One versus three weeks hypofractionated whole breast radiotherapy for early breast cancer treatment: the FAST-Forward phase III RCT

Adrian Murray Brunt,[1,2*] Joanne S Haviland,[2] Duncan A Wheatley,[3] Mark A Sydenham,[2] David J Bloomfield,[4] Charlie Chan,[5] Suzy Cleator,[6] Charlotte E Coles,[7] Ellen Donovan,[8] Helen Fleming,[9] David Glynn,[10] Andrew Goodman,[11] Susan Griffin,[10] Penelope Hopwood,[2] Anna M Kirby,[12] Cliona C Kirwan,[13] Zohal Nabi,[14] Jaymini Patel,[2] Elinor Sawyer,[15] Navita Somaiah,[12] Isabel Syndikus,[16] Karen Venables,[14] John R Yarnold[12] and Judith M Bliss[2] on behalf of the FAST-Forward Trial Management Group

[1]School of Medicine, University of Keele and University Hospitals of North Midlands, Staffordshire, UK
[2]Clinical Trials and Statistics Unit (ICR-CTSU), The Institute of Cancer Research, London, UK
[3]Department of Oncology, Royal Cornwall Hospital NHS Trust, Truro, UK
[4]Sussex Cancer Centre, Brighton and Sussex University Hospitals, Brighton, UK
[5]Women's Health Clinic, Nuffield Health Cheltenham Hospital, Cheltenham, UK
[6]Department of Oncology, Imperial Healthcare NHS Trust, London, UK
[7]Department of Oncology, University of Cambridge, Cambridge, UK
[8]Centre for Vision, Speech and Signal Processing, University of Surrey, Guildford, UK
[9]Clinical and Translational Radiotherapy Research Group, National Cancer Research Institute, London, UK
[10]Centre for Health Economics, University of York, York, UK
[11]Oncology Unit, Torbay Hospital, Devon, UK
[12]Department of Radiotherapy, The Royal Marsden NHS Foundation Trust, Sutton, UK and Division of Radiotherapy and Imaging, The Institute of Cancer Research, London, UK
[13]Division of Cancer Sciences, University of Manchester, Manchester, UK
[14]RTQQA, Mount Vernon Cancer Centre, Middlesex, UK
[15]Comprehensive Cancer Centre, King's College London, London, UK
[16]Clatterbridge Cancer Centre, Clatterbridge Hospital NHS Trust, Cheshire, UK

[*]Corresponding author m.brunt@keele.ac.uk and fastforward-icrctsu@icr.ac.uk

Declared competing interests of authors

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/WWBF1044.

Primary conflicts of interest: Joanne Haviland reports grant funding from NIHR HTA (London, UK) and is a member of the HTA Clinical Evaluation and Trials Committee (2019–23). Duncan Wheatley reports personal fees from Roche (Basel, Switzerland) and Daiichi Sankyo (Tokyo, Japan) and travel support from Roche (Basel, Switzerland). Mark Sydenham reports grant funding from NIHR HTA (London, UK). David Bloomfield reports personal fees from Astra Zeneca (Cambridge, UK). Charlotte Coles reports a NIHR Research Professorship and is a member of HTA Clinical Evaluation and Trials Committee (2017–23). Ellen Donovan reports grant funding from NIHR-HTA (London, UK). David Glynn reports grant funding from NIHR-HTA (London, UK) and from Cancer Research UK (London, UK). Susan Griffin reports grant funding from NIHR-HTA (London, UK) and is a member of PHR Research Funding Board (2022–26). Anna Kirby reports grant funding from Cancer Research UK (London, UK) and is President of the European Society of Radiation Oncology. Zohal Nabi reports grant funding from NIHR-HTA (London, UK). Jaymini Patel reports grant funding from NIHR-HTA (London, UK). Isabel Syndikus reports personal fees from Bayer (Leverkusen, Germany), Pfizer (Sandwich, UK), Astellas (Tokyo, Japan), Janssen (High Wycombe, UK) and travel support from Bayer (Leverkusen, Germany), Roche (Basel, Switzerland). She is a member of the Data Monitoring and Safety Committee for Bristol Myers Squibb (New York City, USA). Karen Venables reports grant funding from NIHR (London, UK) and is a member of the RTTQA management group. Judith Bliss reports grants from NIHR-HTA (London, UK), Astra Zeneca (Cambridge, UK), Merck Sharp Dohme (New Jersey, USA), Puma Biotechnology (Los Angeles, USA), Clovis Oncology (Boulder, USA), Pfizer (Sandwich, UK), Janssen-Cilag (High Wycombe, UK), Novartis (Basel, Switzerland), Roche (Basel, Switzerland), Eli Lilly (Indianapolis, USA) and an AACR Scientific Achievement Award and Honorarium 2022. She is a NIHR Senior Researcher and is a member of the HTA Commissions Committee (2011–16).

Published November 2023
DOI: 10.3310/WWBF1044

Plain language summary

One versus three weeks hypofractionated whole breast radiotherapy for early breast cancer treatment: the FAST-Forward phase III RCT

Health Technology Assessment 2023; Vol. 27: No. 25

DOI: 10.3310/WWBF1044

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Plain language summary

Patients diagnosed with early breast cancer are often recommended to have radiotherapy after surgery because research has shown that it lowers the risk of the cancer returning. However, it may cause some short- and long-term side effects. Previous clinical trials showed that the same, or even better, outcomes with a lower total dose of radiotherapy given in fewer, larger daily doses compared with older historical treatment schedules. The National Institute for Health and Care Research Health Technology Assessment Programme-funded FAST-Forward Trial aimed to see whether the number of doses could be reduced further without reducing the beneficial effects of radiotherapy.

Between November 2011 and June 2014, 4096 patients agreed to take part in the FAST-Forward Main Trial testing three schedules of radiotherapy to the breast. Standard treatment given on 15 days over 3 weeks (Control Group) was compared with two different lower dose schedules where treatment was given on 5 days over 1 week (lower dose Test Groups). An additional 469 patients entered a sub-study where the gland area under the arm also received radiotherapy (Nodal Sub-Study).

Main Trial 5-year results reported in April 2020 showed that the number of patients whose cancer had returned in the treated breast was low in all groups: around 2 in 100 (2.1%) for the Control Group, and 1.7% in the higher dose and 1.4% in the lower dose Test Groups. The majority of reported side effects assessed by patients and doctors up to 5 years after radiotherapy were mild for all treatment groups. Patients in the Control Group and in the lower dose Test Group experienced similar levels of side effects. More side effects were reported in the higher dose Test Group, although differences were small.

Overall, the FAST-Forward findings suggest that the lower dose 1-week schedule gave similar results in terms of the cancer returning and side effects to the standard 3-week treatment and this schedule can now be used to help treat future patients.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 3.6

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 3.6 and is ranked 32nd (out of 105 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2021 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), Embase (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta.

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 09/01/47. The contractual start date was in September 2011. The draft report began editorial review in June 2022 and was accepted for publication in October 2022. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).