**RAS, BRAF and EGFR related genetic mutations as predictive biomarkers in colorectal cancer**

**SUPPLEMENTARY DATA**

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**Table S1. Descriptive statistics of mutation levels (allelic frequencies) of all studied mutations**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **ALL cases included** | | | | | | | |
|  | | **KRAS Q61** | **KRAS G12/G13** | **NRAS Q61** | **NRAS G12/G13** | **BRAF** | **EGFR** |
| LINEAR SCALE | | | | | | | |
| Mean | | 0.72 | 75.76 | 2.81 | 14.84 | 21.58 | 0.23 |
| 95% Confidence Interval for Mean | Lower Bound | 0.57 | 40.74 | -0.56 | -0.72 | 4.52 | -0.15 |
| Upper Bound | 0.87 | 110.77 | 6.18 | 30.39 | 38.65 | 0.60 |
| 5% Trimmed Mean | | 0.69 | 58.35 | 0.45 | 2.59 | 9.84 | 0.00 |
| Median | | 0.82 | 4.95 | 0.00 | 0.76 | 0.00 | 0.00 |
| Variance | | 0.34 | 18377.06 | 170.16 | 3624.54 | 4362.42 | 2.09 |
| Std. Deviation | | 0.58 | 135.56 | 13.04 | 60.20 | 66.05 | 1.44 |
| Minimum | | 0.00 | 0.25 | 0.00 | 0.00 | 0.00 | 0.00 |
| Maximum | | 3.48 | 599.63 | 85.48 | 342.30 | 266.46 | 11.07 |
| Range | | 3.48 | 599.38 | 85.48 | 342.30 | 266.46 | 11.07 |
| Interquartile Range | | 0.96 | 86.94 | 0.86 | 0.88 | 0.04 | 0.00 |
| Skewness | | 1.51 | 1.98 | 5.67 | 4.70 | 3.05 | 7.44 |
| Kurtosis | | 7.30 | 3.44 | 32.42 | 22.25 | 7.97 | 56.54 |
| Percentiles | |  |  |  |  |  |  |
| 25 | | 0.65 | 2.78 | 0.00 | 0.14 | 0.00 | 0.00 |
| 33 | | 0.82 | 3.17 | 0.00 | 0.65 | 0.00 | 0.00 |
| 50 | | 0.90 | 4.95 | 0.00 | 0.76 | 0.00 | 0.00 |
| 67 | | 0.96 | 10.67 | 0.76 | 0.96 | 0.00 | 0.00 |
| 75 | | 0.00 | 89.72 | 0.86 | 1.02 | 0.12 | 0.00 |
| **Mutation-free cases excluded** | | | | | | | |
|  | | **KRAS Q61** | **KRAS G12/G13** | **NRAS Q61** | **NRAS G12/G13** | **BRAF** | **EGFR** |
| LINEAR SCALE | | | | | | | |
| Mean | | 0.99 | 75.76 | 6.25 | 19.78 | 92.50 | 4.51 |
| 95% Confidence Interval for Mean | Lower Bound | 0.85 | 40.74 | -1.30 | 27.3401 | 24.68 | -9.66 |
| Upper Bound | 1.12 | 110.77 | 13.79 | 157.6542 | 147.99 | 18.68 |
| 5% Trimmed Mean | | 0.93 | 58.35 | 2.58 | 5.52 | 87.96 | 0.00 |
| Median | | 0.88 | 4.95 | 0.87 | 0.87 | 22.53 | 1.74 |
| Variance | | 0.20 | 18377.06 | 363.86 | 4760.14 | 12734.88 | 32.54 |
| Std. Deviation | | 0.44 | 135.56 | 19.08 | 68.99 | 112.885 | 5.70 |
| Minimum | | 0.56 | 0.25 | 0.53 | 0.56 | 0.12 | 0.72 |
| Maximum | | 3.48 | 599.63 | 85.48 | 342.30 | 266.46 | 11.07 |
| Range | | 2.92 | 599.38 | 84.95 | 341.74 | 266.34 | 10.35 |
| Interquartile Range | | 0.34 | 86.94 | 0.93 | 0.46 | 233.56 | . |
| Skewness | | 4.33 | 1.98 | 3.71 | 4.01 | .643 | 1.67 |
| Kurtosis | | 23.73 | 3.44 | 13.35 | 15.94 | -1.577 | . |
| Percentiles | |  |  |  |  |  |  |
| 25 | | 0.80 | 2.78 | 0.73 | 0.71 | 0.26 | 0.72 |
| 33 | | 0.82 | 3.17 | 0.77 | 0.75 | 0.32 | 1.05 |
| 50 | | 0.88 | 4.95 | 0.87 | 0.87 | 22.53 | 1.74 |
| 67 | | 0.96 | 10.67 | 1.02 | 1.02 | 172.98 | 8.08 |
| 75 | | 1.15 | 89.72 | 1.66 | 1.17 | 233.82 |  |
| = | | **KRAS Q61** | **KRAS G12/G13** | **NRAS Q61** | **NRAS G12/G13** | **BRAF** | **EGFR** |
| LOG SCALE | | | | | | | |
| Mean | | -0.03 | 1.04 | 0.12 | 0.16 | 0.81 | 0.38 |
| 95% Confidence Interval for Mean | Lower Bound | -0.07 | 0.81 | -0.09 | -.0438 | -0.18 | -1.12 |
| Upper Bound | 0.01 | 1.27 | 0.33 | 1.6555 | 1.51 | 1.89 |
| 5% Trimmed Mean | | -0.04 | 1.03 | 0.05 | 0.05 | 0.81 | . |
| Median | | -0.06 | 0.69 | -0.06 | -0.06 | 0.75 | 0.24 |
| Variance | | 0.02 | 0.80 | 0.28 | 0.47 | 2.16 | 0.37 |
| Std. Deviation | | 0.13 | 0.89 | 0.53 | 0.68 | 1.47 | 0.61 |
| Minimum | | -0.25 | -0.60 | -0.28 | -0.25 | -0.92 | -0.14 |
| Maximum | | 0.54 | 2.78 | 1.93 | 2.53 | 2.43 | 1.04 |
| Range | | 0.79 | 3.38 | 2.21 | 2.79 | 3.35 | 1.19 |
| Interquartile Range | | 0.15 | 1.50 | 0.36 | 0.22 | 2.97 | . |
| Skewness | | 1.85 | 0.64 | 2.80 | 2.83 | 0.00 | 0.99 |
| Kurtosis | | 6.79 | -0.84 | 7.65 | 6.91 | -2.18 | . |
| Percentiles | |  |  |  |  |  |  |
| 25 | | -0.10 | 0.44 | -0.14 | -0.15 | -0.60 | -0.14 |
| 33 | | -0.09 | 0.50 | -0.11 | -0.12 | -0.50 | -0.02 |
| 50 | | -0.06 | 0.69 | -0.06 | -0.06 | 0.75 | 0.24 |
| 67 | | -0.02 | 1.03 | 0.01 | 0.01 | 2.24 | 0.79 |
| 75 | | 0.06 | 1.94 | 0.22 | 0.07 | 2.37 |  |

**Coexistence of mutations and their associations with clinical and histopathological data**

How mutations are mutually influencing each other, the so-called coexistence of mutations was determined by calculating the OR- and RR-type parameters in all possible situations where one of the mutations is considered a determining factor (determinant variable) for the other mutations that were considered dependent on this mutation (outcome variables). We considered the following situations:

1. Coexistence of mutations, regardless of AF‰. We thus distinguish for each mutation two cases: absence (encoded by the symbol 0) and presence (encoded by the symbol 1). In short, we have the following situations for each mutation X,

|  |  |
| --- | --- |
|  | (S1) |

So, if X is the determinant mutation and Y is the outcome variable, we denote by X = 0 if the mutation X is absent and by X = 1 if the mutation X is present. By X or Y, we mean one of the studied mutations, KRAS Q61, KRAS G12 / G13, NRAS Q61, NRAS G12 / G13 or BRAF.

1. Coexistence of mutations taking into account AF‰ values. In this case, we have the following notations:

|  |  |
| --- | --- |
|  | (S2) |

in the first case (in which we first considered that a mutation is present if ), we calculated the following coefficients:

Odds-ratio (OR) is invariable at the change X → Y and is calculated as the ratio of the following probabilities

|  |  |
| --- | --- |
|  | (S3) |

where is the relative probability or frequency of cases for which Y = 0 (Y mutation is absent), knowing that X = 0 (X mutation is present).

Relative risk (*RR*1) is calculated as:

|  |  |
| --- | --- |
|  | (S4) |

The risk of Y mutation in cases X = 0 compared to cases X = 1. If or more precisely , then the cases X = 0 (i.e. the cases in which the determinant mutation X is absent) have RR1 times higher relative risk than the cases X = 1 (when the mutation X is present) to be associated with the presence of the Y mutation (Y = 1). In short, the absence of the X mutation increases by RR1 folds the risk of the Y mutation occurrence compared to the absence of X mutation.

Relative risk calculated as:

|  |  |
| --- | --- |
|  | (S5) |

that is, the risk of Y mutation in cases X = 1 compared to cases X = 0. If (or more precisely ), then the cases X = 1 (in which the determinant mutation X is present) have folds higher relative risk than the cases X = 0 (when the mutation X is absent) to be associated with the presence of the Y mutation (Y = 1). In other words, the presence of the X mutation increases by folds the risk of the Y mutation occurring if X is absent.

Relative risk calculated as

|  |  |
| --- | --- |
|  | (S6) |

that is, the risk of Y mutation absence in cases X = 0 compared to cases X = 1. If (or more precisely), then the cases X = 0 (in which the determinant mutation X is absent) have folds higher relative risk than the cases when the mutation X is present (X = 1) to be associated with the absence of the Y mutation (Y = 0). In other words, the absence of the X mutation increases by folds the risk of the Y mutation absence compared to X mutation presence.

We have the following equations between the four parameters

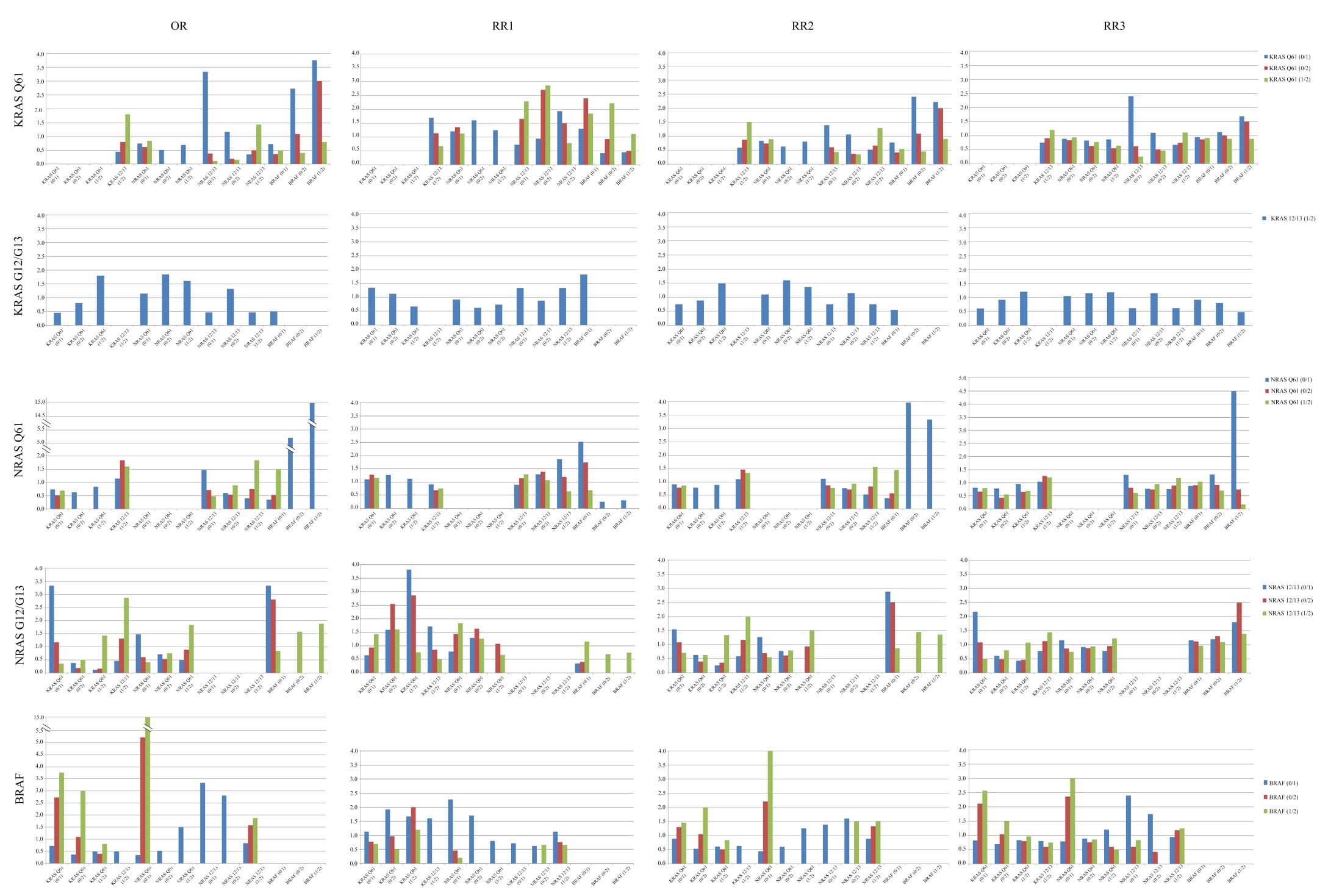
|  |  |
| --- | --- |
|  | (S7) |

The same coefficients OR, RR1 and RR3 were calculated for all possible combinations (X = {0, 1, 2} | Y = {0, 1, 2}) were also calculated in the second case.

Risk factor - mutation association is expressed by the same type of coefficients. The variable Y is associated with the mutation’s absence (Y = 0) or presence (Y = 1) in the above formulas. The variable X will be one of the clinical variables: sex, X → {F, M}; diabetes, X → {no, yes} in which *no*- non diabetic patients, *yes* - diabetic patients; smoking: X → {no, yes}, BMI: X - {1, 2} where *1*- underweight + normal weight, *2*- overweight and obese patients. The meaning of the parameters OR, RR1, RR 2 and RR3 is the same as above. We used the OR and RR parameters defined above to study the association of a mutation as a risk factor for the values of tumour-related variables (laterality, histopathological features, tumour staging) listed in Table S3. In this case, the variable X in the above equations represents the presence or absence of one of the mutations, and Y represents one of the variables listed with the possible values, as shown in Table S3. A significant association between a clinical or a histopathological variable and a mutation will be considered when RR> 1.3.

**Table S2. Expressing associations between mutation levels via risk ratios RR1, RR2 and RR3**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Independent mutations values** | **Outcome mutation values** | **RR1 > 1.3** | **RR2 > 1.3** | | **RR3 > 1.3** |
| X→{0,1} | Y→{0,1} | The absence of the X mutation determines the presence of 0.1 ≤ AF <1 levels of the Y mutation preferentially. | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of AF < 1 levels of the Y mutation preferentially. | | The X mutation’s absence determines the Y mutation’s absence rather than the presence of 0.1 ≤ AF <1 levels of this mutation. |
| The cases with AF = 0 or 0.1 ≤ AF <1 for both X and Y mutations | |
| X→{0,1} i.e.  The cases with AF = 0 or 0.1 ≤ AF <1 | Y→{0,2} i.e.  The cases with AF = 0 or AF ≥ 1 | The absence of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | | The X mutation’s absence determines the Y mutation’s absence. |
| X→{0,1} i.e.  The cases with AF = 0 or 0.1 ≤ AF <1 | Y→{1,2} i.e.  The cases with 0.1 ≤ AF <1 or AF ≥ 1 | The absence of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | | The X mutation’s absence determines the Y mutation’s presence of 0.1 ≤ AF <1 levels preferentially. |
| X→{0,2} i.e.  The cases with AF = 0 or AF ≥ 1 | Y→{0,1} i.e.  The cases with AF = 0 or 0.1 ≤ AF <1 | The absence of the X mutation determines the presence of 0.1 ≤ AF <1 levels of the Y mutation preferentially. | The presence of AF ≥ 1 levels of the X mutation determines the presence of 0.1 ≤ AF <1 levels preferentially. | | The X mutation’s absence determines the absence of the Y mutation preferentially. |
| X→{0,2} i.e | Y→{0,2} i.e. | The absence of the X mutation determines the presence of AF ≥ 1 levels of the Y mutation preferentially. | The presence of AF ≥ 1 levels of the X mutation determines the presence of AF ≥ 1 levels of the Y mutation preferentially. | | The X mutation’s absence determines the absence of the Y mutation preferentially. |
| The cases with AF = 0 or AF ≥ 1 | |
| X→{0,2} i.e.  The cases with AF = 0 or AF ≥ 1 | Y→{1,2} i.e.  The cases with 0 < AF < 1 or AF ≥ 1 | The absence of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | | The absence of the X mutation determines the presence of 0.1 ≤ AF <1 levels of Y mutation preferentially. |
| X→{1,2} i.e.  The cases with 0.1 ≤ AF <1 or AF ≥ 1 | Y→{0,1} i.e.  The cases with AF = 0 or 0.1 ≤ AF <1 | The presence of AF < 1 levels of the X mutation determines the presence of 0.1 ≤ AF <1 levels of the Y-mutation preferentially. | The presence of AF ≥ 1 levels of the X mutation determines the presence of 0.1 ≤ AF <1 levels of Y mutation preferentially. | | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the absence of the Y-mutation preferentially. |
| X→{1,2} i.e.  The cases with 0.1 ≤ AF <1 or AF ≥ 1 | Y→{0,2} i.e.  The cases with AF = 0 or AF ≥ 1 | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y mutation preferentially. | The presence of AF ≥ 1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y mutation than the absence of the Y-mutation preferentially. | | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the absence of the Y-mutation preferentially. |
| X→{1,2} | Y→{1,2} | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y-mutation preferentially. | The presence of AF ≥ 1 levels of the X mutation determines the presence of AF ≥ 1 levels of Y-mutation preferentially. | The presence of 0.1 ≤ AF <1 levels of the X mutation determines the presence of 0.1 ≤ AF <1 levels of the Y-mutation preferentially. | | |
| The cases with 0.1 ≤ AF <1 or AF ≥ 1 | |

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**Figure S1. Risk analysis via OR, RR1, RR2 and RR3 of possible two-by-two associations between the studied mutations, defined according to Table S1**

**Table S3. Models used for OR, RR1, RR2 and RR3 calculation related to mutations status and tumour pathological features**

**Tumour localization / laterality**

L – left colon; R – right colon;

**ALL mutations**

0 – the mutation is absent, 1 – the mutation is present

**Tumour differentiation grade**

***Differentiation grade grouping model 1***

1 – well-differentiated / 2 - moderately and poorly differentiated tumours

***Differentiation grade grouping model 2***

1 – well and moderately / 2 - poorly differentiated tumours

**Histopathological pattern**

***Tubular pattern***

0 – absent, 1 – present

***Cribriform pattern***

0 – absent, 1 – present

***Necrosis***

0 – absent, 1 – present

***Mucoid phenotype***

0 – absent, 1 – present

**Invasion limits**

***Limits of invasion model 1***

1 – tumour invasion limited by the submucosa,

2 – tumour invasion beyond the submucosa;

***Limits of invasion model 2***

1 – tumour invasion limited by the muscularis mucosa,

2 – tumour invasion beyond the muscularis mucosa;

***Limits of invasion model 3***

1 – tumour invasion limited by the subserosa,

2 – tumour invasion beyond the muscularis subserosa;

***Limits of invasion model 4***

1 – tumour invasion limited by the serosa,

2 – tumour invasion beyond the muscularis serosa;

**Desmoplastic reaction**

***Desmoplastic reaction Model1***

1 – "low"; 2 – "moderate and high"

***Desmoplastic reaction Model2***

1 – "low and moderate"; 2 – "high"

**Lymphovascular invasion, perineural invasion, adenomatous polyps or budding**

0 – absent; 1 – present;

**Inflammatory infiltrates**

***Mixed peri- and/or intratumoral infiltrate Model 1***

1 – "absent"; 2 – "present (grade-independent) "

***Mixed peri- and/or intratumoral infiltrate Model 2***

1 – "absent or low"; 2 – "moderate or high"

***Mixed peri- and/or intratumoral infiltrate Model 3***

1 – "absent or low or moderate"; 2 – "high"

***Lymphocyte peri- and/or intratumoral Model 1***

1 – "absent"; 2 – "present (grade-independent)"

***Lymphocyte peri- and/or intratumoral Model 2***

1 – "absent or low"; 2 – "moderate or high"

***Lymphocyte peri- and/or intratumoral Model 3***

1 – "absent or low or moderate"; 2 – "high"

**ypT Staging**

***ypT Model 1***

1 – ypT2 or ypT3; 2 – ypT4

***ypT Model 2***

1 – ypT2; 2 – ypT3 or ypT4

**ypN Staging**

***ypN Model 1***

1 – ypN0 or ypN1; 2 – ypN2

***ypN Model 2***

1 – ypN0; 2 – ypN1 or ypN2

**ypM Staging**

M0 – no metastasis; M1 – metastasis in any organ;

**AJCC Staging**

1 –stage II CRC; 2 – stages III and IV CRC;

**Table S4. Risk estimation calculations using the models presented in table S3. Parameters OR, RR1, RR2 and RR3 have been defined above.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Independent variable (Mutation)** | **Outcome Variable** | **Symbol** | **Value** | **95% IC LB** | **95% IC UB** |
| KRAS Q61 (0/1) | Tumor Localization (left/right) | OR | 1.192 | 0.319 | 4.445 |
| KRAS Q61 (0/1) | Tumor Localization (left/right) | RR1 | 0.882 | 0.340 | 2.290 |
| KRAS Q61 (0/1) | Tumor Localization (left/right) | RR2 | 1.134 | 0.592 | 1.676 |
| KRAS Q61 (0/1) | Tumor Localization (left/right) | RR3 | 1.051 | 0.731 | 1.511 |
| KRAS Q61 (0/1) | HP differentiation model 1 (1/2) | OR | 0.632 | 0.184 | 2.162 |
| KRAS Q61 (0/1) | HP differentiation model 1 (1/2) | RR1 | 1.194 | 0.765 | 1.865 |
| KRAS Q61 (0/1) | HP differentiation model 1 (1/2) | RR2 | 0.838 | 0.409 | 1.267 |
| KRAS Q61 (0/1) | HP differentiation model 1 (1/2) | RR3 | 0.754 | 0.342 | 1.663 |
| KRAS Q61 (0/1) | HP differentiation model 2 (1/2) | OR | 1.842 | 0.198 | 17.179 |
| KRAS Q61 (0/1) | HP differentiation model 2 (1/2) | RR1 | 0.573 | 0.073 | 4.521 |
| KRAS Q61 (0/1) | HP differentiation model 2 (1/2) | RR2 | 1.745 | 1.245 | 2.245 |
| KRAS Q61 (0/1) | HP differentiation model 2 (1/2) | RR3 | 1.056 | 0.888 | 1.256 |
| KRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | OR | 0.696 | 0.072 | 6.773 |
| KRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | RR1 | 1.029 | 0.872 | 1.215 |
| KRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | RR2 | 0.972 | 0.815 | 1.129 |
| KRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | RR3 | 0.717 | 0.087 | 5.917 |
| KRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | OR | 0.632 | 0.184 | 2.162 |
| KRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | RR1 | 1.194 | 0.765 | 1.865 |
| KRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | RR2 | 0.838 | 0.409 | 1.267 |
| KRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | RR3 | 0.754 | 0.342 | 1.663 |
| KRAS Q61 (0/1) | Necrosis (0/1) | OR | 0.552 | 0.166 | 1.829 |
| KRAS Q61 (0/1) | Necrosis (0/1) | RR1 | 1.433 | 0.718 | 2.861 |
| KRAS Q61 (0/1) | Necrosis (0/1) | RR2 | 0.698 | -0.017 | 1.413 |
| KRAS Q61 (0/1) | Necrosis (0/1) | RR3 | 0.791 | 0.472 | 1.326 |
| KRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | OR | 1.464 | 0.123 | 17.415 |
| KRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | RR1 | 0.979 | 0.842 | 1.138 |
| KRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | RR2 | 1.021 | 0.884 | 1.158 |
| KRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | RR3 | 1.433 | 0.140 | 14.693 |
| KRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | OR | 1.292 | 0.365 | 4.570 |
| KRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | RR1 | 0.925 | 0.618 | 1.384 |
| KRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | RR2 | 1.081 | 0.774 | 1.388 |
| KRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | RR3 | 1.194 | 0.504 | 2.828 |
| KRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | OR | 3.107 | 0.923 | 10.462 |
| KRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | RR1 | 0.593 | 0.308 | 1.140 |
| KRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | RR2 | 1.686 | 1.401 | 1.971 |
| KRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | RR3 | 1.843 | 1.015 | 3.346 |
| KRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | OR | 1.630 | 0.444 | 5.984 |
| KRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | RR1 | 0.717 | 0.284 | 1.807 |
| KRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | RR2 | 1.395 | 0.962 | 1.828 |
| KRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | RR3 | 1.168 | 0.797 | 1.712 |
| KRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | OR | 4.222 | 0.485 | 36.767 |
| KRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | RR1 | 0.695 | 0.333 | 1.448 |
| KRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | RR2 | 1.439 | 1.077 | 1.801 |
| KRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | RR3 | 2.933 | 0.653 | 13.183 |
| KRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | RR1 | 0.367 | 0.061 | 2.205 |
| KRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | RR2 | 2.725 | 2.419 | 3.031 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | OR | 4.889 | 1.157 | 20.665 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR1 | 0.375 | 0.132 | 1.064 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR2 | 2.667 | 2.424 | 2.910 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR3 | 1.833 | 1.146 | 2.934 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | OR | 3.545 | 0.683 | 18.397 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR1 | 0.385 | 0.099 | 1.489 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR2 | 2.597 | 2.311 | 2.883 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | OR | 1.500 | 0.271 | 8.300 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR1 | 0.714 | 0.169 | 3.027 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR2 | 1.401 | 0.856 | 1.946 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR3 | 1.071 | 0.817 | 1.404 |
| KRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR3 | 1.364 | 0.978 | 1.902 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | OR | 0.745 | 0.219 | 2.531 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR1 | 1.137 | 0.679 | 1.904 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR2 | 0.880 | 0.422 | 1.338 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR3 | 0.847 | 0.417 | 1.722 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | OR | 0.400 | 0.100 | 1.599 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR1 | 2.000 | 0.719 | 5.561 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR2 | 0.500 | -0.781 | 1.781 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR3 | 0.800 | 0.544 | 1.177 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | OR | 0.400 | 0.023 | 6.848 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR1 | 2.400 | 0.160 | 35.911 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR2 | 0.417 | -1.823 | 2.657 |
| KRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR3 | 0.960 | 0.830 | 1.111 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | OR | 0.783 | 0.225 | 2.723 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.167 | 0.540 | 2.522 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.857 | 0.230 | 1.484 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.913 | 0.566 | 1.472 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | OR | 0.500 | 0.129 | 1.940 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR1 | 1.667 | 0.628 | 4.420 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR2 | 0.600 | -0.439 | 1.639 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR3 | 0.833 | 0.562 | 1.236 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | OR | 0.242 | 0.036 | 1.633 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR1 | 3.500 | 0.650 | 18.852 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR2 | 0.286 | -2.564 | 3.136 |
| KRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR3 | 0.848 | 0.650 | 1.107 |
| NRAS Q61 (0/1) | Tumor Localization (left/right) | OR | 4.160 | 1.226 | 14.113 |
| NRAS Q61 (0/1) | Tumor Localization (left/right) | RR1 | 0.363 | 0.147 | 0.899 |
| NRAS Q61 (0/1) | Tumor Localization (left/right) | RR2 | 2.755 | 2.539 | 2.971 |
| NRAS Q61 (0/1) | Tumor Localization (left/right) | RR3 | 1.510 | 1.042 | 2.188 |
| NRAS Q61 (0/1) | HP differentiation model 1 (1/2) | OR | 1.875 | 0.646 | 5.445 |
| NRAS Q61 (0/1) | HP differentiation model 1 (1/2) | RR1 | 0.774 | 0.502 | 1.193 |
| NRAS Q61 (0/1) | HP differentiation model 1 (1/2) | RR2 | 1.292 | 1.020 | 1.564 |
| NRAS Q61 (0/1) | HP differentiation model 1 (1/2) | RR3 | 1.452 | 0.761 | 2.768 |
| NRAS Q61 (0/1) | HP differentiation model 2 (1/2) | OR | 0.200 | 0.022 | 1.832 |
| NRAS Q61 (0/1) | HP differentiation model 2 (1/2) | RR1 | 4.355 | 0.542 | 35.002 |
| NRAS Q61 (0/1) | HP differentiation model 2 (1/2) | RR2 | 0.230 | -3.583 | 4.043 |
| NRAS Q61 (0/1) | HP differentiation model 2 (1/2) | RR3 | 0.871 | 0.734 | 1.034 |
| NRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | OR | 0.192 | 0.020 | 1.832 |
| NRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | RR1 | 1.136 | 0.959 | 1.346 |
| NRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | RR2 | 0.880 | 0.703 | 1.057 |
| NRAS Q61 (0/1) | For HP phenotype with tubular pattern (0/1) | RR3 | 0.218 | 0.026 | 1.832 |
| NRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | OR | 0.789 | 0.277 | 2.252 |
| NRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | RR1 | 1.103 | 0.712 | 1.710 |
| NRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | RR2 | 0.907 | 0.516 | 1.298 |
| NRAS Q61 (0/1) | HP phenotype with cribriform pattern (0/1) | RR3 | 0.871 | 0.472 | 1.606 |
| NRAS Q61 (0/1) | Mucoid HP phenotype (0/1) | OR | 0.263 | 0.064 | 1.083 |
| NRAS Q61 (0/1) | Mucoid HP phenotype (0/1) | RR1 | 2.903 | 0.890 | 9.472 |
| NRAS Q61 (0/1) | Mucoid HP phenotype (0/1) | RR2 | 0.344 | -1.669 | 2.357 |
| NRAS Q61 (0/1) | Mucoid HP phenotype (0/1) | RR3 | 0.762 | 0.578 | 1.005 |
| NRAS Q61 (0/1) | Necrosis (0/1) | OR | 2.670 | 0.886 | 8.046 |
| NRAS Q61 (0/1) | Necrosis (0/1) | RR1 | 0.536 | 0.263 | 1.094 |
| NRAS Q61 (0/1) | Necrosis (0/1) | RR2 | 1.866 | 1.593 | 2.139 |
| NRAS Q61 (0/1) | Necrosis (0/1) | RR3 | 1.431 | 0.941 | 2.175 |
| NRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | OR | 0.417 | 0.036 | 4.869 |
| NRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | RR1 | 1.045 | 0.923 | 1.184 |
| NRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | RR2 | 0.957 | 0.835 | 1.079 |
| NRAS Q61 (0/1) | Limits of invasion model 1 (1/2) | RR3 | 0.435 | 0.042 | 4.541 |
| NRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | OR | 1.361 | 0.434 | 4.270 |
| NRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | RR1 | 0.915 | 0.658 | 1.272 |
| NRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | RR2 | 1.093 | 0.836 | 1.350 |
| NRAS Q61 (0/1) | Limits of invasion model 2 (1/2) | RR3 | 1.244 | 0.550 | 2.815 |
| NRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | OR | 0.919 | 0.320 | 2.637 |
| NRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | RR1 | 1.034 | 0.680 | 1.574 |
| NRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | RR2 | 0.967 | 0.613 | 1.321 |
| NRAS Q61 (0/1) | Limits of invasion model 3 (1/2) | RR3 | 0.950 | 0.504 | 1.793 |
| NRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | OR | 0.909 | 0.307 | 2.696 |
| NRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | RR1 | 1.065 | 0.521 | 2.174 |
| NRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | RR2 | 0.939 | 0.395 | 1.483 |
| NRAS Q61 (0/1) | Limits of invasion model 4 (1/2) | RR3 | 0.968 | 0.666 | 1.406 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | OR | 3.333 | 0.319 | 34.830 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | RR1 | 0.825 | 0.588 | 1.158 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | RR2 | 1.212 | 0.975 | 1.449 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 1 | RR3 | 2.750 | 0.353 | 21.414 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | OR | 2.917 | 0.594 | 14.327 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | OR | 4.800 | 0.459 | 50.155 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | RR1 | 0.589 | 0.272 | 1.278 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | RR2 | 1.698 | 1.381 | 2.015 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | RR3 | 1.719 | 0.721 | 4.098 |
| NRAS Q61 (0/1) | Desmoplasic Reaction Model 2 | RR3 | 1.760 | 0.934 | 3.317 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | OR | 0.750 | 0.240 | 2.341 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.167 | 0.629 | 2.163 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.857 | 0.319 | 1.395 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.875 | 0.518 | 1.477 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | OR | 0.844 | 0.246 | 2.904 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR1 | 1.125 | 0.474 | 2.670 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR2 | 0.889 | 0.238 | 1.540 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR3 | 0.950 | 0.655 | 1.378 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | OR | 1.082 | 0.252 | 4.645 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR1 | 0.938 | 0.286 | 3.072 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR2 | 1.066 | 0.414 | 1.718 |
| NRAS Q61 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR3 | 1.015 | 0.775 | 1.329 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | OR | 1.167 | 0.379 | 3.587 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR1 | 0.933 | 0.567 | 1.538 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR2 | 1.072 | 0.706 | 1.438 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR3 | 1.089 | 0.583 | 2.034 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | OR | 0.458 | 0.106 | 1.985 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR1 | 1.867 | 0.560 | 6.223 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR2 | 0.536 | -0.771 | 1.843 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR3 | 0.856 | 0.648 | 1.129 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | OR | 1.450 | 0.086 | 24.565 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR1 | 0.700 | 0.046 | 10.575 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR2 | 1.429 | 0.775 | 2.083 |
| NRAS Q61 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR3 | 1.015 | 0.903 | 1.140 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | OR | 0.567 | 0.171 | 1.883 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.448 | 0.649 | 3.233 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.691 | -0.108 | 1.490 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.821 | 0.546 | 1.234 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | OR | 0.370 | 0.087 | 1.585 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR1 | 2.172 | 0.668 | 7.068 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR2 | 0.460 | -1.044 | 1.964 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR3 | 0.805 | 0.596 | 1.086 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | OR | 0.912 | 0.139 | 6.005 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR1 | 1.086 | 0.199 | 5.939 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR2 | 0.921 | 0.034 | 1.808 |
| NRAS Q61 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR3 | 0.991 | 0.823 | 1.193 |
| NRAS G12/G13 (0/1) | Tumor Localization (left/right) | OR | 3.482 | 0.692 | 17.515 |
| NRAS G12/G13 (0/1) | Tumor Localization (left/right) | RR1 | 0.382 | 0.099 | 1.479 |
| NRAS G12/G13 (0/1) | Tumor Localization (left/right) | RR2 | 2.618 | 2.335 | 2.901 |
| NRAS G12/G13 (0/1) | Tumor Localization (left/right) | RR3 | 1.331 | 0.991 | 1.788 |
| NRAS G12/G13 (0/1) | HP differentiation model 1 (1/2) | OR | 1.338 | 0.409 | 4.374 |
| NRAS G12/G13 (0/1) | HP differentiation model 1 (1/2) | RR1 | 0.882 | 0.518 | 1.501 |
| NRAS G12/G13 (0/1) | HP differentiation model 1 (1/2) | RR2 | 1.134 | 0.770 | 1.498 |
| NRAS G12/G13 (0/1) | HP differentiation model 1 (1/2) | RR3 | 1.180 | 0.613 | 2.273 |
| NRAS G12/G13 (0/1) | HP differentiation model 2 (1/2) | OR | 0.300 | 0.053 | 1.684 |
| NRAS G12/G13 (0/1) | HP differentiation model 2 (1/2) | RR1 | 2.867 | 0.647 | 12.700 |
| NRAS G12/G13 (0/1) | HP differentiation model 2 (1/2) | RR2 | 0.349 | -1.871 | 2.569 |
| NRAS G12/G13 (0/1) | HP differentiation model 2 (1/2) | RR3 | 0.860 | 0.659 | 1.122 |
| NRAS G12/G13 (0/1) | HP phenotype with cribriform pattern (0/1) | OR | 1.338 | 0.409 | 4.374 |
| NRAS G12/G13 (0/1) | HP phenotype with cribriform pattern (0/1) | RR1 | 0.882 | 0.518 | 1.501 |
| NRAS G12/G13 (0/1) | HP phenotype with cribriform pattern (0/1) | RR2 | 1.134 | 0.770 | 1.498 |
| NRAS G12/G13 (0/1) | HP phenotype with cribriform pattern (0/1) | RR3 | 1.180 | 0.613 | 2.273 |
| NRAS G12/G13 (0/1) | Mucoid HP phenotype (0/1) | OR | 0.728 | 0.187 | 2.836 |
| NRAS G12/G13 (0/1) | Mucoid HP phenotype (0/1) | RR1 | 1.274 | 0.459 | 3.536 |
| NRAS G12/G13 (0/1) | Mucoid HP phenotype (0/1) | RR2 | 0.785 | -0.030 | 1.600 |
| NRAS G12/G13 (0/1) | Mucoid HP phenotype (0/1) | RR3 | 0.927 | 0.659 | 1.305 |
| NRAS G12/G13 (0/1) | Necrosis (0/1) | OR | 1.798 | 0.491 | 6.581 |
| NRAS G12/G13 (0/1) | Necrosis (0/1) | RR1 | 0.675 | 0.270 | 1.687 |
| NRAS G12/G13 (0/1) | Necrosis (0/1) | RR2 | 1.481 | 1.076 | 1.886 |
| NRAS G12/G13 (0/1) | Necrosis (0/1) | RR3 | 1.213 | 0.822 | 1.790 |
| NRAS G12/G13 (0/1) | Limits of invasion model 1 (1/2) | RR1 | 1.075 | 0.991 | 1.167 |
| NRAS G12/G13 (0/1) | Limits of invasion model 1 (1/2) | RR2 | 0.930 | 0.846 | 1.014 |
| NRAS G12/G13 (0/1) | Limits of invasion model 2 (1/2) | OR | 0.839 | 0.225 | 3.130 |
| NRAS G12/G13 (0/1) | Limits of invasion model 2 (1/2) | RR1 | 1.051 | 0.731 | 1.511 |
| NRAS G12/G13 (0/1) | Limits of invasion model 2 (1/2) | RR2 | 0.951 | 0.631 | 1.271 |
| NRAS G12/G13 (0/1) | Limits of invasion model 2 (1/2) | RR3 | 0.882 | 0.340 | 2.290 |
| NRAS G12/G13 (0/1) | Limits of invasion model 3 (1/2) | OR | 1.020 | 0.307 | 3.386 |
| NRAS G12/G13 (0/1) | Limits of invasion model 3 (1/2) | RR1 | 0.992 | 0.615 | 1.602 |
| NRAS G12/G13 (0/1) | Limits of invasion model 3 (1/2) | RR2 | 1.008 | 0.631 | 1.385 |
| NRAS G12/G13 (0/1) | Limits of invasion model 3 (1/2) | RR3 | 1.012 | 0.492 | 2.082 |
| NRAS G12/G13 (0/1) | Limits of invasion model 4 (1/2) | OR | 1.071 | 0.309 | 3.715 |
| NRAS G12/G13 (0/1) | Limits of invasion model 4 (1/2) | RR1 | 0.956 | 0.419 | 2.178 |
| NRAS G12/G13 (0/1) | Limits of invasion model 4 (1/2) | RR2 | 1.046 | 0.509 | 1.583 |
| NRAS G12/G13 (0/1) | Limits of invasion model 4 (1/2) | RR3 | 1.024 | 0.673 | 1.557 |
| NRAS G12/G13 (0/1) | Desmoplasic Reaction Model 1 | RR1 | 1.313 | 1.033 | 1.667 |
| NRAS G12/G13 (0/1) | Desmoplasic Reaction Model 1 | RR2 | 0.762 | 0.482 | 1.042 |
| NRAS G12/G13 (0/1) | Desmoplasic Reaction Model 2 | OR | 2.200 | 0.329 | 14.726 |
| NRAS G12/G13 (0/1) | Desmoplasic Reaction Model 2 | RR1 | 0.636 | 0.191 | 2.119 |
| NRAS G12/G13 (0/1) | Desmoplasic Reaction Model 2 | RR2 | 1.572 | 1.127 | 2.017 |
| NRAS G12/G13 (0/1) | Desmoplasic Reaction Model 2 | RR3 | 1.400 | 0.680 | 2.882 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | OR | 0.544 | 0.146 | 2.035 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.349 | 0.737 | 2.468 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.741 | 0.129 | 1.353 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.734 | 0.355 | 1.517 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | OR | 0.321 | 0.083 | 1.250 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR1 | 2.056 | 0.922 | 4.584 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR2 | 0.486 | -0.648 | 1.620 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR3 | 0.661 | 0.365 | 1.197 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | OR | 0.581 | 0.121 | 2.797 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR1 | 1.542 | 0.454 | 5.240 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR2 | 0.649 | -0.439 | 1.737 |
| NRAS G12/G13 (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR3 | 0.895 | 0.627 | 1.278 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | OR | 0.833 | 0.225 | 3.085 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR1 | 1.083 | 0.619 | 1.896 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR2 | 0.923 | 0.459 | 1.387 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR3 | 0.903 | 0.426 | 1.912 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | OR | 0.774 | 0.169 | 3.541 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR1 | 1.219 | 0.383 | 3.882 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR2 | 0.820 | -0.016 | 1.656 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR3 | 0.944 | 0.656 | 1.357 |
| NRAS G12/G13 (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR3 | 1.054 | 0.980 | 1.134 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | OR | 1.167 | 0.297 | 4.588 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR1 | 0.905 | 0.367 | 2.230 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR2 | 1.105 | 0.567 | 1.643 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR3 | 1.056 | 0.661 | 1.686 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | OR | 1.786 | 0.332 | 9.592 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR1 | 0.633 | 0.161 | 2.499 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR2 | 1.580 | 1.108 | 2.052 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR3 | 1.131 | 0.824 | 1.552 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | OR | 1.294 | 0.130 | 12.835 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR1 | 0.792 | 0.098 | 6.420 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR2 | 1.263 | 0.569 | 1.957 |
| NRAS G12/G13 (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR3 | 1.025 | 0.837 | 1.254 |
| BRAF (0/1) | Tumor Localization (left/right) | OR | 1.939 | 0.562 | 6.698 |
| BRAF (0/1) | Tumor Localization (left/right) | RR1 | 0.640 | 0.287 | 1.427 |
| BRAF (0/1) | Tumor Localization (left/right) | RR2 | 1.563 | 1.210 | 1.916 |
| BRAF (0/1) | Tumor Localization (left/right) | RR3 | 1.240 | 0.792 | 1.943 |
| BRAF (0/1) | HP differentiation model 1 (1/2) | OR | 1.080 | 0.326 | 3.577 |
| BRAF (0/1) | HP differentiation model 1 (1/2) | RR1 | 0.969 | 0.597 | 1.574 |
| BRAF (0/1) | HP differentiation model 1 (1/2) | RR2 | 1.032 | 0.660 | 1.404 |
| BRAF (0/1) | HP differentiation model 1 (1/2) | RR3 | 1.047 | 0.513 | 2.135 |
| BRAF (0/1) | HP differentiation model 2 (1/2) | OR | 0.543 | 0.058 | 5.062 |
| BRAF (0/1) | HP differentiation model 2 (1/2) | RR1 | 1.744 | 0.221 | 13.754 |
| BRAF (0/1) | HP differentiation model 2 (1/2) | RR2 | 0.573 | -0.950 | 2.096 |
| BRAF (0/1) | HP differentiation model 2 (1/2) | RR3 | 0.947 | 0.796 | 1.126 |
| BRAF (0/1) | For HP phenotype with tubular pattern (0/1) | OR | 1.436 | 0.148 | 13.965 |
| BRAF (0/1) | For HP phenotype with tubular pattern (0/1) | RR1 | 0.972 | 0.823 | 1.147 |
| BRAF (0/1) | For HP phenotype with tubular pattern (0/1) | RR2 | 1.029 | 0.880 | 1.178 |
| BRAF (0/1) | For HP phenotype with tubular pattern (0/1) | RR3 | 1.395 | 0.169 | 11.521 |
| BRAF (0/1) | HP phenotype with cribriform pattern (0/1) | OR | 0.747 | 0.229 | 2.442 |
| BRAF (0/1) | HP phenotype with cribriform pattern (0/1) | RR1 | 1.134 | 0.666 | 1.929 |
| BRAF (0/1) | HP phenotype with cribriform pattern (0/1) | RR2 | 0.882 | 0.414 | 1.350 |
| BRAF (0/1) | HP phenotype with cribriform pattern (0/1) | RR3 | 0.847 | 0.440 | 1.631 |
| BRAF (0/1) | Mucoid HP phenotype (0/1) | OR | 1.374 | 0.353 | 5.352 |
| BRAF (0/1) | Mucoid HP phenotype (0/1) | RR1 | 0.785 | 0.283 | 2.178 |
| BRAF (0/1) | Mucoid HP phenotype (0/1) | RR2 | 1.274 | 0.772 | 1.776 |
| BRAF (0/1) | Mucoid HP phenotype (0/1) | RR3 | 1.078 | 0.766 | 1.517 |
| BRAF (0/1) | Necrosis (0/1) | OR | 1.244 | 0.372 | 4.167 |
| BRAF (0/1) | Necrosis (0/1) | RR1 | 0.872 | 0.415 | 1.832 |
| BRAF (0/1) | Necrosis (0/1) | RR2 | 1.147 | 0.690 | 1.604 |
| BRAF (0/1) | Necrosis (0/1) | RR3 | 1.085 | 0.680 | 1.732 |
| BRAF (0/1) | Limits of invasion model 1 (1/2) | OR | 0.155 | 0.013 | 1.848 |
| BRAF (0/1) | Limits of invasion model 1 (1/2) | RR1 | 1.127 | 0.919 | 1.382 |
| BRAF (0/1) | Limits of invasion model 1 (1/2) | RR2 | 0.887 | 0.679 | 1.095 |
| BRAF (0/1) | Limits of invasion model 1 (1/2) | RR3 | 0.174 | 0.017 | 1.788 |
| BRAF (0/1) | Limits of invasion model 2 (1/2) | OR | 1.192 | 0.319 | 4.445 |
| BRAF (0/1) | Limits of invasion model 2 (1/2) | RR1 | 0.951 | 0.662 | 1.368 |
| BRAF (0/1) | Limits of invasion model 2 (1/2) | RR2 | 1.052 | 0.763 | 1.341 |
| BRAF (0/1) | Limits of invasion model 2 (1/2) | RR3 | 1.134 | 0.437 | 2.944 |
| BRAF (0/1) | Limits of invasion model 3 (1/2) | OR | 0.981 | 0.295 | 3.257 |
| BRAF (0/1) | Limits of invasion model 3 (1/2) | RR1 | 1.008 | 0.624 | 1.626 |
| BRAF (0/1) | Limits of invasion model 3 (1/2) | RR2 | 0.992 | 0.608 | 1.376 |
| BRAF (0/1) | Limits of invasion model 3 (1/2) | RR3 | 0.988 | 0.480 | 2.034 |
| BRAF (0/1) | Limits of invasion model 4 (1/2) | OR | 0.933 | 0.269 | 3.236 |
| BRAF (0/1) | Limits of invasion model 4 (1/2) | RR1 | 1.047 | 0.459 | 2.386 |
| BRAF (0/1) | Limits of invasion model 4 (1/2) | RR2 | 0.955 | 0.367 | 1.543 |
| BRAF (0/1) | Limits of invasion model 4 (1/2) | RR3 | 0.977 | 0.642 | 1.486 |
| BRAF (0/1) | Desmoplasic Reaction Model 1 | OR | 1.500 | 0.138 | 16.268 |
| BRAF (0/1) | Desmoplasic Reaction Model 1 | RR1 | 0.933 | 0.642 | 1.356 |
| BRAF (0/1) | Desmoplasic Reaction Model 1 | RR2 | 1.072 | 0.781 | 1.363 |
| BRAF (0/1) | Desmoplasic Reaction Model 1 | RR3 | 1.400 | 0.187 | 10.503 |
| BRAF (0/1) | Desmoplasic Reaction Model 2 | OR | 1.630 | 0.287 | 9.256 |
| BRAF (0/1) | Desmoplasic Reaction Model 2 | RR1 | 0.788 | 0.352 | 1.760 |
| BRAF (0/1) | Desmoplasic Reaction Model 2 | RR2 | 1.269 | 0.833 | 1.705 |
| BRAF (0/1) | Desmoplasic Reaction Model 2 | RR3 | 1.283 | 0.500 | 3.294 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | OR | 0.754 | 0.202 | 2.812 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.168 | 0.553 | 2.464 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.856 | 0.241 | 1.471 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.880 | 0.497 | 1.560 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | OR | 1.182 | 0.294 | 4.754 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR1 | 0.892 | 0.348 | 2.286 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR2 | 1.121 | 0.577 | 1.665 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR3 | 1.054 | 0.671 | 1.656 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | OR | 1.722 | 0.358 | 8.295 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR1 | 0.649 | 0.191 | 2.205 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR2 | 1.541 | 1.083 | 1.999 |
| BRAF (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR3 | 1.117 | 0.782 | 1.595 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | OR | 1.440 | 0.398 | 5.211 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR1 | 0.855 | 0.506 | 1.446 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR2 | 1.170 | 0.821 | 1.519 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR3 | 1.232 | 0.573 | 2.646 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | OR | 1.125 | 0.249 | 5.080 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR1 | 0.912 | 0.284 | 2.933 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR2 | 1.096 | 0.468 | 1.724 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR3 | 1.026 | 0.730 | 1.442 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | OR | 3.083 | 0.179 | 53.158 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR1 | 0.342 | 0.023 | 5.087 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR2 | 2.924 | 2.605 | 3.243 |
| BRAF (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR3 | 1.055 | 0.894 | 1.245 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | OR | 0.857 | 0.218 | 3.371 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.105 | 0.448 | 2.724 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.905 | 0.248 | 1.562 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.947 | 0.593 | 1.513 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | OR | 1.074 | 0.238 | 4.840 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR1 | 0.947 | 0.305 | 2.945 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR2 | 1.056 | 0.414 | 1.698 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR3 | 1.018 | 0.702 | 1.475 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | OR | 0.773 | 0.078 | 7.664 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR1 | 1.263 | 0.156 | 10.243 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR2 | 0.792 | -0.315 | 1.899 |
| BRAF (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR3 | 0.976 | 0.797 | 1.195 |
| EGFR (0/1) | Tumor Localization (left/right) | RR3 | 0.702 | 0.592 | 0.831 |
| EGFR (0/1) | HP differentiation model 1 (1/2) | RR1 | 0.579 | 0.464 | 0.722 |
| EGFR (0/1) | HP differentiation model 1 (1/2) | RR2 | 1.727 | 1.612 | 1.842 |
| EGFR (0/1) | HP differentiation model 2 (1/2) | RR3 | 0.895 | 0.819 | 0.978 |
| EGFR (0/1) | For HP phenotype with tubular pattern (0/1) | RR1 | 0.912 | 0.842 | 0.989 |
| EGFR (0/1) | For HP phenotype with tubular pattern (0/1) | RR2 | 1.096 | 1.026 | 1.166 |
| EGFR (0/1) | HP phenotype with cribriform pattern (0/1) | RR1 | 0.579 | 0.464 | 0.722 |
| EGFR (0/1) | HP phenotype with cribriform pattern (0/1) | RR2 | 1.727 | 1.612 | 1.842 |
| EGFR (0/1) | Mucoid HP phenotype (0/1) | RR1 | 0.211 | 0.127 | 0.348 |
| EGFR (0/1) | Mucoid HP phenotype (0/1) | RR2 | 4.739 | 4.655 | 4.823 |
| EGFR (0/1) | Necrosis (0/1) | RR3 | 0.632 | 0.518 | 0.770 |
| EGFR (0/1) | Limits of invasion model 1 (1/2) | RR1 | 0.947 | 0.891 | 1.007 |
| EGFR (0/1) | Limits of invasion model 1 (1/2) | RR2 | 1.056 | 1.000 | 1.112 |
| EGFR (0/1) | Limits of invasion model 2 (1/2) | RR1 | 0.702 | 0.592 | 0.831 |
| EGFR (0/1) | Limits of invasion model 2 (1/2) | RR2 | 1.425 | 1.315 | 1.535 |
| EGFR (0/1) | Limits of invasion model 3 (1/2) | RR1 | 0.596 | 0.482 | 0.738 |
| EGFR (0/1) | Limits of invasion model 3 (1/2) | RR2 | 1.678 | 1.564 | 1.792 |
| EGFR (0/1) | Limits of invasion model 4 (1/2) | RR1 | 0.333 | 0.231 | 0.481 |
| EGFR (0/1) | Limits of invasion model 4 (1/2) | RR2 | 3.003 | 2.901 | 3.105 |
| EGFR (0/1) | Desmoplasic Reaction Model 1 | RR3 | 0.154 | 0.062 | 0.379 |
| EGFR (0/1) | Desmoplasic Reaction Model 2 | RR3 | 0.500 | 0.340 | 0.734 |
| EGFR (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR3 | 0.440 | 0.322 | 0.602 |
| EGFR (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR3 | 0.780 | 0.673 | 0.904 |
| EGFR (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR3 | 0.960 | 0.907 | 1.016 |
| EGFR (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR1 | 0.347 | 0.236 | 0.509 |
| EGFR (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR2 | 2.882 | 2.771 | 2.993 |
| EGFR (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR1 | 0.224 | 0.133 | 0.378 |
| EGFR (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR2 | 4.464 | 4.373 | 4.555 |
| EGFR (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR1 | 0.082 | 0.032 | 0.209 |
| EGFR (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR2 | 12.195 | 12.145 | 12.245 |
| Any NRAS-type (0/1) | Tumor Localization (left/right) | RR3 | 1.515 | 1.242 | 1.849 |
| Any NRAS-type (0/1) | HP differentiation model 1 (1/2) | OR | 1.500 | 0.336 | 6.702 |
| Any NRAS-type (0/1) | HP differentiation model 1 (1/2) | RR1 | 0.833 | 0.402 | 1.727 |
| Any NRAS-type (0/1) | HP differentiation model 1 (1/2) | RR2 | 1.200 | 0.769 | 1.631 |
| Any NRAS-type (0/1) | HP differentiation model 1 (1/2) | RR3 | 1.250 | 0.578 | 2.704 |
| Any NRAS-type (0/1) | HP differentiation model 2 (1/2) | OR | 0.106 | 0.017 | 0.674 |
| Any NRAS-type (0/1) | HP differentiation model 2 (1/2) | RR1 | 6.250 | 1.517 | 25.744 |
| Any NRAS-type (0/1) | HP differentiation model 2 (1/2) | RR2 | 0.160 | -4.573 | 4.893 |
| Any NRAS-type (0/1) | HP differentiation model 2 (1/2) | RR3 | 0.665 | 0.387 | 1.142 |
| Any NRAS-type (0/1) | For HP phenotype with tubular pattern (0/1) | RR3 | 1.111 | 1.013 | 1.219 |
| Any NRAS-type (0/1) | HP phenotype with cribriform pattern (0/1) | OR | 0.829 | 0.178 | 3.856 |
| Any NRAS-type (0/1) | HP phenotype with cribriform pattern (0/1) | RR1 | 1.078 | 0.600 | 1.937 |
| Any NRAS-type (0/1) | HP phenotype with cribriform pattern (0/1) | RR2 | 0.928 | 0.450 | 1.406 |
| Any NRAS-type (0/1) | HP phenotype with cribriform pattern (0/1) | RR3 | 0.893 | 0.345 | 2.313 |
| Any NRAS-type (0/1) | Mucoid HP phenotype (0/1) | OR | 0.417 | 0.085 | 2.044 |
| Any NRAS-type (0/1) | Mucoid HP phenotype (0/1) | RR1 | 1.875 | 0.655 | 5.371 |
| Any NRAS-type (0/1) | Mucoid HP phenotype (0/1) | RR2 | 0.533 | -0.687 | 1.753 |
| Any NRAS-type (0/1) | Mucoid HP phenotype (0/1) | RR3 | 0.781 | 0.449 | 1.360 |
| Any NRAS-type (0/1) | Necrosis (0/1) | OR | 4.667 | 0.533 | 40.886 |
| Any NRAS-type (0/1) | Necrosis (0/1) | RR1 | 0.313 | 0.048 | 2.017 |
| Any NRAS-type (0/1) | Necrosis (0/1) | RR2 | 3.195 | 2.930 | 3.460 |
| Any NRAS-type (0/1) | Necrosis (0/1) | RR3 | 1.458 | 1.032 | 2.062 |
| Any NRAS-type (0/1) | Limits of invasion model 1 (1/2) | RR1 | 1.064 | 0.992 | 1.141 |
| Any NRAS-type (0/1) | Limits of invasion model 1 (1/2) | RR2 | 0.940 | 0.868 | 1.012 |
| Any NRAS-type (0/1) | Limits of invasion model 2 (1/2) | OR | 1.543 | 0.325 | 7.333 |
| Any NRAS-type (0/1) | Limits of invasion model 2 (1/2) | RR1 | 0.868 | 0.494 | 1.526 |
| Any NRAS-type (0/1) | Limits of invasion model 2 (1/2) | RR2 | 1.152 | 0.778 | 1.526 |
| Any NRAS-type (0/1) | Limits of invasion model 2 (1/2) | RR3 | 1.339 | 0.493 | 3.637 |
| Any NRAS-type (0/1) | Limits of invasion model 3 (1/2) | OR | 1.632 | 0.364 | 7.305 |
| Any NRAS-type (0/1) | Limits of invasion model 3 (1/2) | RR1 | 0.806 | 0.390 | 1.667 |
| Any NRAS-type (0/1) | Limits of invasion model 3 (1/2) | RR2 | 1.241 | 0.825 | 1.657 |
| Any NRAS-type (0/1) | Limits of invasion model 3 (1/2) | RR3 | 1.316 | 0.604 | 2.865 |
| Any NRAS-type (0/1) | Limits of invasion model 4 (1/2) | OR | 1.688 | 0.308 | 9.249 |
| Any NRAS-type (0/1) | Limits of invasion model 4 (1/2) | RR1 | 0.694 | 0.198 | 2.438 |
| Any NRAS-type (0/1) | Limits of invasion model 4 (1/2) | RR2 | 1.441 | 0.945 | 1.937 |
| Any NRAS-type (0/1) | Limits of invasion model 4 (1/2) | RR3 | 1.172 | 0.747 | 1.839 |
| Any NRAS-type (0/1) | Desmoplasic Reaction Model 1 | RR1 | 1.263 | 1.029 | 1.551 |
| Any NRAS-type (0/1) | Desmoplasic Reaction Model 1 | RR2 | 0.792 | 0.558 | 1.026 |
| Any NRAS-type (0/1) | Desmoplasic Reaction Model 2 | OR | 2.000 | 0.159 | 25.115 |
| Any NRAS-type (0/1) | Desmoplasic Reaction Model 2 | RR1 | 0.667 | 0.128 | 3.470 |
| Any NRAS-type (0/1) | Desmoplasic Reaction Model 2 | RR2 | 1.499 | 0.960 | 2.038 |
| Any NRAS-type (0/1) | Desmoplasic Reaction Model 2 | RR3 | 1.333 | 0.545 | 3.262 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | OR | 0.870 | 0.157 | 4.802 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.075 | 0.454 | 2.545 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.930 | 0.309 | 1.551 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.935 | 0.401 | 2.181 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | OR | 0.387 | 0.068 | 2.191 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR1 | 1.792 | 0.705 | 4.556 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR2 | 0.558 | -0.529 | 1.645 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 2 | RR3 | 0.694 | 0.305 | 1.577 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | OR | 1.143 | 0.117 | 11.177 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR1 | 0.896 | 0.135 | 5.961 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR2 | 1.116 | 0.355 | 1.877 |
| Any NRAS-type (0/1) | Mixed peri- and/or intratumoral infiltrate Model 3 | RR3 | 1.024 | 0.696 | 1.505 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | OR | 0.900 | 0.180 | 4.504 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR1 | 1.048 | 0.522 | 2.101 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR2 | 0.954 | 0.428 | 1.480 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 1 | RR3 | 0.943 | 0.378 | 2.353 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | OR | 0.643 | 0.107 | 3.874 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR1 | 1.397 | 0.378 | 5.168 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR2 | 0.716 | -0.303 | 1.735 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 2 | RR3 | 0.898 | 0.549 | 1.469 |
| Any NRAS-type (0/1) | Lymphocyte peri- and/or intratumoral Model 3 | RR3 | 1.048 | 0.982 | 1.117 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | OR | 0.517 | 0.093 | 2.881 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR1 | 1.467 | 0.597 | 3.605 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR2 | 0.682 | -0.188 | 1.552 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 1 | RR3 | 0.759 | 0.331 | 1.736 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | OR | 0.588 | 0.094 | 3.696 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR1 | 1.467 | 0.418 | 5.150 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR2 | 0.682 | -0.367 | 1.731 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 2 | RR3 | 0.863 | 0.479 | 1.553 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | OR | 0.500 | 0.046 | 5.404 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR1 | 1.833 | 0.244 | 13.799 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR2 | 0.546 | -1.043 | 2.135 |
| Any NRAS-type (0/1) | PMN peri- and/or intratumoral infiltrate Model 3 | RR3 | 0.917 | 0.633 | 1.327 |

**Table S5.** Clinical and demographic data of the studied cohort

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Variable | Mean | Median | Std. Deviation | Min. | Max. |
| **Age (yrs)** | **67.16** | **68.50** | **11.02** | **32** | **87** |
| Female | 69.12 | 69.00 | 9.84 | 50 | 84 |
| Male | 65.54 | 66.00 | 11.44 | 22 | 87 |
| **BMI (kg/m2)** | **26.74** | **26.52** | **3.97** | **18** | 41 |
| Female | 27.18 | 26.30 | 4.55 | 19 | 41 |
| Male | 26.38 | 26.63 | 3.45 | 18 | 33 |
| Variable | Category | | | Frequency | Percentage (%) |
| Sex | Female | | | 26 | 43.3 |
| Male | | | 34 | 56.7 |
| BMI (kg/m2) | Underweight (<18.5) | | | 1 | 1.7 |
| Normal weight (18.5 to 24.9) | | | 16 | 26.7 |
| Overweight (≥ 25) | | | 41 | 71.6 |
| Pre-obesity (25.0 to 29.9) | | | 31 | 51.7 |
| Class 1 obesity (30.0 to 34.9) | | | 9 | 15.0 |
| Class 2 obesity (30.0 to 34.9) | | | 0 | 0 |
| Class 3 obesity (≥ 40) | | | 1 | 1.7 |
| Unreported | | | 2 | NA |
| Diabetes | Diabetic patients | | | 30 | 51.7 |
| Female | | | 12 | 19.0 |
| Male | | | 20 | 32.7 |
| Non-diabetics | | | 28 | 48.3 |
| Female | | | 14 | 24.1 |
| Male | | | 14 | 24.1 |
| Smoking | Smoking patients | | | 12 | 20.7 |
| Female | | | 2 | 4.5 |
| Male | | | 11 | 18.2 |
| Non-smoking patients | | | 46 | 79.3 |
| Female | | | 24 | 41.4 |
| Male | | | 22 | 37.9 |
| Tumor localization | Left (L) | | | 41 | 70.7 |
| Right (R) | | | 17 | 29.3 |
| ypT stage | T2 | | | 6 | 10.3 |
| T3 | | | 39 | 67.2 |
| T4 | | | 13 | 22.4 |
| ypN stage | N0 | | | 31 | 53.4 |
| N1 | | | 20 | 34.5 |
| N2 | | | 7 | 12.1 |
| ypM stage | M0 | | | 40 | 69.0 |
| M1 | | | 18 | 31.0 |
| AJCC Staging | I | | | 5 | 8.6 |
| IIA | | | 18 | 31.0 |
| IIB | | | 2 | 3.4 |
| IIIA | | | 2 | 3.4 |
| IIIB | | | 1 | 1.7 |
| IIIC | | | 8 | 13.8 |
| IV | | | 20 | 34.5 |
| Unreported | | | 2 | NA |

Unreported cases are not included in the percentage calculations.