

HYBRID

Results of the HYBRID trial: A multicentre randomised phase II study of Hypofractionated Bladder Radiotherapy with or without Image guided adaptive-predictive planning

Background

We have provided you with this leaflet because you took part in a clinical trial called HYBRID, a study for patients with muscle-invasive bladder cancer who were having weekly radiotherapy.

This study aimed to find out whether it is possible to deliver adaptive radiotherapy at different hospitals across the UK. This is where each patient has three treatment plans designed with different size safety margins and then the one that fits best is chosen for each particular treatment day. We hoped to show that adaptive radiotherapy reduces non-bladder side effects compared to standard radiotherapy, which uses the same plan for each treatment day. We also hoped to show that no more than 3 in 10 people having treatment, experienced moderate to severe side effects in each treatment group. We wanted to gather more information about how well bladder cancer is treated by weekly radiotherapy, and how well it reduces any symptoms patients experience as a result of bladder cancer.

The results of HYBRID have now been published in the International Journal of Radiation Oncology Biology Physics medical journal. We have written this leaflet to summarise these results. We have also added the link to the publication at the end of this document in case you would like to read the results in more detail. The published results describe how the treatment worked in the two groups of participants and you cannot be identified personally in any of the publications.

Treatment groups

After you agreed to take part in HYBRID you joined one of the following groups:

- **Weekly standard radiotherapy**– weekly radiotherapy using the same treatment plan each time
- **Weekly adaptive radiotherapy** – radiotherapy where one of three different sized plans (small, medium and large) was chosen that best fit the bladder on each day of treatment ('plan of the day')

Trial participation

65 people joined HYBRID between April 2014 and August 2016

- 32 people were in the standard radiotherapy group
- 33 people were in the adaptive radiotherapy group

People from 14 NHS hospitals across the UK joined the study.

Was the delivery of adaptive radiotherapy a success?

All 33 people in the adaptive radiotherapy group, across 14 different NHS hospitals, were treated successfully with adaptive radiotherapy. 28 out of 33 participants in the adaptive radiotherapy group received at least one dose of their radiotherapy using the small or large plan because it fitted their bladder better than the medium plan.

Did radiotherapy treatment reduce symptoms of bladder cancer?

Three months following radiotherapy various urinary symptoms (incontinence, cystitis, and presence of blood in the urine) were improved in the majority of patients in both treatment groups who had these symptoms prior to their treatment.

Did adaptive radiotherapy reduce the non-bladder side effects of radiotherapy?

We found that three months after treatment:

- 5 out of 33 people who received adaptive radiotherapy reported moderate to severe side effects related to radiotherapy of which 2 were non-bladder side effects.
- 7 out of 30 people who received standard radiotherapy reported moderate to severe side effects related to radiotherapy of which 4 were non-bladder side effects.

This showed that fewer than 3 out of 10 patients in each treatment group experienced moderate to severe side effects.

People in the adaptive radiotherapy group did have fewer non-bladder side effects and were less likely to stop treatment early due to side effects than those in the standard radiotherapy group. However, larger clinical trials are required to confirm that this effect was due to the treatment received rather than by chance.

How well did the treatment work?

At 3 months after treatment fewer people had cancer in the bladder than we expected when the study started:

- 22 out of 25 people who received adaptive radiotherapy had no sign of cancer in their bladder
- 17 out of 23 people who received standard radiotherapy had no sign of cancer in their bladder.

Fewer people who had their disease assessed at three months had cancer in their bladder in the adaptive radiotherapy group than those in standard radiotherapy group. However, larger clinical trials are required to confirm that this effect was due to the treatment received rather than by chance.

Two years after radiotherapy nearly 5 out of 10 participants were still alive. With high levels of cancer control in the bladder and a higher than expected number of people alive two years after treatment, we have shown that this weekly radiotherapy schedule can be effective at controlling disease.

What do our researchers say?

The doctor leading the study, Professor Robert Huddart, Professor of Urological Cancer and Honorary Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust, said:

“We would like to thank all the people, who were often elderly, for taking part. Thanks to their support we have been able to develop a way to treat bladder cancer which we will hope will benefit the many people who are not well enough for the standard intensive treatments. They have also helped us develop evidence that new advanced radiotherapy may help reduce side effects and make the treatment more tolerable and effective”

What happens next?

The HYBRID trial was the first study of adaptive ‘plan of the day’ radiotherapy in bladder cancer. Now that we have confirmed that adaptive radiotherapy treatment can be delivered successfully and without causing additional side effects; adaptive radiotherapy will be tested in larger studies. This, we hope, will lead to its widespread use.

We would like to thank you very much for taking part in HYBRID. Without your contribution this trial would not have been possible and we would not have been able to make progress in improving treatment for future patients with muscle-invasive bladder cancer.

If you have any questions about the results of HYBRID, please discuss this information sheet with your doctor or nurse.

You can read the full publication in the International Journal of Radiation Oncology Biology Physics medical journal on the link below:

<https://doi.org/10.1016/j.ijrobp.2020.11.068>

The HYBRID trial is funded by Cancer Research UK.

The Chief Investigator is Prof Robert Huddart at The Royal Marsden NHS Foundation Trust. HYBRID is coordinated by the Clinical Trials and Statistics Unit at the Institute of Cancer Research (ICR-CTSU).

