**Table 1.** Patient and clinical characteristics of the whole and matched cohorts

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| --- | --- | --- | --- | --- | --- | --- |
| **Characteristics** | **Whole cohort (n=1257)** | | | **Matched cohort (n=508)** | | |
| **Synchronous (n=931)** | **Metachronous (n=326)** | ***p* value** | **Synchronous (n= 381)** | **Metachronous (n= 127)** | ***p* value** |
| Age at diagnosis, mean (SD), y | 59.3 (9.2) | 58.7 (9.5) | 0.47 |  |  | 0.24 |
| Sex, male, n (%) | 597 (64.1) | 201 (61.7) | 0.43 |  |  | 0.26 |
| KPS, mean (SD) | 83.6 (6.9) | 84.5 (7.4) | **<0.01** |  |  | 0.50 |
| \*Primary tumor size, mean (SD), cm | 4.7 (1.8) | 3.9 (1.9) | **<0.01** |  |  |  |
| Regional LN enlargement, n (%) | 662 (71.1) | 253 (77.6) | **0.04** |  |  | 0.05 |
| Primary tumor site, n (%) |  |  | **<0.01** |  |  | **0.03** |
| Head & neck | 361 (38.8) | 206 (63.2) |  |  |
| Body & tale | 570 (61.2) | 120 (36.8) |  |  |
| The extent of LM, n (%) |  |  | 0.35 |  |  | 0.95 |
| <25% | 731 (78.5) | 264 (81.0) |  |  |
| ≥25% | 200 (21.5) | 62 (19.0) |  |  |
| Child-Pugh classification, n (%) |  |  | **0.04** |  |  | 0.49 |
| A | 757 (81.3) | 281 (86.2) |  |  |
| B | 169 (18.2) | 44 (13.5) |  |  |
| C | 5 (0.5) | 1 (0.3) |  |  |
| Extrahepatic metastasis, n (%) | 439 (47.2) | 178 (54.6) | **0.03** |  |  | **0.001** |
| Pain, n (%) | 630 (67.7) | 185 (56.7) | **<0.01** |  |  | 0.07 |
| \*\*Weight loss, n (%) | 305 (32.8) | 99 (30.4) | 0.42 |  |  | 0.67 |
| Tumor differentiation, n (%) |  |  | **<0.01** |  |  | **0.001** |
| Dedifferentiation | 8 (0.9) | 3 (0.9) |  |  |
| Poorly | 249 (26.7) | 31 (9.5) |  |  |
| Moderately | 259 (27.8) | 201 (61.7) |  |  |
| Well | 4 (0.4) | 10 (3.1) |  |  |
| Unknown | 411 (44.1) | 81 (24.8) |  |  |
| CEA (ng/ml), n/total n (%) |  |  |  |  |  | 0.32 |
| <5 | 372 (40.0) | 157 (48.2) | **0.02** |  |  |
| ≥5 | 545 (58.5) | 168 (51.5) |  |  |
| Unknown | 14 (1.5) | 1 (0.3) |  |  |
| #CA19-9 (U/ml), n/total n (%) |  |  | **<0.01** |  |  | 0.71 |
| <500 | 390 (41.9) | 190 (58.3) |  |  |
| ≥500 | 534 (57.4) | 136 (41.7) |  |  |
| Unknown | 7 (0.8) | 0 (0) |  |  |
| CA242 (U/ml), n/total n (%) |  |  | **<0.01** |  |  | 0.67 |
| <20 | 237 (25.5) | 110 (33.7) |  |  |
| ≥20 | 594 (63.8) | 182 (55.8) |  |  |
| Unknown | 100 (10.7) | 34 (10.4) |  |  |
| WBC (\*109/ml), n/total n (%) |  |  | **0.03** |  |  | 0.23 |
| <10 | 808 (86.8) | 298 (91.4) |  |  |
| ≥10 | 121 (13.0) | 28 (8.6) |  |  |
| Unknown | 2 (0.2) | 0 |  |  |
| ALT (U/L), n/total n (%) |  |  | **<0.01** |  |  | **0.003** |
| <60 | 722 (77.6) | 290 (89.0) |  |  |
| ≥60 | 207 (22.2) | 36 (11.0) |  |  |
| Unknown | 2 (0.2) | 0 |  |  |
| AST (U/L), n/total n (%) |  |  | **<0.01** |  |  | 0.10 |
| <60 | 747 (80.2) | 290 (89.0) |  |  |
| ≥60 | 182 (19.5) | 36 (11.0) |  |  |
| Unknown | 2 (0.2) | 0 |  |  |
| ALP (U/L), n/total n (%) |  |  | 0.19 |  |  | 0.61 |
| <130 | 470 (50.5) | 180 (55.2) |  |  |
| ≥130 | 452 (48.5) | 146 (44.8) |  |  |
| Unknown | 9 (1.0) | 0 |  |  |
| GGT (U/L), n/total n (%) |  |  | **<0.01** |  |  | 0.06 |
| <54 | 363 (39.0) | 180 (55.2) |  |  |
| ≥54 | 556 (59.7) | 144 (44.2) |  |  |
| Unknown | 12 (1.3) | 2 (0.6) |  |  |
| CRP (mg/L), n/total n (%) |  |  | **0.01** |  |  | 0.99 |
| <8 | 278 (29.9) | 127 (39.0) |  |  |
| ≥8 | 260 (27.9) | 78 (23.9) |  |  |
| Unknown | 393 (42.2) | 121 (37.1) |  |  |
| LDH (U/L), n/total n (%) |  |  | **<0.01** |  |  | 0.48 |
| < 250 | 576 (61.9) | 228 (69.9) |  |  |
| ≥250 | 196 (21.1) | 27 (8.3) |  |  |
| Unknown | 159 (17.1) | 71 (21.8) |  |  |
| Pancreatic tumor resection, n (%) | 36 (3.9) | 194 (59.5) | **<0.01** |  |  | 0.001 |
| First-line SCT regimens, n/total n (%) |  |  | 0.81 |  |  | 0.81 |
| Without SCT | 302 (32.4) | 114 (35.0) |  |  |
| GEM/S-1 monotherapy | 108 (11.6) | 44 (13.5) |  |  |
| GEM + OX/S-1/5-FU/Capecitabine | 143 (15.4) | 37 (11.3) |  |  |
| GEM + nab-PTX | 265 (28.5) | 75 (23.0) |  |  |
| mFOLFIRINOX | 113 (12.1) | 56 (17.2) |  |  |
| Liver-directed therapies, n (%) | 156 (16.8) | 80 (24.5) | **<0.01** |  |  | 0.08 |
| \* Some data (< 5%) was missing. \*\* Weight loss of over 10% of body weight within 3 months. # The data of CA19-9 was mainly from the values in the non-jaundice state. n indicates the number of participants. Abbreviations: SD, standard deviation; KPS, Karnofsky performance status; LN, lymph node; LM, liver metastases; TB, total bilirubin; CB, conjugated bilirubin; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CA242, carbohydrate antigen 242; WBC, white blood cell; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, glutamyl transpeptidase; ALB, albumin; LDH, lactate dehydrogenase; SCT, systemic chemotherapy; HAI, hepatic arterial infusion. | | | | | | |

**Table 2.** Multivariate analysis of variables for the whole cohort

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| **Variables** | **HR (95% CI)** | ***p* value** |
| Timing of LM (S-LM vs. M-LM) | 1.67 (1.13-2.47) | **0.011** |
| Age (<65 vs. ≥65) | 1.17 (0.86-1.61) | 0.320 |
| KPS (≤80 vs. >80) | 0.70 (0.52-0.94) | **0.019** |
| Primary tumor size (<5 vs. ≥5 cm) | 0.86 (0.64-1.15) | 0.318 |
| Regional LN enlargement  (Yes vs. No) | 1.03 (0.76-1.41) | 0.830 |
| Extent of liver involvement  (≥25% vs. <25%) | 0.66 (0.42-1.06) | 0.088 |
| Extrahepatic metastasis (Yes vs. No) | 1.19 (0.90-1.58) | 0.218 |
| Child-Pugh classification (A vs. B vs. C) | 2.47 (1.51-4.02) | **<0.001** |
| Weight loss within 3 months  (<10% vs. ≥10%) | 1.01 (0.75-1.37) | 0.930 |
| CEA (<5 vs. ≥5 ng/ml) | 0.92 (0.69-1.23) | 0.583 |
| CA19-9 (≥500 vs. <500U/ml) | 1.49 (1.05-2.11) | **0.024** |
| CA242 (<20 vs. ≥20U/ml) | 0.90 (0.63-1.30) | 0.586 |
| ALT (<60 vs. ≥60U/L) | 1.00 (0.58-1.73) | 0.992 |
| AST (<60 vs. ≥60U/L) | 0.66 (0.37-1.18) | 0.160 |
| GGT (<54 vs. ≥54U/L) | 1.35 (0.94-1.94) | 0.101 |
| ALP (<130 vs. ≥130U/L) | 0.78 (0.54-1.13) | 0.188 |
| LDH (<250 vs. ≥250U/L) | 1.61 (1.03-2.51) | **0.037** |
| WBC (<10 vs. ≥10 \*109/L) | 1.06 (0.66-1.70) | 0.795 |
| CRP (<8 vs. ≥8mg/L) | 1.21 (0.89-1.63) | 0.218 |
| Cancer pain (Yes vs. No) | 1.26 (0.94-1.70) | 0.124 |
| Tumor differentiation (Dedifferentiation vs. Poorly vs. Moderately vs. Well) | 1.07 (0.82-1.39) | 0.631 |
| Pancreatic tumor resection (Yes vs. No) | 0.62 (0.42-0.94) | **0.022** |
| First-line SCT regimens (Without SCT vs. GEM/S-1 monotherapy vs. GEM + OX/S-1/5-FU/Capecitabine vs. GEM + nab-PTX vs. mFOLFIRINOX) | 0.82 (0.74-0.91) | **<0.001** |
| Liver-directed therapies (Yes vs. No) | 0.55 (0.39-0.79) | **0.001** |
| Abbreviations: HR, hazard ratio; CI, confidence interval; LM, liver metastases; S-, synchronous; M-, metachronous; KPS, Karnofsky performance status; LN, lymph node; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; CA242, carbohydrate antigen 242; TB, total bilirubin; CB, conjugated bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALB, albumin; GGT, glutamyl transpeptidase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; WBC, white blood cell; Hb, hemoglobin; SCT, systemic chemotherapy; HAI, hepatic arterial infusion. | | |