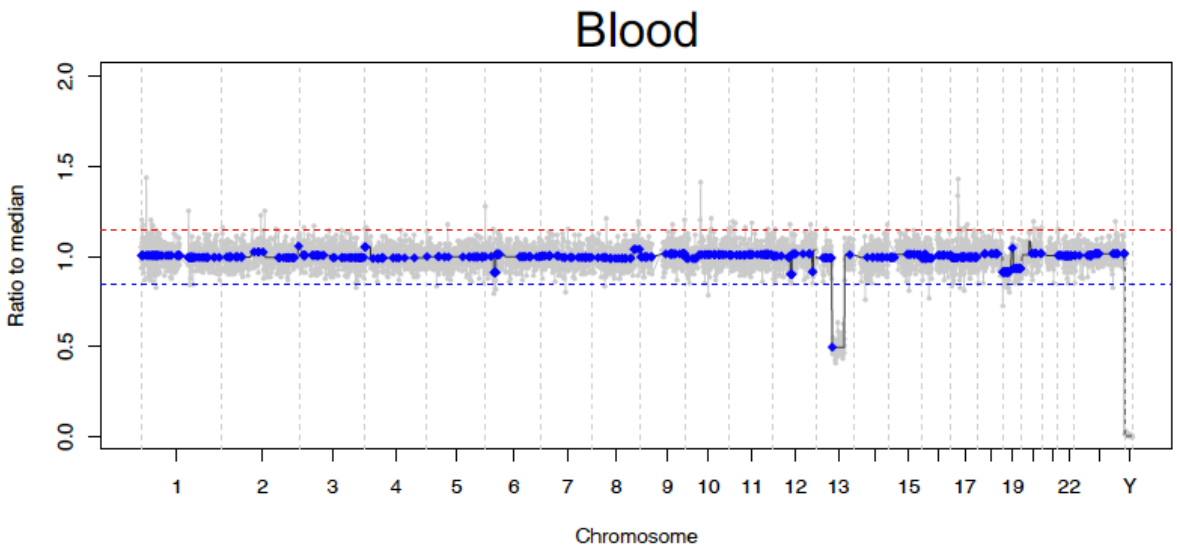
**Supplementary Table 1.** Patient demographics, clinical outcomes, *RB1* mutational analysis, and somatic copy number alterations (SCNAs)

| Case | Eye | Sex | Age at dx (mos) | IIRC Group Class | AJCC | Seeding type at diagnosis | Blood *RB1* mutation | Somatic *RB1* mutation | Total # of AH sam-ples | RB SCNAs | | | | | # SCNA (total) per eye | Req'd ENUC? | Reason for ENUC | Time to ENUC after dx (days) | Follow-up (mos) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | 1q | 2p | 6p | 13q | 16q | | | | | |
| 1 | OD | F | 13 | C | cT2b | dust | 13q & 16p deletion; 13q14.2-q31.1 and 949kb loss of 16p12.2 | 13q deletion c.1981C>T (p.R661W), missense mutation | 3 | ↑(1.3) | | | ↓(0.5) | ↓(0.7) | 3 | no | N/A | N/A | 32 |
| 1 | OS | F | 13 | D | cT2b | sphere | 13q & 16p deletion; 13q14.2-q31.1 and 949kb loss of 16p12.2 | 13q deletion c.1215+1G>A, splice donor variant | 2 | | | ↑(1.8) | ↓(0.5) | | 2 | yes | secondary (recur) | 300 | 32 |

NOTE: Gains or losses are indicated as ↑ (gain) or ↓ (loss), with amplitude of the change (as ratio to median).
Abbreviations: AJCC, American Joint Committee on Cancer; AH, aqueous humor; dx, diagnosis; ENUC, enucleation; IIRC, International Intraocular Retinoblastoma Classification; mos, months; *RB1*, retinoblastoma tumor suppressor gene; SCNA, somatic copy number alteration.




**Supplementary Figure 1.** The germline 13q deletion is seen on somatic copy number alteration (SCNA) profiling of peripheral blood. Due to germline status, this 13q deletion is seen consistently in all other SCNA profiles. Notably, the germline focal 16p deletion seen on peripheral blood *RB1* testing is not detected in SCNA profiling, as it is below our 1Mbp detection threshold.