1. Publishable summary

Summary description of project context and objectives

Summary description and objectives of the project;
The ARTFORCE project introduces very sophisticated tools to improve treatment outcome of patients with advanced tumours by enabling tailored irradiation of the most active parts of the tumour. Furthermore, the work carried out in this project aims to improve quality of life by withholding ineffective, toxic treatments and to decrease community costs by targeting expensive treatments to those who will benefit. To this end, treatment-specific tumour response predictors are developed for patient selection, i.e. genetic predictors for cisplatin and radiation sensitivity as well as functional and anatomical imaging predictors early during the treatment. Also a major aim is to improve the overall level of radiation oncology in Europe by introducing methods for fully-controlled image guided adapted radiotherapy to personalize the very intensive and aggressive treatment for Lung and Head & Neck cancer.

Description of work performed and main results

Description of the work performed during the third period (month 37 to 54)
Most work packages are on schedule (7 out of the 9 work packages).
Within the ARTFORCE project there are several interlinked work packages. Work packages 2 (Adaptive RT to account for anatomical changes), WP3 (Biological adaptive treatment planning in the presence of advanced techniques), WP4 (Three dimensional in-vivo dosimetry) and WP6 (Standardisation and innovative molecular imaging for prediction and decision making) (as well as administrative work packages 1 & 9) run according to schedule. The analysis of the biopsies in work package 5 (Biological markers to predict the response of Head & Neck tumours to Cetuximab or cisplatin+RT) as well as the validation of the biomarkers for predicting the cisplatin and radiation sensitivity are currently postponed to allow for a sufficient number of patients to be analysed. In the meantime however, more extensive work has been performed in characterising biomarkers in lung cancer patients. There is no indication that these work packages will be delayed by factors other than those mentioned above. It has to be mentioned that, within work package 2 (Adaptive RT to account for anatomical changes), the sophisticated treatment planning and validation by dummy runs already allows the participating centres to start the adaptive radiotherapy treatment of patients according to protocol prescription. In work package 3 (Biological adaptive treatment planning in the presence of advanced techniques) it was shown that already in the second week of treatment it is now possible to estimate the radiosensitivity using functional imaging, thus predicting the required radiation dose.
Work package 4 (three dimensional in-vivo dosimetry) has been completed and implemented on time. This allows early on-line detection of errors in treatment delivery of sophisticated radiotherapy in each participating centre.
The two work packages containing a clinical trial are delayed. There are 3 important, external reasons for this delay. In addition to a number of minor reasons, the first major reason was the termination of the free delivery of Cetuximab due to the expiration of the patent and due to budget limitations within Merck. This was unforeseen and unexpected and had a major impact on the project. The second major reason for delay is the long time it took to obtain Medical Ethical Approval and Regulatory Affairs Approval for the trials in all participating centres in the different countries. The third major reason for delay was slow accrual caused by severe restrictions due to radiation safety imposed on the daily life of the patients treated with radiolabelled Cetuximab. The protocol for the Head & Neck trial (work package 8) has been adapted by removing the imaging studies with the radiolabelled Cetuximab. The adapted protocol does not impose the significant life-style restrictions on the patients (they can now freely interact with their close relatives) and this is improving accrual. To further improve accrual we have invited more hospitals to join ARTFORCE as a partner (UMC Utrecht and EMC Rotterdam). These centres were selected because of their large Head & Neck cancer population. For the Lung trial 4 centres will contribute patients, without formerly entering the consortium.
The IDMC recommended to extend the lung trial (work package 7) accrual to 164 (instead of 106) randomized patients, to have a sufficient number of patients alive after 2 years.
Four Third parties are now added to the project to assist in accrual for this trial.
In work package 9 the dissemination of knowledge and expertise is being developed in close cooperation with the European Society for Therapeutic Radiology and Oncology (ESTRO).

Presentations of the project are given at the annual society meetings and published in the ESTRO Newsletter. Involved personnel from consortium institutes are eligible for travel/exchange grants supported by the project and 4 grants for courses and 1 grant for an exchange visit have been awarded during this period.

In Work package 1 a request for a no-cost extension has been made as per May 2015 (first possible date to request an extension) and is currently being evaluated. Despite the initial unforeseen and unexpected delays caused by external factors, we now expect with the actions taken (reduction of the complexity of the Head & Neck protocol, addition of partners/third parties, and monthly teleconferences with all trial partners) we can complete both clinical trial protocols and work package 5 with validation of the predictive assays within the time frame of the extended project.

Expected final results and potential impacts

Expected final results and their potential impact and use
This ARTFORCE project is aimed at improving the treatment outcome in patients with head & neck or lung cancer, treated with a combined modality of radiotherapy and systemic treatment. The improvement in better tumour control will be reached by delivering higher radiation doses to the tumour while minimizing the radiation dose to normal tissues and by reducing toxic side effects of the systemic treatment. This will be obtained by:
1. Novel irradiation methods using information from innovative imaging approaches for the individual treatment design.
2. Adapting the radiation treatment plans to individual patients' anatomical and biological changes during treatment.
3. Designing and validating new QA methods for sophisticated high tech radiation procedures.
4. Validating methods of patient selection for treatment with a combination of radiation and cisplatin.

Expected clinical benefit: Novel irradiation methods by using information from innovative imaging approaches for the individual treatment design, resulting in better treatment outcome.

In over 95 publications the EU has been acknowledged so far as the funding body for the ARTFORCE project, of which 14 publications in the period April 2014-September 2015.

Project public website address:	www.cancerartforce.eu

2. Core of the report

Project objectives, Work progress and achievements, and project management during the period

The Project Summary Pdf document contains the core of the report.