

- Lung cancer is the **leading cause of cancer death** worldwide.
- Lung cancer is often detected at advanced stages. No diagnostic marker has been proven useful in lung cancer clinical practice. The **unmet need** for lung cancer **diagnostic tools** is considered high.
- **C4d**, a complement activation fragment, has been identified as a **new biomarker** for the early diagnostic or prognostic evaluation of lung cancer patients.
- **Indication: lung cancer:**
  - new molecular marker in risk algorithms.
  - patient selection for invasive procedures.

### Scope of the Problem

- In the United States, lung cancer incidence rate is the second highest among men and women and is the most common cause of cancer death in both sexes.
- Lung cancer comprises two subtypes: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). The latter accounts for 80-85% of all cases and includes the two most frequent lung cancer types: adenocarcinomas and squamous cell carcinomas.
- Less than 20% of patients are diagnosed in early stages, when surgical intervention is possible. This explains the poor five-year survival rate (15-20% for all lung cancer tumors and less than 5% in metastatic cases).

### Clinical need

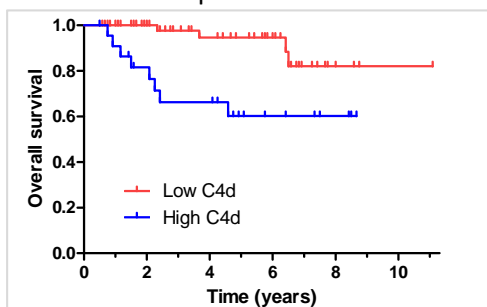
- To significantly increase the percentage of early detected cases is an urgent need.
- Low-dose CT based lung cancer screening studies have reported high rates of detection of cancers in early stages and a reduction in mortality. In this context, the use of **molecular markers** may help in:
  - the implementation of population-based screening programs.
  - the confirmation of the presence of malignant cells.
  - the prediction of its evolution and its biological response to treatment.

### Biomarker Identification

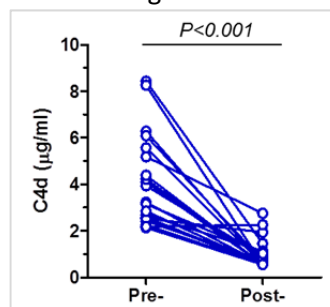
- The role of complement in the control of lung cancer cell growth has been evaluated: lung cancer cells efficiently activate the classical complement pathway.
- C4d, a complement activation fragment, is of value for detection and prognosis of lung cancer.

### Biomarker Validation

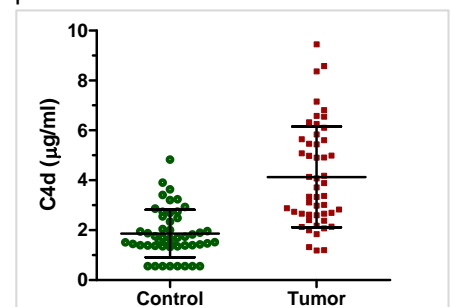
- The value of C4d quantification for the early diagnostic or prognostic evaluation of lung cancer patients is sustained by the use of:
  - different biological samples (tumor tissue, bronchoalveolar lavage fluid and plasma)
  - a range of independent patient cohorts.
- C4d levels in bronchoalveolar lavage fluid and in plasma are increased in samples from lung cancer patients at both advanced (III and IV) and early (I and II) stages compared with control subjects.
- C4d levels in plasma are associated with increased lung cancer risk in asymptomatic individuals.



C4d levels in plasma are associated with shorter survival in lung cancer patients at advanced and early stages. (Figure shows early stages).



C4d levels in plasma are dramatically reduced after surgical removal of lung tumors.



C4d levels in plasma are increased in lung cancer patients at advanced and early stages. (Figure shows advanced stages).

### Competitive Advantage

- C4d is elevated irrespective of the lung cancer histology.
- C4d is not elevated in highly prevalent respiratory diseases such as COPD or emphysema.
- The analytical method is commercially viable and easy to implement in the clinical context.

**Intellectual Property** New lung cancer molecular markers. PCT/EP2013/055823 (licensed to Digna Biotech).

### Reference

Ajona D et al. Investigation of complement activation product c4d as a diagnostic and prognostic biomarker for lung cancer. *J Natl Cancer Inst.* 2013 Sep 18;105(18):1385-93.