

Table S10

| FOCUS H&E slide A | Overall | | | | CMS1 | | | | CMS2 | | | | CMS3 | | | | CMS4 | | | |
|---------------------------------|--------------------|------------|------------------------|---------|-------------------|------------|--------------------------|---------|--------------------|------------|------------------------|---------|-------------------|------------|-------------------------|---------|-------------------|------------|-------------------------|---------|
| | Classified (n=278) | | Unclassified (n=84) | | Classified (n=52) | | Unclassified (n=13) | | Classified (n=120) | | Unclassified (n=26) | | Classified (n=36) | | Unclassified (n=15) | | Classified (n=70) | | Unclassified (n=30) | |
| | Statistics | Statistics | Odds ratio | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value |
| Major molecular features | | | | | | | | | | | | | | | | | | | | |
| <i>CIMP cluster</i> | n=238 | n=75 | | 0.353 | n=41 | n=11 | | 1.000 | n=108 | n=25 | | 0.553 | n=28 | n=13 | | 1.000 | n=61 | n=26 | | 0.462 |
| CIMP-High | 21% | 28% | | | 54% | 45% | | | 6% | 20% | | | 46% | 38% | | | 15% | 23% | | |
| CIMP-Low | 24% | 33% | | | 27% | 45% | | | 27% | 28% | | | 18% | 31% | | | 21% | 35% | | |
| CIMP-Negative | 54% | 39% | | | 20% | 9% | | | 67% | 52% | | | 36% | 31% | | | 64% | 42% | | |
| <i>Microsatellite status</i> | n=258 | n=81 | 0 (0.000,1.249) | 0.353 | n=47 | n=13 | 0 (0.1,504) | 0.353 | n=116 | n=25 | 0 (0,Inf) | 1.000 | n=30 | n=13 | 0 (0,Inf) | 1.000 | n=65 | n=30 | 0 (0.84,39) | 1.000 |
| Stable (MSS) | 96% | 100% | | | 79% | 100% | | | 100% | 100% | | | 100% | 100% | | | 98% | 100% | | |
| Instable (MSI) | 4% | 0% | | | 21% | 0% | | | 0% | 0% | | | 0% | 0% | | | 2% | 0% | | NA |
| Selected mutations | | | | | | | | | | | | | | | | | | | | |
| <i>APC mut status</i> | n=258 | n=81 | 1.772 (0.775,4.575) | 0.480 | n=47 | n=13 | 7.263 (0.924,335.217) | 0.353 | n=116 | n=25 | 0.341 (0.078,1.73) | 0.353 | n=30 | n=13 | 1.325 (0.095,75.72) | 1.000 | n=65 | n=30 | 3.799 (0.783,36.808) | 0.353 |
| Wild-type | 16% | 10% | | | 38% | 8% | | | 6% | 16% | | | 10% | 8% | | | 22% | 7% | | |
| Mutated | 84% | 90% | | | 62% | 92% | | | 94% | 84% | | | 90% | 92% | | | 78% | 93% | | |
| <i>BRAF mut status</i> | n=258 | n=81 | 0.748 (0.265,1.839) | 1.000 | n=47 | n=13 | 0.846 (0.188,3.47) | 1.000 | n=116 | n=25 | 0 (0,Inf) | 1.000 | n=30 | n=13 | 0.755 (0.013,10.566) | 1.000 | n=65 | n=30 | 0.342 (0.007,3.028) | 0.913 |
| Wild-type | 89% | 91% | | | 57% | 62% | | | 100% | 100% | | | 90% | 92% | | | 91% | 97% | | |
| Mutated | 11% | 9% | | | 43% | 38% | | | 0% | 0% | | | 10% | 8% | | | 9% | 3% | | |
| <i>KRAS mut status</i> | n=258 | n=81 | 1.91 (1.116,3.308) | 0.229 | n=47 | n=13 | 0.863 (0.168,3.724) | 1.000 | n=116 | n=25 | 1.795 (0.694,7.85) | 0.479 | n=30 | n=13 | 0.822 (0.163,4.699) | 1.000 | n=65 | n=30 | 3.346 (1.181,10.571) | 0.229 |
| Wild-type | 54% | 38% | | | 66% | 69% | | | 59% | 44% | | | 27% | 31% | | | 51% | 23% | | |
| Mutated | 46% | 62% | | | 34% | 31% | | | 41% | 56% | | | 73% | 69% | | | 49% | 77% | | |
| <i>TP53 mut status</i> | n=258 | n=81 | 0.936 (0.529,1.685) | 1.000 | n=47 | n=13 | 1.389 (0.325,7.105) | 1.000 | n=116 | n=25 | 0.473 (0.165,1.439) | 0.462 | n=30 | n=13 | 1.511 (0.34,6.945) | 1.000 | n=65 | n=30 | 1.455 (0.497,4.687) | 1.000 |
| Wild-type | 29% | 31% | | | 38% | 31% | | | 18% | 32% | | | 57% | 46% | | | 31% | 23% | | |
| Mutated | 71% | 69% | | | 62% | 69% | | | 82% | 68% | | | 43% | 54% | | | 69% | 77% | | |

| FOCUS H&E slide B | Overall | | | | CMS1 | | | | CMS2 | | | | CMS3 | | | | CMS4 | | | |
|---------------------------------|--------------------|---------------------|---------------------|---------|-------------------|---------------------|---------------------|---------|--------------------|---------------------|---------------------|---------|-------------------|---------------------|---------------------|---------|-------------------|---------------------|---------------------|---------|
| | Classified (n=265) | Unclassified (n=84) | Odds ratio (95% CI) | P value | Classified (n=48) | Unclassified (n=17) | Odds ratio (95% CI) | P value | Classified (n=118) | Unclassified (n=25) | Odds ratio (95% CI) | P value | Classified (n=31) | Unclassified (n=13) | Odds ratio (95% CI) | P value | Classified (n=68) | Unclassified (n=29) | Odds ratio (95% CI) | P value |
| Major molecular features | Statistics | Statistics | | | Statistics | Statistics | | | Statistics | Statistics | | | Statistics | Statistics | | | Statistics | Statistics | | |
| <i>CIMP cluster</i> | n=258 | n=75 | | 0.305 | n=41 | n=11 | | 0.662 | n=108 | n=25 | | 0.221 | n=28 | n=12 | | 1.000 | n=61 | n=27 | | 0.521 |
| CIMP-High | 21% | 28% | | | 54% | 36% | | | 6% | 24% | | | 46% | 42% | | | 15% | 22% | | |
| CIMP-Low | 24% | 33% | | | 27% | 55% | | | 27% | 28% | | | 18% | 25% | | | 21% | 33% | | |
| CIMP-Negative | 54% | 39% | | | 20% | 9% | | | 67% | 48% | | | 36% | 33% | | | 64% | 44% | | |
| <i>Microsatellite status</i> | n=258 | n=81 | 0 | 0.305 | n=47 | n=12 | 0 | 0.549 | n=116 | n=26 | 0 | 1.000 | n=30 | n=12 | 0 | 1.000 | n=65 | n=31 | 0 | 1.000 |
| Stable (MSS) | 96% | 100% | (0.1,249) | | 79% | 100% | (0.1,645) | | 100% | 100% | (0,Inf) | | 100% | 100% | (0,Inf) | | 98% | 100% | (0.81,671) | |
| Instable (MSI) | 4% | 0% | | | 21% | 0% | | | 0% | 0% | | | 0% | 0% | | | 2% | 0% | | |
| Selected mutations | | | | | | | | | | | | | | | | | | | | |
| <i>APC mut status</i> | n=258 | n=81 | 1.772 | 0.520 | n=47 | n=12 | Inf | 0.221 | n=116 | n=26 | 0.273 | 0.267 | n=30 | n=12 | 1.217 | 1.000 | n=65 | n=31 | 3.934 | 0.305 |
| Wild-type | 16% | 10% | (0.775,4.575) | | 38% | 0% | (1,471,Inf) | | 6% | 19% | (0.067,1.199) | | 10% | 8% | (0.086,69.894) | | 22% | 6% | (0.813,38.108) | |
| Mutated | 84% | 90% | | | 62% | 100% | | | 94% | 81% | | | 90% | 92% | | | 78% | 94% | | |
| <i>BRAF mut status</i> | n=258 | n=81 | 0.748 | 1.000 | n=47 | n=12 | 0.679 | 1.000 | n=116 | n=26 | Inf | 0.499 | n=30 | n=12 | 0.822 | 1.000 | n=65 | n=31 | 0.331 | 0.845 |
| Wild-type | 89% | 91% | (0.265,1.839) | | 57% | 67% | (0.131,2.982) | | 100% | 96% | (0,114,Inf) | | 90% | 92% | (0.014,11.596) | | 91% | 97% | (0.007,2.922) | |
| Mutated | 11% | 9% | | | 43% | 33% | | | 0% | 4% | | | 10% | 8% | | | 9% | 3% | | |
| <i>KRAS mut status</i> | n=258 | n=81 | 1.91 | 0.221 | n=47 | n=12 | 1.376 | 1.000 | n=116 | n=26 | 1.413 | 0.904 | n=30 | n=12 | 1.089 | 1.000 | n=65 | n=31 | 2.932 | 0.221 |
| Wild-type | 54% | 38% | (1.116,3.308) | | 66% | 58% | (0.295,6.011) | | 59% | 50% | (0.55,3.638) | | 27% | 25% | (0.196,7.821) | | 51% | 26% | (1.071,8.746) | |
| Mutated | 46% | 62% | | | 34% | 43% | | | 41% | 50% | | | 73% | 75% | | | 49% | 74% | | |
| <i>TP53 mut status</i> | n=258 | n=81 | 0.936 | 1.000 | n=47 | n=12 | 1.237 | 1.000 | n=116 | n=26 | 0.5 | 0.499 | n=30 | n=12 | 1.299 | 1.000 | n=65 | n=31 | 1.517 | 0.887 |
| Wild-type | 29% | 31% | (0.529,1.685) | | 38% | 33% | (0.28,6.448) | | 18% | 31% | (0.177,1.512) | | 57% | 50% | (0.275,6.175) | | 31% | 23% | (0.52,4.872) | |
| Mutated | 71% | 69% | | | 62% | 67% | | | 82% | 69% | | | 43% | 50% | | | 69% | 77% | | |

| TCGA H&E slide A | Overall | | | | CMS1 | | | | CMS2 | | | | CMS3 | | | | CMS4 | | | |
|---------------------------------|--------------------|------------|---------------------|---------|-------------------|------------|---------------------|---------|--------------------|------------|---------------------|---------|-------------------|------------|---------------------|---------|--------------------|------------|---------------------|---------|
| | Classified (n=430) | | Unclassified (n=33) | | Classified (n=73) | | Unclassified (n=1) | | Classified (n=189) | | Unclassified (n=21) | | Classified (n=58) | | Unclassified (n=5) | | Classified (n=110) | | Unclassified (n=6) | |
| | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value |
| Major molecular features | | | | | | | | | | | | | | | | | | | | |
| <i>CIMP-cluster</i> | | | | | | | | | | | | | | | | | | | | |
| CIMP.High | n=337 | n=30 | | 1.000 | n=67 | n=0 | | | n=142 | n=10 | | 1.000 | n=46 | n=5 | | 0.850 | n=82 | n=5 | | 0.188 |
| CIMP.Low | 17% | 10% | | | 67% | 0% | | | 2% | 0% | | | 20% | 20% | | | 20% | 20% | | |
| CIMP.Negative | 20% | 20% | | | 16% | 0% | | | 15% | 10% | | | 41% | 20% | | | 17% | 40% | | |
| | 64% | 70% | | | 16% | 0% | | | 82% | 30% | | | 39% | 60% | | | 83% | 40% | | |
| <i>Microsatellite status</i> | | | | | | | | | | | | | | | | | | | | |
| Stable (MSS) | n=402 | n=32 | 0 | 0.144 | n=67 | n=1 | 0 | 0.758 | n=174 | n=21 | 0 | 1.000 | n=55 | n=5 | 0 | 1.000 | n=106 | n=5 | 0 | 1.000 |
| Instable (MSI) | 82% | 100% | (0.0,588) | | 15% | 100% | (0.7,526) | | 99% | 100% | (0,321,524) | | 84% | 100% | (0,6,587) | | 96% | 100% | (0,38,731) | |
| | 18% | 0% | | | 85% | 0% | | | 1% | 0% | | | 16% | 0% | | | 4% | 0% | | |
| Selected mutations | | | | | | | | | | | | | | | | | | | | |
| <i>APC mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 | n=29 | 2.084 | 0.758 | n=60 | n=1 | Inf | 0.760 | n=152 | n=18 | 2.713 | 1.000 | n=49 | n=4 | 0.449 | 0.585 | n=102 | n=6 | 0.835 | 1.000 |
| Mutated | 30% | 17% | (0.753,7.175) | | 73% | 0% | (0,066,Inf) | | 6% | 6% | (0,383,119.188) | | 31% | 50% | (0,036,731) | | 29% | 33% | (0,113,9.695) | |
| | 70% | 83% | | | 27% | 100% | | | 86% | 94% | | | 69% | 50% | | | 71% | 67% | | |
| <i>BRAF mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 | n=29 | 0 | 0.433 | n=60 | n=1 | 0 | 1.000 | n=152 | n=18 | 0 | 1.000 | n=49 | n=4 | 0 | 1.000 | n=102 | n=6 | 0 | 1.000 |
| Mutated | 89% | 100% | (0,1,119) | | 43% | 100% | (0,30,971) | | 100% | 100% | (0,Inf) | | 96% | 100% | (0,72,542) | | 95% | 100% | (0,21,874) | |
| | 11% | 0% | | | 57% | 0% | | | 0% | 0% | | | 4% | 0% | | | 5% | 0% | | |
| <i>KRAS mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 | n=29 | 2.427 | 0.302 | n=60 | n=1 | Inf | 0.760 | n=152 | n=18 | 1.972 | 0.758 | n=49 | n=4 | 0.871 | 1.000 | n=102 | n=6 | 7.315 | 0.758 |
| Mutated | 60% | 38% | (1.05,5.863) | | 73% | 0% | (0,066,Inf) | | 66% | 50% | (0,65,5.994) | | 22% | 25% | (0,062,49.684) | | 60% | 17% | (0,778,356.801) | |
| | 40% | 62% | | | 27% | 100% | | | 34% | 50% | | | 78% | 75% | | | 40% | 83% | | |
| <i>TP53 mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 | n=29 | 0.897 | 1.000 | n=60 | n=1 | Inf | 0.802 | n=152 | n=18 | 0.579 | 0.760 | n=49 | n=4 | 0.633 | 1.000 | n=102 | n=6 | 1 | 1.000 |
| Mutated | 42% | 45% | (0,391,2,092) | | 65% | 0% | (0,045,Inf) | | 32% | 44% | (0,192,1,802) | | 65% | 75% | (0,011,8.993) | | 33% | 33% | (0,135,11,577) | |
| | 58% | 55% | | | 35% | 100% | | | 68% | 56% | | | 35% | 25% | | | 67% | 67% | | |

| TCGA H&E slide B | Overall | | | | CMS1 | | | | CMS2 | | | | CMS3 | | | | CMS4 | | | |
|---------------------------------|--------------------|--------------|------------------------|---------|-------------------|-------------|---------------------|---------|--------------------|--------------|--------------------------|---------|-------------------|-------------|-------------------------|---------|--------------------|-------------|-------------------------|---------|
| | Classified (n=430) | | Unclassified (n=33) | | Classified (n=73) | | Unclassified (n=1) | | Classified (n=189) | | Unclassified (n=21) | | Classified (n=58) | | Unclassified (n=5) | | Classified (n=110) | | Unclassified (n=6) | |
| | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value |
| Major molecular features | | | | | | | | | | | | | | | | | | | | |
| <i>CIMP-cluster</i> | | | | | | | | | | | | | | | | | | | | |
| CIMP-High | n=337 17% | n=20 10% | | 1.000 | n=67 67% | n=0 0% | | | n=142 2% | n=10 0% | | 1.000 | n=46 20% | n=5 20% | | 1.000 | n=62 20% | n=5 20% | | 0.188 |
| CIMP-Low | 20% | 20% | | | 18% | 18% | | | 15% | 10% | | | 41% | 20% | | | 17% | 40% | | |
| CIMP-Negative | 64% | 70% | | | 15% | 15% | | | 82% | 80% | | | 39% | 60% | | | 82% | 40% | | |
| <i>Microsatellite status</i> | | | | | | | | | | | | | | | | | | | | |
| Stable (MSS) | n=402 82% | n=22 100% | 0 (0.0,588) | 0.144 | n=67 15% | n=1 100% | 0 (0.7,526) | 0.758 | n=174 99% | n=20 100% | 0 (0.337,516) | 1.000 | n=55 84% | n=5 100% | 0 (0.6,587) | 1.000 | n=106 96% | n=6 100% | 0 (0.31,059) | 1.000 |
| Instable (MSI) | 18% | 0% | | | 85% | 0% | | | 1% | 0% | | | 16% | 0% | | | 4% | 0% | | |
| Selected mutations | | | | | | | | | | | | | | | | | | | | |
| <i>APC mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 30% | n=29 17% | 2.084 (0.753,7.175) | 0.758 | n=60 73% | n=1 0% | Inf (0.066,Inf) | 0.760 | n=152 14% | n=17 6% | 2.554 (0.358,112.565) | 1.000 | n=49 31% | n=4 50% | 0.449 (0.036,731) | 1.000 | n=102 29% | n=7 29% | 1.041 (0.159,11.51) | 1.000 |
| Mutated | 70% | 83% | | | 27% | 100% | | | 86% | 94% | | | 69% | 50% | | | 71% | 71% | | |
| <i>BRAF mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 89% | n=29 100% | 0 (0.1,119) | 0.433 | n=60 43% | n=1 100% | 0 (0.30,971) | 1.000 | n=152 100% | n=17 100% | 0 (0,Inf) | 1.000 | n=49 96% | n=4 100% | 0 (0.72,542) | 1.000 | n=102 95% | n=7 100% | 0 (0.18,175) | 1.000 |
| Mutated | 11% | 0% | | | 57% | 0% | | | 0% | 0% | | | 4% | 0% | | | 5% | 0% | | |
| <i>KRAS mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 60% | n=29 38% | 2.427 (1.05,5.863) | 0.302 | n=60 73% | n=1 0% | Inf (0.066,Inf) | 0.760 | n=152 66% | n=17 47% | 2.217 (0.712,7.038) | 0.758 | n=49 22% | n=4 25% | 0.871 (0.062,49.684) | 1.000 | n=102 60% | n=7 29% | 3.675 (0.569,40.347) | 0.758 |
| Mutated | 40% | 62% | | | 27% | 100% | | | 34% | 53% | | | 78% | 75% | | | 40% | 71% | | |
| <i>TP53 mut status</i> | | | | | | | | | | | | | | | | | | | | |
| Wild-type | n=363 42% | n=29 45% | 0.897 (0.391,2.092) | 1.000 | n=60 65% | n=1 0% | Inf (0.045,Inf) | 0.902 | n=152 32% | n=17 47% | 0.521 (0.167,1.657) | 0.760 | n=49 65% | n=4 75% | 0.633 (0.011,8.593) | 1.000 | n=102 33% | n=7 29% | 1.248 (0.192,13.745) | 1.000 |
| Mutated | 58% | 55% | | | 35% | 100% | | | 68% | 53% | | | 35% | 25% | | | 67% | 71% | | |

| GRAMPIAN H&E slide A | Overall | | | | CMS1 | | | | CMS2 | | | | CMS3 | | | | CMS4 | | | |
|---------------------------------|--------------------|------------|---------------------|---------|-------------------|------------|---------------------|---------|-------------------|------------|---------------------|---------|-------------------|------------|---------------------|---------|-------------------|------------|---------------------|---------|
| | Classified (n=144) | | Unclassified (n=79) | | Classified (n=20) | | Unclassified (n=16) | | Classified (n=63) | | Unclassified (n=41) | | Classified (n=35) | | Unclassified (n=8) | | Classified (n=26) | | Unclassified (n=14) | |
| | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value |
| Major molecular features | | | | | | | | | | | | | | | | | | | | |
| <i>CIMP cluster</i> | n=86 | n=12 | | 0.26 | n=11 | n=5 | | 0.647 | n=40 | n=20 | | 0.134 | n=24 | n=5 | | 0.847 | n=11 | n=2 | | 0.295 |
| CIMP High | 17% | 19% | | | 45% | 40% | | | 5% | 10% | | | 33% | 40% | | | 0% | 0% | | |
| CIMP Low | 37% | 22% | | | 36% | 20% | | | 45% | 20% | | | 38% | 20% | | | 9% | 50% | | |
| CIMP Negative | 45% | 59% | | | 18% | 40% | | | 49% | 70% | | | 29% | 40% | | | 91% | 50% | | |
| <i>Microsatellite status</i> | n=121 | n=60 | 0 | 0.552 | n=19 | n=14 | 0 | 0.244 | n=51 | n=30 | 0 | 1 | n=30 | n=7 | 0 | 1 | n=21 | n=9 | 0 | 1 |
| Stable (MSS) | 98% | 100% | (0.4,886) | | 84% | 100% | (0.3,22) | | 100% | 100% | (0,Inf) | | 100% | 100% | (0,Inf) | | 100% | 100% | (0,Inf) | |
| Instable (MSI) | 2% | 0% | | | 16% | 0% | | | 0% | 0% | | | 0% | 0% | | | 0% | 0% | | |
| Selected mutations | | | | | | | | | | | | | | | | | | | | |
| <i>APC mut status</i> | n=121 | n=60 | 2.084 | 0.292 | n=19 | n=14 | Inf | 0.013 | n=51 | n=30 | 0.584 | 1 | n=30 | n=7 | 0.675 | 1 | n=21 | n=9 | 0.414 | 0.517 |
| Wild-type | 10% | 5% | (0.533,1.971) | | 37% | 0% | (1.31,Inf) | | 2% | 3% | (0.007,47.083) | | 10% | 14% | (0.044,40.764) | | 5% | 11% | (0.005,35.29) | |
| Mutated | 90% | 95% | | | 63% | 100% | | | 98% | 97% | | | 90% | 86% | | | 95% | 89% | | |
| <i>BRAF mut status</i> | n=121 | n=60 | 0 | 0.552 | n=19 | n=14 | 0 | 0.244 | n=51 | n=30 | 0 | 1 | n=30 | n=7 | 0 | 1 | n=21 | n=9 | 0 | 1 |
| Wild-type | 98% | 100% | (0.4,886) | | 84% | 100% | (0.3,22) | | 100% | 100% | (0,Inf) | | 100% | 100% | (0,Inf) | | 100% | 100% | (0,Inf) | |
| Mutated | 2% | 0% | | | 16% | 0% | | | 0% | 0% | | | 0% | 0% | | | 0% | 0% | | |
| <i>KRAS mut status</i> | n=121 | n=60 | 1.203 | 0.636 | n=19 | n=14 | 0.368 | 0.257 | n=51 | n=30 | 1.467 | 0.485 | n=30 | n=7 | 2.925 | 0.649 | n=21 | n=9 | 2.579 | 0.427 |
| Wild-type | 48% | 43% | (0.617,2.36) | | 21% | 43% | (0.057,2.085) | | 63% | 53% | (0.533,4.048) | | 33% | 14% | (0.288,151.455) | | 57% | 33% | (0.411,20.449) | |
| Mutated | 52% | 57% | | | 79% | 57% | | | 37% | 47% | | | 67% | 86% | | | 43% | 67% | | |
| <i>TP53 mut status</i> | n=121 | n=60 | 1.604 | 0.309 | n=19 | n=14 | Inf | 0.057 | n=51 | n=30 | 0.798 | 0.753 | n=30 | n=7 | Inf | 0.306 | n=21 | n=9 | 0.635 | 0.666 |
| Wild-type | 20% | 13% | (0.64,4.433) | | 26% | 0% | (0.744,Inf) | | 14% | 17% | (0.194,3.542) | | 23% | 0% | (0.333,Inf) | | 24% | 33% | (0.087,5.376) | |
| Mutated | 80% | 87% | | | 74% | 100% | | | 86% | 83% | | | 77% | 100% | | | 76% | 67% | | |

| GRAMPIAN H&E slide B | Overall | | | | CMS1 | | | | CMS2 | | | | CMS3 | | | | CMS4 | | | |
|---------------------------------|---------------------------|---------------------------|-------------------------|---------|---------------------------|--------------------------|-------------------------|---------|---------------------------------|--------------------------|-------------------------|---------|---------------------------|-------------------------|--------------------------|---------|-------------------------|-------------------------|-------------------------|---------|
| | Classified (n=144) | | Unclassified (n=79) | | Classified (n=14) | | Unclassified (n=17) | | Classified (n=53) | | Unclassified (n=41) | | Classified (n=26) | | Unclassified (n=9) | | Classified (n=21) | | Unclassified (n=12) | |
| | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value | Statistics | Statistics | Odds ratio (95% CI) | P value |
| Major molecular features | | | | | | | | | | | | | | | | | | | | |
| <i>CIMP-cluster</i> | n=86 17% 37% 45% | n=32 19% 22% 59% | | 0.26 | n=11 45% 36% 18% | n=5 40% 20% 40% | | 0.647 | n=40 5% 10% 45% 29% | n=20 2% 25% 50% | | 0.315 | n=24 33% 38% 29% | n=5 40% 0% 60% | | 0.321 | n=11 0% 9% 50% | n=2 0% 50% 50% | | 0.295 |
| <i>Microsatellite status</i> | n=121 98% 2% | n=60 100% 0% | 0 (0.4,886) | 0.552 | n=19 84% 16% | n=12 100% 0% | 0 (0.3,791) | 0.265 | n=51 100% 0% | n=22 100% 0% | 0 (0,Inf) | 1 | n=30 100% 0% | n=8 100% 0% | 0 (0,Inf) | 1 | n=21 100% 0% | n=8 100% 0% | 0 (0,Inf) | 1 |
| Selected mutations | | | | | | | | | | | | | | | | | | | | |
| <i>APC mut status</i> | n=121 10% 90% | n=60 5% 95% | 2.084 (0.533,11.971) | 0.392 | n=19 37% 63% | n=12 0% 100% | Inf (1.106,Inf) | 0.026 | n=51 2% 98% | n=22 3% 97% | 0.624 (0.008,50.222) | 1 | n=30 10% 90% | n=8 25% 75% | 0.346 (0.031,4.981) | 0.279 | n=21 5% 95% | n=8 0% 100% | Inf (0.01,Inf) | 1 |
| <i>BRAF mut status</i> | n=121 98% 2% | n=60 100% 0% | 0 (0.4,886) | 0.552 | n=19 84% 16% | n=12 100% 0% | 0 (0.3,791) | 0.265 | n=51 100% 0% | n=22 100% 0% | 0 (0,Inf) | 1 | n=30 100% 0% | n=8 100% 0% | 0 (0,Inf) | 1 | n=21 100% 0% | n=8 100% 0% | 0 (0,Inf) | 1 |
| <i>KRAS mut status</i> | n=121 48% 52% | n=60 43% 57% | 1.203 (0.617,2.36) | 0.636 | n=19 21% 79% | n=12 50% 50% | 0.28 (0.041,1.667) | 0.127 | n=51 37% 63% | n=22 50% 50% | 1.674 (0.625,4.531) | 0.265 | n=30 33% 67% | n=8 25% 75% | 1.485 (0.211,117.637) | 1 | n=21 57% 43% | n=8 25% 75% | 3.812 (0.518,47.338) | 0.215 |
| <i>TP53 mut status</i> | n=121 20% 80% | n=60 13% 87% | 1.604 (0.64,4.433) | 0.309 | n=19 26% 74% | n=12 8% 92% | 3.78 (0.346,202.168) | 0.363 | n=51 14% 86% | n=22 12% 88% | 1.112 (0.254,5.67) | 1 | n=30 23% 77% | n=8 0% 100% | Inf (0.39,Inf) | 0.307 | n=21 24% 76% | n=8 38% 62% | 0.534 (0.068,4.669) | 0.646 |