Study type	open, non-interventional , prospective, multi-center clinical research platform
Contact details	Sponsor: AIO-Studien-gGmbH, Berlin, info@aio-studien-ggmbh.de Main Project: Steering Board Spokesperson: Prof. Dr. Frank Griesinger Pius Hospital, Oldenburg, frank.griesinger@pius-hospital.de Satellite Stage I/II/III: Steering Board Spokesperson: PD Dr. Wilfried Eberhardt, University Hospital Essen, wilfried.eberhardt@uni-duisburg-essen.de Satellite SCLC: Steering Board Spokesperson: Dr. Martin Sebastian, University Hospital Frankfurt, sebastian@med.uni-frankfurt.de Concept, Project Management and Analyses: iOMEDICO AG, Freiburg, Annette Fleitz, annette.fleitz@iomedico.com (Main Project) Adrian Binninger, Adrian.binninger@iomedico.com (Satellite Stage I/II/III) Adrian Binninger, Adrian.binninger@iomedico.com (Satellite SCLC)
Purpose and rationale	Thorough knowledge of the treatment reality, e.g. characteristics, diagnostic, treatment and outcome of unselected patients in real-life practice, is crucial to evaluate and improve the quality of care for patients with non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). The purpose of CRISP is to set up a national clinical research platform to document uniform data on the molecular testing, treatment, course of disease in patients with NSCLC or SCLC. A particular focus is on molecular biomarker testing before the start of first-line treatment of patients with advanced or metastatic NSCLC. The data shall be used to assess the current state of care and to develop recommendations concerning topics that could be improved. PRO assessment will provide large-scale data on quality of life and anxiety/depression for real-life patients with NSCLC or SCLC in routine practice. In addition, two questionnaires (concerning individual quality of life and patient-caregiver communication) will be validated in German patients with metastatic NSCLC. Furthermore, CRISP will set up a decentralized clinically annotated tissue repository for future collaborative, investigational scientific biomarker testing.
Objectives	To assess molecular biomarker testing, treatment and outcome of patients with NSCLC or SCLC in Germany, in particular: • To collect data on the frequency, methodology and results of molecular biomarker testing before first-line and later-line treatment • To describe types of surgeries, systemic treatments, radiochemotherapies, radiation therapies and sequential treatments thereof applied in real-life practice • To assess effectiveness of treatments in regards to response rate, progression-free survival and overall survival • To describe physician-reported factors affecting treatment decision making besides biomarker profiling • To collect key data on specific supportive therapies • To investigate changes in diagnostics, treatment or outcome during the course of the project • To evaluate patient-reported outcomes concerning (1) general health-related and individual quality of life (QoL), (2) physical and psychological well-being, (3) anxiety and depression, (4) patient-caregiver communication
Population / Number of patients	Main Project: Up to 10.000 patients with locally advanced or metastatic NSCLC at the start of palliative first-line systemic therapy or receiving best supportive care. Of all patients recruited, 5,000 patients will be patients with non-squamous cell

	carcinoma tested for molecular alterations at the start of first-line treatment or patients with squamous cell carcinoma (CRISP patients). The remainder will be patients with untested non-squamous carcinoma (CRISP satellite untested patients stage IIIB/IIIC/IV). Patients included: **7331** (01.October 2021) Satellite Stage I/II/III: Up to 2400 patients with NSCLC stage I, II, stage IIIA, or with NSCLC stage IIIB/C if they are eligible for curative surgery and/or radiochemotherapy, or are receiving best supportive care will be recruited (CRISP satellite I/II/III patients). Satellite Stage II/III started in August 2018. Patients included: **1140** (01.October 2021) Satellite SCLC: Up to 1200 patients with SCLC (limited stage (LD) or extensive stage (ED)) if they are eligible for surgery and/or radio(chemo)therapy and/or systemic therapy, or are receiving best supportive care will be recruited (CRISP satellite SCLC patients). Satellite SCLC started in September 2019. Patients included: **712** (01.October 2021)
Number of sites	Patients will be recruited in up to 150 study sites (certified lung cancer centers, comprehensive cancer centers, hospitals and office-based oncology practices) in Germany. Target number: 170, 186 Initiated
Inclusion criteria	Patients who meet all of the following criteria are eligible for the project: • Age ≥ 18 years • Able to understand and willing to sign written Informed Consent and to complete patient-reported-outcome assessment instruments Main Project: • Confirmed non-small cell lung cancer (NSCLC) • Informed consent no later than four weeks after start of first-line systemic treatment or no later than four weeks after diagnosis for patients receiving “best supportive care only” • Stage IV, or Stage IIIB/C (UICC8) if patient is ineligible for curative surgery and/or radiochemotherapy • Systemic therapy or best supportive care Satellite Stage I/II/III: • Confirmed non-small cell lung cancer (NSCLC) • Informed consent no later than four weeks after start of first anti-tumor treatment (including surgery and radiotherapy) or no later than four weeks after diagnosis for patients receiving “best supportive care only” (i.e. no anti-tumor treatment = no surgery, radiotherapy or systemic therapy) • Stage I, Stage II, Stage IIIA, or Stage IIIB/C (UICC8) if patient is eligible for curative surgery and/or radiochemotherapy • Systemic (chemo)therapy and/or radiation therapy and/or surgery, or best supportive care Satellite SCLC: • Confirmed small cell lung cancer (SCLC) • Informed consent no later than four weeks after start of first anti-tumor treatment or no later than four weeks after diagnosis for patients receiving “best supportive care only” (i.e. no anti-tumor treatment = no surgery, radiotherapy or systemic therapy) • Systemic (chemo)therapy and/or radiation therapy and/or surgery or best supportive care

	Main Project: It is strongly recommended that patients' tumor samples are tested for EGFR mutation in exons 18-21, ALK rearrangement and ROS1 rearrangement as well as PD-L1 expression by a certified molecular pathology laboratory before the start of first-line treatment.
Exclusion criteria	None
Data collection	Baseline (demographic, clinical, tumor) characteristics, details on biomarker testing, including re-testing, treatment decision making, all systemic anti-cancer therapies including details, key data on radiotherapies, surgeries and specified supportive therapies, outcome (response, progression, survival), course of disease. Data will be documented at baseline and updated at least every three months.
Patient-reported outcomes	Patient-reported outcomes will be assessed using the questionnaires Functional Assessment of Cancer Therapy General (FACT-G) core questionnaire, plus the FACT-L, the lung specific module, Patient Health Questionnaire for Depression and Anxiety – ultra brief form (PHQ4), Schedule for the Evaluation of Individual Quality of Life Questionnaire (SEIQoL-Q), and Cancer Communication Assessment tool for Patients and Families – Short (CCAT-PF-Short, (disclosure scale) will be validated in 1,000 patients with advanced NSCLC each. PROs will be assessed at the time of recruitment (baseline), every 2 months for up to 12 months, and every 3 months thereafter for a maximum of 3 years.
Statistics	Descriptive and exploratory statistics will be performed as described in the statistical analysis plan.
Planned timelines	Main Project (Recruitment of up to 6500 patients): First Patient In (FPI) Q4/ 2015 Last Patient In (LPI) Q4/ 2020 Last Patient Out (LPO) Q4/ 2023 Interim analysis Annually Final analysis 2023 CRISP 10000 (Amendment, inclusion of further 3500 Patients) Start Recruitment for another 3 years: Q1/2021 LPI (approx. 10000 patients) Q2/2023 LPO Q2/2026 Final report CRISP 10000 Q4/2027 Satellite Stage II/III (first 800 patients): First Patient In (FPI) Q3/ 2018 Last Patient In (LPI) Q1/ 2020 Last Patient Out (LPO) Q1/ 2023 Interim analysis Annually Final analysis 2023 Satellite I/II/III (additional 1600 patients): Restart of recruitment Q3 2020 LPI Satellite I/II/III Q3 2023 LPO Satellite I/II/III Q3 2026 Final analysis Satellite I/II/III 12 months after LPO (planned 2027) Satellite SCLC: First Patient In (FPI) Q3/ 2019 Last Patient In (LPI) Q3/ 2023 Last Patient Out (LPO) Q3/ 2025 Interim analysis Annually Final analysis 12 months after LPO (planned Q3 2026)

	The individual observation time is until death or end of project (LPO). Publication: Various publications during and after the project