

Independent review committee report - Mermaid-III

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Mermaid-III: “Ovarian Cancer Early detection, screening, and long-term survival”

Lead: Prof Susanne Kruger Kjaer

Funding: DKR 15,512,752

COMMENT

Overall this workstream has been extremely productive leading to 71 publications (131 if we include other contributions to international consortia), numerous presentations and collaborations. It has also created a large biobank and linkage of registries/databases to be able to drive future research. Sections B-F have been very productive. Prof Kjaer (and her team) is to be congratulated on the overall outputs from the work-stream.

Aspects of the work has included collaborative working with the need to ship samples to collaborators in other countries including the USA. This has been negatively impacted by the COVID19 pandemic and also by GDPR. While legal and regulatory issues are being addressed by institutional lawyers we don't know about the progress achieved and likely outcome.

The lack of adequate deliverables from the early detection biomarker Sections A1 and A2 remain a criticism of this section of the programme.

SECTION A

As previously highlighted, the Papgene/Papseek test appears to have extremely limited sensitivity for ovarian cancer. The committee had highlighted in its earlier reports the importance/need for validating the data as planned in study A2 before focusing huge time and resource in study A3. The utility of the LBC biobank (A3) for early diagnosis of ovarian cancer using the proposed strategy depended on this.

Unfortunately the work was hampered by issues beyond the control of the investigators such as COVID19 pandemic and implications of GDPR restricting sample transport to the USA.

It is unfortunate that Surepath collection was not the optimum medium to run PAPSEEK. The sample collection obtained from Sweden using Thinprep is also stuck and has not been able to be transported to the USA due to regulatory issues.

What is the best collection medium for this test?

Ideally these issues should be resolved prior to large sample collections.

The collaboration with Prof Widschwendter's team around the WID-OC index is a welcome step forward.

157K Thinprep LBC samples from 137K women undergoing cervical screening have been biobanked. This can undoubtedly provide an extremely important and valuable resource for future translational work.

However, the main aim of this section of the workstream remains to be delivered. We understand the research team is engaged with taking this forward.

Outputs – 3 publications, 5 presentations

SECTION B

This section covers research into serous borderline tumours, their histopathological and genomic characterisation and associated risk of progression. The risk of benign ovarian tumours progressing to SBOT has also been explored.

While important research, this does not fall within early detection or screening.

Outputs:

B1- 9 publications and 1 presentation.

B2 & B3- 6 publications and 1 presentation

SECTION C

This evaluates variety of factors potentially related to the risk of ovarian cancer or borderline tumours.

Data collection including Swedish data is ongoing.

Outputs-

large number of publications particularly as part of international consortia.

28 publications + in preparation

4 presentations.

SECTION D

Survival from ovarian cancer treatment and Survivorship

Linkage of different databases / registries has been undertaken with data cleaning to undertake prognostic studies and form the basis for translational work

Outputs:

20 publications + 2 in progress

4 presentations

SECTION E

Oophorectomy - health outcomes and cancer risk

Outputs:

One paper published and three important ones undergoing peer review.

SECTION F

Non-epithelial ovarian cancer

Outputs:

2 publications + 1 in preparation

Mermaid-III: Biomarkers and/or Prognostic markers

Leads: Prof Claus Hogdall and Prof Estrid Hogdall

Funding: DKR 18,309,434

COMMENT:

This work-stream has been extremely successful and productive.

Two large OC cohorts, GOVEC and PELVIC MASS studies, have been consolidated in Denmark. 6596 OC patients have been enrolled in the study with corresponding clinical variables and matched bio-banked samples for a number of patients, which is commendable. These cohort data have been linked to other national Danish databases. A number of translational studies have been completed. It has led to numerous academic outputs including, 114 publications (76 Danish led and 38 being contributions to international consortia), 3400 citations, 30 invited talks, number of international collaborations across 10 countries. The CPH index for ovarian cancer diagnosis has been adopted nationally in clinical practice and this is an important achievement.

As expected the COVID19 pandemic has affected planned timelines and progress of sample collection and analyses of section B in particular but this is being addressed through mitigating strategies where necessary.

Sections:

Major sections in this part of the programme included (a) development of GOVEC/ Pelvic Mass cohorts, (b) miRNA.nRNA studies, (c) sequencing studies, (d) methylation studies and (e) other studies/analyses.

Progress has been achieved across all sections since the last review.

A number of outputs from these sections can form the basis of future translational research projects.

The adoption of the CPH index for ovarian cancer diagnosis in clinical practice is a valuable achievement. Further optimization of this is being explored with the IOTA group.

The methylation algorithm reported is new /not published. Can the methylation biomarker/signature developed be evaluated in the biobank established in Prof Kjaer's work-stream.

Mermaid-III: "The Infection Theory"

Lead: Professor Jan Blaakaer

Funding: DKR 1,534,353

Prof Blaaker's group has published 3 papers over 7 years. There is now one more paper in progress, which is good to see.

COMMENT

While the last paper being readied for submission (after a gap) is welcome, unfortunately this section of Mermaid-III has been plagued by slow and poor progress for a long time. Arguably there should have been a clearer focus with a better study design, sample size and planned implementation to adequately investigate this theory/approach.

Programme administration

The committee would like to congratulate the Mermaid-III administration team for fundraising and delivering the funding to sustain this research, which has overall led to number of important academic outputs. The programme has provided an important scaffolding and number of outputs which can be the building blocks for and drive future translational research. That the administration has been achieved with minimal use of funds for administrative costs (DKR 609,785) over 7 years is commendable and highlights the team's sustained commitment to maximising the research effort.

Independent Audit Committee report: Executive Summary

Mermaid III

Early detection & screening; Biomarkers &/or Prognostic markers; Infection Theory

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The Mermaid-III programme has funded three work-streams of research into ovarian cancer: (a) Early detection & screening; (b) Biomarkers &/or Prognostic markers; and (c) Infection Theory, to the tune of DKR 35,356,539 over the last 7 years. The three work-streams have been led by Prof Susanne Kruger Kjaer, Profs Claus & Estrid Hogdall and Prof Jan Blaakaer respectively. Overall the research programme has been extremely productive leading to a large number of academic outputs including 249 publications and 45 presentations. Two of the three work-streams, particularly stood out: Prof Kjaer- 131 publications and 15 presentations and Profs Hogdall- 114 publications and 30 presentations. Prof Blaakaer's work-stream contributed 4 publications. Besides these outputs, the programme has led to the creation of a large biobank by Prof Kjaer, a bio resource of two large cohorts of ovarian cancer cases by Profs Hogdall, and enabled linkage of registries/databases and clinical outcomes. It has helped build resource and capacity, enabled national and international collaborations. This along with outcomes from this programme has laid a strong foundation for driving future translational research.

Unfortunately some of the work was hampered along the way. Two issues beyond the control of the investigators were the COVID19 pandemic and implications of GDPR implementation restricting sample transport and some collaborative work. These issues were dealt with by mitigating strategies and plans being put in place to take the work forward.

Overall the audit committee congratulates the investigators for completing 7 years of the programme and dealing with a number of challenges that arose along the way. We would also like to highlight the critically important role played by the MERMAID team in raising funding for the programme and administering the programme in such an efficient way at minimal cost.



(On behalf of the Audit Committee)

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