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Paclitaxel with or without GSK1120212 for treatment of melanoma

Submission date	Recruitment status	[_] Prospectively registered
27/04/2012	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
27/04/2012	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/01/2020	Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-at-gsk1120212-people-melanoma

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2011-002545-35

Protocol serial number
12095

Study information

Scientific Title
A randomised phase II study of paclitaxel with or without GSK1120212 in advanced wild type BRAF melanoma

Acronym
PACMEL

Study objectives
This is a randomised multi-centre study. 80 patients (forty in each of 2 arms) with melanoma will be randomly assigned to receive treatment with paclitaxel chemotherapy or the same drug along with GSK1120212, a new medicine. To take part the patient's melanoma must have a normal BRAF gene (at V600), which is about 60% of people with melanoma. This can be checked on a sample of the patient's tumour (usually one that has already been taken as part of their treatment). Prior to the randomised part of the study, between 9 and 18 patients will take part in the trial to establish the best dose of GSK1120212 and paclitaxel in combination.

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Committee South Central - Oxford, 23/01/2012, ref: 11/SC/0458

Primary study design
Interventional

Study design
Randomised interventional phase II trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Melanoma

Interventions
Dose Escalation Phase: Patients with advanced melanoma will be recruited into 3 dose level cohorts. Three dose levels of GSK1120212, starting at 1.0 mg for the first cohort and escalating by 0.5 mg to 1.5 mg and 2.0 mg for the second and third cohorts respectively. At all dose levels, GSK1120212 will be administered once daily orally in combination with an 80 mg/m2 IV infusion of paclitaxel on Days 1, 8 and 15 of each 4 week cycle. This phase will determine the maximum tolerated dose of GSK1120212 in combination with paclitaxel for the randomisation phase. Paclitaxel will be administered for up to 6 cycles, but GSK1120212 may be continued until disease progression or intolerable toxicity.

Randomisation Phase: Two treatment arms:
1. Maximum 6 cycles of single agent Paclitaxel alone as an 80mg/m2 IV infusion on Days 1, 8 and 15 of each 4 week cycle
2. Maximum 6 cycles of Paclitaxel as an 80mg/m2 IV infusion on Days 1, 8 and 15 of each 4 week

cycle in combination with maximum tolerated dose of GSK1120212 once daily orally. GSK1120212 may be continued until disease progression or intolerable toxicity.

Patients will be followed up every 3 months until disease progression.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
trametinib (GSK1120212), paclitaxel

Primary outcome(s)
1. Efficacy of GSK1120212 in combination with paclitaxel compared to paclitaxel alone
2. Progression free survival

Key secondary outcome(s)
1. Further efficacy of GSK1120212 in combination with paclitaxel compared to paclitaxel alone
2. Overall survival
3. Objectine response rate
4. Progression free survival at 6 months

Completion date
30/04/2016

Eligibility

Key inclusion criteria
1. Aged = 18 years
2. Able to provide evidence from an accredited laboratory of wt BRAF status for their melanoma, or ascertainment of wild type BRAF status from a sample of melanoma provided for mutational analysis in Oxford (phase 2 part only).
3. Unresectable stage 3 or 4, histologically proven cutaneous or unknown primary melanoma
4. Measurable disease as defined by RECIST 1.1 (phase 2 part only)
5. ECOG performance score of 0 or 1
6. Life expectancy of at least 12 weeks.
7. Maximum 2 prior lines of treatment for advanced disease.
8. Adequate cardiac function (NYHA 0-1), and LVEF within normal limits on echocardiogram.
9. The patient is willing to give consent to the main study and able to comply with the protocol for the duration of the study, including scheduled follow-up visits and examinations.
10. Adequate haematological, hepatic and renal function
11. Target Gender: Male & Female
12. Lower Age Limit 18 years

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
111

Key exclusion criteria
1. Any systemic anti-cancer therapy (including participation in other clinical trials) within 28 days prior to Day 1.
2. Any radiotherapy within 14 days prior to Day 1.
3. Prior taxane or BRAF or MEK inhibitors for metastatic melanoma.
4. Any unresolved toxicity from prior anti-cancer therapy that is greater than CTCAE grade 2.
5. Pregnancy or breastfeeding women. Female patients must have a negative urinary or serum pregnancy test or have evidence of post-menopausal status (defined as absence of menstruation for > 12 months, bilateral oophrectomy or hysterectomy).
6. Grade =2 peripheral neuropathy at study entry.
7. Patients of reproductive potential who are not willing to use adequate contraceptive measures for the duration of the study (both male and female patients)
8. Known severe hypersensitivity reactions to paclitaxel or other drugs formulated in Cremophor EL and ethanol
9. Ocular or mucosal malignant melanoma
10. Another active malignancy within the past three years.
11. Evidence of brain metastases, unless surgically resected/stereotactic radiosurgery treated brain metastasis with no evidence of relapse on cerebral MRI, or treated brain metastasis and stable off treatment, including steroids, for 3 months.
12. Clinically significant and uncontrolled major medical condition(s): such as active infection, bleeding diathesis.
13. Patients who are known to be serologically positive for Hepatitis B, Hepatitis C or HIV.
14. Inability to swallow tablets, refractory nausea and vomiting, chronic gastrointestinal diseases (eg, inflammatory bowel disease) or significant bowel resection that would preclude adequate absorption.
15. Ocular disease predisposing to central serous retinopathy and/or retinal vein occlusion, including increased intraocular pressure, glaucoma, uncontrolled hypertension or uncontrolled diabetes.

Date of first enrolment
20/04/2012

Date of final enrolment
30/04/2016

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Oxford
Oxford
United Kingdom
OX3 7DQ

Sponsor information

Organisation
University of Oxford (UK)

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline (UK)

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results for dose escalation phase	01/02/2015		Yes	No
Results article	results	01/02/2019		Yes	No
Results article	results	01/02/2019	29/01/2020	Yes	No
HRA research summary			28/06/2023	No	No
Plain English results				No	Yes