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| **Study Order** | **Molecular Analysis** | **Sample Comparison** | **Follow-Up Requirement** | **Rationale for Follow-Up Requirement** |
| 1 | 12-gene expression classifier | Class 1 (n = 216)  Class 2 (n = 173) | None | Performed on all study participants |
| 2 | PCA analysis of  12-gene expression classifier | Class1met+ (n = 12) Class1met- (n = 96) | None | Performed on all samples for which expression of the 12 genes was available before outsourcing to DecisionDx-UM |
| 3 | Global transcriptome analysis | Class1met+ (n = 5) Class1met- (n = 8) | >1 year follow-up for Class1met- tumors | Class 1 tumors are usually smaller than Class 2 tumors and less commonly treated by enucleation, which is preferred to obtain enough tissue for this analysis. A less strict (shorter) time requirement was used to allow more samples to be included. |
| 4 | qPCR validation of *PRAME* | Class1met+ (n = 7) Class1met- (n = 19) | >3 years follow-up for Class1met- tumors | Less RNA is needed for qPCR than for global transcriptome analysis, so more samples were available that had sufficient RNA remaining. A stricter (longer) time requirement could be used. |
| 5 | qPCR validation of *PRAME* for Kaplan-Meier analysis | Class1PRAME+ (n = 25) Class1PRAME- (n = 39) | None | Performed on all retrospective samples that were available |
| 6 | SNP array | Class1PRAME+/met+ (n = 6) Class1PRAME+/met- (n = 3)  Class1PRAME-/met- (n = 3) | None | Class 1 tumors are usually smaller than Class 2 tumors and less commonly treated by enucleation, which is required to obtain enough tissue for this analysis. These were the only samples available. |

**Supplementary Table 1.** Molecular analyses and the order in which they were conducted in this study.