Supplementary Table 2. Multivariate analyses for RFS as a sensitivity analysis of the MSS/MSI-L subset

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Standard model (Prespecified 11 factors) |  | Tested model 1 (11 factors and Gradeconv) |  | Tested model 2(11 factors and GradePOR) |
| Parameter | Category |  | HR (95% CI) | *P* value |  | HR (95% CI) | *P* value |  | HR (95% CI) | *P* value |
| Sex | Female |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | Male |  | 1·22 (0·85–1·74) | 0·277 |  | 1·20 (0·84–1·72) | 0·310 |  | 1·18 (0·83–1·69) | 0·362 |
| Age (years) | ≤70 |  | 1 |  |  | 1 |  |  |  |  |
| 　 | 71–80 |  | 1·46 (1·03–2·07) | 0·032 |  | 1·46 (1·03–2·06) | 0·035 |  | 1·47 (1·04–2·08) | 0·031 |
| Tumour location | Right-sided colon |  | 1 |  |  | 1 |  |  | 1 |  |
|  | Left-sided colon |  | 1·05 (0·72–1·54) | 0·789 |  | 1·05 (0·72–1·54) | 0·785 |  | 1·06 (0·72–1·54) | 0·779 |
| 　 | Rectosigmoid |  | 1·18 (0·74–1·87) | 0·484 |  | 1·17 (0·74–1·87) | 0·499 |  | 1·19 (0·75–1·89) | 0·460 |
| No. of LN examined | ≥12 |  | 1 |  |  | 1 |  |  | 1 |  |
|  | <12 |  | 1·30 (0·89–1·91) | 0·177 |  | 1·29 (0·88–1·90) | 0·189 |  | 1·28 (0·87–1·89) | 0·208 |
| Size of tumour | <50 mm |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | ≥50 mm |  | 1·33 (0·94–1·89) | 0·107 |  | 1·33 (0·94–1·88) | 0·107 |  | 1·30 (0·91–1·84) | 0·147 |
| T-stage | T3 |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | T4 |  | 2·30 (1·60–3·30) | <0·001 |  | 2·33 (1·62–3·35) | <0·001 |  | 2·23 (1·55–3·21) | <0·001 |
| Lymphatic invasion | Negative  |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | Positive |  | 0·98 (0·69–1·39) | 0·906 |  | 0·99 (0·70–1·40) | 0·948 |  | 0·98 (0·69–1·38) | 0·892 |
| Venous invasion | Negative |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | Positive |  | 1·01 (0·7–1·44) | 0·974 |  | 1·00 (0·69–1·43) | 0·982 |  | 1·04 (0·72–1·49) | 0·845 |
| Preoperative CEA  | ≤5·0 ng/ml |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | >5·0 ng/ml |  | 1·47 (1·04–2·08) | 0·031 |  | 1·46 (1·03–2·07) | 0·034 |  | 1·43 (1·01–2·03) | 0·043 |
| Treatment arm | Surgery-alone |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | UFT |  | 0·90 (0·64–1·25) | 0·517 |  | 0·89 (0·64–1·25) | 0·499 |  | 0·87 (0·63–1·22) | 0·426 |
| Tumour budding | BD1 |  | 1 |  |  | 1 |  |  | 1 |  |
|  | BD2 |  | 1·49 (0·94–2·36) | 0·089 |  | 1·50 (0·95–2·37) | 0·085 |  | 1·25 (0·70–2·23) | 0·453 |
|  | BD3 |  | 2·86 (1·84–4·43) | <0·001 |  | 2·81 (1·81–4·37) | <0·001 |  | 1·98 (1·09–3·60) | 0·026 |
| Gradeconv | G1 |  | **–** | **–** |  | 1 |  |  | **–** | **–** |
|  | G2 |  | **–** | **–** |  | 1·19 (0·84–1·68) | 0·332 |  | **–** | **–** |
|  | G3 |  | **–** | **–** |  | 1·11 (0·34–3·57) | 0·868 |  | **–** | **–** |
| GradePOR | G1 |  | **–** | **–** |  | **–** | **–** |  | 1 |  |
|  | G2 |  | **–** | **–** |  | **–** | **–** |  | 1·31 (0·72–2·40) | 0·377 |
|  | G3 |  | **–** | **–** |  | **–** | **–** |  | 2·14 (1·07–4·29) | 0·032 |
| Test to investigate the addition of Gradeconv or GradePOR to standard model\* |
| Wald test for ordered grade (d.f. = 1) |  | **–** |  |  | 1·15 (0·84–1·58) | 0·371 |  | 1·51 (1·09–2·10) | 0·014 |
| Wald test for grade with non-G3/G3 (d.f. = 1） |  | **–** |  |  | 1·00 (0·32–3·19) | 0·995 |  | 1·67 (1·09–2·57) | 0·019 |

RFS, relapse-free survival; LN, lymph node; MSS, microsatellite stable; MSI, microsatellite instability; UFT, tegafur–uracil; Gradeconv, conventional tumour grade based on the predominant histological type; GradePOR, tumour grade based on the extent of the poorly differentiated component; HR, hazard ratio; CI, confidence interval; DF, degrees of freedom.

\*Estimated model was constructed with all variables included in the standard model and a tumor grading system (Gradeconv or GradePOR).