

ROSETTA Lung-202: a phase 3 trial of first-line pumitamig monotherapy vs pembrolizumab in locally advanced/metastatic NSCLC and PD-L1 expression ≥ 50%



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Background

- Despite advancements in the treatment of advanced non-small cell lung cancer (NSCLC) with the approval of immune checkpoint inhibitor (ICI)-based therapies (with or without chemotherapy), many patients do not achieve a durable clinical response or experience disease progression, limiting long-term survival¹⁻⁴
- Pumitamig (BNT327/BMS986545) is an investigational bispecific antibody engineered to simultaneously target both programmed death ligand-1 (PD-L1) and vascular endothelial growth factor (VEGF)-A within the tumor and tumor microenvironment, a dual mechanism intended to enhance antitumor immunity and inhibit angiogenesis⁵ (Figure 1)

Study rationale

- Combining PD-L1 and VEGF inhibition may enhance treatment efficacy, potentially addressing the unmet need for more effective therapies in advanced disease stages^{6,7}
 - Clinical trials have demonstrated significantly improved progression-free survival (PFS) and overall survival (OS) and an acceptable safety profile with programmed death-1 (PD-1)/PD-L1 and VEGF combinations in metastatic or advanced NSCLC, including atezolizumab plus bevacizumab⁸ and ivonescimab⁹
 - Specifically, in HARMONI-2, PFS for ivonescimab vs pembrolizumab was 11.1 months vs 5.8 months, respectively (HR 0.51 [95% CI, 0.38-0.69]; $P < 0.0001$), with similar results in patients with PD-L1 tumor proportional score (TPS) 1-49% (HR 0.54 [95% CI, 0.37-0.78]) and $\geq 50\%$ (HR 0.48 [95% CI, 0.29-0.79])⁹
 - Pumitamig preclinical studies support the synergistic effects of PD-(L)1 blockade and VEGF inhibition (Figure 2)^{5,10}
 - In vitro*, blockade of the PD-1/PD-L1 interaction by the binding of pumitamig to PD-L1 restores effector T-cell function, leading to the killing of tumor cells⁵
 - Specifically, pumitamig blocked VEGF-A/VEGF receptor 2 engagement, induced VEGF-A-dependent clustering with PD-L1 on the cell surfaces, and led to more robust internalization than PD-L1 monospecific antibody⁵
 - Antitumor activity is shown in various *in vivo* tumor mouse models, confirming biological activity and therapeutic potential of pumitamig for cancer therapy⁵
 - Phase 1 and 2 studies showed pumitamig has an acceptable and manageable safety profile, and preliminary efficacy data supports its antitumor activity in advanced solid tumors, including lung cancer¹⁰⁻¹³
 - In the ongoing phase 1b/2a PM8002-A001 dose expansion monotherapy study in patients with advanced solid tumors, encouraging efficacy was observed with pumitamig in patients with advanced NSCLC¹¹
 - Median PFS was 13.6 months in the overall population, 13.6 months in patients with PD-L1 1-49%, and 17.9 months in patients with PD-L1 $\geq 50\%$
 - In the ongoing randomized, open-label, global phase 2/3 ROSETTA Lung-02 study investigating pumitamig plus chemotherapy in patients with first-line (1L) NSCLC, encouraging efficacy was observed across histologies and at each PD-L1 level¹⁰
 - Confirmed objective response rate (ORR) was 63.6% in NSQ and 72.7% in SQ NSCLC populations, and was 47.6% in patients with PD-L1 $< 1\%$, 77.8% in PD-L1 1-49%, and 100% in PD-L1 $\geq 50\%$
- ROSETTA Lung-202 is designed to evaluate the efficacy of pumitamig monotherapy in patients with previously untreated advanced NSCLC and PD-L1 TPS $\geq 50\%$

Figure 1. Pumitamig proposed mechanism of action⁵

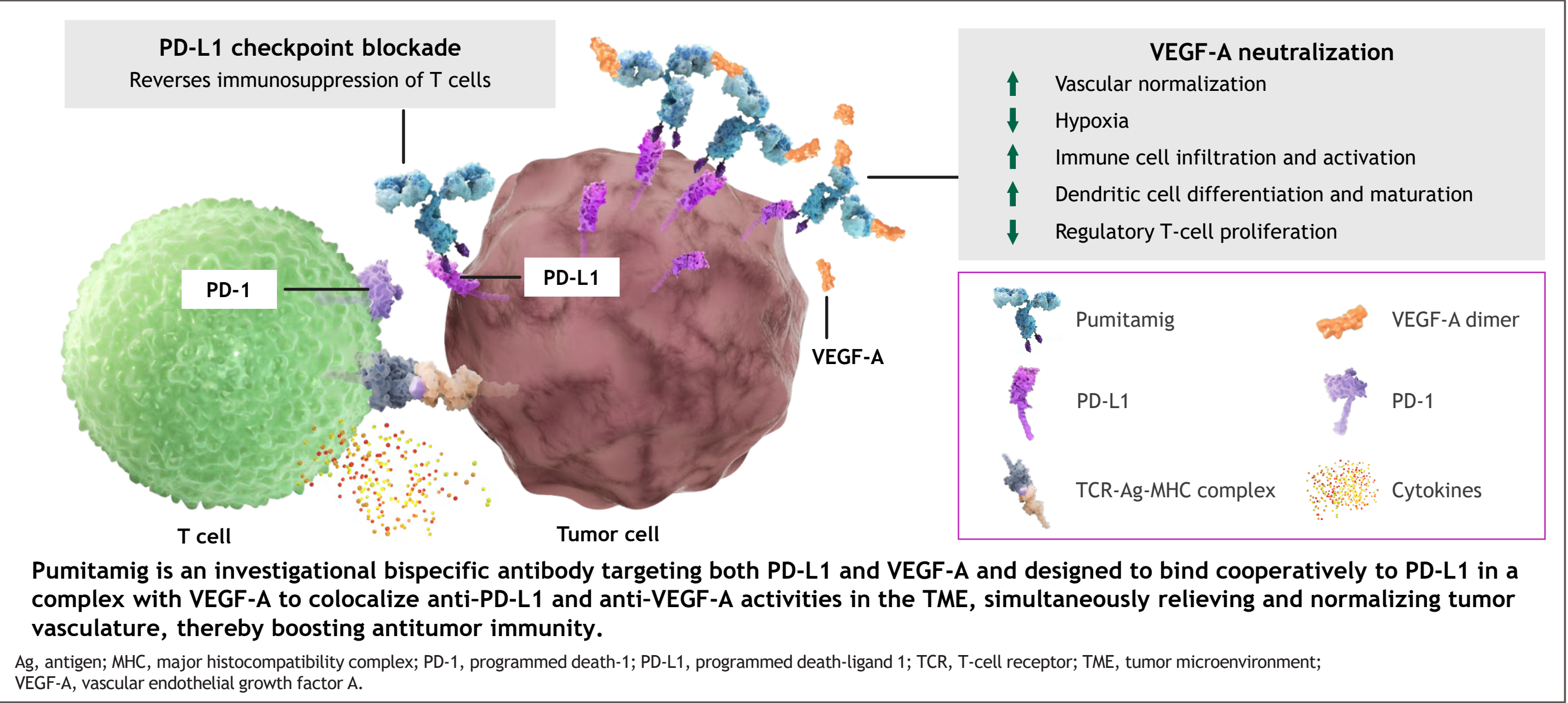
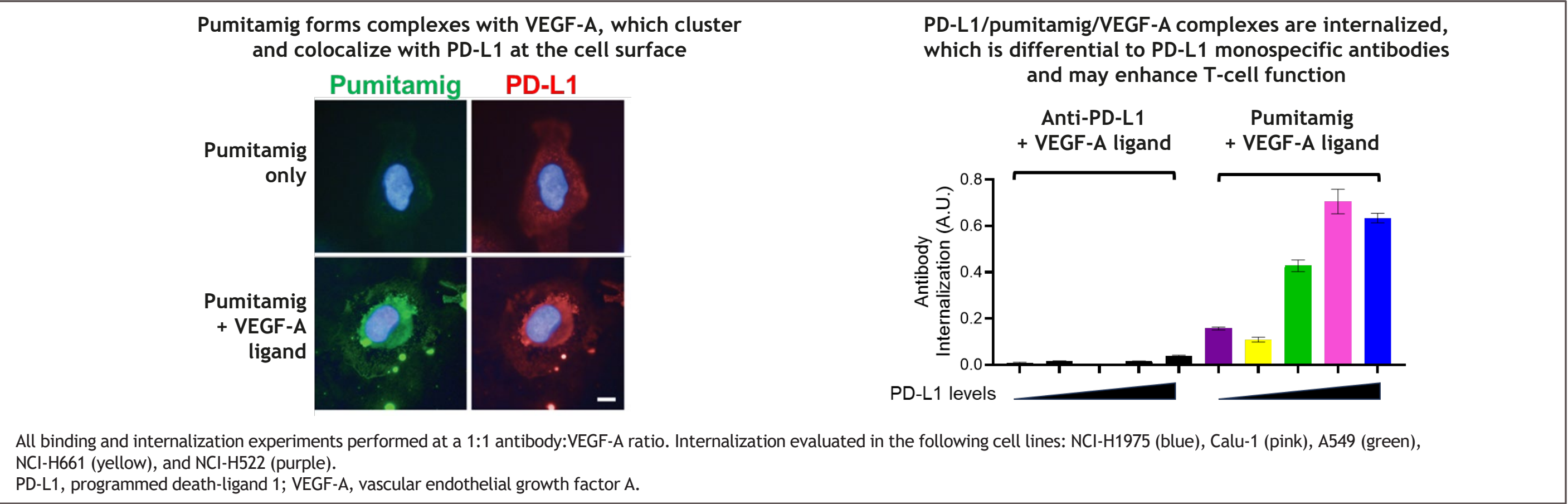


Figure 2. Pumitamig-VEGF-A colocalization with PD-L1 and internalization^{5,10}



Study design

- ROSETTA Lung-202 (NCT07361510) is an ongoing global, randomized, multicenter, double-blind, phase 3 clinical trial investigating the efficacy and safety of pumitamig monotherapy vs pembrolizumab monotherapy in patients with previously untreated advanced NSCLC and PD-L1 TPS $\geq 50\%$ (Figure 3)
- The key eligibility criteria and endpoints for the study are listed in Tables 1 and 2, respectively

Figure 3. ROSETTA Lung-202 double-blind, phase 3 study design

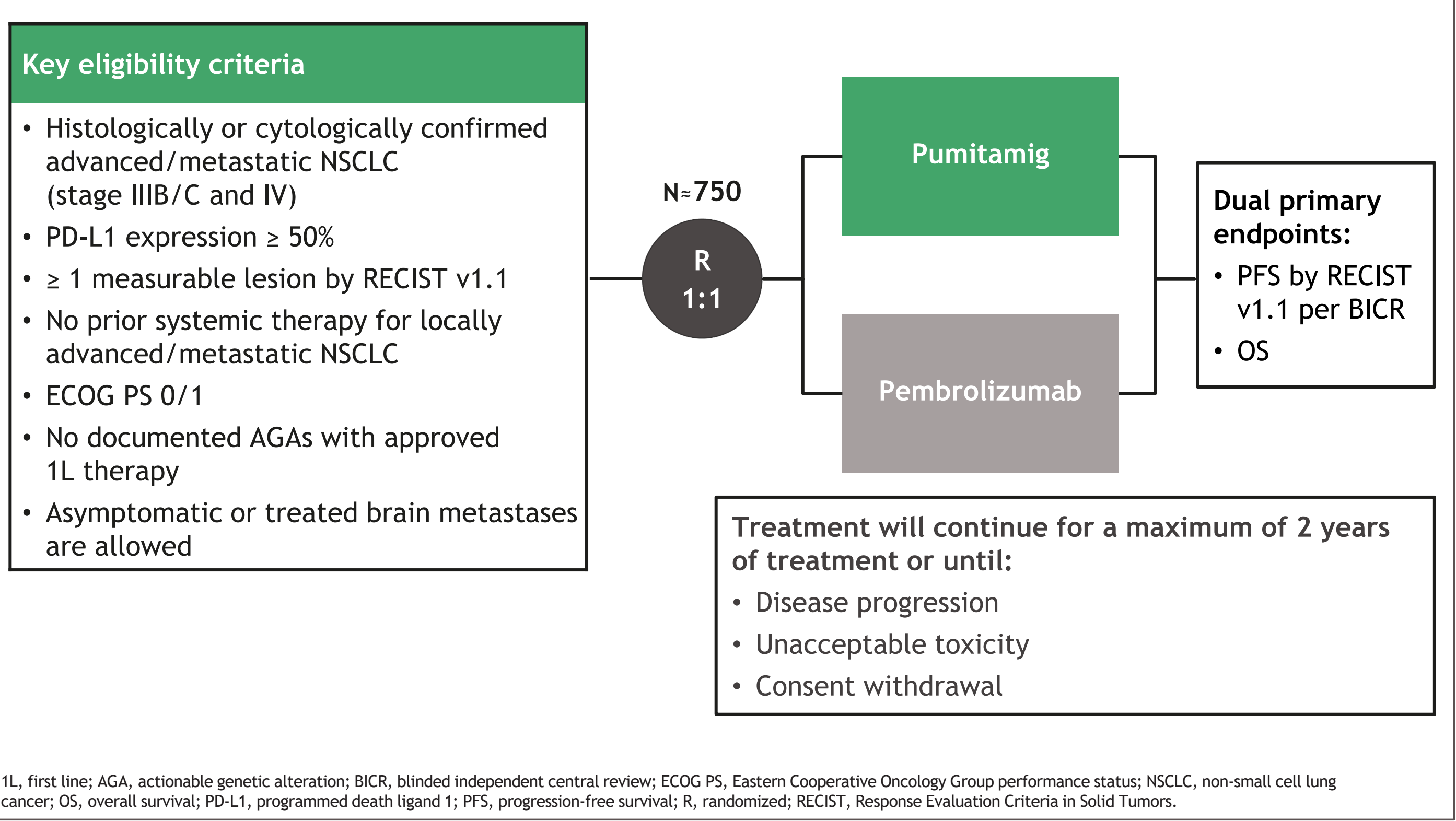


Table 1. ROSETTA Lung-202 key eligibility criteria

Key inclusion criteria
- Aged ≥ 18 years - Histologically or cytologically confirmed diagnosis of stage IIIB/IIIC or stage IV NSCLC (NSQ and SQ) - PD-L1 expression $\geq 50\%$^a - Measurable disease as defined by RECIST v1.1 - No prior systemic antitumor therapy for locally advanced or metastatic NSCLC - ECOG PS 0/1
Key exclusion criteria
- AGA for which 1L approved therapies are indicated - Symptomatic untreated CNS metastases, leptomeningeal metastases (carcinomatous meningitis), or spinal cord compression - Significant cardiovascular impairment, major thrombotic or embolic events or major hemorrhagic events (within 6 months prior to randomization), or significant risk of pulmonary hemorrhage - Active autoimmune disease

^aAs determined by Sponsor preapproved local PD-L1 IHC assays (VENTANA PD-L1 [SP263] assay, Agilent PD-L1 IHC 22C3 pharmDx, or Agilent PD-L1 IHC 28-8 pharmDx) or central test, performed in accordance with the intended use of the assays. Testing must comply with local diagnostic regulations, and documentation of which PD-L1 test was used must be provided. 1L, first-line; AGA, actionable genetic alteration; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; IHC, immunohistochemistry; NSCLC, non-small cell lung cancer; NSQ, nonsquamous; PD-L1, programmed death ligand 1; RECIST, Response Evaluation Criteria in Solid Tumors; SQ, squamous.

Table 2. ROSETTA Lung-202 endpoints

Dual primary endpoints
- PFS by RECIST v1.1 per BICR - OS
Secondary endpoints
- PFS by RECIST v1.1 per investigator - OR, DOR, DCR, and TTR by RECIST v1.1 per BICR - TTDD based on the NSCLC-SAQ total score

BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response; NSCLC-SAQ, non-small cell lung cancer-symptom assessment questionnaire; OR, objective response; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TTDD, time to definitive deterioration; TTR, time to response.

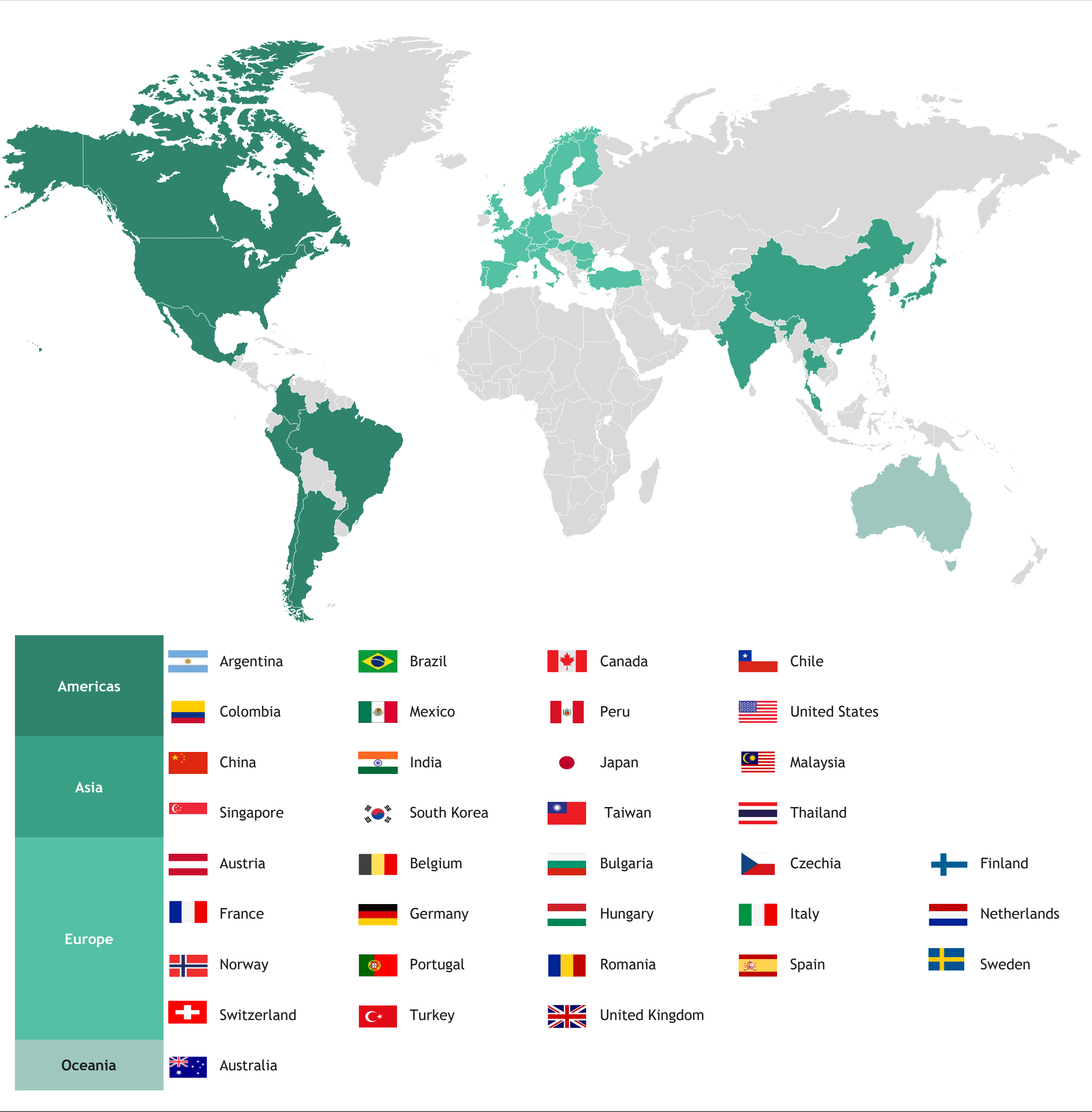
Acknowledgments

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- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Jessie Arries, PhD, Melissa Kirk, PhD, and Kathleen Blake of Ashfield MedComms, an Inizio company, funded by Bristol Myers Squibb

Study sites and dates

- ROSETTA Lung-202 is currently enrolling at 272 study sites across 35 countries as of July 2026; sites and countries are subject to change as enrollment progresses (Figure 4)
- Study start date: March 2026
- Estimated enrollment number: 750
- Estimated primary completion date: October 2031
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- Also presented at WCLC 2026 is the ROSETTA Lung-201 (NCT07361497) study where pumitamig is being investigated as monotherapy in patients with unresectable stage III NSCLC post-chemoradiation (See TiP poster P2.330)

Figure 4. ROSETTA Lung-202 study sites



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