PORTEC-4a Newsletter no 3 27 May 2019

First international patients included in PORTEC-4a

We are delighted to report that on 15th February 2019 the University Hospital of Ghent (Belgium) was activated for the PORTEC-4a trial, rapidly followed by University Hospital Tübingen (Germany) on 1st March 2019.
Tübingen has randomised the first international patient in PORTEC-4a in February, and Ghent randomised their first participant in April 2019. We thank the local PIs and their teams for all the work they have done for activation of the trial in their centres. Currently, two other German sites are preparing for participation: Essen and Bad Homburg. The molecular profiles for these sites will be determined at Tübingen, once the pathology validation of their lab has been completed.

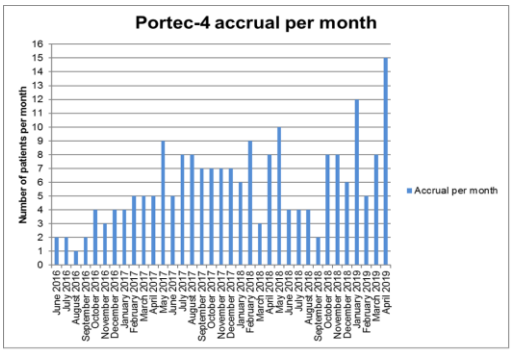
International groups and sites preparing for participation are:

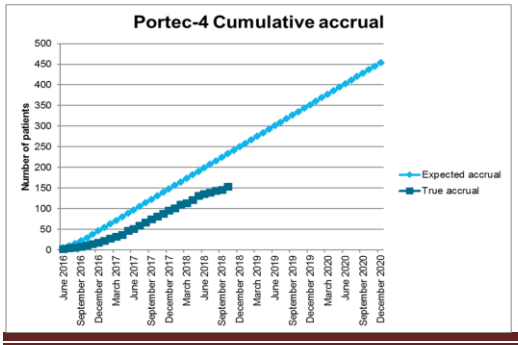
- Cancer Trials Ireland/St Luke's Hospital, Dublin (Ireland) – in set up, pending validation of the pathology lab for the molecular profile
- CEEGOG/University Hospital Prague (Czech Republic) – in set up
- GINECO group (France) – preparing ethics application and validation of path lab
- ANZGOG group Australia and New Zealand) is awaiting funding opportunities.

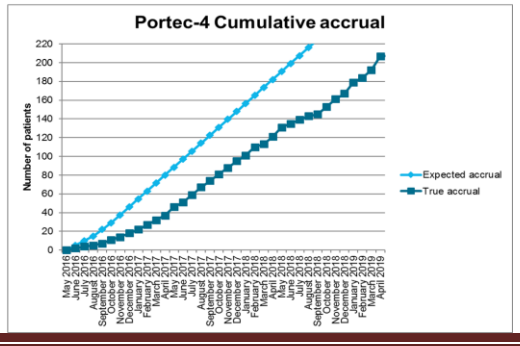
Accrual to the PORTEC-4a trial has reached 200 on April 20th 2019, and 214 on 27th of May

Accrual to PORTEC-4a has continued to increase over the past year. In 2017 and 2018, 76 and 72 patients have been randomised, compared with 47 between January 1st and May 27, 2019.

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







Recruitment status on May 27, 2019:

Center	control arm	molecular profile	Total
Amsterdam UMC	5	11	16
Catharina Hospital	4	6	10
Erasmus Medical Center	4	6	10
Haaglanden Medical Center	2	3	5
Isala Hospital	3	0	3
Leiden UMC	11	27	38
Maastro Clinic	15	31	46
NKI/AvL	2	6	8
Radboud UMC	1	2	3
Radiotherapy Group Arnhem	7	23	30
Radiotherapy Institute Friesland	5	12	17
UMC Groningen	2	4	6
UMC Utrecht	1	1	2
Verbeeten Institte	8	5	13
Radiotherapy Group Deventer	0	1	1
Tuebingen University Hospital (D)	0	4	4
University Hostpital Gent (B)	0	1	1
Zeeuws Radiotherapy Institute	1	0	1
Total	**71**	**143**	**214**

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
Trial documents can be found at www.msbi.nl/portec4

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 has been resumed in 2018, Dorien Berends-vd Meer being the study monitor. All sites are visited once every 2 years, with an extra visit after 1 year in case of specific issues. In 2018 and early 2019 the sites with the largest inclusion have been visited, and at the end of 2019 all sites will have been visited at least once. Monitoring has turned out to be useful; although most sites are doing very well there have been suggested improvements based on the monitor findings which have led to enhanced study quality.

It should be emphasized that it is essential that a subject screening log be kept up to date, and that all study personnel should have a valid GCP or BROK certificate.

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

Pathology workflow and result of the molecular profile

Thanks to the tremendous efforts of the central pathologists Tjalling Bosse and Vincent Smit and their team – and the rapid work of all the investigators and research staff involved - the result of the molecular profile is almost always reported

within the protocol period of 2 working weeks. Delayed profile results are most often due to delayed receipt of materials.
Please **always** ensure and double check if the pathology lab and original pathology number have been entered correctly on the randomization form!

DSMB

The Data and Safety Monitoring Board have had their annual teleconference in December 2018, and were pleased with the increased accrual although this is still being followed on a 6-monthly basis. Their report has been sent to the Ethics committee and to the local PIs. The next DSMB teleconference will be held in the late autumn of 2019.

Dummyrun and QA checks

As specified in the protocol, all sites are required to have completed the dummy run procedure before their site initiation. After inclusion of the first few patients, a quality assurance check of one brachytherapy plan is conducted for each site on an annual basis. In 2018 and 2019 the first QA round has been performed which has proven relevant, as some sites had changed applicator types, protocols, etc.
Bastiaan Wortman has given an oral presentation on the PORTEC-4a QA at the Annual ESTRO meeting in Milan, April 2019. A manuscript will be prepared in the coming months.

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

PORTEC-4a information and update meetings are begin held at each GCIG meeting. Next meeting will be in Chicago, May 31st 2019.

There has been substantial interest of the GCIG groups, and the current and coming international participation has resulted from these meeetings.

Presentations and publications

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

In 2018, a paper reporting on the results of the pilot phase has been published in Gynecologic Oncology - Wortman et al, Gynecol Oncol 2018 151(1): 69-75.

Remi Nout has presented the dummy run at ESTRO 2017 and Bastiaan Wortman the QA results at ESTRO 2019.

The background and design of the PORTEC-4a trial have been presented at many international meetings, such as IGCS in Kyoto, 2018 and ESMO 2018