SUPPLEMENTARY FIGURE

| study | label | HR (95% CI) | % Wei |
|------------------------------------|---------------------------------------|--|--------------|
| I–IV stage | | | |
| Castells (1999) | | ♦ 3.30 (1.56, 6.99) | 3.04 |
| Earl (2015) | | 12.68 (3.54, 45.41) | 1.78 |
| Kinugasa (2015) | cohort1 | 1.84 (1.08, 3.25) | 3.67 |
| Kinugasa (2015) | cohort2 | 2.84 (1.41, 6.07) | 3.10 |
| Adamo (2017) | | 2.89 (1.20, 7.30) | 2.60 |
| Kim (2018) | | 2.54 (1.41, 4.56) | 3.55 |
| Lin (2018) | i i i | 6.72 (3.34, 13.49) | 3.20 |
| Subtotal (I-square | = 55.2%, p = 0.037) | 3.37 (2.22, 5.12) | 20.9 |
| III–IV stage | | | |
| Chen (2010) | | 9.84 (5.16, 18.76) | 3.36 |
| Tjensvoll (2016) | K-ras | 5.86 (0.72, 47.96) | 0.86 |
| Tjensvoll (2016) | ctDNA level | 1.43 (1.09, 1.88) | 4.49 |
| Chen (2017) | · · · · · · · · · · · · · · · · · · · | 1.42 (1.19, 1.69) | 4.69 |
| Cheng (2017) | ERBB2 | 1.73 (1.10, 2.72) | 3.98 |
| Cheng (2017) | K–ras G12V | 1.48 (1.08, 2.02) | 4.39 |
| Pietrasz (2017) | | - 2.24 (1.41, 3.54) | 3.96 |
| Perets (2018) | | ◆ 5.71 (1.31, 24.93) | 1.47 |
| Bernard (2019) | | 2.80 (1.40, 5.70) | 3.19 |
| Mohan (2019) | | 3.46 (1.76, 6.77) | 3.27 |
| Patel (2019) | | 2.76 (1.47, 5.18) | 3.41 |
| Strijker (2019) | | 1.06 (1.03, 1.09) | 4.84 |
| Watanabe (2019) | | 2.12 (0.99, 4.57) | 2.99 |
| Cheng (2020) | K-ras G12V | 1.62 (1.19, 2.18) | 4.41 |
| Cheng (2020) Subtotal (I-square | K-ras G12D = 89.0%, p = 0.000) | 1.58 (1.19, 2.09) 2.01 (1.58, 2.57) | 4.47 53.7 |
| I–II stage | | | |
| Hadano (2016) | | ♦ 3.18 (1.93, 5.25) | 3.83 |
| Pietrasz (2017) | i | 4.49 (1.05, 19.24) | 1.50 |
| Nakano (2018) | Baseline | 0.31 (0.04, 2.38) | 0.90 |
| Nakano (2018) | Post-operative | ♦ 3.18 (0.95, 10.66) | 1.91 |
| Yang (2018) | Baseline | 8.74 (1.57, 48.81) | 1.18 |
| Yang (2018) | Post-operative | ▶ 10.55 (1.87, 59.46) | 1.17 |
| Groot (2019) | | 2.89 (1.26, 6.67) | 2.80 |
| Lee (2019) | Baseline | 3.60 (1.00, 13.10) | 1.76 |
| Lee (2019) | Post-operative | 5.50 (1.00, 17.40) | 1.54 |
| Watanabe (2019) | | 0.66 (0.14, 3.00) | 1.39 |
| Guo (2020) | K–ras G12V | 2.10 (1.30, 3.50) | 3.85 |
| Guo (2020) | K–ras G12D | 3.50 (1.90, 6.50) | 3.46 |
| Subtotal (I-square | = 28.0%, p = 0.170) | 2.95 (2.11, 4.12) | 25.2 |
| Overall (I–squared | = 87.7%, p = 0.000) | 2.54 (2.05, 3.14) | 100 |
| NOTE: Weights are | om random effects analysis | | |

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| study | label | HR (95% CI) | % Weight |
|-----------------------------------|----------------------------|---------------------------|-------------|
| Baseline | | | |
| Castells (1999) | · · · · · | 3.30 (1.56, 6.99) | 3.04 |
| Chen (2010) | | 9.84 (5.16, 18.76) | 3.36 |
| Earl (2015) | | ◆ 12.68 (3.54, 45.41) | 1.78 |
| Kinugasa (2015) | cohort1 | 1.84 (1.08, 3.25) | 3.67 |
| Kinugasa (2015) | cohort2 | 2.84 (1.41, 6.07) | 3.10 |
| Hadano (2016) | | 3.18 (1.93, 5.25) | 3.83 |
| Tjensvoll (2016) | K–ras | 5.86 (0.72, 47.96) | 0.86 |
| Tjensvoll (2016) | ctDNA level | 1.43 (1.09, 1.88) | 4.49 |
| Adamo (2017) | | 2.89 (1.20, 7.30) | 2.60 |
| Chen (2017) | | 1.42 (1.19, 1.69) | 4.69 |
| Cheng (2017) | ERBB2 | 1.73 (1.10, 2.72) | 3.98 |
| Cheng (2017) | K–ras G12V | 1.48 (1.08, 2.02) | 4.39 |
| Pietrasz (2017) | | 2.24 (1.41, 3.54) | 3.96 |
| Kim (2018) | · · · · · | - 2.54 (1.41, 4.56) | 3.55 |
| Lin (2018) | | 6.72 (3.34, 13.49) | 3.20 |
| Nakano (2018) | < | 0.31 (0.04, 2.38) | 0.90 |
| Perets (2018) | | ◆ 5.71 (1.31, 24.93) | 1.47 |
| Yang (2018) | | ♦ 8.74 (1.57, 48.81) | 1.18 |
| Bernard (2019) | | 2.80 (1.40, 5.70) | 3.19 |
| Groot (2019) | • | 2.89 (1.26, 6.67) | 2.80 |
| Lee (2019) | · · · · · · | 3.60 (1.00, 13.10) | 1.76 |
| Mohan (2019) | | 3.46 (1.76, 6.77) | 3.27 |
| Patel (2019) | | 2.76 (1.47, 5.18) | 3.41 |
| Strijker (2019) | _ • | 1.06 (1.03, 1.09) | 4.84 |
| Watanabe (2019) | I–II stage | 0.66 (0.14, 3.00) | 1.39 |
| Watanabe (2019) | III–IV stage | 2.12 (0.99, 4.57) | 2.99 |
| Cheng (2020) | K–ras G12V | 1.62 (1.19, 2.18) | 4.41 |
| Cheng (2020) | K–ras G12D | 1.58 (1.19, 2.09) | 4.47 |
| Guo (2020) | K–ras G12V | 2.10 (1.30, 3.50) | 3.85 |
| Guo (2020) | K–ras G12D | 3.50 (1.90, 6.50) | 3.46 |
| Subtotal (I–squared | = 88.4%, p = 0.000) | 2.42 (1.95, 3.01) | 93.89 |
| Post–operative Pietrasz (2017) | | 4.49 (1.05, 19.24) | 1.50 |
| Nakano (2018) | | 3.18 (0.95, 10.66) | 1.91 |
| Yang (2018) | 1 | ◆ → 10.55 (1.87, 59.46) | 1.17 |
| Lee (2019) | | 5.50 (1.00, 17.40) | 1.54 |
| Subtotal (I–squared | = 0.0%, p = 0.733) | 4.84 (2.38, 9.85) | 6.11 |
| Overall (I–squared : | 87.7%, p = 0.000) | 2.54 (2.05, 3.14) | 100.00 |
| NOTE: Weights are f | om random effects analysis | | |
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| study | label | HR (95% CI) | Weight |
|-----------------------------|---------------------------|---|--------|
| (-ras | | | |
| Castells (1999) | | 3.30 (1.56, 6.99) | 2.80 |
| Chen (2010) | | 9.84 (5.16, 18.76) | 3.11 |
| arl (2015) | | 12.68 (3.54, 45.41) | 1.62 |
| (inugasa (2015) | cohort1 | 1.84 (1.08, 3.25) | 3.40 |
| (inugasa (2015) | cohort2 | 2.84 (1.41, 6.07) | 2.86 |
| ladano (2016) | | - 3.18 (1.93, 5.25) | 3.56 |
| jensvoll (2016) | | 5.86 (0.72, 47.96) | 0.77 |
| Adamo (2017) | | 2.89 (1.20, 7.30) | 2.39 |
| (im (2018) | | | 3.29 |
| .in (2018) | | 2.54 (1.41, 4.56) | 2.95 |
| lin (2018) Vakano (2018) | Baseline | 6.72 (3.34, 13.49) 0.31 (0.04, 2.38) | 0.81 |
| | | | |
| Vakano (2018) | Post-operative | 3.18 (0.95, 10.66) | 1.74 |
| Perets (2018) | | 5.71 (1.31, 24.93) | 1.34 |
| Bernard (2019) | | 2.80 (1.40, 5.70) | 2.94 |
| Groot (2019) | | 2.89 (1.26, 6.67) | 2.57 |
| _ee (2019) | Baseline | 3.60 (1.00, 13.10) | 1.61 |
| _ee (2019) | Post–operative | 5.50 (1.00, 17.40) | 1.40 |
| Mohan (2019) | | 3.46 (1.76, 6.77) | 3.02 |
| Watanabe (2019) | I–II stage | 0.66 (0.14, 3.00) | 1.26 |
| Watanabe (2019) | III–IV stage | 2.12 (0.99, 4.57) | 2.76 |
| Subtotal (I–squared = | 48.6%, p = 0.008) | 3.31 (2.53, 4.34) | 46.18 |
| (–ras G12V | | | |
| Kinugasa (2015) | cohort1 | 2.05 (1.19, 3.47) | 3.45 |
| Kinugasa (2015) | cohort2 | 3.25 (1.40, 7.20) | 2.61 |
| Cheng (2017) | | 1.48 (1.08, 2.02) | 4.10 |
| rang (2018) | Baseline | 8.74 (1.57, 48.81) | 1.07 |
| /ang (2018) | Post–operative | 10.55 (1.87, 59.46) | 1.05 |
| Cheng (2020) | | 1.62 (1.19, 2.18) | 4.12 |
| Guo (2020) | | 2.10 (1.30, 3.50) | 3.57 |
| Subtotal (I—squared = | 49.3%, p = 0.066) | 2.03 (1.51, 2.74) | 19.97 |
| K–ras G12D | | | |
| Kinugasa (2015) | cohort1 | 1.27 (0.74, 2.12) | 3.48 |
| (inugasa (2015) | cohort2 | 1.62 (0.82, 3.16) | 3.02 |
| Cheng (2020) | | 1.58 (1.19, 2.09) | 4.17 |
| Guo (2020) | | 3.50 (1.90, 6.50) | 3.20 |
| subtotal (I–squared = | 55.6%, p = 0.080) | 1.77 (1.22, 2.58) | 13.87 |
| tDNA level | | | |
| jensvoll (2016) | | 1.43 (1.09, 1.88) | 4.19 |
| Chen (2017) | | 1.42 (1.19, 1.69) | 4.39 |
| Patel (2019) | | 2.76 (1.47, 5.18) | 3.16 |
| Strijker (2019) | • | 1.06 (1.03, 1.09) | 4.53 |
| subtotal (I–squared = | 87.2%, p = 0.000) | 1.40 (1.07, 1.83) | 16.28 |
| ERBB2 | | | |
| Cheng (2017) | | 1.73 (1.10, 2.72) | 3.70 |
| Subtotal (I—squared = | %, p = .) | 1.73 (1.10, 2.72) | 3.70 |
| Overall (I–squared = 8 | 5.9%, p = 0.000) | 2.42 (1.98, 2.97) | 100.00 |
| NOTE: Weights are from | n random effects analysis | | |
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Supplementary Figure 1. (A) Subgroup analyses of OS according to tumor stage. (B) Subgroup analyses of OS according to sampling time. (C) Subgroup analyses of OS according to detection marker.