

218eTiP - The PULMO-01 phase I/IIa study of roginolisib in combination with dostarlimab, with or without docetaxel, in patients with advanced non-squamous NSCLC who have progressed on standard of care therapy

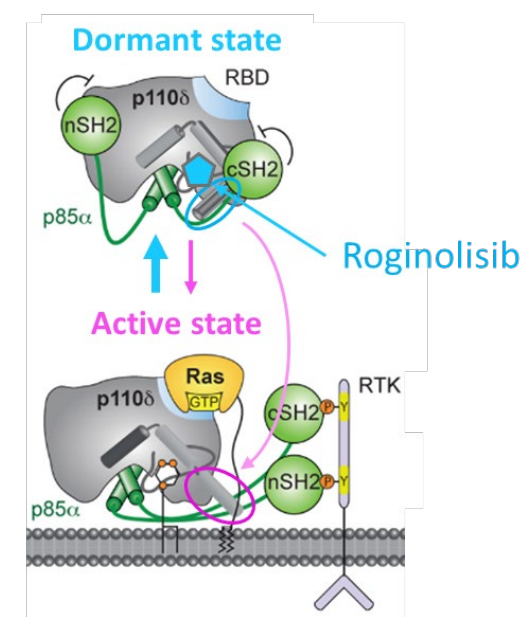
R Wener¹, A Azkàrate², A Bearz³, A Delmonte⁴, E Nadal⁵, I Demedts⁶, A Santoro⁷, O J Juan-Vidal⁸, A Sánchez-Gastaldo⁹, M Cantarini¹⁰, G di Conza¹¹, M Emig¹⁰, T Hammett¹⁰, P Kaur¹⁰, K Tonge¹⁰, L van der Veen¹⁰, M Lahn¹⁰, M Hojouj¹¹, M Maio¹²

¹ Universitair Ziekenhuis Antwerpen, Antwerp, Belgium, ² Hospital Universitari Son Espases, Palma, Spain, ³CRO Aviano, National Cancer Institute, IRCCS, Aviano, Italy, ⁴Istituto Scientifico Romagnolo per lo Studio e la cura dei Tumori, Meldola, Italy, ⁵Catalan Institute of Oncology, Bellvitge Biomedical Research Institute, Barcelona, Spain, ⁶AZ Delta Hospital, Roeselare, Belgium, ⁷IRCCS Humanitas Research Hospital - Humanitas Cancer Center, Milan, Italy, ⁸Hospital Universitari i Politecnic La Fe, Valencia, Spain, ⁹Hospital Virgen del Rocío, Sevilla, Spain, ¹⁰iOnctura SA, Geneva, Switzerland, ¹¹Simbec Orion, United Kingdom, ¹²University of Siena, Center for Immuno-Oncology, University Hospital of Siena, Siena, Italy.

BACKGROUND

Patients with advanced non-small cell lung cancer (NSCLC) without actionable driver mutations who progress on immune checkpoint inhibitors (ICI) and platinum-based chemotherapy, are in need of well-tolerated and effective new therapies.

Roginolisib - Allosteric Modulator of PI3Kδ

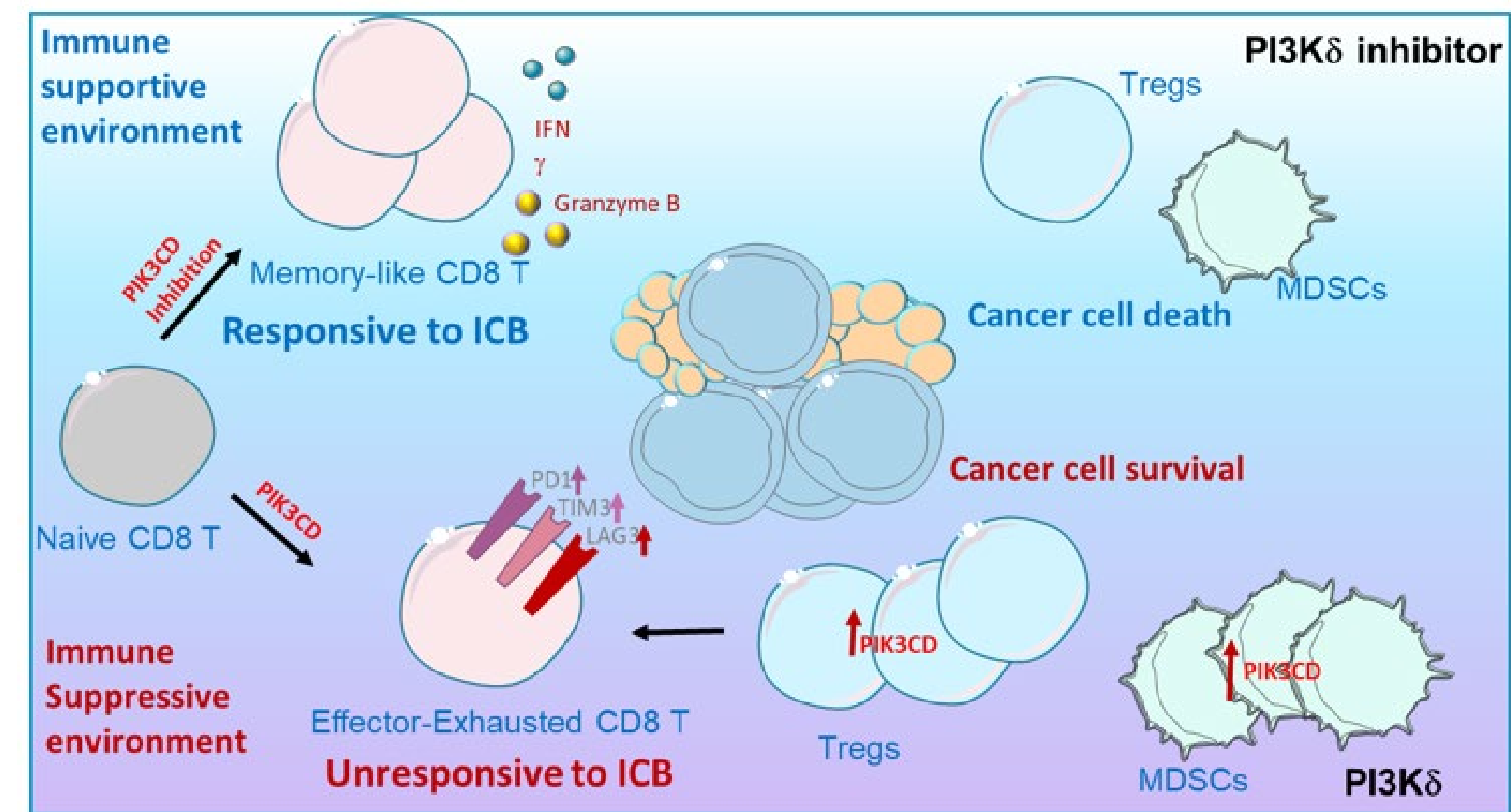


Roginolisib precisely binds and locks dormant PI3Kδ preventing activation to inhibit oncogenic signaling & restore normal signaling.

- **Roginolisib** (IOA-244) is a novel highly selective, non-ATP competitive, small molecule inhibiting phosphoinositide 3-kinase delta (PI3Kδ) through allosteric modulation locking PI3Kδ in an inactive “dormant” state.
- **Dostarlimab** is a humanized IgG4 monoclonal antibody that binds to the programmed death receptor-1 (PD-1) on T cells and blocks its interaction with the ligands PD-L1 and PD-L2, thereby releasing PD-1–mediated inhibition of the anti-tumor immune response.
- In NSCLC, *PIK3CD* gene expression is upregulated and strongly correlated with regulatory T cells (Tregs) abundance (Di Giacomo 2021, Kalla et al. 2024)
- The accumulation of Tregs in the tumour microenvironment is often associated with immune evasion and resistance to ICI resulting in poor response to treatment and worse prognosis (Spiliopoulou 2024).
- Roginolisib is designed to block both, tumour-cell intrinsic (i.e. PI3Kδ up regulation) and extrinsic mechanisms, including Treg cells, B cells, and myeloid-derived suppressor cells (MDSCs).

We hypothesise that roginolisib, through PI3Kδ inhibition, induces a reduction in Tregs and MDSCs and induces proliferation of memory like CD8+ T cells, thereby increasing the responsiveness to immunotherapy (i.e. dostarlimab). Furthermore, the addition of chemotherapy to both immunologically active compounds (i.e., dostarlimab and roginolisib) might enhance the immunogenic-induced cell death (Fabian et al. 2021).

Figure 1: Role of PI3Kδ across immune and cancer cells in solid tumours



IFNγ=interferon γ; LAG3=lymphocyte-activation gene 3; PD-1=programmed cell death protein 1; PIK3CD=phosphoinositide-4,5-bisphosphate 3-kinase catalytic subunit delta; TIM3=T cell immunoglobulin domain and mucin domain-containing protein 3; Treg=T regulatory cell (Ali 2014, Abu Eid 2017, Yoon 2021, Johnson 2023)

METHODS

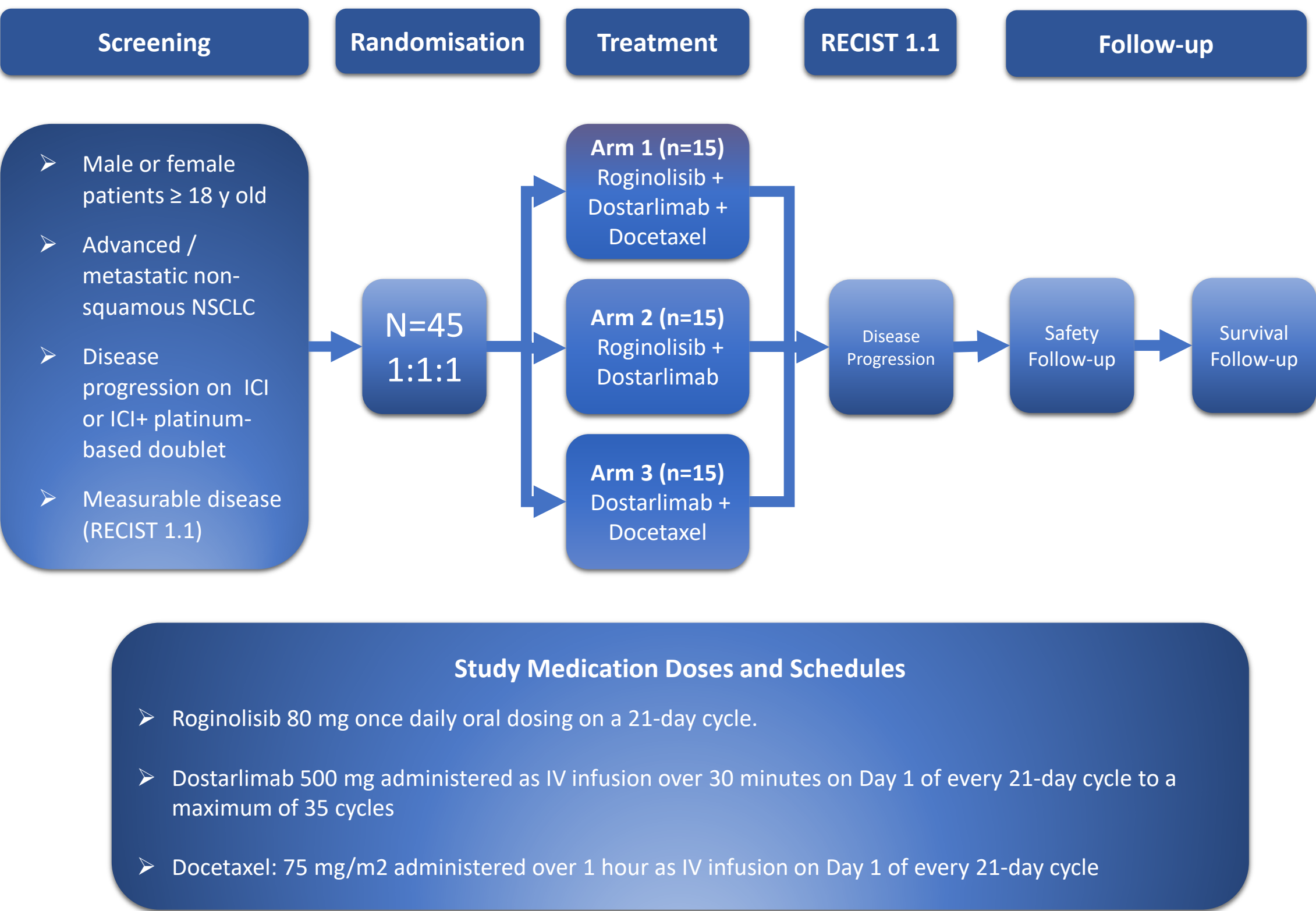
Design:

PULMO-01 (NCT06879717) is a Phase I/II open-label, randomised, parallel-arm, multi-centre study

Key Eligibility Criteria:

- Male and female patients ≥18 years of age
- ECOG performance status of 0 or 1
- Histologically or cytologically confirmed stage IIIb/IV or recurrent non-squamous NSCLC
- Have measurable disease per RECIST v1.1 as determined by the investigator
- Documented radiographic disease progression on or after prior anti-PD(L)1 therapy and platinum chemotherapy or after standard immunotherapy without chemotherapy in accordance with standard of care
- Have not been previously treated with dostarlimab or docetaxel
- Have no known active CNS metastases and/or carcinomatous meningitis (patients with previously treated brain metastases may participate provided they are stable)

Figure 2: Study Schema



STUDY STATUS

- Enrolment started in April 2025 and was completed in December 2025
- A total of 63 patients were enrolled at 10 sites across Italy, Spain and Belgium.
- 51 patients were randomised and 49 were dosed.

STUDY OBJECTIVES AND ENDPOINTS

Primary Objective

- To assess the safety and tolerability of roginolisib plus dostarlimab, with or without docetaxel, and dostarlimab plus docetaxel
- To compare across treatment arms the proportion of patients with a reduction in peripheral blood Tregs (for example as defined by CD4⁺CD25⁺CD127⁻ expression)

Secondary Objectives

- To further evaluate across treatment arms immune cell subsets in peripheral blood (such as naive, activated, memory and exhausted CD8+ and CD4+ T-cells, B cells, NK cells, dendritic cells, monocytes and granulocytes) following treatment
- To evaluate preliminary signs of clinical efficacy across treatment arms
- To determine the pharmacokinetic (PK) parameters of roginolisib when given in combination with dostarlimab with or without docetaxel

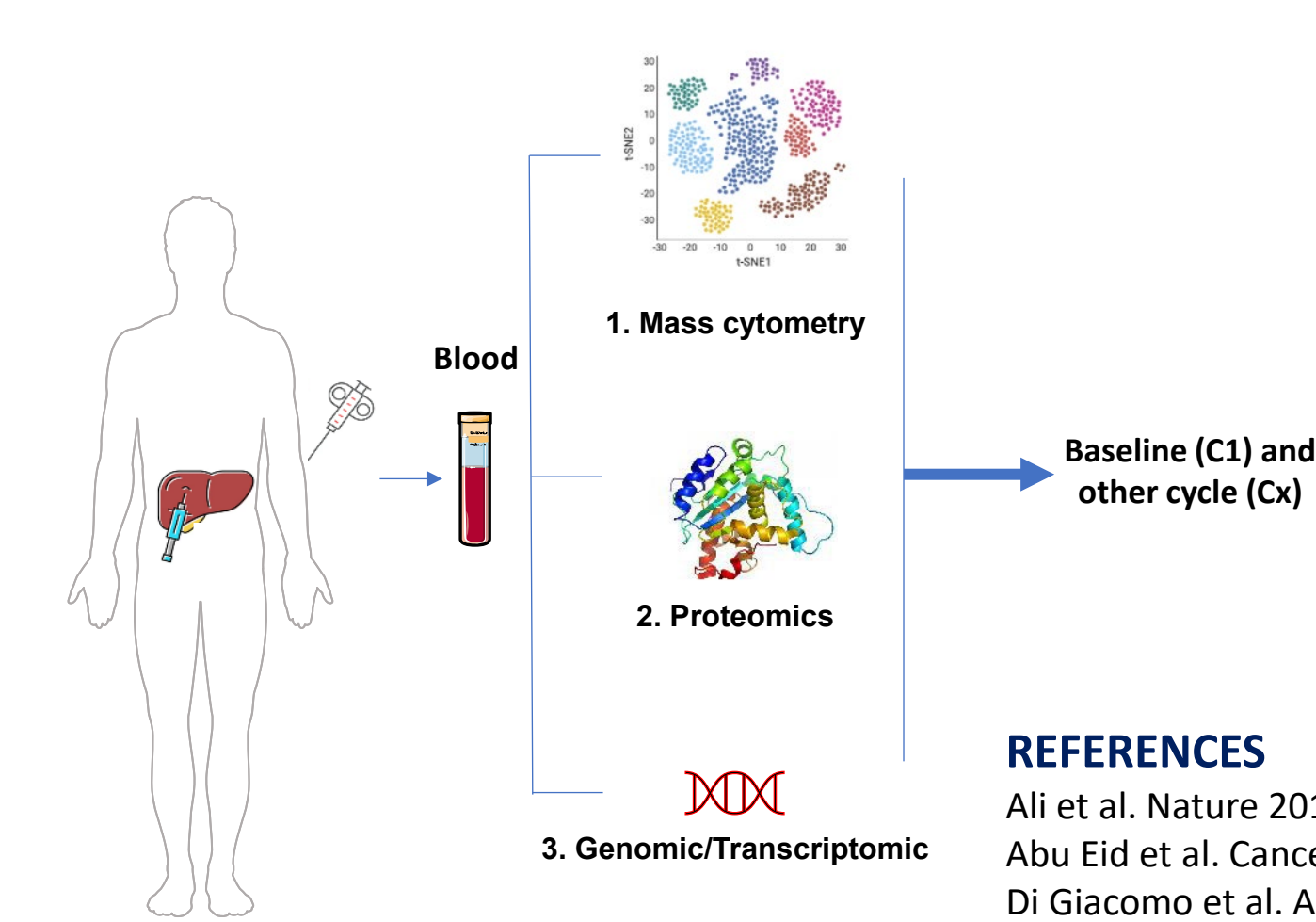
Exploratory Objectives

- To evaluate the effect of roginolisib on chemokine and cytokine levels in plasma
- To determine genetic mutations and gene expression to evaluate potential predictive markers for response to treatment

Assessments of Endpoints

- Toxicities graded to Common Terminology Criteria for Adverse Events (CTCAE) version 5.0
- Change from baseline in peripheral blood Tregs of at least 50% by Day 42 as assessed by mass cytometry (cytometry by time of flight, CyTOF)
- Change from baseline in immune related signatures as assessed by mass cytometry (expanded analyses), proteomics, genomics/transcriptomics (DNA/mRNA, including ctDNA)
- Objective response rate, duration of response, disease control rate, clinical benefit rate and progression free survival per RECIST v1.1 as assessed by the investigator, and overall survival

Figure 3: Translational Analyses Performed on Blood Samples



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