ISRCTN17674794 https://doi.org/10.1186/ISRCTN17674794

A study to measure the accuracy of a new test for the diagnosis of melanoma

Submission date
29/10/2021

Recruitment status
No longer recruiting

Registration date
03/11/2021

Overall study status
Completed

Last Edited
20/09/2022

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Melanoma is the most common fatal skin cancer in the United States. Skin lesions that are changing, have multiple colors, or bleeding may be melanomas. Early diagnosis before it spreads outside the skin can save lives. If a doctor suspects a lesion may be a melanoma, they will take a biopsy of it and send it to the pathology laboratory for analysis. In the pathology laboratory, the biopsy will be processed into glass slides that can be examined under a microscope. Dermatopathologists are specialized medical doctors who look at these slides to make the final diagnosis of the lesion. However, dermatopathologists do not always agree on whether a lesion is a melanoma or not. Additional special testing may help to determine what the best diagnosis is. One of these special tests is called the PRAME stain. Slides of melanomas often are colored brown by the PRAME stain. The aim of this study is to determine how accurate the PRAME stain is by analyzing a large group of melanomas and benign non-melanoma skin tumors for how often they are positive for PRAME. A secondary aim of this study is to see how good the agreement is between two different dermatopathologists on whether the PRAME stain is positive or not.

Who can participate?
Patients who had a skin biopsy after 11/02/2021 to rule out melanoma at the University of Kansas Medical Center with PRAME and MART1 stains

What does the study involve?
Participants' slides will be reviewed by a board-certified dermatopathologist to confirm the original pathology diagnosis of either melanoma or not melanoma. Then, two separate dermatopathologists will each score the PRAME slide from 0 to 4+. Scores of 4+ will be considered a positive PRAME test, defined at PRAME staining of more than 75% of the cells that make up the lesion. These dermatopathologists will not have access to the other slides from the biopsy or the original pathology diagnosis to avoid biasing their interpretation of the PRAME slide. The study will last 8 months in total.

What are the possible benefits and risks of participating?
There will be no immediate direct benefit to those taking part but there should be benefits to future patients with lesions that are suspected to be melanomas because the results of the study are likely to influence how dermatopathologists will use the PRAME stain to diagnose

melanoma in the future. These benefits include reducing the risk of misdiagnosing a melanoma as a benign lesion and misdiagnosing a benign lesion as a melanoma. Since this study involves only the review of existing pathology slides and does not involve any additional testing or intervention, there is minimal risk to the subjects' welfare. The primary risks are loss of the participants' slides during the retrieval/return process and disclosure of private health information. To minimize the risk of these events, the researchers will only withdraw small batches of cases at a time (20 subject cases per run) and return all slides to the file before withdrawing a new batch for analysis. To avoid disclosure of protected information, acquired pathology data will be unidentified and securely stored on an encrypted server specifically designed for medical research. The data will be destroyed 1 year from the date of the study publication.

Where is the study run from?
University of Kansas Medical Center (USA)

When is the study starting and how long is it expected to run for?
October 2021 to June 2022

Who is funding the study?
Investigator initiated and funded

Who is the main contact?
Dr Garth Fraga
gfraga@kumc.edu

Contact information

Type(s)
Scientific

Contact name
Dr Garth Fraga

ORCID ID
https://orcid.org/0000-0001-5567-0165

Contact details
KUMC Mail Stop #3045
3901 Rainbow Boulevard
Kansas City
United States of America
66160
+1 (0)913 588 1180
gfraga@kumc.edu

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Protocol serial number
1.1

Study information

Scientific Title
PRAME immunohistochemistry for melanoma: a STARD-compliant diagnostic accuracy study

Acronym
DAPRAME

Study objectives
A PRAME score of 4+ (76+% of lesional melanocytes with nuclear positive signal) has a positive likelihood ratio of >10 for diagnosis of melanoma in the setting of difficult to diagnose primary melanocytic lesions

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 29/10/2021, Human Research Protection Program at the University of Kansas Medical Center (Mail-Stop 1032, 3901 Rainbow Blvd., Kansas City, KS 66160, USA; +1(0) 913 5881240; IRBhelp@kumc.edu), ref. STUDY00147914

Study design
Retrospective cohort selection cross-sectional study

Primary study design
Observational

Study type(s)
Diagnostic

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

Interventions
PRAME expression will be scored by visual estimation as 0, 1+ (1-25%), 2+, (26-50%), 3+ (51-75%), or 4+ (76-100%), utilizing a corresponding MART1 stained slide to help determine the localization and density of melanocytes in the tumor. Both total tumor and hot spot measures will be obtained (hot spot = two adjacent 400X original magnification fields). The PRAME is from BioCare Medical, EPR20330 is the clone and it is a rabbit monoclonal antibody. Opti View is used for detection on the Benchmark Ultra IHC stainer, with Standard CC1 antigen retrieval for 64 minutes, utilizing the primary antibody in a predilute form for 32 minutes incubation at 36 degrees C. With the OptiView kit, select pre-primary hydrogen peroxide inhibitor for the procedure and with 8 minutes for the OV HQ Universal Linker and OV HRP Multimer.

Intervention Type
Other

Primary outcome(s)
Diagnosis of melanoma in the final pathology report at baseline

Key secondary outcome(s))
1. Diagnostic accuracy of 2+ (> 25%) PRAME positivity at baseline
2. Diagnostic accuracy of 3+ (> 50%) PRAME positivity at baseline
3. Diagnostic accuracy of 4+ (> 75%) PRAME positivity at baseline
4. Diagnostic accuracy of hotspot 4+ PRAME positivity (two adjacent 40X fields) at baseline
5. Diagnostic accuracy of single hotspot 4+ PRAME positivity (single 40X field) at baseline
6. Interrater concordance of visual estimates of PRAME positivity at baseline

PRAME is measured by microscopic examination of immunostained slides on a score of 0-4+ (0 = 0% of lesional melanocytes are positive; 1+ = 1-25% of lesional melanocytes are positive; 2+ = 26-50% of lesional melanocytes are positive; 3+ = 51-75% of lesional melanocytes are positive; and 4+ = 76-100% of lesional melanocytes are positive)

Completion date
30/06/2022

Eligibility

Key inclusion criteria
1. Pathology sample of a primary pigmented skin lesion
2. PRAME immunohistochemistry performed on that sample prior to final diagnosis
3. MART1 immunohistochemistry performed on that sample prior to final diagnosis

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
All

Sex
All

Total final enrolment
143

Key exclusion criteria
1. Uncertain final diagnosis (e.g., MELTUMP)
2. Re-excision
3. Spindle cell melanoma
4. Desmoplastic melanoma
5. Metastatic melanoma
6. Nonmelanocytic lesion
7. Missing slides
8. Unreadable PRAME or MART1 slides due to technical error

Date of first enrolment
11/02/2021

Date of final enrolment
30/06/2022

Locations

Countries of recruitment
United States of America

Study participating centre
University of Kansas Medical Center
3901 Rainbow Boulevard
Kansas City
United States of America
66160

Sponsor information

Organisation
University of Kansas Medical Center

ROR
https://ror.org/036c9yv20

Funder(s)

Funder type
Other

Funder Name
Investigator initiated and funded

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study are not expected to be made available due to the need to protect the participants' privacy. To avoid disclosure of protected information, acquired pathology data will be unidentified and securely stored on an

encrypted server specifically designed for medical research. The data will be destroyed 1 year from the date of the study publication.

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		28/06/2022	20/09/2022	Yes	No