Hamlet.rt Trans - a prospective single centre translational sub-study evaluation of liquid biomarkers of radiation response

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Background and Hypothesis

- Hamlet.rt is a translational biosampling pilot sub-study, leveraging the infrastructure of Cancer Research UK RadNet Cambridge to explore multiple liquid biomarkers of radiation response.
- Studies have shown that biomarkers such as cell free DNA (cfDNA) are released into the bloodstream during radiotherapy (Lo et al. 2000) and studies have found to be similarly informative.

The primary objective of Hamlet.rt Trans is to establish proof of concept of DBS as a cancer liquid biopsy for monitoring treatment response and detection of minimal residual disease.

Study Objectives

- The study examines biomarkers of treatment response in patients with lung and head and neck cancers, and markers of treatment response and toxicity in patients with prostate cancer.
- Up to 50 patients will be recruited per cancer type.
- In addition to conventional urine and blood sampling, the study collects dried blood spots (DBS) from fingerpick samples onto Whatman FTA cards. DBS may replace frequent peripheral venepuncture in future studies if found to be similarly informative.
- The primary objective of Hamlet.rt Trans is to establish proof of concept of DBS as a cancer liquid biopsy for monitoring treatment response and detection of minimal residual disease.

Patient Selection

- Head and Neck: squamous cell lung cancer receiving primary radical radiotherapy +/- chemotherapy regardless of human papilloma virus status
- Lung: non-small cell lung cancer treated with radical radiotherapy +/- chemotherapy
- Prostate: high-risk (Cambridge Prognostic Group 4-5) adenocarcinoma, receiving 60 Gy in 20 fractions to prostate gland and seminal vesicles only

Sampling Schedule

- At each time point, the following samples are collected:
  - Whole blood samples are collected via venepuncture (up to 30ml) into Paxgene and EDTA tubes.
  - Up to four DBS samples (~50 µl each) are collected via fingerpicking sampling.
  - 25 – 200ml of urine are collected into universal containers and stabilised with Streck Urine Preservative.
- Plasma for cfDNA analysis and senescence-related profiling is extracted from the biosamples in addition to buffy coat at selected time points.
- A typical sampling schedule for a patient receiving radiotherapy for non-small cell lung cancer includes 10 sampling time points in total.

Recruitment & Sampling

- Total: 30
  - Lung: 17
  - H&N: 10
  - Prostate: 3

Conclusions

- This prospective single-centre study – currently in progress- demonstrates good acceptability of combined blood sampling methods at frequent intervals during radiotherapy treatment.
- Recruitment will continue, and preliminary translational analyses will commence in parallel to identify novel strategies for evaluating treatment response to radical radiotherapy in common solid cancers treated with radiotherapy as a primary modality.
- Based on these analyses, a follow-on study will further examine the most informative time points and techniques.
- Patient feedback will continue to be sought on the sampling schedule and techniques.

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