

P1.082: Early Detection of *KRAS* G12C Mutations in Bronchoscopy Specimens Using Digital PCR: Expanding the Molecular Utility of Bronchial Washings

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INTRODUCTION

Lung cancer remains a leading cause of cancer-related mortality, with prognosis strongly dependent on disease stage at diagnosis. Bronchoscopy is routinely used to investigate suspected lung cancer and provides specimens including bronchial washings, brushings and guided sheath samples. However, these materials are often underutilized for molecular testing despite being collected in close proximity to the tumour.

Digital PCR (dPCR) enables sensitive detection of low-abundance genetic variants and may facilitate molecular testing of these routinely collected specimens.

Aim: To evaluate the feasibility of detecting *KRAS* G12C mutations using dPCR in bronchoscopy-derived specimens from patients with known *KRAS* mutation status.

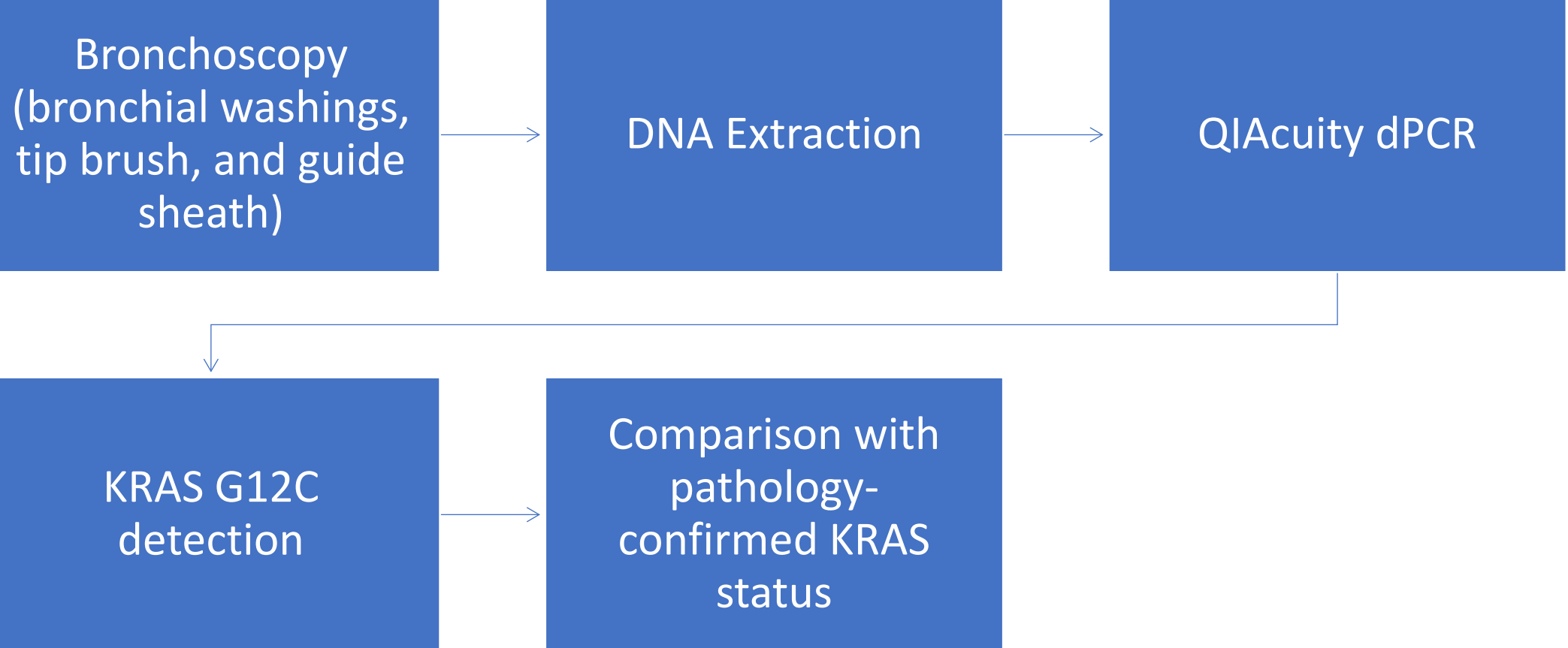
METHODS

Bronchoscopy specimens from 41 participants with pathology-confirmed *KRAS* G12 status were retrospectively analyzed: 21 *KRAS* G12 wildtype and 20 *KRAS* G12C-mutant cases.

Four bronchoscopy-derived specimen types were evaluated:

- Bronchial wash cell pellet (BWCP; n=44)
- Bronchial wash supernatant (BWSP; n=41)
- Guided sheath cell pellet (GSCP; n=21)
- Brushing tip cell pellet (BTCP; n=22)

Participant-matched plasma was also analysed where available. DNA was extracted and *KRAS* G12C mutation detection performed using the QIAcuity digital PCR platform. A positive result was defined as ≥4 mutant partitions above the assay threshold.



DISCUSSION AND CONCLUSION

Actionable Take Away Message:

Bronchoscopy specimens represent a valuable and potentially underutilised source for molecular testing. ***KRAS* G12C mutations can be detected by dPCR even in some early-stage cancers with non-malignant cytology**, while testing multiple specimen types may further improve detection and maximise the clinical information obtained from a single bronchoscopy procedure.

Future Direction for Research:

Larger prospective studies are needed to validate these findings and optimise sample processing and DNA input to improve detection sensitivity. Expanding this approach to **multi-gene and multi-omics testing** could broaden the clinical utility of bronchoscopy specimens, supporting earlier molecular characterisation and identification of actionable targets for patients with lung cancer.

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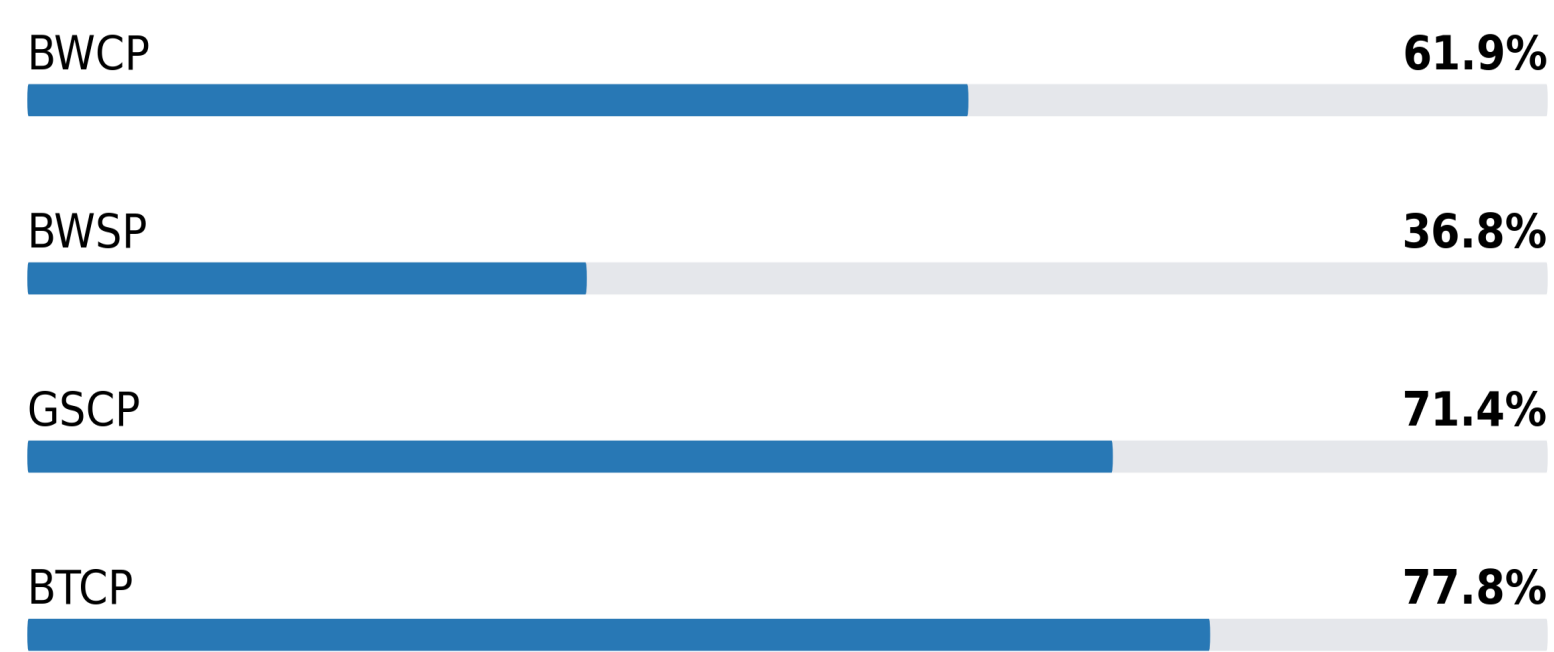
Artificial Intelligence (AI) Use Disclaimer

Tool	Use	Prompt(s)
ChatGPT	Generate results graphics	Generate graphics that shows <i>KRAS</i> G12C detected in 4/8 stage 1, 2/3 stage 2, 5/6 stage 3, and 5/5 stage 4 LC based on these results and discussions. Generate another graphic that shows no <i>KRAS</i> G12C detected in matched plasma.

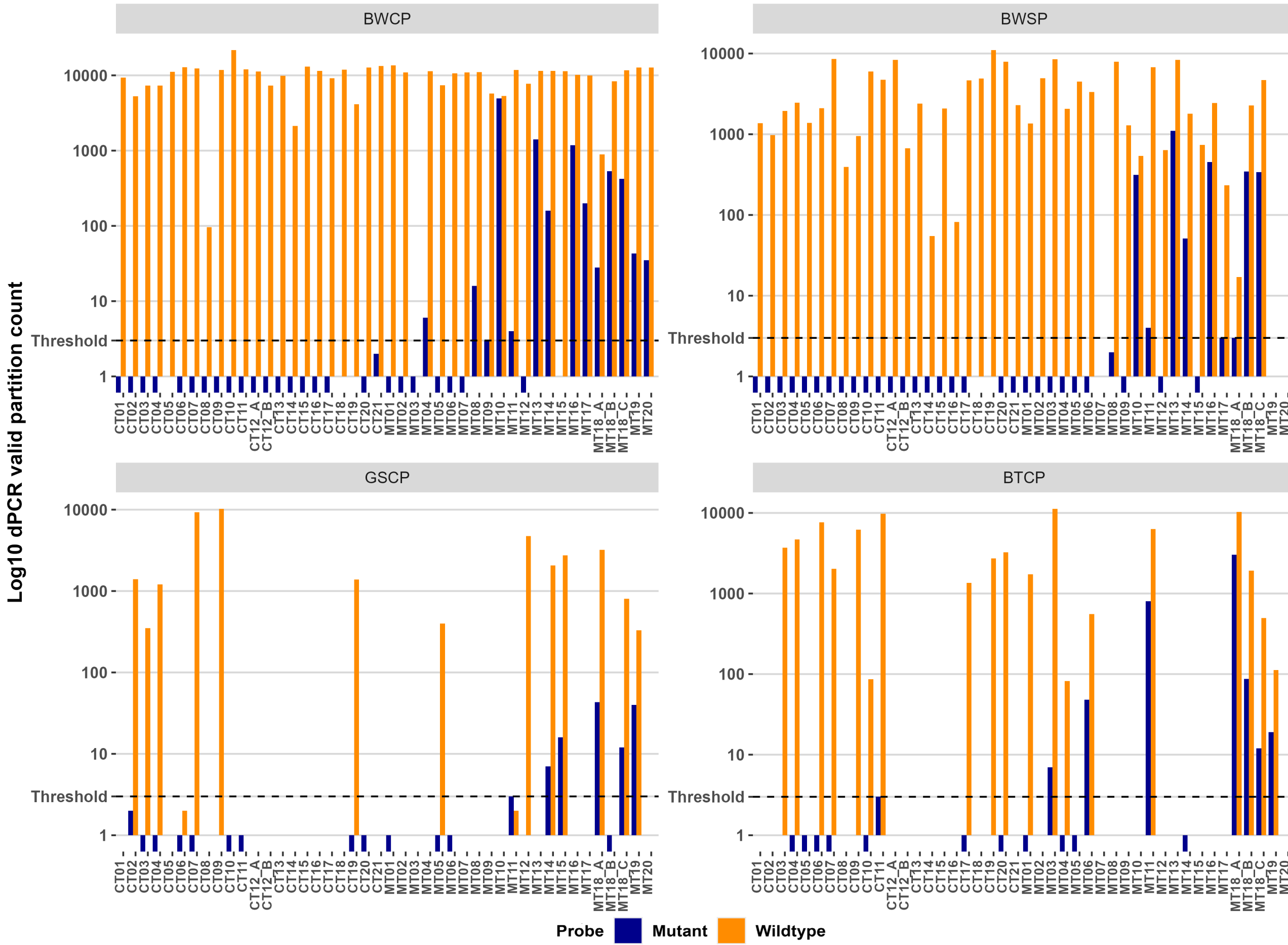
RESULTS

KRAS G12C is detectable in bronchoscopy specimens using digital PCR

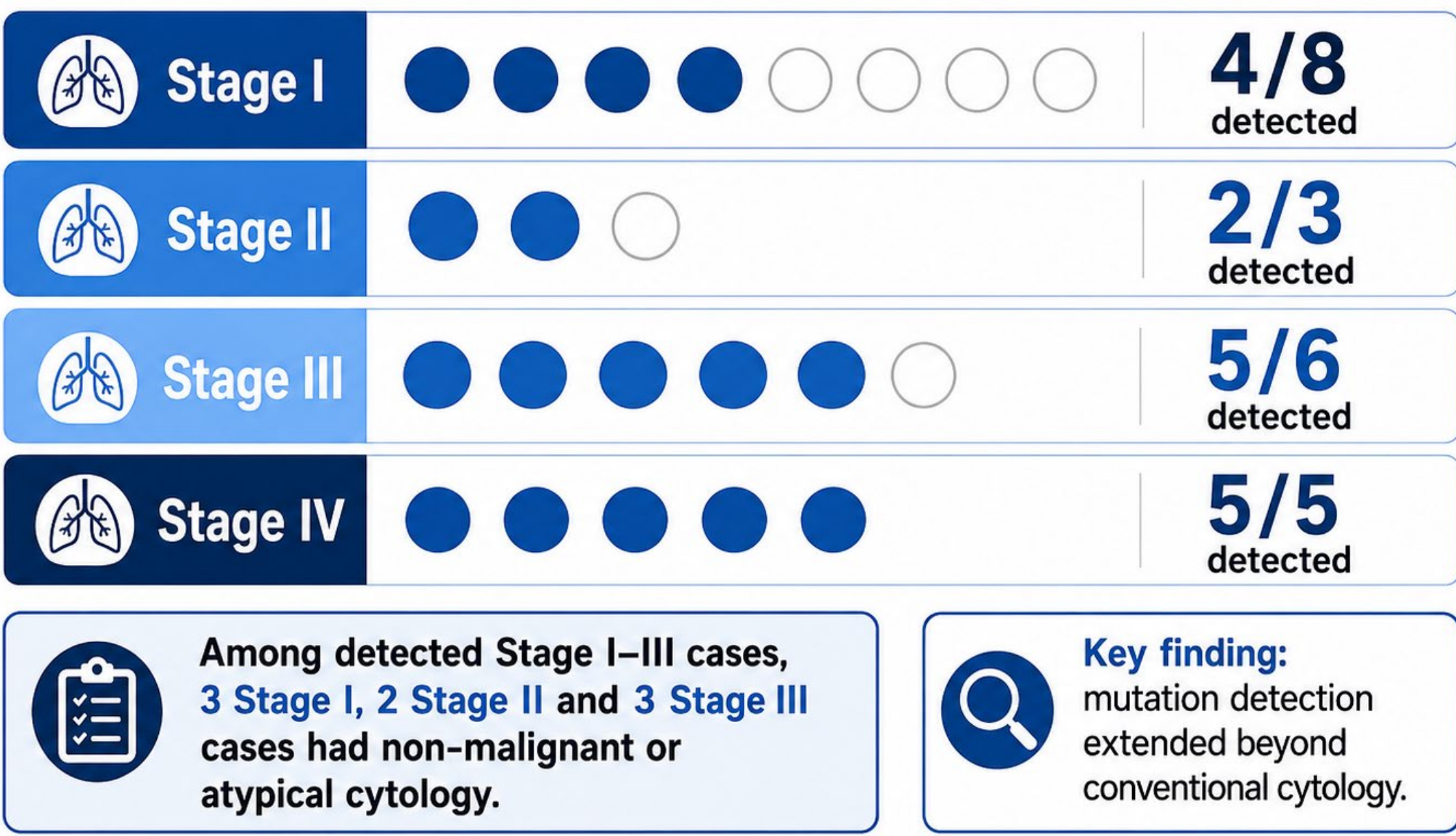
KRAS G12C was detected in **13/21 BWCP, 7/19 BWSP, 5/7 GSCP and 7/9 BTCP** samples from mutation-positive cases using dPCR. No *KRAS* G12C mutation was detected in specimens from *KRAS* G12 wildtype cases.



72.7% Overall sensitivity
100% Specificity
86.4% Concordance

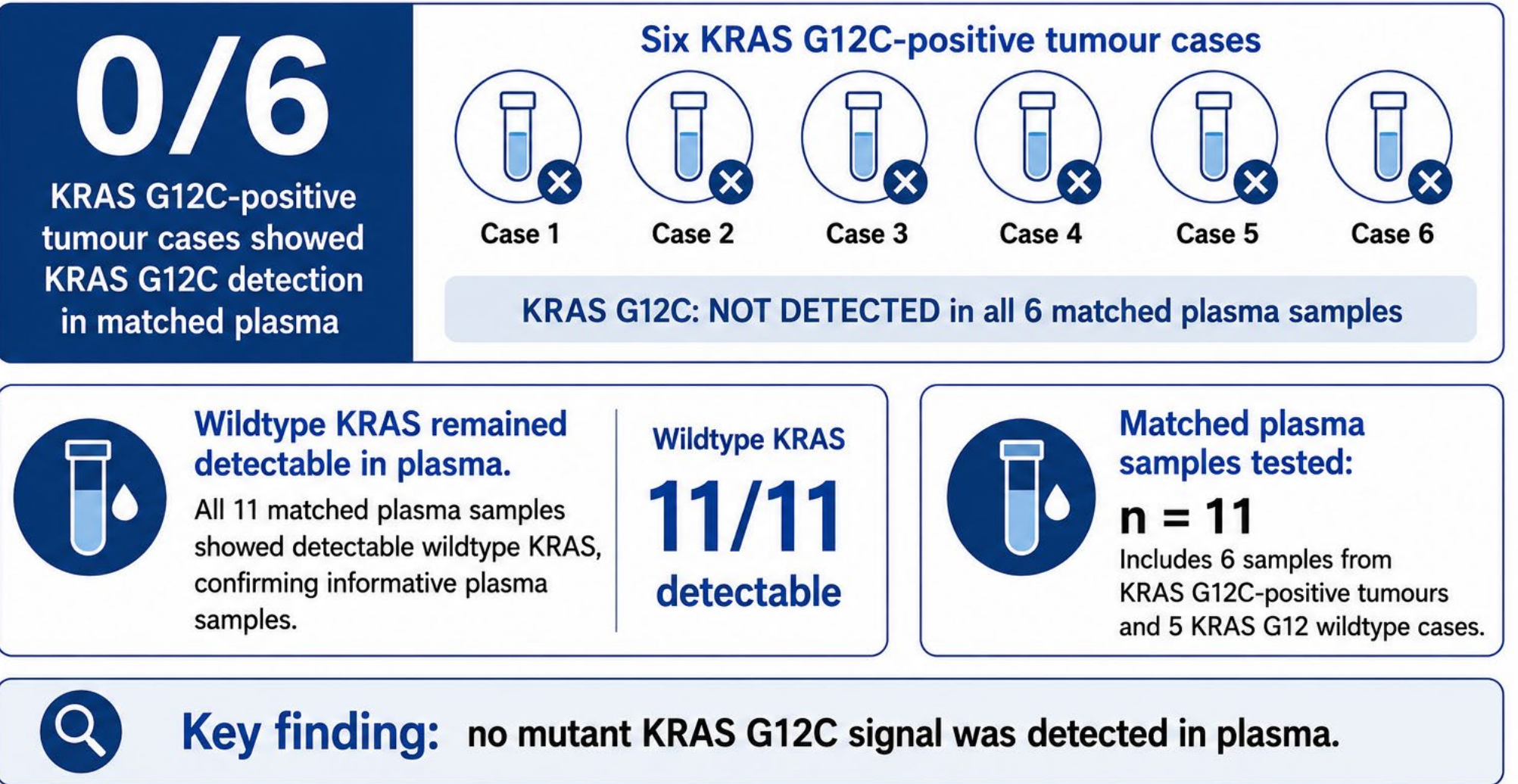


KRAS G12C mutation was detected despite non-malignant cytology



The lung cancer diagnosis determined from the bronchoscopy specimens varied from the pathology results on the corresponding bronchial biopsy or surgical tissue. No malignant cells were detected in all tumour stage I bronchoscopy specimens, and some of tumour stage II, III and IV bronchoscopy specimens. Despite this, *KRAS* G12C mutation was successfully detected in bronchoscopy specimens with tumour stage and cytological diagnosis: Stage I (4/8, 3 non-malignant), Stage II (2/3, both non-malignant), Stage III (5/6, 3 non-malignant or atypia) and Stage IV (5/5).

No *KRAS* G12C mutation was detected in matched plasma



A subset of participant-matched plasma samples was available for *KRAS* G12C mutation testing— five cases carried wildtype *KRAS* G12 while six cases carried *KRAS* G12C mutation (tumour stage I to stage IV). None of these samples showed mutant *KRAS* G12C partition despite all were detected with substantial amount of wildtype *KRAS* G12 partitions.