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DANTE: Duration of Anti-PD1 therapy for melanoma

Submission date 15/01/2018	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 31/07/2018	**Overall study status** Completed	
Last Edited 14/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/a-study-find-out-how-long-people-melanoma-treatment-pembrolizumab-nivolumab-dante

Contact information

Type(s)
Scientific

Contact name
Dr Sue Bell

Contact details
Clinical Trials Research Unit
Leeds Institute of Clinical Trials Research
University of Leeds
Leeds
United Kingdom
LS2 9JT
+44 (0)113 343 1492
s.e.bell@leeds.ac.uk

Additional identifiers

EudraCT/CTIS number
2017-002435-42

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

35180

Study information

Scientific Title
DANTE: A randomised phase III trial to evaluate the Duration of ANti-PD1 monoclonal antibody Treatment in patients with metastatic mElanoma

Acronym
DANTE

Study objectives
This trial aims to determine whether anti-PD1 monotherapy to treat advanced melanoma can be stopped after 1 year, rather than the current standard practice (i.e. continuing to treat until disease progression/unacceptable toxicity, or for at least 2 years), and achieve and maintain as good an outcome (in terms of the cancer coming back).

The hypothesis is that continuing treatment beyond 1 year is unnecessary, as there is no biological evidence that justifies continuous therapy; many responses occur in the first year and can continue even after treatment is stopped. Also, continuing treatment exposes patients to an increased risk of developing immune-related toxicities and is a considerable burden to patients and the National Health Service.

Ethics approval required
Old ethics approval format

Ethics approval(s)
East Midlands – Leicester South Research Ethics Committee, 18/01/2018, ref: 17/EM/0440

Study design
Randomised; Interventional; Design type: Treatment, Drug, Immunotherapy, Active Monitoring

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Metastatic melanoma

Interventions
Population: Patients with advanced (unresectable stage III or IV) melanoma who are due to start (or are within 12 months of starting) anti-PD1 monotherapy as their 1st line treatment

Consenting patients will be registered with the CTRU within the first 12 months of starting anti-PD1 monotherapy. The registration phase is not considered part of this clinical trial. Patients will receive anti-PD1 monotherapy and undergo monitoring and scans as per standard of care. When they are approaching 12 months of treatment, patients who have not progressed and remain on treatment will be approached for formal eligibility assessment and be consented for randomisation into the trial.

Baseline (pre-randomisation) assessments:
1. CT scan at 12 months post start of treatment (standard practice)
2. Quality of life and health economics questionnaire completion

Intervention: Stop anti-PD1 therapy at randomisation (12 months after starting therapy)
Comparator (control): Continue anti-PD1 therapy until disease progression or unacceptable toxicity (or a minimum of 2 years in the absence of progression/unacceptable toxicity)

Follow-up assessments
1. Every 3 months for the first 12 months post randomisation, then every 6 months in years 2 to 4 post-randomisation. A CT and/or MRI scan will be performed at each timepoint (standard practice)
2. Patients will complete quality of life and health economic questionnaires every 3 months until 18 months post-randomisation

Intervention Type
Other

Phase
Phase IV

Primary outcome measure
Progression-free survival is measured according to RECIST v1.1 at 12 months post-randomisation, using the pre-randomisation (12 month post-start of treatment) scan as the baseline

Secondary outcome measures
1. Quality of life is measured using the participant self-reported EORTC QLQ-C30, QLQ-MEL38 and the EQ-5D-5L questionnaires at baseline (pre-randomisation), 3, 6, 9, 12, 15 and 18 months post-randomisation (key secondary outcome)
2. Overall survival is calculated from the date of randomisation to the date of death from any cause, or the date last known to be alive for patients who are not known to have died
3. Objective response rate is measured according to RECIST v1.1 at 12 months post-randomisation of the final participant, using the pre-randomisation (12 month post-start of treatment) scan as the baseline
4. Best tumour response rate is measured according to RECIST v1.1 at 12 months post-randomisation of the final participant, using the pre-randomisation (12 month post-start of treatment) scan as the baseline
5. Duration of response is measured according to RECIST v1.1 at 12 months post-randomisation of the final participant, using the pre-randomisation (12 month post-start of treatment) scan as

the baseline
6. Safety and toxicity is measured according to CTCAE v5.0 at 12 months and 4 years post-randomisation of the final participant
7. Cost-effectiveness is measured using the incremental cost effectiveness ratio (ICER) and compared against the NICE threshold of £20,000 per QALY. This will be done both within trial (using data collected to 18 months post-randomisation) and across patient lifetime using a Markov model (at 4 years post-randomisation of the final participant

Overall study start date
01/02/2017

Completion date
15/10/2024

Eligibility

Key inclusion criteria
Eligibility for REGISTRATION
1. Histologically or cytologically confirmed unresectable AJCC stage III or stage IV (metastatic) melanoma, including cutaneous and non-cutaneous melanoma
2. Aged ≥ 18 years
3. Planned or currently receiving (<12 months) treatment with first-line pembrolizumab or nivolumab
4. Written informed consent for registration

Inclusion criteria for RANDOMISATION
1. Registered in DANTE
2. Progression-free by RECIST v1.1 criteria at 12 months (+/- 4 weeks) from the start of pembrolizumab or nivolumab
3. 12 months (+/- 4 weeks) from start of pembrolizumab or nivolumab
4. ECOG performance status 0-2
5. Considered fit by the treating clinician to continue to receive ongoing treatment with pembrolizumab or nivolumab
6. Written informed consent for randomisation

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 1208; UK Sample Size: 1208

Key exclusion criteria
Exclusion criteria for RANDOMISATION
1. Severe comorbidities, including severe autoimmune disease or pneumonitis
2. Active infection requiring systemic therapy
3. Known history of HIV, hepatitis B or C
4. Other malignancy within past 5 years, excluding adequately treated Stage 1 or Stage 2 basal /squamous cell carcinoma of the skin, carcinoma in situ of the cervix or breast, or other in situ cancers
5. Pregnant, breast-feeding or patients with reproductive potential (female and male) unwilling to use adequate contraception while receiving anti-PD1 therapy and for 6 months after the last dose. Women of reproductive potential are defined as: following menarche and until becoming post-menopausal, unless permanently sterile. Men of reproductive potential are defined as: post-pubescent and not sterile by vasectomy or bilateral orchidectomy.
6. Prior systemic treatment for advanced melanoma, including ipilimumab and combination ipilimumab and nivolumab, other than BRAF and MEK inhibitors and the current treatment for advanced melanoma. Prior adjuvant or neo-adjuvant therapy is allowed as long as it was completed at least 12 months prior to starting anti-PD1 therapy
7. Treated brain metastases with MRI evidence of progression and/or requirement for high doses of systemic corticosteroids that could result in immunosuppression (> 10 mg/day prednisolone equivalents)
8. Untreated brain metastases that are symptomatic and/or require local intervention (surgery, radiosurgery, corticosteroid therapy) or other systemic therapy

Date of first enrolment
13/08/2018

Date of final enrolment
15/09/2023

Locations

Countries of recruitment
England

Northern Ireland

Scotland

United Kingdom

Wales

Study participating centre
Weston Park Hospital (lead centre)
Whitham Rd
Sheffield
United Kingdom
S10 2SJ

Study participating centre
Addenbrooke's Hospital
Hills Rd
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Rd
Glasgow
United Kingdom
G12 0YN

Study participating centre
Belfast City Hospital
10 Jubilee Rd
Belfast
United Kingdom
BT9 7JL

Study participating centre
Broomfield Hospital
Court Rd
Broomfield
Chelmsford
United Kingdom
CM1 7ET

Study participating centre
Castle Hill Hospital
Castle Rd
Cottingham
United Kingdom
HU16 5JQ

Study participating centre
Charing Cross Hospital
Fulham Palace Rd

Hammersmith
London
United Kingdom
W6 8RF

Study participating centre
Cheltenham General Hospital
Sandford Rd
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
Churchill Hospital
Old Rd
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
City Hospital
Hucknall Rd
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Derriford Hospital
Derriford Rd
Crownhill
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Freeman Hospital
Freeman Rd
High Heaton

Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Gloucestershire Royal Hospital
Great Western Rd
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Kent & Canterbury Hospital
Ethelbert Rd
Canterbury
United Kingdom
CT1 3NG

Study participating centre
Mount Vernon Hospital
Rickmansworth Rd
Northwood
United Kingdom
HA6 2RN

Study participating centre
Ninewells Hospital
James Arrott Dr
Dundee
United Kingdom
DD2 1SY

Study participating centre
Norfolk and Norwich University Hospital
Colney Ln
Norwich
United Kingdom
NR4 7UY

Study participating centre
Queen Alexandra Hospital
Southwick Hill Rd
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
Queen Elizabeth Queen Mother Hospital
St Peter's Rd
Margate
United Kingdom
CT9 4AN

Study participating centre
Raigmore Hospital
Old Perth Rd
Inverness
United Kingdom
IV2 3UJ

Study participating centre
Royal Cornwall Hospital
Treliske
Truro
United Kingdom
TR1 3LQ

Study participating centre
Royal Derby Hospital
Uttoxeter Rd

Derby
United Kingdom
DE22 3NE

Study participating centre
Royal Devon and Exeter Hospital
Barrack Rd
Exeter
United Kingdom
EX2 5DW

Study participating centre
Royal Free Hospital
Pond St
Hampstead
London
United Kingdom
NW3 2QG

Study participating centre
Royal Preston Hospital
Sharoe Green Lane North
Fulwood
Preston
United Kingdom
PR2 9HT

Study participating centre
Royal Stoke University Hospital
Newcastle Rd
Stoke-on-Trent
United Kingdom
ST4 6QG

Study participating centre
Royal Sussex County Hospital
Eastern Rd
Brighton
United Kingdom
BN2 5BE

Study participating centre
Southampton General Hospital
Tremona Rd
Southampton
United Kingdom
SO16 6YD

Study participating centre
St Helens Hospital
Marshalls Cross Rd
Saint Helens
United Kingdom
WA9 3DA

Study participating centre
St James's University Hospital
Beckett St
Leeds
United Kingdom
LS9 7TF

Study participating centre
The Christie
Wilmslow Rd
Manchester
United Kingdom
M20 4BX

Study participating centre
The Clatterbridge Cancer Centre
Clatterbridge Rd
Birkenhead
Wirral
United Kingdom
CH63 4JY

Study participating centre
Velindre Hospital
Velindre Rd

Cardiff
United Kingdom
CF14 2TL

Study participating centre
William Harvey Hospital
Kennington Rd
Willesborough
Ashford
United Kingdom
TN24 0LZ

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust

Sponsor details
c/o Dr Dipak Patel
Northern General Hospital
Herries Road
Sheffield
England
United Kingdom
S5 7AU
+44 (0)114 2265941
Dipak.Patel@sth.nhs.uk

Sponsor type
Hospital/treatment centre

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The study protocol will be published. Planned publication of the study results in a high-impact peer reviewed journal. Primary analysis publication anticipated February 2025. Long-term results publication anticipated February 2028.

Intention to publish date
01/02/2025

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		01/07/2021	05/07/2021	Yes	No
HRA research summary			28/06/2023	No	No