Supplementary Table 1. Multivariate analyses for RFS as sensitivity analysis of the full analysis set

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | Standard model (Prespecified 12 factors) |  | Tested model 1 (12 factors and Gradeconv) |  | Tested model 2(12 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 |  | 1·20 (0·85–1·70) | 0·307 |  | 1·18 (0·83–1·68) | 0·345 |  | 1·17 (0·82–1·66) | 0·386 |
| Age (years) | ≤70 |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | 71–80 |  | 1·50 (1·07–2·11) | 0·020 |  | 1·49 (1·06–2·1) | 0·023 |  | 1·51 (1·07–2·12) | 0·019 |
| Tumour location | Right-sided colon |  | 1 |  |  | 1 |  |  | 1 |  |
|  | Left-sided colon |  | 1·07 (0·74–1·55) | 0·729 |  | 1·06 (0·73–1·54) | 0·761 |  | 1·07 (0·74–1·56) | 0·712 |
| 　 | Rectosigmoid |  | 1·19 (0·75–1·88) | 0·471 |  | 1·16 (0·73–1·85) | 0·524 |  | 1·20 (0·75–1·89) | 0·447 |
| No. of LN examined | ≥12 |  | 1 |  |  | 1 |  |  | 1 |  |
|  | <12 |  | 1·27 (0·87–1·86) | 0·222 |  | 1·26 (0·86–1·85) | 0·231 |  | 1·25 (0·85–1·83) | 0·261 |
| Size of tumour | <50 mm |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | ≥50 mm |  | 1·31 (0·93–1·85) | 0·121 |  | 1·32 (0·94–1·86) | 0·114 |  | 1·28 (0·91–1·81) | 0·163 |
| T-stage | T3 |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | T4 |  | 2·38 (1·66–3·40) | <0·001 |  | 2·40 (1·68–3·44) | <0·001 |  | 2·32 (1·62–3·32) | <0·001 |
| Lymphatic invasion | Negative  |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | Positive |  | 0·97 (0·69–1·37) | 0·876 |  | 0·98 (0·70–1·39) | 0·919 |  | 0·97 (0·68–1·37) | 0·847 |
| Venous invasion | Negative |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | Positive |  | 1·02 (0·71–1·45) | 0·929 |  | 1·01 (0·70–1·44) | 0·971 |  | 1·05 (0·73–1·50) | 0·809 |
| Preoperative CEA  | ≤5.0 ng/ml |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | >5.0 ng/ml |  | 1·42 (1·00–2·01) | 0·048 |  | 1·41 (1·00–1·99) | 0·053 |  | 1·39 (0·98–1·96) | 0·063 |
| MSI status | MSS/MSI-low |  | 1 |  |  | 1 |  |  | 1 |  |
|  | MSI-high |  | 0·26 (0·08–0·84) | 0·024 |  | 0·30 (0·09–1·01) | 0·052 |  | 0·22 (0·07–0·72) | 0·012 |
| Treatment arm | Surgery-alone |  | 1 |  |  | 1 |  |  | 1 |  |
| 　 | UFT |  | 0·90 (0·65–1·25) | 0·527 |  | 0·89 (0·64–1·24) | 0·494 |  | 0·88 (0·63–1·22) | 0·445 |
| Tumour budding | BD1 |  | 1 |  |  | 1 |  |  | 1 |  |
|  | BD2 |  | 1·53 (0·97–2·42) | 0·068 |  | 1·53 (0·97–2·42) | 0·068 |  | 1·30 (0·73–2·31) | 0·375 |
|  | BD3 |  | 2·89 (1·87–4·48) | <0·001 |  | 2·85 (1·84–4·41) | <0·001 |  | 2·07 (1·14–3·73) | 0·016 |
| Gradeconv | G1 |  | **–** | **–** |  | 1 |  |  | **–** | **–** |
|  | G2 |  | **–** | **–** |  | 1·15 (0·82–1·61) | 0·435 |  | **–** | **–** |
|  | G3 |  | **–** | **–** |  | 0·75 (0·22–2·52) | 0·636 |  | **–** | **–** |
| GradePOR | G1 |  | **–** | **–** |  | **–** | **–** |  | 1 |  |
|  | G2 |  | **–** | **–** |  | **–** | **–** |  | 1·30 (0·71–2·36) | 0·397 |
|  | G3 |  | **–** | **–** |  | **–** | **–** |  | 2·02 (1·02–4·03) | 0·045 |
| Test to investigate the addition of Gradeconv or GradePOR to standard model\* |
| Wald test for ordered grade (d.f. = 1) |  | **–** |  |  | 1·07 (0·79–1·45) | 0·657 |  | 1·46 (1·06–2·03) | 0·023 |
| Wald test for grade with non-G3/G3 (d.f. = 1） |  | **–** |  |  | 0·70 (0·21–2·32) | 0·555 |  | 1·60 (1·05–2·45) | 0·030 |

RFS, relapse-free survival; LN, lymph node; MSI, microsatellite instability; MSS, microsatellite stable; 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).