



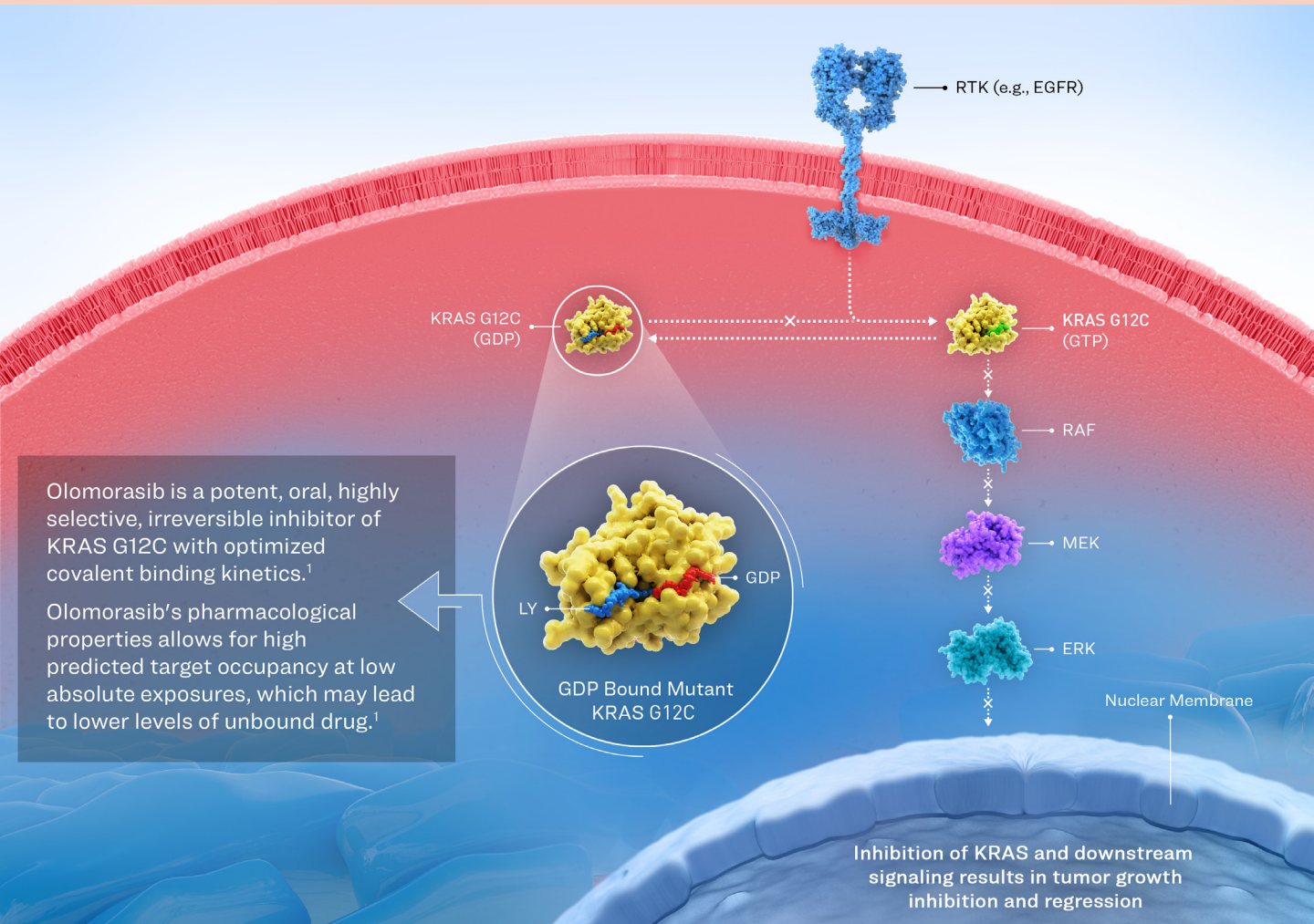
# **OLOMORASIB** (LY3537982)

## **KRAS G12C INHIBITOR**

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# OLOMORASIB KRAS G12C INHIBITOR (LY3537982) | MECHANISM OF ACTION<sup>1-4</sup>



Peng SB, et al<sup>1</sup>; Kano Y, et al<sup>2</sup>; Janes MR, et al<sup>3</sup>; Ji J, et al<sup>4</sup>

**Abbreviations:** EGFR=Epidermal Growth Factor Receptor; ERK=Extracellular Signal-Regulated Kinase; GDP=Guanosine Diphosphate; GTP=Guanosine Triphosphate; KRAS=Kirsten Rat Sarcoma Viral Oncogene Homolog; LY=Olomorasib; MEK=Mitogen-Activated Protein Kinase; RAF=Rapidly Accelerated Fibrosarcoma; RTK=Receptor Tyrosine Kinase.

**References:** 1. Peng SB, et al. *Cancer Res.* 2021;81(suppl 13):1259. 2. Kano Y, et al. *Nat Commun.* 2019;10(1):224. 3. Janes MR, et al. *Cell.* 2018;172(3):578-589. 4. Ji J, et al. *Onco Targets Ther.* 2022;15:747-756.

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## TARGET

*KRAS* is the most common oncogene across all tumor types. *KRAS* G12C represents a *KRAS* mutation in patients with non-small cell lung cancer (14%), colorectal cancer (3%), and other solid tumors (1%-3%).<sup>1</sup>

## MOLECULE

Olomorasib is a selective covalent inhibitor of *KRAS* G12C; in preclinical models, it demonstrates activity as monotherapy and in combination with other anticancer therapies. It has competitive pharmacokinetic properties supporting its advancement into clinical testing. Olomorasib has been shown in vitro to target a *KRAS* G12C mutation, thereby inhibiting mutant *KRAS*-dependent signaling.<sup>2</sup>

## CLINICAL DEVELOPMENT

Olomorasib is being studied in clinical trials in patients with non-small cell lung cancer, colorectal cancer, or other solid tumors.

**References:** 1. Ji J, et al. *Onco Targets Ther.* 2022;15:747-756. 2. Peng SB, et al. *Cancer Res.* 2021;81(suppl 13):1259.

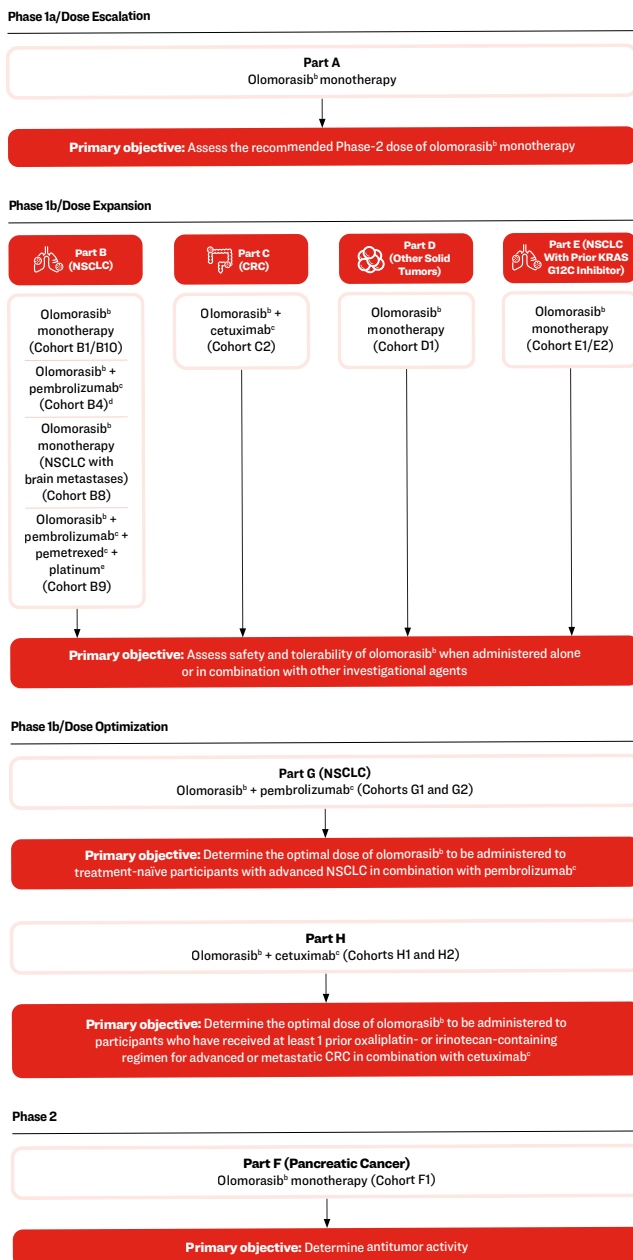
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# OLOMORASIB KRAS G12C INHIBITOR (LY3537982)

**NCT04956640**

**A Phase 1/2 Study of Olomorasib in Patients With KRAS G12C-Mutant Advanced Solid Tumors<sup>a</sup>**



<sup>a</sup>This clinical trial is being conducted globally; <sup>b</sup>Administered orally; <sup>c</sup>Administered intravenously. <sup>d</sup>Prior KRAS G12C inhibitor allowed. <sup>e</sup>Platinum (cisplatin or carboplatin) is administered intravenously.

**Abbreviations:** CRC=Colorectal Cancer; KRAS=Kirsten Rat Sarcoma Virus; NSCLC=Non-Small Cell Lung Cancer.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT04956640].



# OLOMORASIB KRAS G12C INHIBITOR (LY3537982)

**NCT04956640**

**A Phase 1/2 Study of Olomorasib in Patients With KRAS G12C-Mutant Advanced Solid Tumors (Cont.)**

## KEY INCLUSION CRITERIA

- Measurable disease as defined by Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1)
- Evidence of KRAS G12C mutation in tumor tissue or circulating tumor DNA
- Histological or a cytologically proven diagnosis of locally advanced, unresectable, and/or metastatic cancer and meet cohort-specific criteria
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Adequate organ function
- Discontinued all previous treatments for cancer with resolution of any significant ongoing adverse events (AEs), except in certain scenarios
- Able to swallow capsules/tablets
- Agree and adhere to contraceptive use, if applicable
- For some parts of the study (eg, one of the two arms with olomorasib plus pembrolizumab and the arm of olomorasib plus pembrolizumab, pemetrexed, and platinum therapy), histologically or cytologically confirmed stage IIIB-IIIC or stage IV NSCLC that is previously untreated in the advanced/metastatic setting and not suitable for curative intent radical surgery or radiation therapy. Previously untreated patients who received adjuvant and neoadjuvant therapy are eligible if the last dose of the systemic treatment was completed at least 6 months prior to enrollment. For untreated patients in the arm with olomorasib plus pembrolizumab noted above, a single cycle of pembrolizumab may be initiated within 21 days prior to enrollment. For untreated patients in the arm of olomorasib plus pembrolizumab, pemetrexed, and platinum therapy, a single cycle of any or all of the drugs other than olomorasib may be initiated within 21 days prior to enrollment. Start of study treatment may be delayed to allow sufficient time for recovery from treatment-related toxicity
- For one part of the study, participants must have received at least one prior oxaliplatin- or irinotecan-containing regimen for advanced or metastatic colorectal cancer (CRC)

## KEY EXCLUSION CRITERIA

- Disease suitable for local therapy administered with curative intent
- Active, ongoing, or untreated infection
- Serious preexisting medical condition(s) that, in the judgment of the investigator, would preclude participation in this study
- Serious cardiac conditions
- A second active primary malignancy or have been diagnosed and/or treated for an additional malignancy within 3 years prior to enrollment
- Symptomatic central nervous system (CNS) malignancy or metastasis and/or carcinomatous meningitis. Patients with treated CNS metastases are eligible for this study if their disease is asymptomatic, radiographically stable for at least 30 days, and they do not require treatment with steroids in the 2-week period prior to study treatment. This only applies to some parts of the study
- Prior treatment with any KRAS G12C small molecule inhibitor, except in certain scenarios where such prior therapy is allowed as per protocol
- The following patients will be excluded from some parts of the study:
  - Experienced certain serious side effects with prior immunotherapy
  - Have an active autoimmune disease that has required systemic anti-autoimmune treatment in the past 2 years
  - Have received a live vaccine within 30 days prior to the first dose of study drug
- Pregnant, breastfeeding, or expecting to conceive or father children within the projected duration of the trial through 35 days after the last dose of study medication
- Known allergic reaction against any of the components of the study treatments

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT04956640].

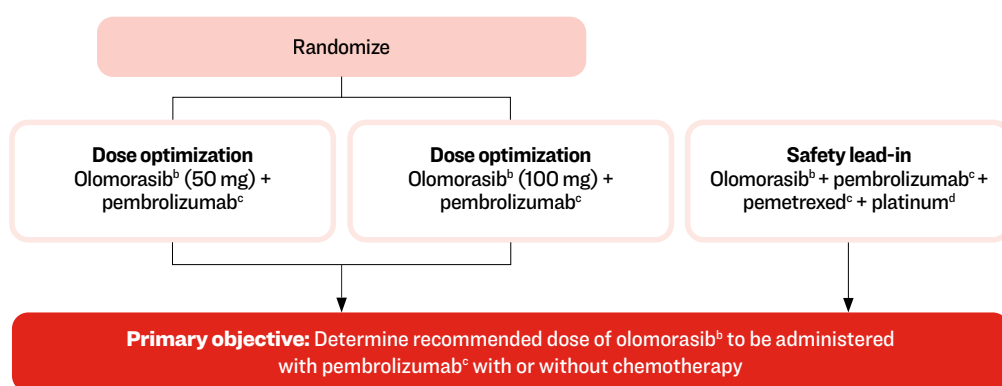


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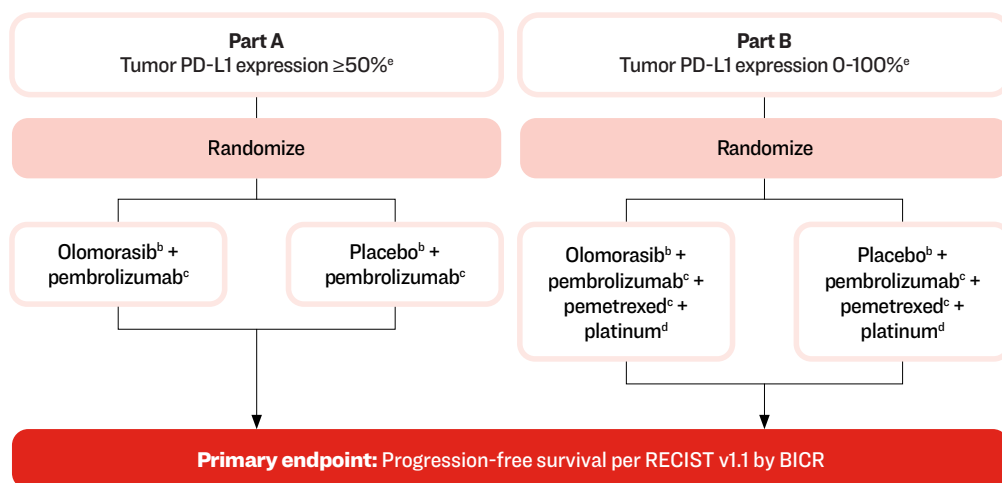
## SUNRAY-01

**A Global Pivotal Study in Participants With KRAS G12C-Mutant, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Comparing First-Line Treatment of Olomorasib and Pembrolizumab vs Placebo and Pembrolizumab in Those With PD-L1 Expression  $\geq 50\%$  or Olomorasib and Pembrolizumab, Pemetrexed, Platinum vs Placebo and Pembrolizumab, Pemetrexed, Platinum Regardless of PD-L1 Expression<sup>a</sup>**

### Dose Optimization/Safety Lead-in



### Phase 3



<sup>a</sup>This clinical trial is being conducted globally; <sup>b</sup>Administered orally; <sup>c</sup>Administered intravenously. <sup>d</sup>Platinum (cisplatin or carboplatin) administered intravenously. <sup>e</sup>Participants with PD-L1  $\geq 50\%$  are eligible to be enrolled in Part A or Part B at the discretion of the investigator.

**Abbreviations:** BICR=Blinded Independent Central Review; KRAS=Kirsten Rat Sarcoma Virus; PD-L1=Programmed Death-Ligand 1; RECIST v1.1=Response Evaluation Criteria in Solid Tumors Version 1.1.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT06119581].

# OLOMORASIB KRAS G12C INHIBITOR (LY3537982)

## SUNRAY-01

**A Global Pivotal Study in Participants With KRAS G12C-Mutant, Locally Advanced or Metastatic Non-Small Cell Lung Cancer Comparing First-Line Treatment of Olomorasib and Pembrolizumab vs Placebo and Pembrolizumab in Those With PD-L1 Expression  $\geq$ 50% or Olomorasib and Pembrolizumab, Pemetrexed, Platinum vs Placebo and Pembrolizumab, Pemetrexed, Platinum Regardless of PD-L1 Expression (Cont.)**

## KEY INCLUSION CRITERIA

- Histologically or cytologically confirmed non-small cell lung cancer (NSCLC) with stage IIIB-IIIC or stage IV disease, not suitable for curative intent radical surgery or radiation therapy
- Part B and safety lead-in part B: the histology of the tumor must be predominantly non-squamous (in line with pemetrexed label)
- Disease with evidence of KRAS G12C mutation
- Known programmed death-ligand 1 (PD-L1) expression
  - Part A:  $\geq$ 50%
  - Part B: 0%-100%
- Measurable disease as defined by Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST v1.1)
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Estimated life expectancy  $\geq$ 12 weeks
- Ability to swallow capsules
- Adequate laboratory parameters
- Contraceptive use should be consistent with local regulations for those participating in clinical studies
- Women of childbearing potential must:
  - Have a negative pregnancy test
  - Not be breastfeeding during treatment

## KEY EXCLUSION CRITERIA

- A documented additional validated targetable oncogenic driver mutation or alteration in genes such as epidermal growth factor receptor (*EGFR*), anaplastic lymphoma kinase (*ALK*), *BRAF* (V600E), human epidermal growth factor receptor 2 (*HER2*), *MET* (exon 14), *ROS1*, rearranged during transfection (*RET*), or neurotrophic tyrosine receptor kinase (*NTRK*)1/2/3
- Had any of the following prior to randomization:
  - Prior systemic therapy (chemotherapy, immunotherapy, targeted therapy, or biological therapy) for advanced or metastatic NSCLC
  - One cycle of standard-of-care treatment prior to study enrollment will be allowed for cases where immediate treatment is clinically indicated
- Central nervous system (CNS) metastases and/or carcinomatous meningitis
- For participants receiving pemetrexed and platinum (part B and safety lead-in part B):
  - Squamous cell and/or mixed small cell/non-small cell histology is not permitted
  - Is unable to interrupt aspirin or other nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Is unable or unwilling to take folic acid or vitamin B12 supplementation

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT06119581].

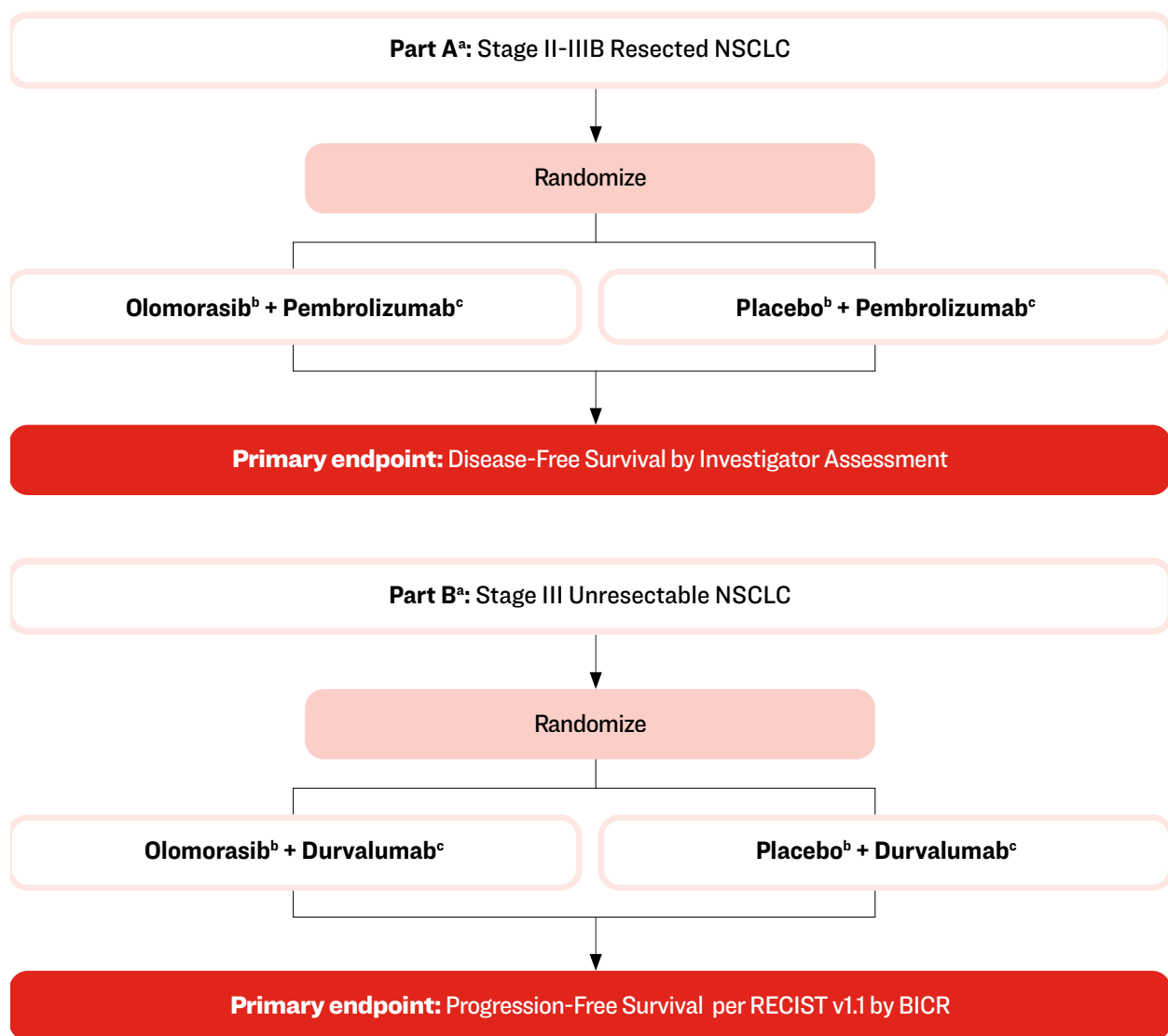
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# OLOMORASIB KRAS G12C INHIBITOR (LY3537982)

## SUNRAY-02

A Phase 3, Multicenter, Double-Blind, Placebo-Controlled Study Assessing the Efficacy and Safety of Olomorasib in Combination With Standard of Care Immunotherapy in Participants With Resected or Unresectable KRAS G12C-Mutant, Non-Small Cell Lung Cancer



<sup>a</sup>Combination treatment for up to approximately 1 year followed by olomorasib/placebo monotherapy to complete up to 3 years of total treatment; <sup>b</sup>Administered orally BID up to 3 years; <sup>c</sup>Administered intravenously up to 1 year.

**Abbreviations:** BICR=Blinded Independent Central Review; BID=Twice Daily; KRAS=Kirsten Rat Sarcoma; NSCLC=Non-Small Cell Lung Cancer; RECIST=Response Evaluation Criteria In Solid Tumors.

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT06890598].



# OLOMORASIB KRAS G12C INHIBITOR (LY3537982)

## SUNRAY-02

**A Phase 3, Multicenter, Double-Blind, Placebo-Controlled Study Assessing the Efficacy and Safety of Olomorasib in Combination With Standard of Care Immunotherapy in Participants With Resected or Unresectable KRAS G12C-Mutant, Non-Small Cell Lung Cancer (Cont.)**

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### KEY INCLUSION CRITERIA

- Histologically/cytologically confirmed non-small cell lung cancer (NSCLC)
- For Part A:
  - Clinical Stage II-IIIB (N2) NSCLC treated via presurgical chemoimmunotherapy, with the residual tumor being present at time of surgery
  - Pathologic Stage II-IIIB (N2) NSCLC treated via initial upfront resection
- For Part B:
  - Clinical Stage III unresectable NSCLC without progression on concurrent platinum-based chemoradiotherapy
- Disease with evidence of KRAS G12C mutation
- Disease with known programmed death-ligand 1 (PD-L1) expression
- Eastern cooperative oncology group (ECOG) performance status of 0 or 1
- Ability to swallow oral medication
- Adequate laboratory parameters
- Contraceptive use consistent with local regulations
- Women of childbearing potential must
  - Have a negative pregnancy test
  - Not be breastfeeding during treatment

### KEY EXCLUSION CRITERIA

- Known changes in the epidermal growth factor receptor (*EGFR*) or anaplastic lymphoma kinase (*ALK*) genes
- Another type of cancer that is either progressing or required active treatment in the last 3 years before screening
- An active autoimmune disease that required systemic treatment in the past 2 years, with the exception of endocrine replacement therapy
- Any immune-related side effect or allergic reaction (Grade  $\geq 3$ ) from a previous immunotherapy medicine or any unresolved Grade  $>1$  immune-related side effect, except in patients with hormone-related diseases who are now on stable hormone replacement therapy

Please visit [clinicaltrials.gov](https://clinicaltrials.gov) for more information on this clinical trial [NCT06890598].

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Pipeline information is current through March 26, 2025.

