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When biomarkers evolve faster than PICOs

Evidence-based JCA mapping in KRAS-mutated non-small cell lung cancer (NSCLC) using REAL-SLR

BACKGROUND

Successful EU **Joint Clinical Assessments (JCAs)** depend on establishing the PICO framework (Population, Intervention, Comparator, Outcome) early and with transparent and evidence-based definitions. In advanced NSCLC, KRAS mutations occur in up to 30% of patients. Emerging KRAS-targeted therapies are expanding beyond the currently approved KRAS G12C population. As treatment pathways, biomarkers, and comparator landscapes evolve, continuous evidence monitoring becomes increasingly important for JCA preparedness.

OBJECTIVES

To evaluated the use of a **Oncoscope** Real-Time AI-Assisted Systematic Literature Review **(REAL-SLR)** database to support evidence-based PICO mapping in KRAS-mutated NSCLC.

METHODS

A **PRISMA-compliant**, **continuously updated** REAL-SLR was conducted using the NSCLC database. Evidence from clinical trials, regulatory sources, clinical guidelines, and HTA documents was systematically identified and synthesized. Studies were mapped by population, intervention, comparator, outcomes, biomarker, line of therapy and subgroups. This continuously updated evidence base was used to map JCA-relevant PICOs.

Table1. **Oncoscope REAL-SLR PICOS & JCA mapping**

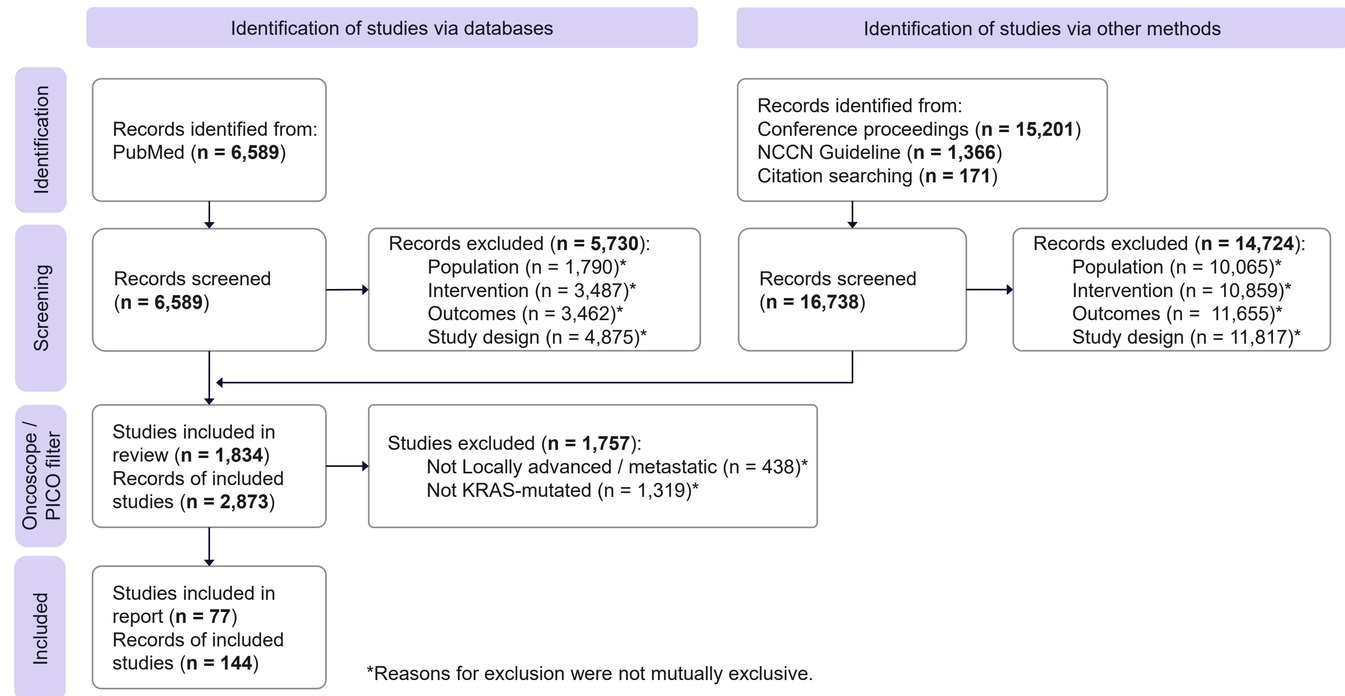
PICOS	REAL-SLR PICOS	JCA Mapping
Patient population	Patients diagnosed with NSCLC at any stage	Disease stage: **metastatic NSCLC**; Histology: Any; Biomarker: **KRAS G12C, KRAS G12C, other KRAS/RAS;** Treatment path: Any
Interventions and Comparators	Any intervention used for the treatment of NSCLC (surgery, radiotherapy, drugs, biologics, cell treatments, vaccines, etc.)	Same as REAL-SLR PICOS
Outcomes measures	Efficacy (OS, PFS, other progression, response), PROs, safety	Same as REAL-SLR PICOS
Study design	RCTs, non-RCTs, single arm, Phase 1, Phase 1/2, Phase 2, Phase 2/3, Phase 3, Phase 4; Pooled analyses of RCTs; ECTs	**Phase 2, Phase 2/3, Phase 3 studies**

KEY TAKEAWAYS

REAL-SLR-enabled, continuously updated evidence based on KRAS-mutated NSCLC identified EVOLVING POPULATIONS and COMPARATOR CLASSES likely to influence future JCA scope.

Living evidence approaches may improve transparency, reduce evidence-generation risk, support EARLIER IDENTIFICATION of HTA-relevant subgroups and comparators, and enhance JCA PREPAREDNESS in rapidly evolving oncology indications.

Figure 1. **Continuously updated PRISMA (REAL-SLR framework) in NSCLC (updated Sep 10, 2026)**



RESULTS

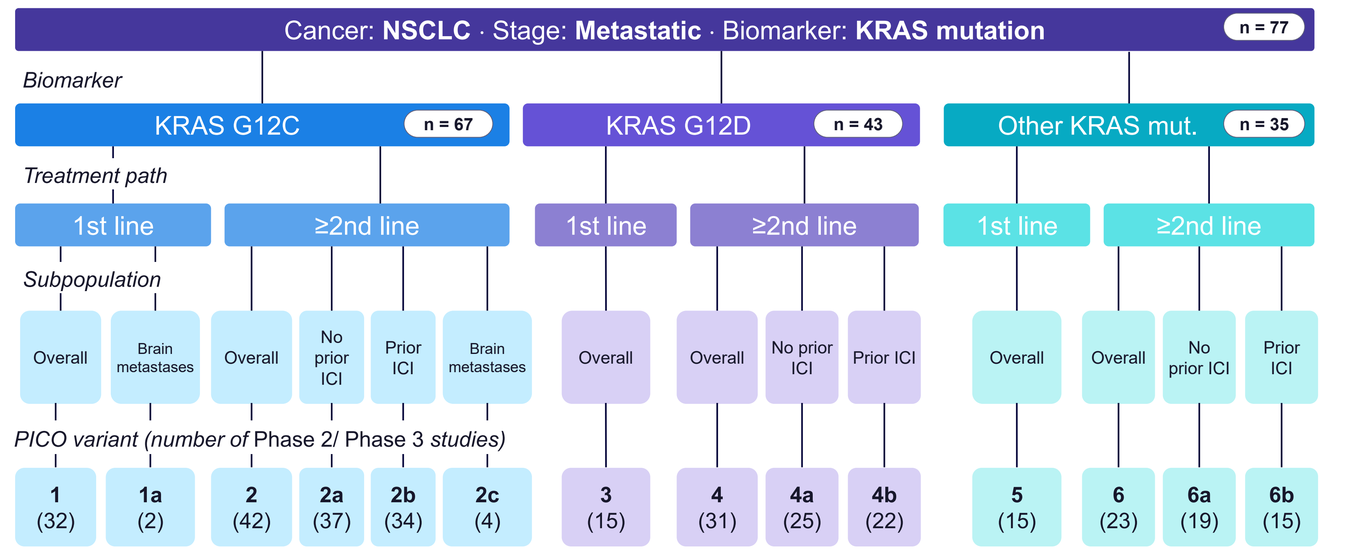
as of September 10, 2026

77 published studies in metastatic KRAS-mutated NSCLC

52 trials in the ≥2nd line setting

3 extended populations based on KRAS-mutation subtype

Figure 2. **Preliminary mapping of possible PICO in KRAS+ mNSCLC**



JCA-relevant additional stratification

HISTOLOGY · PRIOR THERAPY · BRAIN / CNS · CO-MUTATIONS / PD-L1

Figure 3. **Evolving intervention landscape**

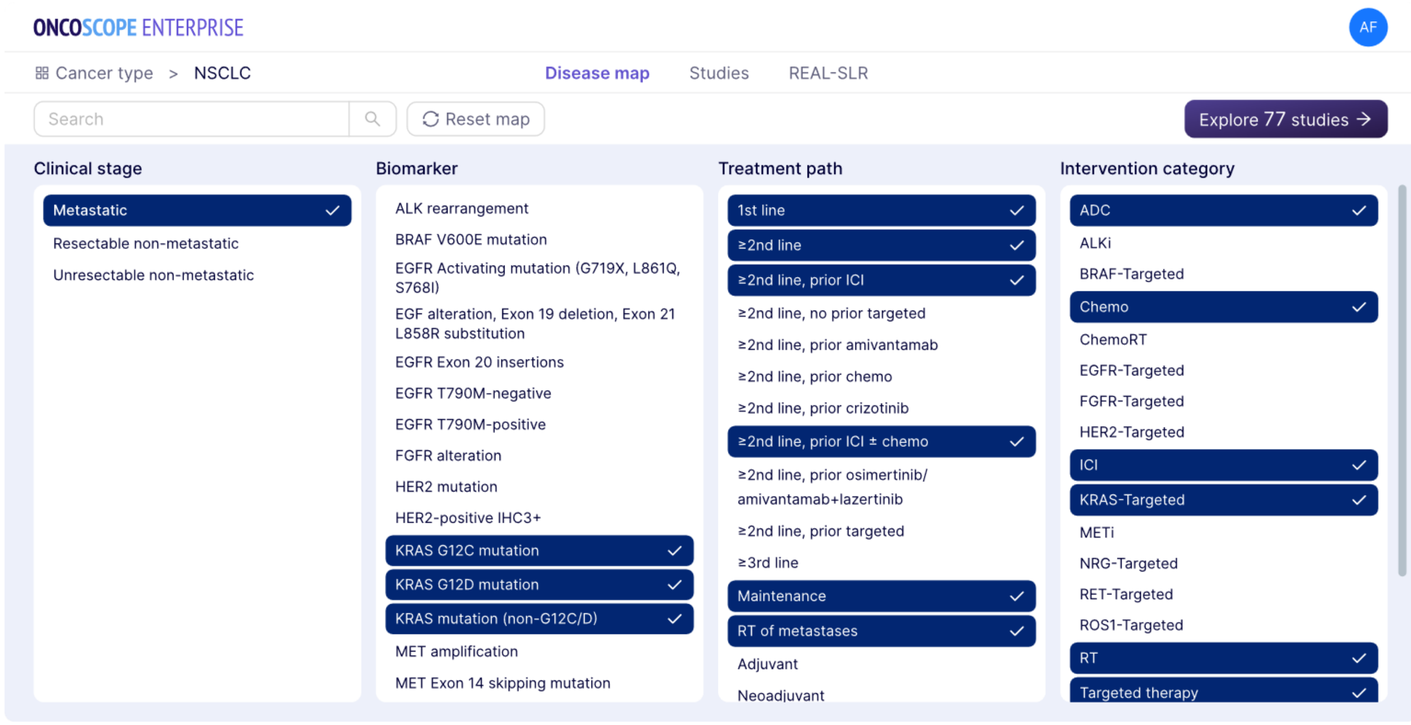
31 G12C-targeted therapies

7 G12D-targeted therapies

1 pan-RAS (ON/OFF) inhibitors

Emerging
- ADCs
- non-covalent inhibitors
- degraders

Figure 4. **Future RAS-targeted disease map**



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ABBREVIATIONS

ADCs, antibody-drug conjugates; **CNS**, central nervous system; **ECTs**, emerging cancer therapies; **HTA**, health technology assessment; **ICI**, immune checkpoint inhibitor; **JCA**, Joint Clinical Assessment; **KRAS**, Kirsten rat sarcoma viral oncogene homolog; **mNSCLC**, metastatic NSCLC; **NSCLC**, non-small cell lung cancer; **OS**, overall survival; **PFS**, progression-free survival; **PICO**, population, intervention, comparator, outcome; **PRISMA**, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; **PROs**, patient-reported outcomes; **QoL**, quality of life; **RAS**, rat sarcoma; **RCT**, randomized controlled trial; **REAL-SLR**, Real-Time AI-Assisted Systematic Literature Review.