**Supplementary Table S2. Clinical outcomes according to HER2, MMR, and CPS status**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Anti-PD1 monotherapy cohort | | | REGONIVO plus LENPEM cohort | | |
|  |  | ORR (%) | 95% CI | *P*-value | ORR (%) | 95% CI | *P*-value |
| HER2 | positive | 10 | 3–29 |  | 46% | 17–77 |  |
|  | negative | 19 | 12–29 | 0.3108 | 61% | 44–75 | 0.3727 |
| MMR | Deficient | 62 | 36–82 |  | 50% | 1–99 |  |
|  | Proficient | 11 | 6–20 | 0.0001 | 58% | 43–71 | 0.8297 |
| PD-L1 CPS | ≥1 | 20 | 12–30 |  | 76% | 57–90 |  |
|  | <1 | 0 | 0–18 | 0.9904 | 38% | 19–59 | 0.0062 |
|  |  | median PFS  (months) | 95% CI | *P*-value | median PFS  (months) | 95% CI | *P*-value |
| HER2 | positive | 1.8 | 0.9 to 3.0 |  | 7.2 | 2.0 to 17.1 |  |
|  | negative | 2.0 | 1.6 to 2.3 | 0.3419 | 7.0 | 5.4 to 10.4 | 0.6572 |
| MMR | Deficient | 24.1 | 3.7 to not reached |  | 7.2 | 4.6 to unpredictable |  |
|  | Proficient | 1.8 | 1.4 to 2.2 | <0.0001 | 7.0 | 5.4 to 9.7 | 0.6032 |
| PD-L1 CPS | ≥1 | 1.9 | 1.4 to 2.3 |  | 9.8 | 2.6 to 7.4 |  |
|  | <1 | 2.2 | 1.2 to 3.0 | 0.5540 | 4.7 | 6.9 to 13.8 | 0.0857 |
|  |  | median OS  (months) | 95% CI | *P*-value | median OS  (months) | 95% CI | *P*-value |
| HER2 | positive | 10.5 | 9.0 to 19.6 |  | 12.4 | 4.3 to unpredictable |  |
|  | negative | 6.6 | 5.0 to 9.4 | 0.1704 | 17.8 | 10.5 to 24.5 | 0.9112 |
| MMR | Deficient | 25.3 | 5.4 to not reached |  | 20.0 | 15.5 to unpredictable |  |
|  | Proficient | 7.1 | 5.1 to 10.1 | 0.0039 | 15.6 | 10.5 to 25.6 | 0.8097 |
| PD-L1 CPS | ≥1 | 7.7 | 5.1 to 10.5 |  | 18.6 | 12.4 to 27.2 |  |
|  | <1 | 6.0 | 3.4 to 10.9 | 0.2594 | 10.4 | 5.0 to 24.5 | 0.2037 |

Abbreviations: REGONIVO, Regorafenib plus nivolumab; LENPEM, Lenvatinib plus pembrolizumab; ORR, objective response rate; PFS, progression-free survival; OS, overall survival; HER2, human epidermal growth factor receptor 2; MMR, mismatch repair; CPS, combined positive score.