Chromosome 8q in Uveal Melanoma prognosis: interdependent prognostic factor or related to genomic parameters

Dear colleagues,

The Rotterdam Ocular Melanoma Studygroup (ROMS) would like to invite you for a collaboration regarding a study in which the role of chromosome 8q is evaluated as a prognostic factor in uveal melanoma patients.

Prognostication of UM relies on recurrent mutations in secondary driver genes, as well as CNV and GEP. Previous studies using FISH probes and array-CGH have shown that the gain of chromosome 8q in UM is strongly correlated with a shorter survival.[1-3] A study of UM patients with different iris colour found that 8q gain was associated with a worse survival in those with light iris color.[4] UM patients with *BAP1* and *SF3B1* mutations have different CNV profiles, and *BAP1*-mutated tumours have a worse prognosis whenever 8q gain is present. And if monosomy 3 and 8q gain are added to the AJCC classification this group showed worst prognosis.[5] In contrast, there is no correlation between 8q gain and early-onset metastasis in *SF3B1*-mutated tumours.[6] A larger cohort study with a uniform approach towards analysis of CNV, mutation status, and transcriptomic data over a longer follow-up period is needed to establish the role of 8q gain in UM. Validation in clinically well-typed patient cohorts with CNV profiles, transcriptome, and mutation data would strengthen these findings.

Aim of this study

To evaluate the role of chromosome 8q regarding prognosis in uveal melanoma patients.

Inclusion criteria

Adult uveal melanoma patients of which genetic data is evaluated or tumour material available for genetic sequencing and a follow-up until death or period of at least 10 years.
If the inclusion criteria are fulfilled, we would like to receive the following data

- Clinical data:
  - age of onset (years)
  - gender (M/F)
  - presence of metastasis (Y/N)
  - location of metastasis
  - disease free survival: time from diagnosis until metastatic disease or current date (months)
  - overall survival: time from diagnosis until death or current date (months)
  - status (dead or alive)
- Genetic data:
  - SNP-array molecular karyotyping and or FISH of chromosome 3p, 3q, 6p, 6q 8p, 8q
- Histopathological data:
  - Tumor LBD (mm)
  - Tumor height (mm)
  - Cell type (spindle/epithelioid/mixed)

- Treatment:
    - Primary treatment
    - Secondary treatment
    - Treatment of metastasis
- If available:
    - BAP1 immunohistochemistry
    - Cause of death
    - 3cen status (normal/loss/gain), (SNP-array/FISH/karyotyping)
    - 6cen status (normal/loss/gain), (SNP-array/FISH/karyotyping)
    - 8cen status (normal/loss/gain), (SNP-array/FISH/karyotyping)
    - 1p
    - 1q
    - 1cen status (normal/loss/gain), (SNP-array/FISH/karyotyping)
    - GNAQ
    - GNA11
    - CYSLTR2
    - PLCB4
    - BAP1
    - EIF1AX
    - SF3B1
    - SRSF2
    - U2AF1
    - MBD4
    - GEP class (1 or 2)
    - RNA sequencing (yes/no)
    -

Minimal dataset in red, these items are selection criterium

All data will be collected in a secured digital environment.

Ethical considerations

This study will adhere to the principles of the Declaration of Helsinki.

Reporting

The results will solely be used for this study and will be published in an international, peer reviewed journal. Authors will include researchers involved in this project and members of the Ophthalmic Oncology Group who provided valid cases for this study, listed in the order of patients enrolled.

Authors will include researchers involved in this project and members of the Ophthalmic Oncology Group who provided valid cases for this study, listed in the order of patients enrolled. Initiators of the study will appear as first and last authors.

Financing
XXXXXXX

Instructions
Please let us know if you would like to join this study by sending an e-mail to n.vanpoppelen@erasmusmc.nl with the subject “inclusion in uveal melanoma 8q study” so we can provide you with the needed information regarding the online database.

References

1. Sisley K, Rennie IG, Parsons MA, et al. Abnormalities of chromosomes 3 and 8 in posterior uveal melanoma correlate with prognosis. *Genes Chromosomes Cancer* 1997;19(1):22-8.
2. Versluis M, de Lange MJ, van Pelt SI, et al. Digital PCR validates 8q dosage as prognostic tool in uveal melanoma. *PLoS One* 2015;10(3):e0116371.
3. Patrone S, Maric I, Rutigliani M, et al. Prognostic value of chromosomal imbalances, gene mutations, and BAP1 expression in uveal melanoma. *Genes Chromosomes Cancer* 2018;57(8):387-400.
4. Wierenga APA, Brouwer NJ, Gelmi MC, et al. Chromosome 3 and 8q Aberrations in Uveal Melanoma Show Greater Impact on Survival in Patients with Light Iris versus Dark Iris Color. *Ophthalmology* 2022;129(4):421-30.
5. Dogrusoz M, Bagger M, van Duinen SG, et al. The Prognostic Value of AJCC Staging in Uveal Melanoma Is Enhanced by Adding Chromosome 3 and 8q Status. *Invest Ophthalmol Vis Sci* 2017;58(2):833-42.
6. Nguyen JQN, Drabarek W, Vaarwater J, et al. 8q Gain Has No Additional Predictive Value in SF3B1MUT Uveal Melanoma but Is Predictive for a Worse Prognosis in Patients with BAP1MUT Uveal Melanoma. *Ophthalmol Sci*. 2023;4(2):100413. doi: 10.1016/j.xops.2023.100413.