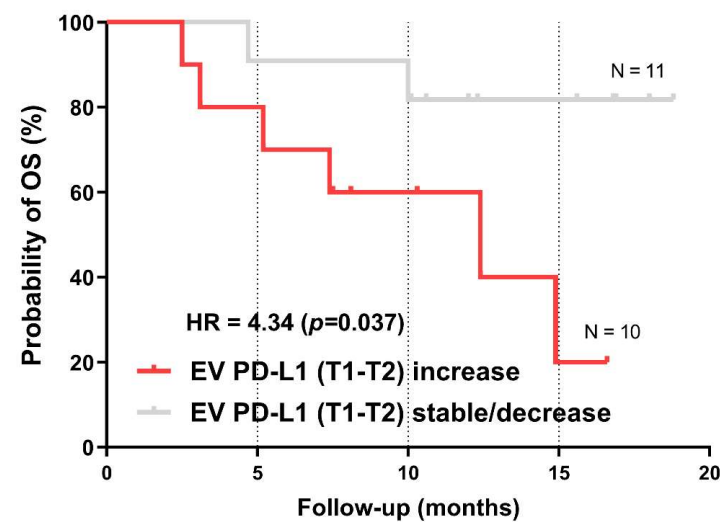
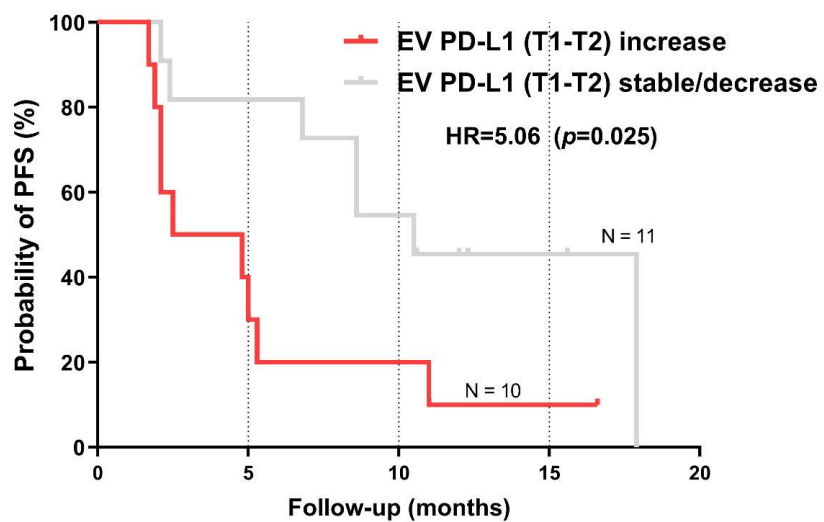
- Tissue and EV levels of PD-L1:



# Results



## Results



## Conclusions - Take home

- The dynamic levels of EV PD-L1 can be used as predictive and prognostic biomarker for the response to immune-checkpoint inhibitors in NSCLC, outperforming the current IHC testing.
- This project lays a first stone for larger studies that would validate the clinical impact of this biomarker.

EV PD-L1 is a promising candidate for guiding treatment decisions in near real-time and for identifying and improving the outcome of NSCLC patients that could benefit from immunotherapy.

Thanks to the patients who participated in the study and the support from our institutions.

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35<sup>th</sup> Anniversary Annual Meeting & Pre-Conference Programs



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