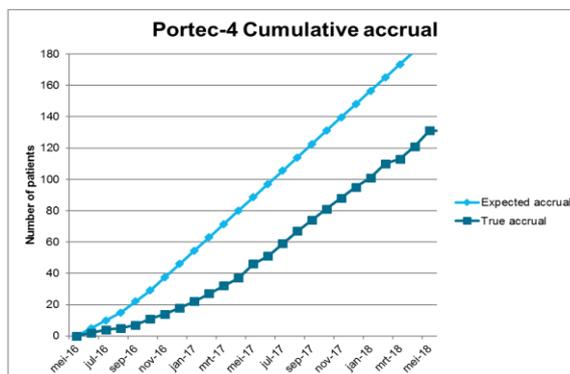
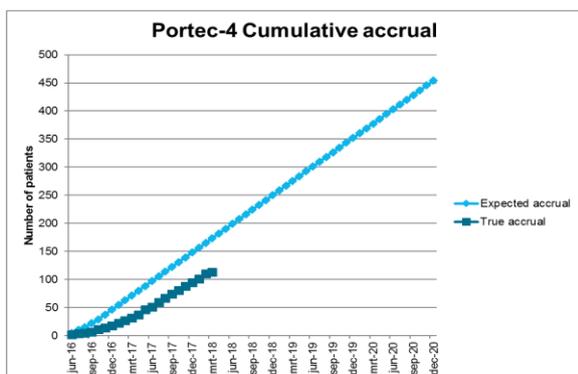
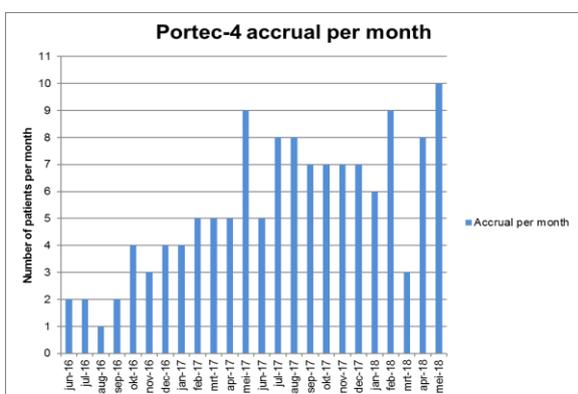


Accrual to the PORTEC-4a trial has reached 131 on May 25th 2018

Accrual to PORTEC-4a has continued to increase since completing the pilot phase of the study on June 12th 2017. The first 50 patients in the pilot phase had been recruited since the activation of the first site on June 15th 2016, and in the period until June 1st 2018 a further 81 have been recruited, for a total of about 90 per year.

See the graphs below and the table on the next page showing the accrual by month and by site, respectively.



Data management and monitoring

Karen Verhoeven-Adema is the PORTEC-4a central datamanager and coordinator at the Trial Office, please email her at portec@iknl.nl

Central monitoring and data checks of CRF entered via the TRIAS system are done on a continuous basis and queries sent accordingly.

On-site monitoring will be resumed in the autumn of 2018, and all sites will be visited at least once every 2 years, with an extra visit after 6-12 months in case of specific issues.

SAE – 2 SAE have been reported in March and July 2017, one unrelated and one possibly related; no new SAE have been reported since 2017.

Recruitment status on May 31st 2018:

Site	No of patients	Arm 1	Arm 2
Academic Medical Center	13	4	9
Arnhem - Radiotherapy Group	12	2	10
Catharina Ziekenhuis	7	2	5
Verbeeten Instituut	11	6	5
Erasmus Medical Center	3	0	3
Leiden University Medical Center	25	7	18
NKI/Antoni v. Leeuwenhoekhuis	3	1	2
Maastricht Radiation Oncology Clinic	32	11	21
Medical Spectre Twente	0	0	0
Haaglanden Medisch Centrum	4	2	2
Radiotherapy Institute Friesland	14	4	10
Deventer - Radiotherapy Group	0	0	0
Isala Zwolle	3	3	0
University Medical Center Groningen	1	1	0
University Medical Center Radboud	1	0	1
University Medical Center Utrecht	2	0	2
Zuidwest Radiotherapeutisch Instituut	0	0	0
TOTAL	131	43	88

DSMB

The Data and Safety Monitoring Board had their annual teleconference on September 8, 2017, to evaluate the report on the pilot phase and overall progress of the trial.

The pilot phase was approved and continuation of the trial was recommended. The DSMB requested an update on accrual after 6 months to see if the improved accrual would be sustained, which has been sent. The next annual DSMB teleconference will be held in October 2018.

Dummy run and QA checks

As specified in the protocol, all sites have completed the dummy run procedure before their site initiation. After inclusion of the first few patients, a QA check of 1 brachytherapy plan will be conducted each year. Sites will be contacted for the 2018 QA round.

PORTEC-4a update meeting at GCIG, May 31st

A PORTEC-4a information and update meeting was held in Chicago, during the GCIG meeting on Thursday, May 31st 2018.

There was substantial interest of the GCIG groups and quite a number of groups are currently looking for funds to be able to participate in the trial:

- o ANZGOG – grant application submitted Feb 2018; result expected Nov 2018
- o Belgian site Gent – in set-up (Ethics and CTA being processed)
- o Irish group Clinical Trials Ireland – funding OK, in preparatory phase
- o French group GINECO– funding application submitted, in preparatory phase
- o US group NRG – interested, discussing participation
- o Canadian group CCTG – interested, preparing grant application for Nov 2018
- o German site Tubingen – highly interested, exploring funding/pathology
- o German site Essen – interested, however funding doubtful

We hope that international participation will be accelerating recruitment into the trial as of early 2019.

Protocol amendments

Currently a number of minor protocol amendments are being prepared and the new version will be sent shortly. The amendments are mainly administrative updates, specification of international participation, and some specific guidelines for pathology decision in case of multiple classifiers.

Presentations and publications

A clinical trial article has been published in NTVO in 2017.

A paper reporting on the results of the pilot phase has been written by Bastiaan Wortman and submitted to Gynecologic Oncology (late April 2018). The results of the pilot phase have been presented at LPRGT (March 2018) and at GCIG (May 2018).

Remi Nout has presented the dummy run at ESTRO 2017. After completion of the first round of QA checks, a paper will be prepared.