

ROSETTA Lung-201: a phase 3 trial of pumitamig monotherapy vs durvalumab in unresectable stage III NSCLC post-chemoradiation

P2.330



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Background

- The standard of care for patients with unresectable stage III non-small cell lung cancer (NSCLC) is typically concurrent chemoradiotherapy (cRT) followed by consolidation durvalumab, based on the significantly improved progression-free survival (PFS) and overall survival (OS) vs placebo in the PACIFIC study¹⁻³
- Long-term outcomes for these patients remain suboptimal, with 5-year PFS and OS rates of 33.1% and 42.9%, respectively, as well as suboptimal efficacy in patients with PD-L1 expression < 1%,¹ highlighting the need for more effective treatment strategies
- 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 angiogenesis⁴ (Figure 1)

Study rationale

- Combining PD-L1 and VEGF inhibition may enhance treatment efficacy, potentially addressing the unmet need for more effective therapies in locally advanced, unresectable NSCLC^{5,6}
 - Clinical trials have demonstrated significantly improved PFS and 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 bevacizumab⁷ and ivonescimab⁸
 - Pumitamig preclinical studies support the synergistic effects of PD-(L)1 blockade and VEGF inhibition (Figure 2)^{4,9}
 - 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 cells⁴
 - 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 antibody⁴
 - Antitumor activity is shown in various *in vivo* tumor mouse models, confirming biological activity and therapeutic potential of pumitamig for cancer therapy⁴
- Phase 1 and 2 studies showed pumitamig has an acceptable and manageable safety profile, and preliminary efficacy data support its antitumor activity in advanced solid tumors, including lung cancer⁹⁻¹²
 - 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 NSCLC¹⁰
 - Confirmed objective response rate (ORR) was 46.7%; median PFS was 13.6 months overall, 13.6 months in patients with PD-L1 expression 1-49%, and 17.9 months in patients with PD-L1 ≥ 50%
 - In the ongoing randomized, open-label, global phase 2/3 ROSETTA Lung-02 study investigating pumitamig plus chemotherapy in patients with first-line NSCLC, encouraging efficacy was observed in nonsquamous (NSQ) and squamous (SQ) NSCLC and at each PD-L1 level⁹
 - Confirmed ORR was 63.6% in NSQ and 72.7% in SQ NSCLC cohorts, and 47.6% in patients with PD-L1 < 1%, 77.8% in PD-L1 1-49%, and 100% in PD-L1 ≥ 50%
- ROSETTA Lung-201 is designed to investigate the efficacy and safety of pumitamig monotherapy vs durvalumab monotherapy in patients with unresectable stage III NSCLC without disease progression after prior platinum-based cCRT

Figure 1. Pumitamig proposed mechanism of action⁴

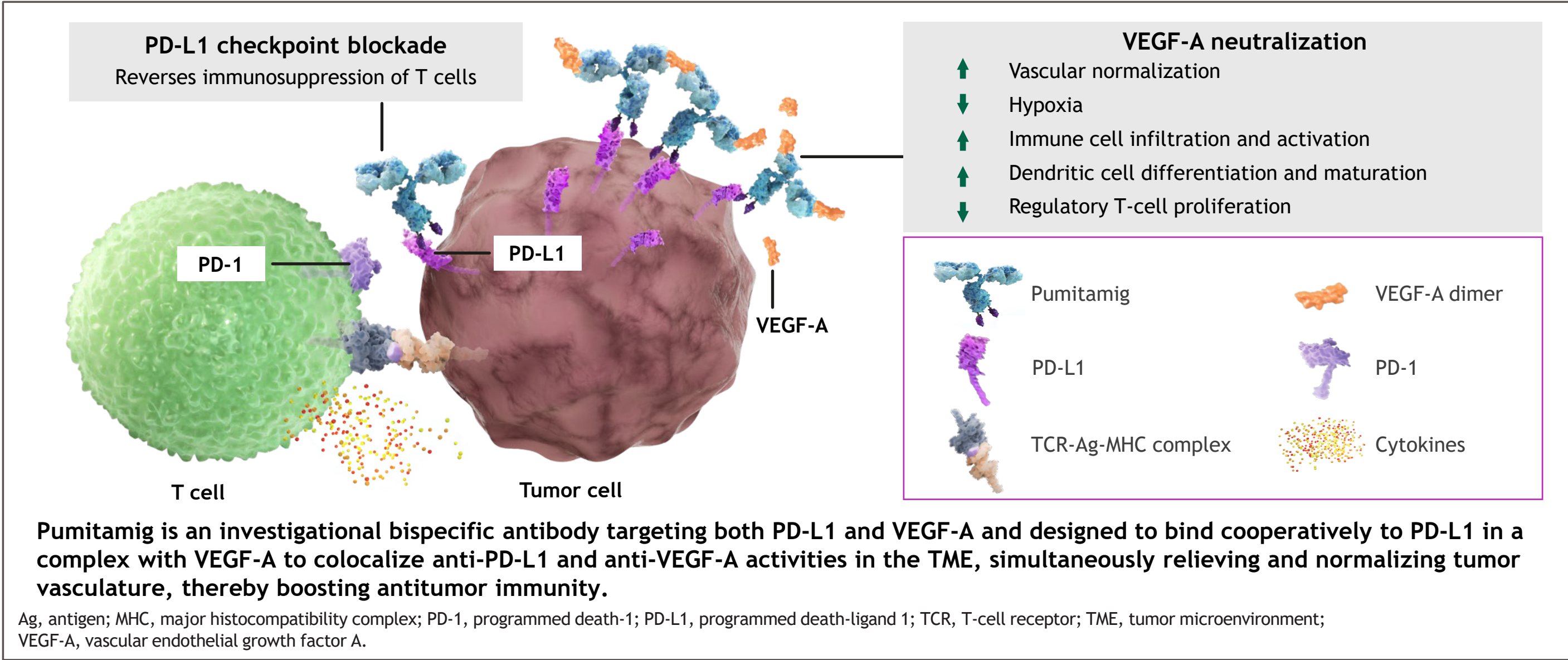
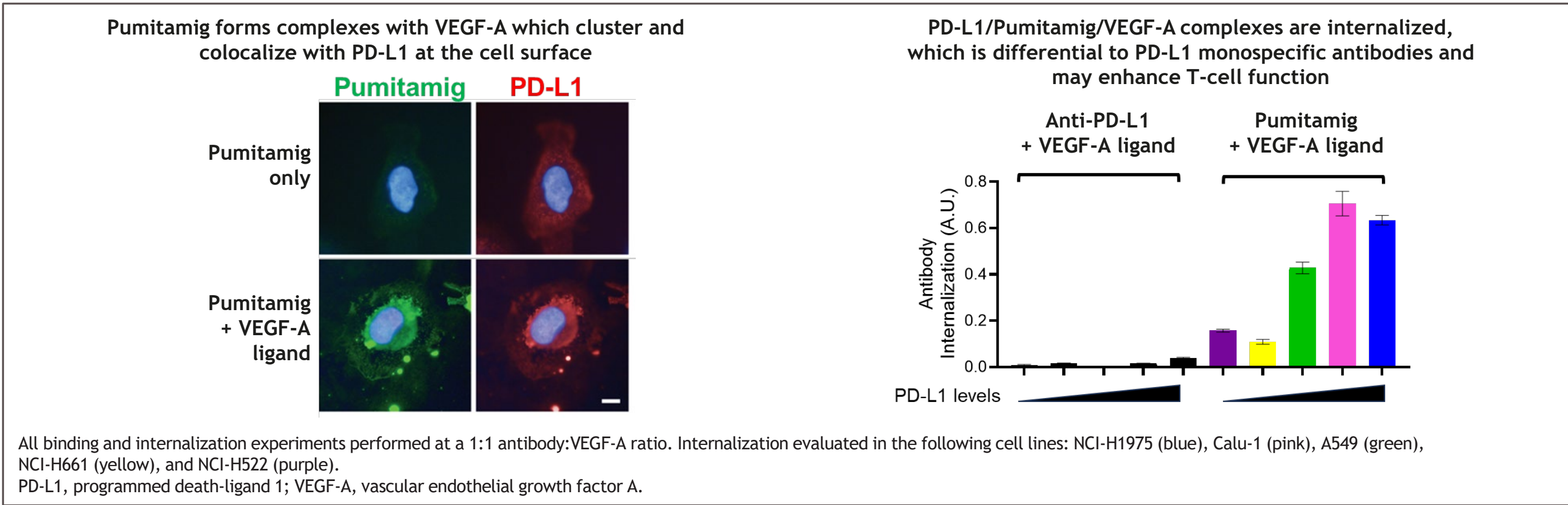


Figure 2. Pumitamig/VEGF-A colocalization with PD-L1 and internalization^{4,9}



Study design

- ROSETTA Lung-201 (NCT07361497) is an ongoing global, randomized, multicenter, open-label, parallel group, phase 3 clinical trial investigating the efficacy and safety of pumitamig monotherapy vs durvalumab monotherapy in patients with unresectable stage III NSCLC without disease progression after prior platinum-based cCRT (Figure 3)
- The key eligibility criteria and endpoints for the study are listed in Tables 1 and 2, respectively

Figure 3. ROSETTA Lung-201 open-label, phase 3 study design

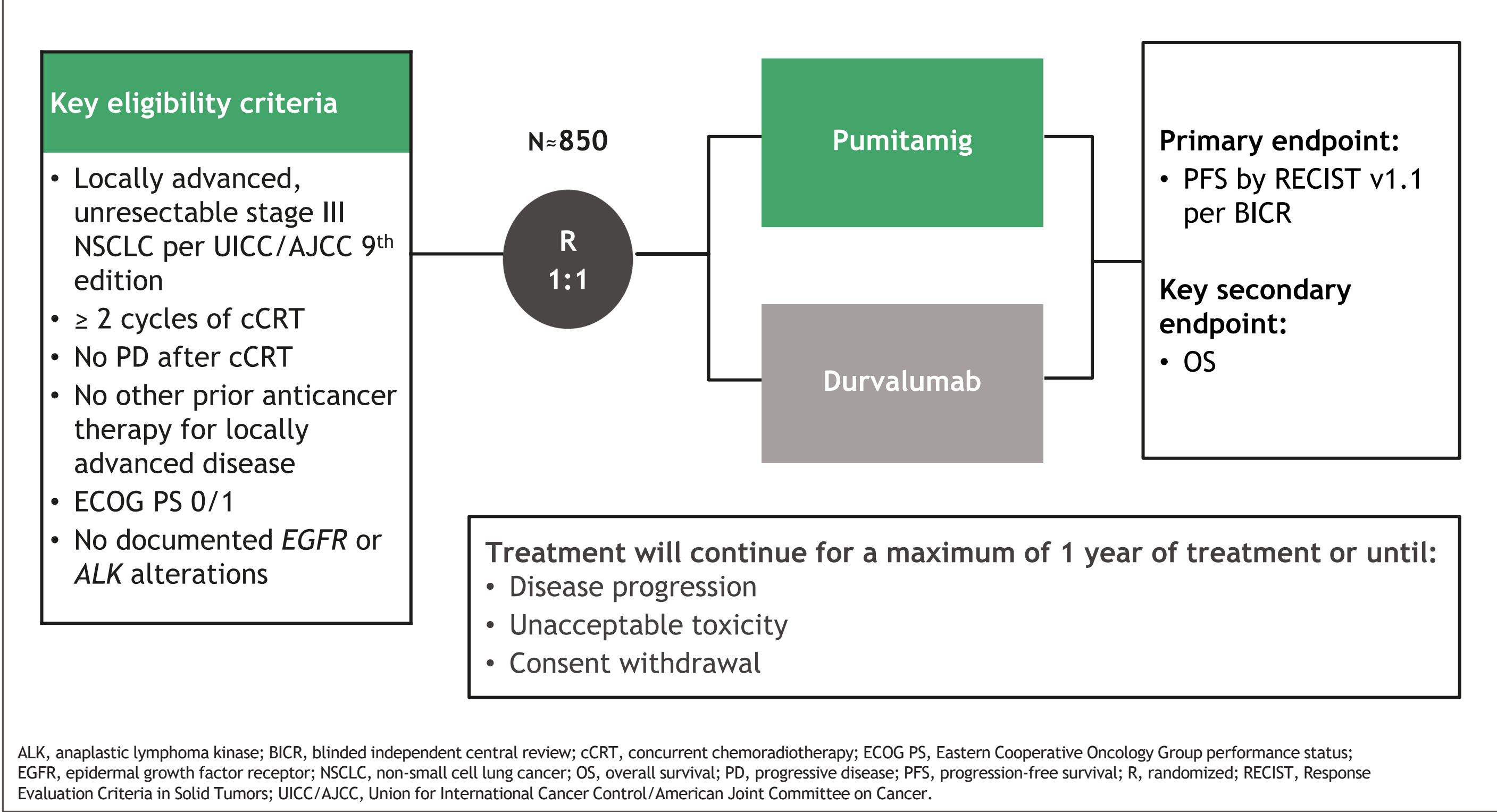


Table 1. ROSETTA Lung-201 key eligibility criteria

Key inclusion criteria
- Aged ≥ 18 years - Histologically or cytologically confirmed unresectable locally advanced (stage III) NSCLC ≥ 2 cycles of platinum-based cCRT (total dose of radiation: ≥ 54 Gy) - No PD following treatment with cCRT - ECOG PS 0/1
Key exclusion criteria
- NSQ histology with documented <i>EGFR</i> or <i>ALK</i> alterations - Active autoimmune disease - Significant cardiovascular impairment such as uncontrolled hypertension (despite optimal medical attention), congestive heart failure, active coronary disease (within 6 months prior to randomization), ventricular arrhythmias, major thrombotic or embolic events or major hemorrhagic events within 6 months prior to randomization, or significant risk of pulmonary hemorrhage - Advanced/clinically significant lung disease (within 6 months prior to randomization) or history of ILD or pneumonitis requiring treatment with systemic steroids (grade ≥ 2), or current or suspected ILD or pneumonitis - Prior anticancer therapy (outside of cCRT) for locally advanced stage III disease

ALK, anaplastic lymphoma kinase; cCRT, concurrent chemoradiotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; ILD, interstitial lung disease; NSCLC, non-small cell lung cancer; NSQ, nonsquamous; PD, progressive disease.

Table 2. ROSETTA Lung-201 endpoints

Primary endpoint
PFS by RECIST v1.1 per BICR
Secondary endpoints
- OS - PFS by RECIST v1.1 per investigator - OR, DCR, DOR, and TTR by RECIST v1.1 per BICR

BICR, blinded independent central review; DCR, disease control rate; DOR, duration of response; OR, objective response; OS, overall survival; PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors; TTR, time to response.

Acknowledgments

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- Pumitamig (BNT327/BMS986545) is being jointly developed by BioNTech and Bristol Myers Squibb
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Jessie Arries, PhD, Melissa Kirk, PhD, and Andrea M. Michels of Ashfield MedComms, an Inizio company, funded by Bristol Myers Squibb

Study sites and dates

- ROSETTA Lung-201 is currently enrolling at 255 study sites across 31 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: 850
- Estimated primary completion date: September 2030
- Estimated study completion date: December 2033
- Also presented at WCLC 2026 is the ROSETTA Lung-202 (NCT07361510) study where pumitamig is being investigated vs pembrolizumab monotherapy as first-line treatment in patients with locally advanced or metastatic NSCLC and PD-L1 expression ≥ 50% (See TiP poster P2.355)

Figure 4. ROSETTA Lung-201 study sites



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