**Supplementary figure 1 (Fig. S1):** Funnel plots and p values of Egger and Begg bias tests for [i]: overall survival (OS) and [ii]: progression-free survival (PFS).

**Fig. S1 [i]: OS**

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|  |  |  |
| --- | --- | --- |
| **Outcome** | **Eager p value** | **Beg p value** |
| OS | P = 0.639 | 0.209 |

**Fig. S1 [ii]: PFS**

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|  |  |  |
| --- | --- | --- |
| **Outcome** | **Eager p value** | **Beg p value** |
| PFS | P = 0.011 | 0.113 |

**Supplementary figure 2 (Fig. S2):** Sensitivity plots for [i]: overall survival (OS) and [ii]: progression-free survival (PFS).

**Fig. S2 [i]: OS**

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**Fig. S2 [ii]: PFS**

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|  |  |  |  |
| --- | --- | --- | --- |
| **Supplementary table 1 (Table S1)**: Search strategy and the combination keywords used for the systematic search. | | | |
| Pubmed (n=146) | Scopus & Embase (n=193) (excluding reviews) | WOS (n=189) | Cochrane (n=8)  (Trials only) |
| (((miR-31[Title/Abstract] OR miRNA-31[Title/Abstract]) OR microRNA-31[Title/Abstract]) OR "microRNA 31"[Title/Abstract]) AND ((((("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields]) AND (("medical subject headings"[MeSH Terms] OR ("medical"[All Fields] AND "subject"[All Fields] AND "headings"[All Fields]) OR "medical subject headings"[All Fields] OR "mesh"[All Fields]) AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields]) AND Title/Abstract[All Fields] AND ("tumour"[All Fields] OR "neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "tumor"[All Fields]) AND Title/Abstract[All Fields] AND ("neoplasms"[MeSH Terms] OR "neoplasms"[All Fields] OR "cancer"[All Fields]) AND Title/Abstract[All Fields] AND ("carcinoma"[MeSH Terms] OR "carcinoma"[All Fields]) AND Title/Abstract[All Fields] AND ("adenocarcinoma"[MeSH Terms] OR "adenocarcinoma"[All Fields]) AND Title/Abstract[All Fields]) AND (("colon"[MeSH Terms] OR "colon"[All Fields]) AND ("medical subject headings"[MeSH Terms] OR ("medical"[All Fields] AND "subject"[All Fields] AND "headings"[All Fields]) OR "medical subject headings"[All Fields] OR "mesh"[All Fields]))) OR colorectal[Title/Abstract]) OR colon[Title/Abstract]) OR rectal[Title/Abstract]) | ( TITLE-ABS-KEY ( mir-31 OR mirna-31 OR microrna-31 OR "microRNA 31" ) AND TITLE-ABS-KEY ( rectal OR colorectal OR colon ) AND TITLE-ABS-KEY ( cancer OR tumor OR neoplasm OR adenocarcinoma OR carcinoma ) ) | TS=( mir-31 OR mirna-31 OR microrna-31 OR "microRNA 31" ) AND TS=( rectal OR colorectal OR colon ) AND TS=( cancer OR tumor OR neoplasm OR adenocarcinoma OR carcinoma ) | ( TITLE-ABS-KEY ( mir-31 OR mirna-31 OR microrna-31 OR "microRNA 31" ) AND TITLE-ABS-KEY ( rectal OR colorectal OR colon ) AND TITLE-ABS-KEY ( cancer OR tumor OR neoplasm OR adenocarcinoma OR carcinoma ) ) |

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Supplementary table 2 (Table S2)**: Quality assessment of the included studies based on the Newcastle-Ottawa Scale (NOS). | | | | | | | | | | | | | | | | | |
| **Quality assessment**  **criteria** | **Acceptable(\*)** | Gayathri Anandappa | Antonia Strippoli | Cristina Caramés | Jitka Mlcochova | Martha L. Slattery | Siân Pugh | Anne Haahr Mellergaard Eriksen | Hisayoshi Igarashi | Pierre Laurent-Puig | Kei Mitsuhashi | Miki Ito | Yalun Li | Gilles Manceau | Katsuhiko Nosho | Nobuhito Kubota | Min-Hui Yang |
| 2019 | 2020 | 2016 | 2015 | 2017 | 2017 | 2017 | 2014 | 2019 | - | 2014 | 2018 | 2014 | 2014 | 2020 | 2013 |
| Representativeness  of exposed cohort? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |
| Selection of the  non-exposed  cohort? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **-** | **\*** | **\*** | **\*** | **-** | **\*** | **-** |
| Ascertainment of  exposure? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |
| Demonstration that  outcome of interest  was not present at  start of study? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |
| Study controls for  age/sex? |  | **\*** | **-** | **-** | **-** | **-** | **\*** | **-** | **-** | **-** | **\*** | **-** | **-** | **-** | **\*** | **-** | **-** |
| Study controls for  at least 3 additional  risk factors? |  | - | - | - | - | - | - | - | - | \* | - | - | - | - | \* | - | - |
| Assessment of  outcome? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |
| Was follow-up long  enough for outcome  to occur? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |
| Adequacy of  follow-up of  cohorts? |  | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** | **\*** |
| Overall Quality Score (Maximum = 9) | | 8 | 7 | 7 | 7 | 7 | 8 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 9 | 7 | 7 |

|  |  |  |
| --- | --- | --- |
| **Table S3:** The relationship between miR-31 expression levels (binary: high vs. low) with tumor location and KRAS/BRAF mutational status | | |
|  |  | High miR-31 expression |
| Colon tumor location | Number of cohorts | 5 |
| Odds ratio (95% CI) | 1.13 (1.03-1.25) |
| p value | 0.252 |
| I2 (%) | 25.4 |
| Mutated KRAS | Number of cohorts | 4 |
| Odds ratio (95% CI) | 1.01 (0.53-1.93) |
| p value | 0.000 |
| I2 (%) | 86.8 |
| Mutated BRAF | Number of cohorts | 5 |
| Odds ratio (95% CI) | 4.08 (2.24-7.43) |
| p value | 0.049 |
| I2 (%) | 58.0 |