

Supplemental Tables for:

Muscle Loss is Associated with Overall Survival in Patients with Metastatic Colorectal Cancer Independent of Tumor Mutational Status and Weight Loss Till Dominik Best et al.

Supplemental Table 1. Days Between Baseline Scan and 3-, 6-, and 12-month Follow-up Scans. To account for the fluctuation of scan intervals we performed linear interpolation to calculate percent change from baseline to exactly 3-, 6- and 12-month follow-up (see *Patients and Methods*).

CT, computed tomography; SD, standard deviation.

| Characteristic | N | mean ± SD | minimum | maximum |
|--|-----|--------------|---------|---------|
| Baseline CT scan to 3-month follow-up, days | 193 | 89 ± 20 | +52 | +133 |
| Baseline CT scan to 6-month follow-up, days | 164 | 181 ± 22 | +140 | +227 |
| Baseline CT scan to 12-month follow-up, days | 135 | 362 ± 22 | +320 | +409 |
| basenne C1 scan to 12-month follow-up, days | 155 | 302 ± 22 | +320 | +409 |

Supplemental Table 2. Patient Characteristics at Time of Metastatic Diagnosis by Availability of Scans at Follow-up Time Points.

n, number; SD, standard deviation.

| Characteristic | 3-month follow-up 6-month follow-up 12-month | | 12-month follow-up |
|----------------|--|-------------|--------------------|
| | n = 193 | n = 164 | n = 135 |
| Age, years | | | |
| Mean ± SD | 58.9 ± 13.1 | 59.3 ± 13.5 | 58.0 ± 13.1 |

| Median [25 th , 75 th percentile] | 59 [50, 68] | 60 [50, 69] | 58 [48, 68] |
|---|-------------|-----------------|-------------|
| Minimum - maximum | 26 - 92 | 26 - 92 | 32 - 92 |
| Sex, n (%) | | | |
| Male | 103 (53.4%) | 89 (54.3%) | 70 (51.9%) |
| Female | 90 (46.6%) | 75 (45.7%) | 65 (48.1%) |
| Race and ethnicity, n (%) | | | |
| Caucasian | 174 (90.2%) | 148 (90.2%) | 122 (90.4%) |
| Asian | 8 (4.1%) | 7 (4.3%) | 6 (4.4%) |
| African American | 2 (1.0%) | 2 (1.2%) | 1 (0.7%) |
| Hispanic or Latino | 0 (0.0%) | 1 (0.6%) | 1 (0.7%) |
| Other | 3 (1.5%) | 2 (1.2%) | 2 (1.5%) |
| Unavailable | 6 (3.1%) | 4 (2.4%) | 3 (2.2%) |
| Body weight at metastatic diagnosis, kg | | | |
| Mean ± SD | 80.1 ± 19.7 | 80.0 ± 19.8 | 79.6 ±19.4 |
| Median [25 th , 75 th percentile] | 77 [66, 91] | 78 [66, 91] | 77 [66, 89] |
| Minimum - maximum | 44 - 153 | 44 - 143 | 44 - 153 |

| Height, cm | | | |
|---|------------------|------------------|------------------|
| Mean ± SD | 169.5 ± 10.2 | 169.7 ± 10.4 | 169.0 ± 10.7 |
| Median [25 th , 75 th percentile] | 168 [163, 178] | 169 [163, 178] | 168 [162, 178] |
| Minimum - maximum | 145 - 196 | 145 - 193 | 145 - 196 |
| Body mass index, kg/m ² | | | |
| Mean ± SD | 27.5 ± 5.4 | 27.5 ± 5.5 | 27.6 ± 5.5 |
| Median [25 th , 75 th percentile] | 27 [24, 30] | 27 [24, 30] | 27 [24, 31] |
| Minimum - maximum | 17 - 42 | 17 - 42 | 17 - 44 |
| Organ of cancer origin, n (%) | | | |
| Colon | 148 (76.7%) | 122 (74.3%) | 100 (74.1%) |
| Rectum | 45 (23.3%) | 42 (25.6%) | 35 (25.9%) |
| Location of tumor, n (%) | | | |
| Left | 123 (63.7%) | 105 (64.0%) | 90 (66.7%) |
| Right | 57 (29.5%) | 50 (30.5%) | 39 (28.9%) |
| Transverse | 13 (6.7%) | 9 (5.5%) | 6 (4.4%) |
| Tumor mutation, n (%) | | | |

| Wild type | 78 (40.4%) | 72 (43.9%) | 67 (49.6%) |
|---|---------------|---------------|---------------|
| KRAS | 79 (40.9%) | 59 (36.0%) | 48 (35.6%) |
| NRAS | 6 (3.1%) | 6 (3.7%) | 5 (3.7%) |
| BRAF | 30 (15.5%) | 27 (16.5%) | 15 (11.1%) |
| Therapy type of first treatment, n (%) | | | |
| Standard chemotherapy | 185 (95.9%) | 156 (95.16%) | 125 (92.6%) |
| Targeted + standard chemotherapy | 8 (4.1%) | 8 (4.9%) | 10 (7.4%) |
| No. of lines of systemic therapy after | | | |
| metastatic diagnosis, n | | | |
| Mean ± SD | 2.3 ± 1.5 | 2.4 ± 1.5 | 2.5 ± 1.6 |
| Median [25 th , 75 th percentile] | 2 [1, 3] | 2 [1, 3] | 2 [1, 3] |
| Minimum - maximum | 0 - 9 | 0 - 9 | 0 - 9 |

Supplemental Table 3. Univariate survival estimates for skeletal muscle loss at 3 months, weight loss at 3 months, and tumor mutational status.

CI, confidence interval; n, number; OS, overall survival; SD, standard deviation.

| | Median OS (95% CI), | 25 th percentile OS (95% CI), | 75 th percentile OS (95% CI), | 5-year-survival rate |
|----------------------------------|---------------------|--|--|----------------------|
| | in months | in months | in months | (95% CI) |
| Skeletal muscle loss at 3 months | | | | |
| >5% skeletal muscle loss | 27 (16 - 42) | 11 (7 - 16) | 62 (42 - NA) | 25% (13% - 39%) |
| ≤5% skeletal muscle loss | 44 (61 - NA) | 24 (32 - 51) | 24 (22 - 28) | 37% (27% - 39%) |
| Weight loss at 3 months | | | | |
| >5% weight loss | 42 (20 - 56) | 14 (8 - 23) | NA (49.8 - NA) | 31% (15% - 48%) |
| ≤5% weight loss | 45 (34 - 61) | 25 (18 - 31) | 72.5 (61.0 - NA) | 39% (27% - 51%) |
| Tumor mutational status | | | | |
| wild-type | 50 (35 - 62) | 28 (22 - 35) | 80 (62 - NA) | 14% (3% - 32%) |
| RAS-mutant | 34 (26 - 51) | 21 (14 - 26) | 71 (51 - NA) | 36% (23% - 48%) |
| BRAF-mutant | 19 (11 - 28) | 11 (7 - 14) | 43 (24 - NA) | 40% (26% - 53%) |

Supplemental Table 4. Multivariable Model Demonstrating the Relationship Between >5% Loss of Body Composition and

Tumor Mutation Status. Body composition change was evaluated at scans obtained 3, 6, and 12 months from metastatic diagnosis.

Estimates are adjusted for potential confounders including age, sex, and baseline skeletal muscle or baseline body weight. **Table 3** is a shortened version of this table.

CI, confidence interval; OR, odds ratio; WT, wild type.

| Timepoint | Covariable | >5% body weight loss | | >5% skeletal musc | le loss |
|-----------|------------|----------------------|---------|-------------------|---------|
| | | OR (95% CI) | P value | OR (95% CI) | P value |

| | ıtation | | | | |
|--------------------|-----------------------------------|-----------------------|-------|----------------------------|-------|
| E | BRAF-mutant vs WT | 1.543 (0.521 - 4.568) | .4332 | 1.786 (0.727 - 4.387) | .2057 |
| K | RAS-mutant vs WT | 0.840 (0.366 - 1.926) | .6801 | 0.972 (0.483 - 1.953) | .9355 |
| Age | e, years | | | | |
| ≥ | ≥70 vs <70 | 0.677 (0.243 - 1.889) | .4567 | 0.829 (0.348 - 1.975) | .6720 |
| Sex | ĸ | | | | |
| fe | female vs male | 3.521 (1.510 - 8.210) | .0036 | 1.439 (0.536 - 3.861) | .4698 |
| Bas | seline | | | | |
| b | oody weight | 1.028 (1.007 - 1.048) | .0080 | _ | _ |
| S | skeletal muscle | | _ | 1.008 (0.996 - 1.021) | .2067 |
| Sex for Base | female vs male seline body weight | 3.521 (1.510 - 8.210) | .0036 | 1.439 (0.536 - 3.861) – | ∠. |

| Mutation | | | | |
|-------------------|--|--|--|---|
| BRAF-mutant vs WT | 2.379 (0.778 - 7.274) | .1284 | 3.372 (1.273 - 8.933) | .0144 |
| RAS-mutant vs WT | 1.188 (0.493 - 2.862) | .7016 | 1.114 (0.538 - 2.435) | .7261 |
| Age, years | | | | |
| ≥70 vs <70 | 1.455 (0.560 - 3.783) | .4412 | 0.748 (0.300 - 1.866) | .5341 |
| Sex | | | | |
| female vs male | 3.225 (1.359 - 7.657) | .0079 | 1.376 (0.506 - 3.740) | .5321 |
| Baseline | | | | |
| weight | 1.027 (1.005 - 1.049) | .0159 | _ | _ |
| skeletal muscle | _ | _ | 1.017 (1.004 - 1.031) | .0107 |
| | BRAF-mutant vs WT RAS-mutant vs WT Age, years ≥70 vs <70 Sex female vs male Baseline weight | BRAF-mutant vs WT $2.379 (0.778 - 7.274)$ RAS -mutant vs WT $1.188 (0.493 - 2.862)$ Age , years $2.70 vs < 70$ $2.379 (0.778 - 7.274)$ 3.2862 $2.379 (0.778 - 7.274)$ $2.379 (0.778 - 7.274)$ 3.2862 | $BRAF$ -mutant vs WT $2.379 (0.778 - 7.274)$ $.1284$ RAS -mutant vs WT $1.188 (0.493 - 2.862)$ $.7016$ Age , years $\geq 70 \text{ vs} < 70$ $1.455 (0.560 - 3.783)$ $.4412$ Sex s | BRAF-mutant vs WT 2.379 (0.778 - 7.274) .1284 3.372 (1.273 - 8.933) RAS-mutant vs WT 1.188 (0.493 - 2.862) .7016 1.114 (0.538 - 2.435) Age, years 270 vs < 70 |

| 12-months | Mutation | | | | |
|-----------|-------------------|------------------------|-------|------------------------|-------|
| | BRAF-mutant vs WT | 4.426 (0.982 - 19.957) | .0529 | 5.533 (1.604 - 19.091) | .0068 |
| | RAS-mutant vs WT | 2.217 (0.717 - 6.853) | .1666 | 1.577 (0.667 - 3.727) | .2991 |
| | Age, years | | | | |
| | ≥70 vs <70 | 4.297 (1.166 - 15.835) | .0285 | 0.833 (0.265 - 2.618) | .7538 |
| | Sex | | | | |
| | female vs male | 7.497 (2.299 - 24.326) | .0008 | 2.430 (0.739 - 7.990) | .1437 |
| | Baseline | | | | |
| | weight | 1.025 (0.996 - 1.053) | .0886 | _ | _ |
| | skeletal muscle | - | _ | 1.010 (0.995 - 1.026) | .1910 |
| | | | | | |