## APPENDIX. Survey questions and responses for T790M testing in Hong Kong from the expert panel (n=8)

**Key question 1: When do you conduct T790M testing?**

Do you recommend T790M testing upon:

- Radiological disease progression? Yes–100%
- Symptomatic disease progression? Yes–100%
- Oligoprogression? Yes–50%, No–50%
- Central nervous system (CNS)–only progression? Yes–100%

Which of the following factors would you consider in a referral for testing?

- Whether the patient is symptomatic–100%
- Patient's performance status–67%
- Presence of oligometastatic disease–83%
- Presence of CNS metastasis–100%
- Carcinoembryonic antigen level–33%

**Key question 2: How do you test for the T790M mutation?**

Which type of biopsy do you use for the initial test?

- Liquid biopsy–100%
- Tissue biopsy–0%

When liquid biopsy is used as the initial test, do you proceed to tissue biopsy if the liquid biopsy result is negative?

*Scenario A: No mutations were detected, including the original sensitising mutation (ie, triple-negative result)*

- Yes–63%
- No, conduct a second liquid biopsy with the same platform–0%
- No, conduct a second liquid biopsy with a different platform–38%
- No, declare the patient T790M-negative and proceed to treatment–0%

*Scenario B: Only the sensitising mutation was detected and T790M is negative*

- Yes–63%
- No, conduct a second liquid biopsy with the same platform–0%
- No, conduct a second liquid biopsy with a different platform–0%
- No, declare the patient T790M-negative and proceed to treatment–38%

When tissue biopsy is used as the initial test, do you request liquid biopsy if the tissue biopsy result is negative?

- Yes–88%
- No–12%

If there is no accessible site for tissue biopsy, what is the next step in management?

- Continue epidermal growth factor receptor–tyrosine kinase inhibitor (EGFR-TKI) treatment and perform repeated liquid biopsy later–86%
- Switch to chemotherapy and perform repeated liquid biopsy if disease progresses after chemotherapy–14%

If there is no accessible site for tissue biopsy and EGFR-TKI treatment is continued, what is the optimal timing for repeated liquid biopsy?

- 4 weeks–0%
- 6 weeks–0%
- 8 weeks–14%
- 12 weeks–0%
- If there is further evidence of progression or patient exhibits more symptoms–86%

  

**APPENDIX. (cont'd)**

How many times would you perform repeated liquid biopsy to consider the disease truly T790M-negative?
- 1–0%
- 2–83%
- 3–17%
- 4–0%
- ≥5–0%

If pleural fluid is available, would you send it for liquid biopsy?
- Yes–88%
- No–13%

If the patient has CNS metastasis, would you send the CSF for liquid biopsy?
- Yes–80%
- No–20%

**Key question 3: What is the most effective method for T790M testing?**

What is your preferred platform for initial liquid biopsy to determine T790M mutation status?
- Reverse transcription (RT) polymerase chain reaction (PCR) (eg, Cobas, ARMS)–0%
- Digital PCR (eg, droplet digital PCR, BEAMing [beads, emulsions, amplification, magnetics])–100%
- Next-generation sequencing (NGS) with large panel–0%
- NGS with small panel–0%

What is your preferred platform for liquid biopsy as the repeated test to determine T790M mutation status?
- RT PCR (eg, Cobas, ARMS)–0%
- Digital PCR (eg, droplet digital PCR, BEAMing)–88%
- NGS with large panel–0%
- NGS with small panel–13%

What is your preferred platform for tissue biopsy to determine T790M mutation status?
- RT PCR (eg, Cobas, ARMS)–63%
- Digital PCR (eg, ddPCR, BEAMing)–12.3%
- NGS with large panel–12.3%
- NGS with small panel–12.3%

 