**Supplementary Table**

Supplementary Table 1. Genomic profiling of repotrectinib-resistant patient biopsy

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Gene** | **Chr** | **Start base position** | **End base position** | **REF** | **ALT** | **Variant classification** | **Amino acid change** | **Tumor allele frequency** | | |
| **P-A pre** | **P-A post** | **P-B post** |
| *MCL1* | 1 | 150550935 | 150550935 | C | G | Missense\_Mutation | p.D241H | 0 | 0 | 0.026 |
| *MSH2* | 2 | 47656972 | 47656972 | C | T | Missense\_Mutation | p.L390F | 0.51 | 0.473 | 0 |
| *MAP3K1* | 5 | 56111633 | 56111634 | TC | CT | Missense\_Mutation | p.L78P | 0.515 | 0.579 | 0 |
| *APC* | 5 | 112173656 | 112173656 | C | T | Nonsense\_Mutation | p.Q789\* | 0.261 | 0.489 | 0 |
| *CCND3* | 6 | 41903800 | 41903800 | C | G | Missense\_Mutation | p.E253Q | 0 | 0.073 | 0 |
| *ETV1* | 7 | 13971284 | 13971284 | C | T | Missense\_Mutation | p.M215I | 0 | 0 | 0.027 |
| *MET* | 7 | 116411986 | 116411986 | C | T | Missense\_Mutation | p.P1009S | 0.465 | 0.541 | 0 |
| *GNAQ* | 9 | 80537095 | 80537095 | G | T | Nonsense\_Mutation | p.Y101\* | 0.025 | 0.027 | 0 |
| *RET* | 10 | 43606856 | 43606856 | G | A | Missense\_Mutation | p.D489N | 0.499 | 0.438 | 0 |
| *KMT2A* | 11 | 118307445 | 118307445 | G | A | Missense\_Mutation | p.G73E | 0 | 0 | 0.551 |
| *FLT3* | 13 | 28623579 | 28623580 | TC | AA | Missense\_Mutation | p.G326V | 0 | 0.027 | 0 |
| *RB1* | 13 | 48955548 | 48955548 | A | G | Missense\_Mutation | p.H555R | 0 | 0 | 0.446 |
| *NUTM1* | 15 | 34648635 | 34648635 | C | T | Missense\_Mutation | p.T781M | 0 | 0 | 0.54 |
| *IDH2* | 15 | 90645555 | 90645555 | G | C | Missense\_Mutation | p.P23R | 0.564 | 0.468 | 0 |
| *TP53* | 17 | 7578395 | 7578396 | GG | AC | Missense\_Mutation | p.178\_179HH>QY | 0 | 0.526 | 0 |
| *TP53* | 17 | 7578418 | 7578418 | T | C | Missense\_Mutation | p.E171G | 0 | 0 | 0.094 |
| *ERBB2* | 17 | 37864776 | 37864776 | G | A | Missense\_Mutation | p.R143Q | 0 | 0 | 0.514 |
| *SMAD4* | 18 | 48604790 | 48604790 | G | T | Nonsense\_Mutation | p.E538\* | 0 | 0.472 | 0 |
| *DOT1L* | 19 | 2226943 | 2226943 | G | A | Missense\_Mutation | p.A1475T | 0.502 | 0.548 | 0 |
| *SMARCA4* | 19 | 11141492 | 11141492 | C | T | Missense\_Mutation | p.R1157W | 0 | 0 | 0.039 |
| *NOTCH3* | 19 | 15276289 | 15276289 | C | T | Missense\_Mutation | p.R1902H | 0.236 | 0.225 | 0 |
| *BRD4* | 19 | 15366124 | 15366124 | C | G | Missense\_Mutation | p.K677N | 0 | 0 | 0.044 |
| *CEBPA* | 19 | 33792731 | 33792732 | - | GCGGGT | In\_Frame\_Ins | p.196\_197insHP | 0 | 0 | 0.406 |
| *GNAS* | 20 | 57415219 | 57415219 | C | A | Missense\_Mutation | p.L20M | 0.426 | 0.471 | 0 |
| *ZNRF3* | 22 | 29438495 | 29438495 | G | T | Missense\_Mutation | p.V147L | 0.518 | 0.452 | 0 |

Chr, chromosome; REF, reference allele; ALT, tumor alternative allele; P-A, Patient A; P-B, Patient B

Germline variant filtering criteria;

- The Exome Aggregation Consortium global population variant allele frequency (EXAC\_AF < 0.01)