The REQUITE project: validating predictive models and biomarkers of radiotherapy toxicity to reduce side-effects and improve quality-of-life in cancer survivors

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INTRODUCTION

Recently the first replicated genetic associations for adverse reactions to radiotherapy were reported. Predictive clinical models for radiotherapy side effects are also being developed. It is now timely to start a project that aims to validate known clinical and genetic predictors of adverse reactions and develop the statistical models for clinical use. REQUITE is a European Union funded FP7 project aiming to validate clinical models and biomarkers of radiotherapy toxicity and design future trials using the models.

OBJECTIVES

1. Perform a multi-centre, cohort study collecting: blood samples, epidemiology and treatment data, and longitudinal side-effect and quality-of-life data (before and after treatment, years 1 & 2) in 5,300 patients with prostate, breast or lung cancer.
2. Produce a centralised biobank of DNA and a centralised database including radiotherapy plans
3. Validate published biomarkers of radiosensitivity – genetic and apoptosis assays
4. Validate clinical predictive models of radiotherapy toxicity in breast, prostate and lung cancer and incorporate biomarker data.
5. Design interventional trials to reduce long-term side-effects.
6. Provide a resource for dissemination and exploitation to the radiotherapy community.

WORK FLOW
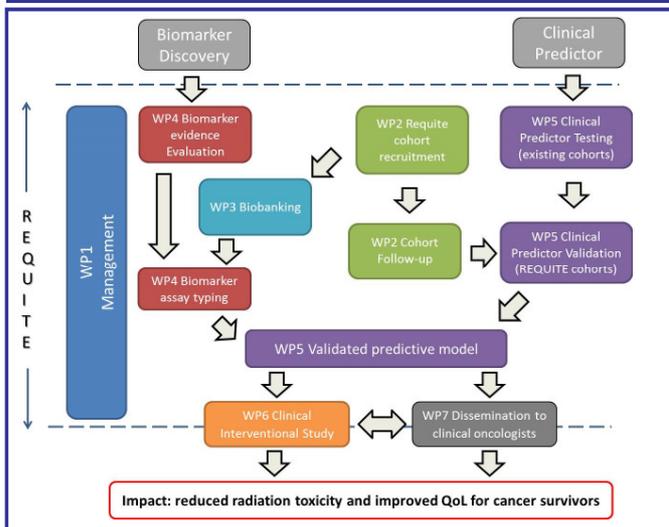
CURRENT STATUS

- Standardised data collection forms generated
- A questionnaire for collecting patient reported toxicity according to Common Toxicity Criteria for Adverse Events was developed for lung patients. The lung and an already validated male pelvic questionnaire were translated into multiple languages, back translated and checked for consistency. The final questionnaires were tested in small cohorts of patients for acceptability. These validated questionnaires and the standardised data collection forms are available at www.requite.eu/.
- A centralised database for electronic data capture and storage was developed
- Database training and site initiation visits for the main sites completed
- Ethical approvals for the observational study obtained February-July 2014
- >408 patients recruited
- Apoptosis assay standardised operating procedure and inter-laboratory testing completed (Leicester, Mannheim, Montpellier), >110 patients assayed
- Breast cancer cohorts for clinical model validation collected and validation of literature reported risk factors, association and prediction statistical modelling for late side-effects applied to the Cambridge IMRT trial data.
- Website developed (www.requite.eu).

BIOMARKERS

- All 5,300 samples will be genotyped for SNPs and CNVs with evidence for association with radiotherapy toxicity. Scale will depend upon costs in project year 5.
- 1,800 samples will be assayed for radiation-induced lymphocyte apoptosis using FACS analysis.
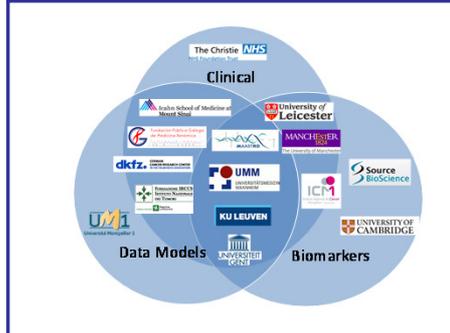
TIMESCALE

Project start	Oct 2013
Recruitment starts	Apr 2014
Recruitment ends	Mar 2016
Follow-up ends	Mar 2018
Project complete	Sep 2018

PARTNERS

KICK OFF MEETING

SUMMARY

- REQUITE has developed standardised data collection forms including questionnaires for collecting patient reported CTCAE toxicity in multiple languages. These forms are freely available via the website to improve the standardisation of data collection in other studies.
- The REQUITE project will develop and validate statistical models incorporating biomarker data to predict radiotherapy side effects. Future interventional trials will use these models to help optimise radiotherapy.
- The project welcomes collaborations that add value to the project, particularly additional datasets for validating clinical models.