**Supplemental material**

**KRAS Mutation Status, Comorbidity, and Mortality in Patients with Metastatic Colorectal Cancer in Denmark**

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**Supplemental Table 1.** **Descriptive characteristics of 7,245 Danish patients with metastatic colorectal cancer by KRAS status, 2009-2013.**

|  | **KRAS wild-type****n (%)** | **KRAS mutant1****n (%)** | **No KRAS test****n (%)** | **All****n (%)** |
| --- | --- | --- | --- | --- |
| **Number of patients** | 1,389 | 1,082 | 4,774 | 7,245 |
| **Sex** |  |  |  |  |
| Female | 549 (39.5) | 465 (43.0) | 2,265 (47.4) | 3,279 (45.3) |
| Male | 840 (60.5) | 617 (57.0) | 2,509 (52.6) | 3,966 (54.7) |
| **Median age at diagnosis (interquartile range)** | 66.7 (59.6, 72.6) | 66.4 (59.7, 72.3) | 73.0 (64.8, 80.5) | 70.3 (62.7, 78.1) |
| **Age group** |  |  |  |  |
| <50 years | 104 (7.5) | 87 (8.0) | 198 (4.1) | 389 (5.4) |
| 50-59 years | 261 (18.8) | 193 (17.8) | 495 (10.4) | 949 (13.1) |
| 60-69 years | 532 (38.3) | 437 (40.4) | 1,250 (26.2) | 2,219 (30.6) |
| >=70 years | 492 (35.4) | 365 (33.7) | 2,831 (59.3) | 3,688 (50.9) |
| **mCRC diagnosis type** |  |  |  |  |
| Primary mCRC | 896 (64.5) | 695 (64.2) | 2,947 (61.7) | 4,538 (62.6) |
| mCRC at recurrence | 493 (35.5) | 387 (35.8) | 1,827 (38.3) | 2,707 (37.4) |
| **Location of the primary tumor** |  |  |  |  |
| Proximal to splenic flexure | 362 (26.1) | 313 (28.9) | 1,475 (30.9) | 2,150 (29.7) |
| Splenic flexure and distal colon | 470 (33.8) | 319 (29.5) | 1,305 (27.3) | 2,094 (28.9) |
| Unspecified/multiple sites  | 67 (4.7) | 50 (4.6) | 460 (9.6) | 577 (8.0) |
| Rectum  | 490 (35.3) | 400 (37.0) | 1,534 (32.1) | 2,424 (33.5) |
| **Comorbidity Index score** |  |  |  |  |
| No comorbidity (CCI score =0) | 937 (67.5) | 747 (69.0) | 2,772 (58.1) | 4,456 (61.5) |
| Low comorbidity (CCI score =1-2) | 385 (27.7) | 287 (26.5) | 1,586 (33.2) | 2,258 (31.2) |
| Moderate/severe comorbidity (CCI score >=3) | 67 (4.8) | 48 (4.4) | 416 (8.7) | 531 (7.3) |
| **Specific comorbidities** |  |  |  |  |
| Myocardial infarction | 66 (4.8) | 48 (4.4) | 292 (6.1) | 406 (5.6) |
| Congestive heart failure | 50 (3.6) | 32 (3.0) | 307 (6.4) | 389 (5.4) |
| Peripheral vascular disease | 54 (3.9) | 46 (4.3) | 324 (6.8) | 424 (5.9) |
| Cerebrovascular disease | 103 (7.4) | 81 (7.5) | 545 (11.4) | 729 (10.1) |
| Dementia | 13 (0.9) | 2 (0.2) | 80 (1.7) | 95 (1.3) |
| Chronic pulmonary disease | 104 (7.5) | 81 (7.5) | 511 (10.7) | 696 (9.6) |
| Connective tissue disease | 45 (3.2) | 28 (2.6) | 185 (3.9) | 258 (3.6) |
| Ulcer disease | 76 (5.5) | 45 (4.2) | 306 (6.4) | 427 (5.9) |
| Mild liver disease | 15 (1.1) | 13 (1.2) | 74 (1.6) | 102 (1.4) |
| Diabetes type I and II | 106 (7.6) | 87 (8.0) | 450 (9.4) | 643 (8.9) |
| Hemiplegia | 3 (0.2) | 2 (0.2) | 25 (0.5) | 30 (0.4) |
| Moderate to severe renal disease | 22 (1.6) | 14 (1.3) | 127 (2.7) | 163 (2.2) |
| Diabetes with end-organ damage | 44 (3.2) | 31 (2.9) | 201 (4.2) | 276 (3.8) |
| Moderate to severe liver disease | 5 (0.4) | 6 (0.6) | 18 (0.4) | 29 (0.4) |
| AIDS | 0 (0.0) | 0 (0.0) | <5 (0.0) | <5 (0.0) |
| **KRAS mutation** | NA |  | NA |  |
| KRAS codon 12 (exon 2) |  | 567 (52.4) |  | 567 (52.4) |
| KRAS mutation codon 13 (exon 2) |  | 121 (11.2) |  | 121 (11.2) |
| KRAS mutation codon 61 (exon 3) |  | 4 (0.4) |  | 4 (0.4) |
| KRAS mutation codon 58, 59, 117, 147 |  | 5 (0.5) |  | 5 (0.5) |
| KRAS mutation present but not specified |  | 387 (35.8) |  | 387 (35.8) |
| 1Mutation in codon 12 (exon 2), codon 13 (exon 2), codon 61 (exon 3), codon 58, 59, 117, 147, and mutation not specified. |

**Supplemental Table 2. One-year standardized mortality rates and adjusted mortality rate ratios associated with KRAS mutation status by comorbidity burden among 2,471 Danish patients with metastatic colorectal cancer diagnosed between 2009 and 2013 and tested for KRAS through 2014.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Patients at risk** | **Deaths** | **Person-years** | **Standardized mortality rate (95%CI)a per 1000 person-years** | **aHR (95%CI)b** | **Interaction contrast (95%CI), per 1000 person-years** |
| **No comorbidity (CCI=0)** |  |  |  |  |  |  |
| Wild type | 937 | 662 | 681.333 | 985.65 (911.94, 1063.8) | Ref | Ref |
| Mutant | 747 | 509 | 541.648 | 958.87 (876.69, 1046.9) | 1.00 (0.89-1.12) |  |
| **Low comorbidity (CCI=1-2)** |  |  |  |  |  |  |
| Wild type | 385 | 269 | 278.657 | 952.88 (841.05, 1076.7) | Ref |  |
| Mutant | 287 | 195 | 207.357 | 903.54 (778.71, 1045.2) | 0.98 (0.81, 1.17) | -22.6 (-22.4, -22.8) |
| **Moderate to severe comorbidity (CCI ≥3)** |  |  |  |  |  |  |
| Wild type | 67 | 58 | 41.439 | 1664.5 (1112.6, 3629.4) | Ref |  |
| Mutant | 48 | 36 | 33.591 | 1088.6 (722.33-1637.2) | 0.83 (0.54, 1.28) | -549.1 (-548.1, -550.2) |

aStandardized to the sex- and age distribution of the baseline population of all mCRC patients with a KRAS test.
bAdjusted for sex, age, and index year.