Expert workshop: Uveal Melanoma

POTENTIAL TRIAL DESIGNS:

1. **Diagnostic/prognosis/prediction:** Detection of UM-ctDNA in pts. with suspected uveal melanoma; baseline and follow-up, single-arm, multicenter.
   → Easy to design and conduct.

2. **Localized disease: Detection of MRD and monitoring:** Patients with uveal melanoma before local treatment and during follow-up;
   Trial design might be:
   a) observatory: prediction of relapse/progression
   b) interventional: MRD-versus imaging guided treatment of residual disease/early dissemination/relapse in patients with initially ctDNA +ive pts. (attractive however positivity rate might be low)
   c) adjuvant design: SOC follow-up versus adjuvant treatment (e.g. tebentafusp in HLA A2), stratified by MRD positive and negative pts.

3. **Metastatic disease: Therapy response and treatment resistance:**
   a) (observatory: prediction of response/relapse during systemic/local treatment → easy to set up)
   b) interventional: → difficult: Low response rates; But: ctDNA clearance correlates with OS. Possibilities would be:
   - systemic treatment until ctDNA progression versus imaging progression
   - interventional: Switch between local/systemic or systemic/systemic treatments based on MRD e.g. switch between tebentafusp and locoregional treatment at ctDNA progression versus imaging progression

4. **Analyte/technique/scientific approach:** focus on ctDNA and CTCs; MRD, fragementomics; methylation and clonal evolution.