

**Supplementary Table 1.** Incidences and subhazard ratios of ischemic stroke or TIA in head and neck cancer patient with and without statin during radiotherapy stratified by demographics and comorbidity in the competing-risk regression model

| Ischemic stroke or TIA   | Statin |       |       |       |       |       | Crude SHR<br>(95% CI)         | Adjusted SHR <sup>†</sup><br>(95% CI) |  |  |
|--------------------------|--------|-------|-------|-------|-------|-------|-------------------------------|---------------------------------------|--|--|
|                          | No     |       |       | Yes   |       |       |                               |                                       |  |  |
|                          | Event  | PY    | Rate* | Event | PY    | Rate* |                               |                                       |  |  |
| Overall                  | 45     | 2,708 | 16.6  | 64    | 3,090 | 20.7  | 1.45 (1.04–2.00) <sup>‡</sup> | 1.35 (0.95–1.91)                      |  |  |
| Age group (yr)           |        |       |       |       |       |       |                               |                                       |  |  |
| ≤49                      | 4      | 444   | 9.00  | 9     | 511   | 17.6  | 1.12 (0.70–1.80)              | 1.15 (0.67–1.95)                      |  |  |
| 50–64                    | 23     | 1,430 | 16.1  | 25    | 1,550 | 16.1  | 0.77 (0.62–0.97) <sup>‡</sup> | 0.83 (0.65–1.05)                      |  |  |
| ≥65                      | 18     | 834   | 21.6  | 30    | 1,028 | 29.2  | 0.69 (0.53–0.91) <sup>§</sup> | 0.74 (0.56–0.99) <sup>‡</sup>         |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.87                                  |  |  |
| Gender                   |        |       |       |       |       |       |                               |                                       |  |  |
| Women                    | 3      | 371   | 8.08  | 9     | 453   | 19.9  | 4.37 (0.70–27.5)              | 4.19 (1.03–17.0) <sup>‡</sup>         |  |  |
| Men                      | 42     | 2,337 | 18.0  | 55    | 2,636 | 20.9  | 1.15 (0.80–1.65)              | 1.02 (0.69–1.52)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.24                                  |  |  |
| Comorbidity              |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 0      | 44    | 0.00  | 1     | 52    | 19.3  | -                             | -                                     |  |  |
| Yes                      | 45     | 2,664 | 16.9  | 63    | 3,038 | 20.7  | 1.23 (0.86–1.76)              | 1.09 (0.74–1.61)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | <0.001                                |  |  |
| Medication               |        |       |       |       |       |       |                               |                                       |  |  |
| Aspirin                  |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 4      | 413   | 9.68  | 3     | 345   | 8.69  | -                             | -                                     |  |  |
| Yes                      | 41     | 2,295 | 17.9  | 61    | 2,744 | 22.2  | 1.17 (0.80–1.71)              | 1.10 (0.74–1.64)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.28                                  |  |  |
| Clopidogrel              |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 42     | 2,497 | 16.8  | 50    | 2,370 | 21.1  | 1.17 (0.79–1.74)              | 1.00 (0.63–1.57)                      |  |  |
| Yes                      | 3      | 211   | 14.2  | 14    | 719   | 19.5  | 2.00 (0.56–7.09)              | 3.85 (0.36–41.7)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.26                                  |  |  |
| ACEI                     |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 11     | 1,171 | 9.39  | 15    | 1,090 | 13.8  | 2.07 (0.71–6.03)              | 1.53 (0.46–5.07)                      |  |  |
| Yes                      | 34     | 1,537 | 22.1  | 49    | 1,999 | 24.5  | 1.13 (0.74–1.74)              | 1.10 (0.70–1.71)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.26                                  |  |  |
| ARB                      |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 22     | 1,469 | 15.0  | 34    | 1,276 | 26.7  | 2.16 (1.09–4.28) <sup>‡</sup> | 1.89 (0.92–3.89)                      |  |  |
| Yes                      | 23     | 1,239 | 18.6  | 30    | 1,814 | 16.5  | 0.93 (0.51–1.70)              | 0.74 (0.36–1.51)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.36                                  |  |  |
| Warfarin                 |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 44     | 2,607 | 16.9  | 61    | 2,879 | 21.2  | 1.45 (1.00–2.09) <sup>‡</sup> | 1.31 (0.88–1.94)                      |  |  |
| Yes                      | 1      | 101   | 9.92  | 3     | 210   | 14.3  | -                             | -                                     |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               | 0.10                                  |  |  |
| Treatment                |        |       |       |       |       |       |                               |                                       |  |  |
| Surgery                  | 37     | 2,187 | 16.9  | 56    | 2,513 | 22.3  | 1.34 (0.90–1.99)              | 1.32 (0.86–2.01)                      |  |  |
| No                       | 8      | 521   | 15.3  | 8     | 577   | 13.9  | 0.81 (0.23–2.91)              | 0.85 (0.27–2.61)                      |  |  |
| Yes                      |        |       |       |       |       |       |                               | 0.23                                  |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       |                               |                                       |  |  |
| Chemotherapy             |        |       |       |       |       |       |                               |                                       |  |  |
| No                       | 9      | 853   | 10.6  | 24    | 1,031 | 23.3  | 2.53 (0.99–6.44)              | 2.05 (0.74–5.69)                      |  |  |

**Supplementary Table 1.** Continued

| Ischemic stroke or TIA   | Statin |       |       |       |       |       | Crude SHR<br>(95% CI) | Adjusted SHR <sup>†</sup><br>(95% CI) |  |  |
|--------------------------|--------|-------|-------|-------|-------|-------|-----------------------|---------------------------------------|--|--|
|                          | No     |       |       | Yes   |       |       |                       |                                       |  |  |
|                          | Event  | PY    | Rate* | Event | PY    | Rate* |                       |                                       |  |  |
| Yes                      | 36     | 1,855 | 19.4  | 40    | 2,059 | 19.4  | 1.11 (0.69–1.77)      | 1.03 (0.58–1.84)                      |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       | 0.12                  |                                       |  |  |
| Cetuximab                |        |       |       |       |       |       |                       |                                       |  |  |
| No                       | 45     | 2,689 | 16.7  | 64    | 3,042 | 21.0  | 1.27 (0.89–1.81)      | 1.13 (0.76–1.67)                      |  |  |
| Yes                      | 0      | 19    | 0.00  | 0     | 47    | 0.00  | -                     | -                                     |  |  |
| <i>P</i> for interaction |        |       |       |       |       |       | 0.82                  |                                       |  |  |

TIA, transient ischemic attack; PY, person-year; SHR, subhazard ratio; CI, confidence interval; ACEI, angiotensin-converting-enzyme inhibitor; ARB, angiotensin II receptor blocker.

\*Incidence rate per 1,000 person-years; <sup>†</sup>Variable found to be significant in the Table 1 were further examined in the multivariable analysis (use of aspirin, clopidogrel, ACEI, and ARB); <sup>‡</sup>*P*<0.05; <sup>§</sup>*P*<0.01.