Clinical Genomics | Oncology

Unlock *KRAS* G12C for lung cancer treatment decisions

The *therascreen*® KRAS RGQ PCR Kit is now FDA approved and clinically validated as a companion diagnostic test to aid the identification of NSCLC patients who may be eligible for treatment with LUMAKRAS™ (sotorasib)

Reliable detection of *KRAS* G12C is the key to a new treatment option

Lung cancer is the second most common cancer in the US, with over 228,000 new cases and 138,000 deaths per year. Of these cases, non-small cell lung cancer (NSCLC) accounts for ~84% (1). Although development of NSCLC is associated with many forms of mutation in a large number of genes, activating mutations in the proto-oncogene *KRAS* are among the most frequent (2), with the specific mutation *KRAS* G12C present in ~13% of NSCLC cases (3). Each year in the US, >25,000 patients are diagnosed with *KRAS* G12C-positive cancers (4) and despite decades of research, until now there has been no targeted treatment option available for them.

The FDA-approved *therascreen* KRAS RGQ PCR Kit is the first tissue companion diagnostic (CDx) test to aid patient selection and guide treatment options in *KRAS* G12C-positive NSCLC.

The *therascreen* KRAS RGQ PCR Kit identifies patients that may be eligible for treatment with the K-Ras G12C-selective inhibitor LUMAKRAS (sotorasib), based on the detection of the clinically actionable *KRAS* G12C mutation in tumor DNA isolated from FFPE tissue samples. This rapid and sensitive test is part of a simple and reliable workflow with automated result reporting. It has proven analytical and clinical validity, having been evaluated in 123 patients during the CodeBreaK 100 clinical trial (5).

Response to LUMAKRAS linked to the presence of the *KRAS* G12C mutation

The CodeBreaK 100 trial (clinical trial 20170543) is an ongoing open-label, multicenter, phase 1/2 study designed to evaluate the efficacy and safety of LUMAKRAS (sotorasib) in adult subjects with advanced solid tumors that harbor the *KRAS* G12C mutation (5).

The primary endpoint of the NSCLC phase 2 portion of this study was to evaluate tumor objective response rate (ORR), assessed by RECIST 1.1 criteria, of LUMAKRAS as monotherapy in subjects with *KRAS* G12C-mutated advanced tumors.

Of a total of 126 subjects, 124 subjects were included in the full analysis set.

The primary endpoint of ORR (complete response + partial response) measured by computed tomography or magnetic resonance imaging and assessed per RECIST 1.1 by blinded independent centralized review (BICR) for subjects with *KRAS* G12C-mutated NSCLC was 36% (45 of 124 subjects; 95% CI: 28–45%); 1.6% (two subjects) achieved complete response and 35.8% (43 subjects) achieved partial response.

The *therascreen* KRAS RGQ PCR Kit enables the selection of *KRAS* G12C-positive patients with advanced NSCLC who may benefit from treatment with LUMAKRAS (sotorasib).

Sample to Insight® workflow

The simple testing workflow begins with manual DNA extraction from formalin-fixed, paraffin-embedded (FFPE) NSCLC tumor tissue using the QIAamp® DSP DNA FFPE Tissue Kit, followed by sensitive real-time PCR on the Rotor-Gene® Q MDx (US) instrument and automated data analysis with Rotor-Gene Q software (Figure 1).

The *therascreen* KRAS RGQ PCR Kit targets seven mutations in codons 12 and 13 of the *KRAS* gene (G12A; G12D; G12R; G12C; G12S; G12V; G13D). Qualitative results are displayed in Rotor-Gene Q software, informing the system operator if one or more of the seven mutations detected by the kit are present. The assay can be completed in ~8 hours, providing next-day results.

Figure 1. Simple, efficient workflow with the *therascreen* KRAS RGQ PCR System.

Ordering Information

Product	Contents	Cat. no.
therascreen KRAS RGQ PCR Kit (24)	For 24 reactions: 1 Control Assay, 7 Mutation Assays, Positive Control, Water, *Taq* DNA Polymerase	870021
Related products		
QIAamp DSP DNA FFPE Tissue Kit (50)	For 50 DNA preps: QIAamp MinElute® columns, Proteinase K, Buffers, and Collection Tubes (2 ml)	60404
Rotor-Gene Q MDx (US) System	Real-time PCR cycler with 6 channels, laptop computer, software, accessories, 1-year warranty on parts and labor, installation and training	9002036

The *therascreen* KRAS RGQ PCR Kit is intended for in vitro diagnostic use.

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN® kit handbook or user manual. QIAGEN kit handbooks and user manuals are available at www.qiagen.com or can be requested from QIAGEN Technical Services or your local distributor.

References

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2. Fernandez-Medarde, A., et al. (2011) Genes Cancer. **2**, 344.
3. Hong, D.S., et al. (2020) N. Engl. J. Med. 383, 1207.
4. Stephen, A.G., et al. (2014) Cancer Cell. **25**, 272.
5. *therascreen* KRAS RGQ PCR Kit Instructions for Use (Handbook). May 2021