

DAREON®-Lung-1: Phase III Trial of First-Line Obixtamig Plus Standard of Care (Atezolizumab, Carboplatin, and Etoposide) Versus Standard of Care in ES-SCLC

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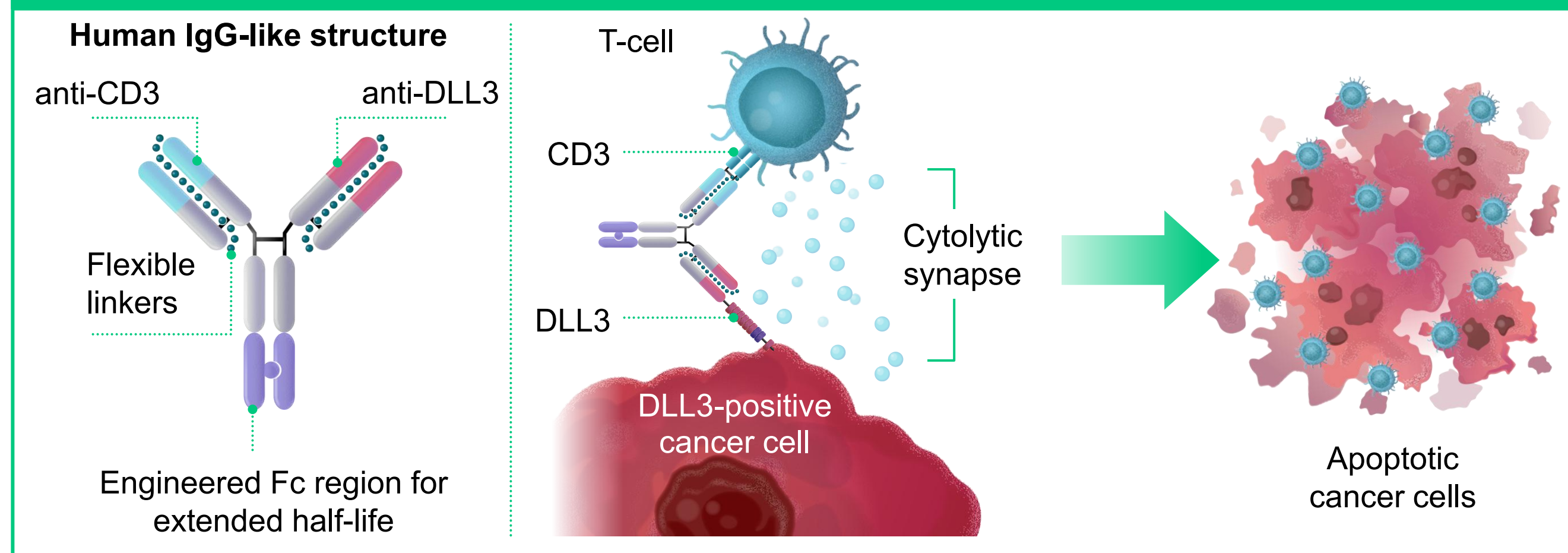
Ticiana Leal^{1*}, Anne-Marie C. Dingemans², Rafal Dziadziuszko³, Shun Lu⁴, Martin Wermke⁵, Tatsuya Yoshida⁶, Yiyuan Ma⁷, Wibke Fader-Schwerin⁸, Dian Yang⁹, Valeria Lifke¹⁰, Solange Peters¹¹

¹Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA, USA; ²Department of Pulmonary Medicine, Erasmus MC Cancer Institute, Erasmus University Medical Center, Rotterdam, The Netherlands; ³Department of Oncology and Radiotherapy, Medical University of Gdańsk, Gdańsk, Poland; ⁴Department of Thoracic Oncology, Shanghai Jiao Tong University, School of Medicine, Shanghai Chest Hospital, Shanghai, China; ⁵NCT/UCG Early Clinical Trial Unit, TU Dresden University of Technology, Dresden, Germany; ⁶Department of Thoracic Oncology, National Cancer Center Hospital, Tokyo, Japan; ⁷Department of Medical Oncology, Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; ⁸Global Clinical Development Operations, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim am Rhein, Germany; ⁹Global Biostatistics & Data Sciences, Boehringer Ingelheim (China) Investment Co., Ltd., Shanghai, China; ¹⁰Global Experimental Medicine Oncology, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an der Riss, Germany; ¹¹Department of Oncology, Centre Hospitalier Universitaire Vaudois, Lausanne University, Lausanne, Switzerland

Introduction

- Due to the aggressive nature of SCLC,¹ early initiation of optimal induction therapy is essential
- The current 1L SoC for ES-SCLC is platinum/etoposide combined with a PD-L1 inhibitor.¹ However, median OS (~12–13 months) remains poor,^{2,3} indicating an unmet need for improved therapeutic options
- DLL3 is an inhibitory Notch ligand that is expressed on tumors in ~94% of patients with SCLC, but with minimal expression in healthy adult tissue^{4–6}
- Obixtamig is a novel IgG-like DLL3/CD3 T-cell engager designed to selectively target DLL3-positive tumor cells: simultaneous binding to DLL3 and CD3 redirects T-cells to kill tumor cells^{7–9}

Mechanism of action of obixtamig^{7–9}



- In the Phase I DAREON®-8 study (NCT06077500), 1L obixtamig plus carboplatin, etoposide, and atezolizumab demonstrated manageable safety and encouraging clinical activity in patients with ES-SCLC, particularly with the selected obixtamig target dose (60 mg),¹⁰ providing evidence to support further clinical development in a Phase III trial

DAREON®-8 study: safety and efficacy¹⁰

1L obixtamig + SoC showed a safety profile consistent with individual treatments	No patients experienced grade ≥3 CRS, ICANS, or potential ICANS-like neurotoxicity events	The most common grade ≥3 AEs were cytopenias and were almost wholly related to chemotherapy
	Obixtamig 60 mg (n=29)	All patients [†] (N=44)
Confirmed ORR, % (95% CI)	76 (58–88)	73 (58–84)
Confirmed DCR, % (95% CI)	90 (74–96)	91 (79–96)
PFS rates, [‡] % (95% CI)		
6-month	85 (72–99)	78 (66–91)
9-month	73 (55–90)	62 (47–77)
6-month DoR rate, % (95% CI)	81 (65–98)	74 (59–90)
Median duration of follow-up for PFS: 10.5 months (95% CI: 9.0–11.2)		

Here, we describe DAREON®-Lung-1 (NCT07472517), an ongoing multicenter, open-label, randomized Phase III trial evaluating obixtamig in combination with SoC (atezolizumab + carboplatin + etoposide) versus SoC alone as 1L treatment in patients with ES-SCLC

[†]Includes patients treated with obixtamig 10 mg (n=10), 30 mg (n=5), and 60 mg (n=29); [‡]Kaplan–Meier estimates 1L, first-line; AEs, adverse events; CD3, cluster of differentiation 3; CI, confidence interval; CRS, cytokine release syndrome; DCR, disease control rate; DLL3, delta-like ligand 3; DoR, duration of response; ES-SCLC, extensive-stage small cell lung cancer; Fc, fragment crystallizable; ICANS, immune effector cell-associated neurotoxicity syndrome; IgG, immunoglobulin G; ORR, objective response rate; OS, overall survival; PD-L1, programmed death ligand 1; PFS, progression-free survival; SCLC, small cell lung cancer; SoC, standard of care

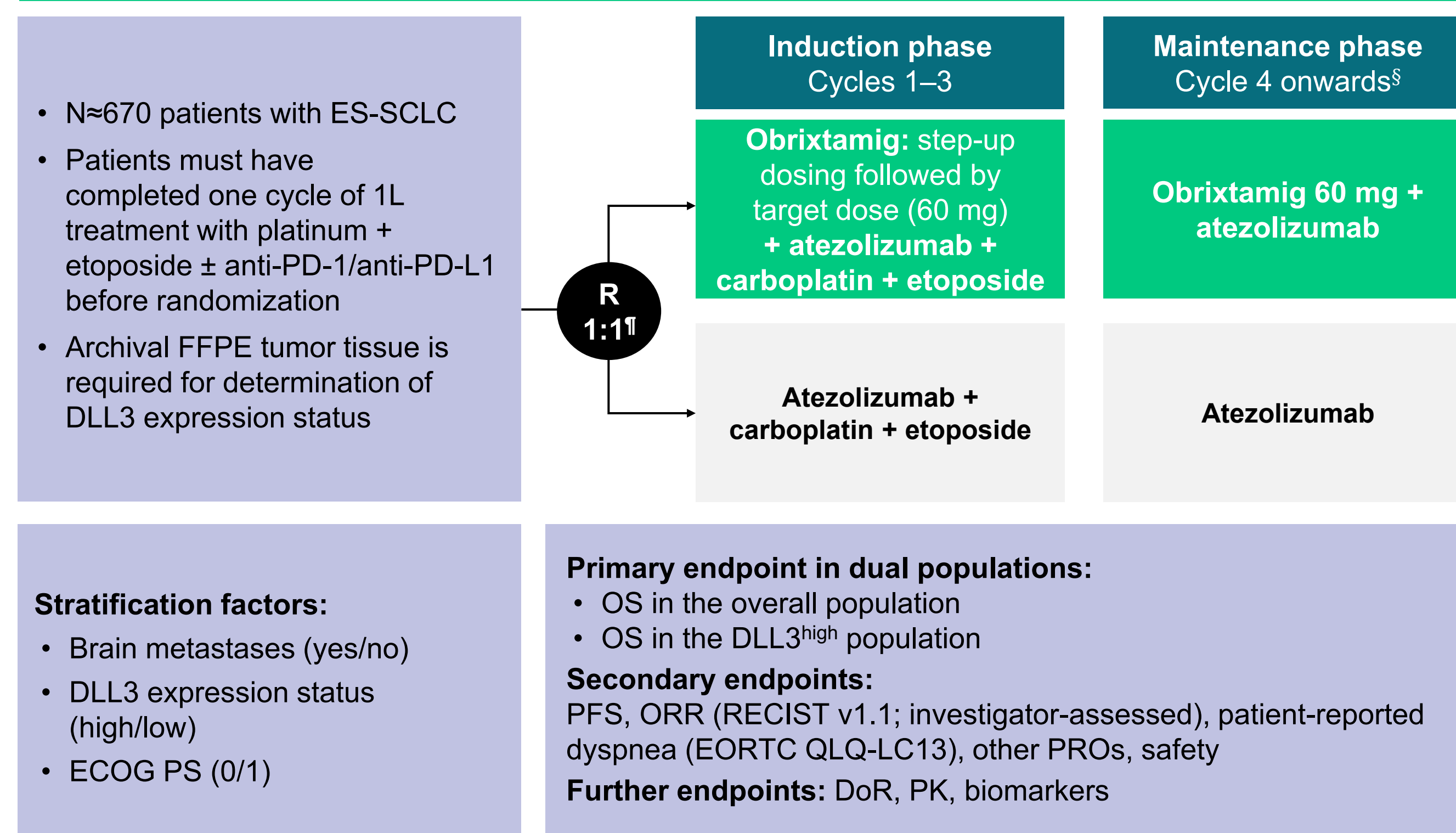
Plain Language Summary

- Small cell lung cancer (SCLC) is an aggressive type of lung cancer. New treatments are needed to help people live longer and improve outcomes
- Obixtamig is an investigational treatment. It targets a protein called DLL3, which is found on tumor cells of most patients with SCLC
- DAREON®-Lung-1 is a study comparing standard treatment for SCLC with standard treatment plus obixtamig in people who have not previously received treatment for their cancer
- The study will look at whether adding obixtamig to standard treatment helps people with SCLC live longer. It will also evaluate safety and side effects

Key Points

- DAREON®-Lung-1 (NCT07472517) is a Phase III trial evaluating obixtamig in combination with SoC (atezolizumab, carboplatin, and etoposide) versus SoC alone as 1L induction and maintenance treatment in patients with ES-SCLC
- Randomization will be prospectively stratified by DLL3 expression status; however, patients with any DLL3 expression status are eligible
- The primary endpoint is OS in the overall population and DLL3^{high} expressing population
- Planned enrollment is ~670 patients. The trial is recruiting patients in Asia, Africa, Europe, North America, South America, and Oceania

Trial Design



- Obixtamig will be administered intravenously as step-up doses in Cycle 1, followed by three fixed 60 mg doses (QW) in Cycle 2, and one fixed 60 mg dose (Q3W) from Cycle 3 onward
- SoC will be given per label

[‡]Treatment will continue until disease progression, unacceptable toxicity, or other protocol-defined discontinuation criteria, for a maximum of 36 months; [†]crossover to the investigational arm is not permitted
ECOG PS, Eastern Cooperative Oncology Group performance status; EORTC QLQ-LC13, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Lung Cancer 13; FFPE, formalin-fixed paraffin-embedded; PD-1, programmed cell death protein 1; PK, pharmacokinetics; PROs, patient-reported outcomes; QW, once weekly; Q3W, once every three weeks; R, randomization; RECIST v1.1; Response Evaluation Criteria in Solid Tumours version 1.1

Key Inclusion and Exclusion Criteria

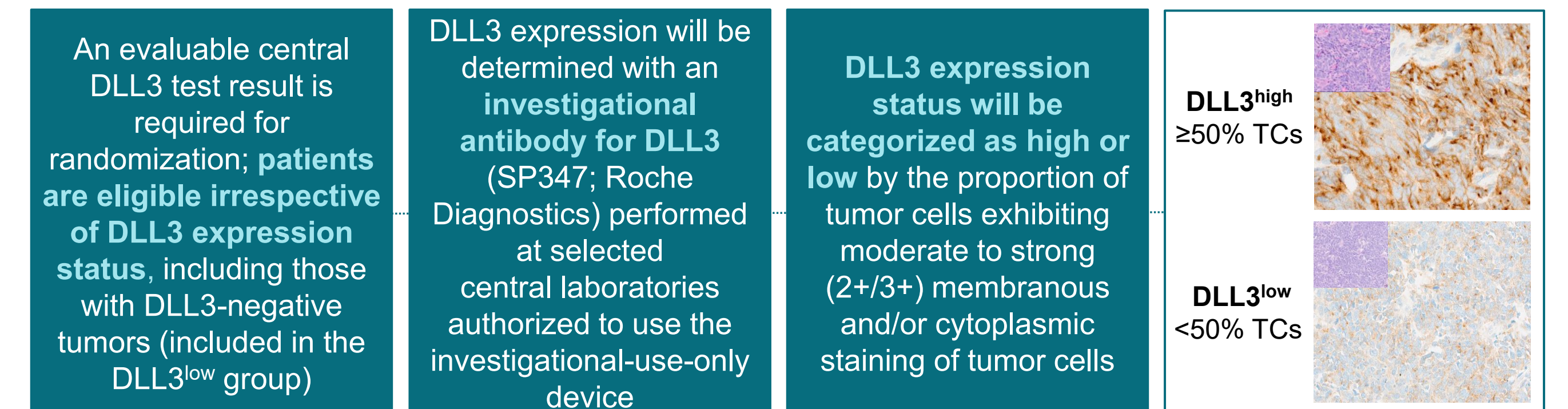
Inclusion criteria	Exclusion criteria
- Age ≥18 years - Histologically confirmed ES-SCLC - ECOG PS 0 or 1 - No prior extensive stage systemic therapy, except for one mandatory cycle of platinum + etoposide ± anti-PD-1/anti-PD-L1 - Available archival FFPE tumor tissue and confirmation of evaluable DLL3 expression status test result	- Symptomatic brain metastases - Leptomeningeal disease - Carcinomatous meningitis - Other previous or concomitant malignancy within past 5 years - History of severe, life-threatening immune-mediated AEs or IRRs

Not all criteria are listed. Further details available at: <https://clinicaltrials.gov/study/NCT07472517>

IRRs, infusion-related reactions

DLL3 Testing

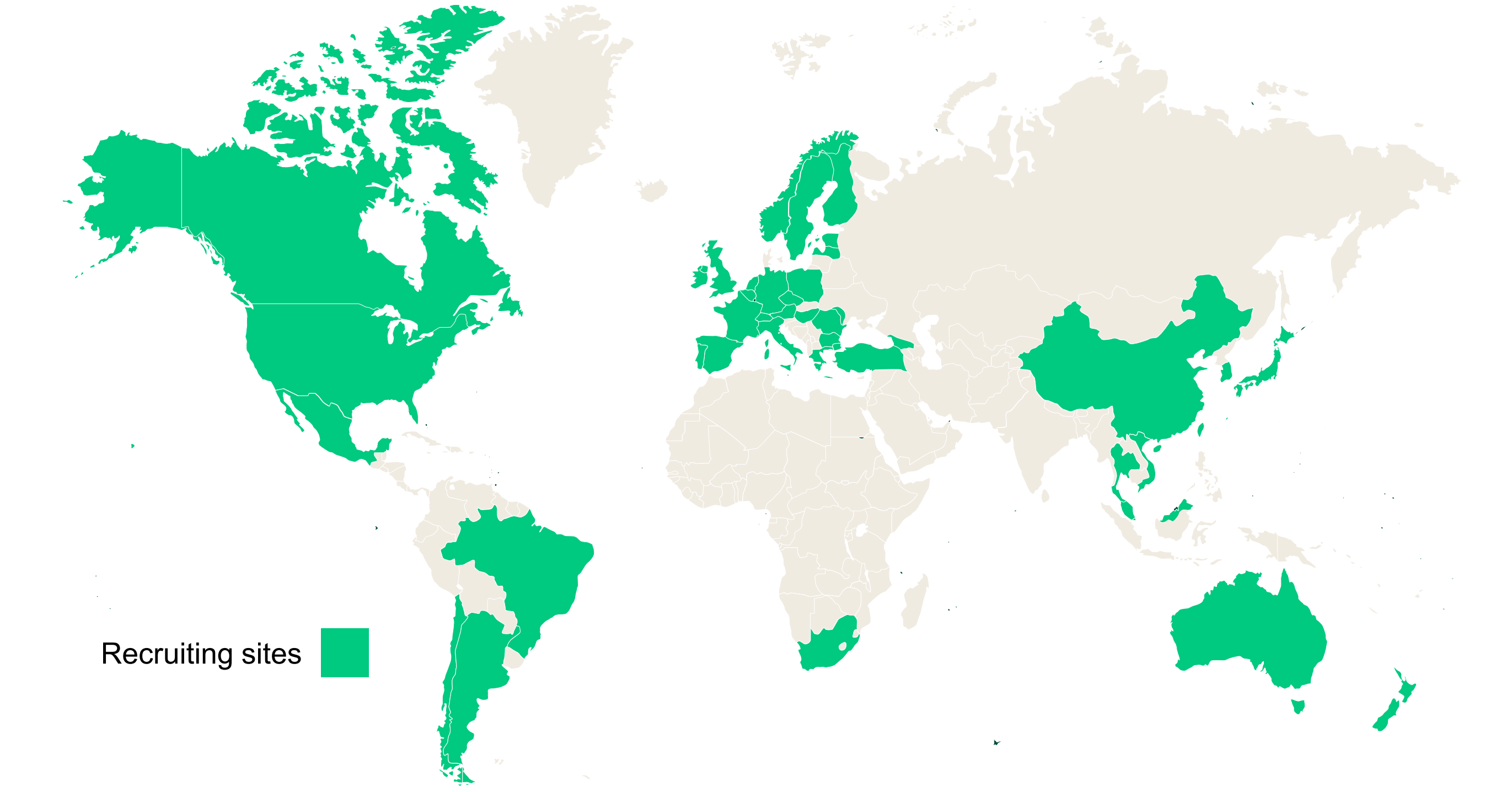
- DAREON®-Lung-1 is a Phase III trial prospectively evaluating the predictive relevance of DLL3 expression for obixtamig in ES-SCLC, with dual primary OS analyses in the overall and DLL3^{high} populations



TCs, tumor cells

Recruitment

- Planned enrollment is ~670 patients
- The trial is currently recruiting patients at 246 sites in 43 countries across
 - Asia
 - Africa
 - Europe
 - North and South America
 - Oceania



- Argentina
- Australia
- Austria
- Belgium
- Brazil
- Bulgaria
- Canada
- Chile
- China
- Czech Republic
- Estonia
- Finland
- France
- Georgia
- Germany
- Greece
- Hong Kong
- Hungary
- Ireland
- Italy
- Japan
- Latvia
- Malaysia
- Mexico
- Moldova
- Netherlands
- New Zealand
- Norway
- Poland
- Portugal
- Romania
- Singapore
- South Korea
- Spain
- Sweden
- Switzerland
- Taiwan
- Thailand
- Turkey
- United Kingdom
- United States
- Vietnam
- South Africa (TBC)

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*Corresponding author email address: ticiana.a.leal@emory.edu



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