|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Supplementary table 1. Associations between HuR C/N ratio and clinicopathological parameters in pancreatobiliary adenocarcinomas | | | | | | | | | |
|  | |  | |  | |  | |  | |
|  |  | | HuR C/N ratio | | | | | |
|  |  | | low (n=54) | | high (n=55) | | p-value | |
| Excluded, neoadjuvant treatment | | |  | | 2 | |  | |
| Lost to follow up | | | 1 | |  | |  | |
| hENT1 | | |  | |  | | 0.564 | |
|  | low | | 29 (54%) | | 25 (46%) | |  | |
|  | high | | 25 (47%) | | 28 (53%) | |  | |
| dCK | | |  | |  | | 0.442 | |
|  | low | | 25 (46%) | | 29 (54%) | |  | |
|  | high | | 29 (55%) | | 24 (45%) | |  | |
| HuR C | | |  | |  | | **<0.001** | |
|  | low | | 40 (74%) | | 14 (26%) | |  | |
|  | high | | 14 (26%) | | 39 (74%) | |  | |
| Year of surgery, M (IQR) | | | 2010 (2005–2011) | | 2008 (2006–2010) | | 0.456 | |
| Age, M (IQR) | | | 66 (61–73) | | 67 (62–72) | | 0.469 | |
| Sex | | |  | |  | | **0.001** | |
|  | Women | | 34 (68%) | | 16 (32%) | |  | |
|  | Men | | 20 (35%) | | 37 (65%) | |  | |
| Tumour origin | | |  | |  | | 0.051 | |
|  | Ampulla Vateri | | 5 (26%) | | 14 (74%) | |  | |
|  | Distal bile duct | | 27 (60%) | | 18 (40%) | |  | |
|  | Pancreas | | 22 (51%) | | 21 (49%) | |  | |
| Tumour size, mm, M (IQR) | | | 30 (24–35) | | 30 (23–38) | | 0.985 | |
| Differentiation grade | | |  | |  | | 0.072 | |
|  | Well/moderate | | 15 (38%) | | 24 (62%) | |  | |
|  | Poor | | 39 (57%) | | 29 (43%) | |  | |
| T-stage | | |  | |  | | 1.000 | |
|  | T1/T2 | | 6 (50%) | | 6 (50%) | |  | |
|  | T3/T4 | | 48 (51%) | | 47 (49%) | |  | |
| N-stage | | |  | |  | | 1.000 | |
|  | N0 | | 15 (50%) | | 15 (50%) | |  | |
|  | N1 | | 39 (51%) | | 38 (49%) | |  | |
| Perineural growth | | |  | |  | | 0.347 | |
|  | No | | 9 (41%) | | 13 (59%) | |  | |
|  | Yes | | 45 (53%) | | 40 (47%) | |  | |
| Growth in lymphatic vessels | | |  | |  | | 0.140 | |
|  | No | | 20 (63%) | | 12 (37%) | |  | |
|  | Yes | | 34 (45%) | | 41 (55%) | |  | |
| Growth in blood vessels | | |  | |  | | 0.546 | |
|  | No | | 37 (53%) | | 33 (47%) | |  | |
|  | Yes | | 17 (46%) | | 20 (54%) | |  | |
| Growth in peripancreatic fat | | |  | |  | | 0.474 | |
|  | No | | 13 (59%) | | 9 (41%) | |  | |
|  | Yes | | 41 (48%) | | 44 (52%) | |  | |
| Margins | | |  | |  | | **0.027** | |
|  | R0 | | 6 (100%) | | 0 (0%) | |  | |
|  | R1/Rx | | 48 (48%) | | 53 (52%) | |  | |
| Adjuvant treatment | | |  | |  | | 0.699 | |
|  | No gemcitabine | | 31 (52%) | | 28 (47%) | |  | |
|  | Gemcitabine | | 23 (48%) | | 25 (52%) | |  | |
| Recurrence | | |  | |  | | 0.294 | |
|  | None | | 10 (53%) | | 9 (47%) | |  | |
|  | Local | | 18 (62%) | | 11 (38%) | |  | |
|  | Distant | | 26 (44%) | | 33 (56%) | |  | |
|  | |  | |  | |  | |  | |
| M, median. IQR, interquartile range. Bold text indicates significant values. | | | | | | | | | |

Supplementary table 2. Cox proportional hazards analysis of the impact of expression of hENT1, dCK, HuR and HuR cytoplasmic/nuclear ratio on overall survival in patients with pancreatobiliary type tumours

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Number (events)** | **OS HR (95% CI)** | | ***P for interaction*** |
|  |  | *unadjusted* | adjusted |  |
| **hENT1** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 53 (42) | 1.00 | 1.00 |  |
| High | 53 (40) | 0.89 (0.57–1.37) | 1.59 (0.97–2.61) |  |
| *No gemcitabine* |  |  |  | *NS* |
| Low | 32 (27) | 1.00 | 1.00 |
| High | 26 (20) | 0.98 (0.55–1.76) | **2.20 (1.12–4.30)** |
| *Gemcitabine* |  |  |  |
| Low | 21 (15) | 1.00 | 1.00 |
| High | 27 (20) | 0.87 (0.44–1.71) | 1.46 (0.69–3.08) |
| **dCK** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 53 (40) | 1.00 | 1.00 |  |
| High | 53 (42) | 1.15 (0.75–1.78) | 1.20 (0.77–1.87) |  |
| *No gemcitabine* |  |  |  | *NS* |
| Low | 28 (21) | 1.00 | 1.00 |
| High | 30 (26) | 1.55 (0.86–2.79) | **1.89 (1.03–3.46)** |
| *Gemcitabine* |  |  |  |
| Low | 25 (19) | 1.00 | 1.00 |
| High | 23 (16) | 0.71 (0.36–1.42) | 0.69 (0.35–1.37) |
| ***HuR*** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 53 (40) | 1.00 | 1.00 |  |
| High | 53 (42) | 1.09 (0.70–1.68) | 1.16 (0.75–1.80) |  |
| *No Gemcitabine* |  |  |  | *NS* |
| Low | 32 (27) | 1.00 | 1.00 |
| High | 26 (20) | 0.83 (0.46–1.48) | 0.81 (0.44–1.50) |
| *Gemcitabine* |  |  |  |
| Low | 21 (13) | 1.00 | 1.00 |
| High | 27 (22) | 1.74 (0.87–3.47) | 1.62 (0.81–3.26) |
| ***HuR C/N ratio*** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 53 (39) | 1.00 | 1.00 |  |
| High | 53 (43) | 1.09 (0.71–1.69) | 1.07 (0.68–1.67) |  |
| *No Gemcitabine* |  |  |  | ***0.028*** |
| Low | 30 (26) | 1.00 | 1.00 |
| High | 28 (21) | 0.72 (0.40–1.28) | 0.56 (0.31–1.01) |
| *Gemcitabine* |  |  |  |
| Low | 23 (13) | 1.00 | 1.00 |
| High | 25 (22) | **2.07 (1.03–4.17)** | **2.19 (1.08–4.45)** |

The multivariable model included age (continuous), T-stage (1–2 vs 3–4), N-Stage, differentiation grade (well-moderate vs poor), lymphatic invasion, vascular invasion, perineural growth, and in the analysis including all cases also gemcitabine treatment (yes/no). C/N ratio= cytoplasmic/nuclear ratio. Bold text indicates significant values. NS= non-significant.

Supplementary table 3. Cox proportional hazards analysis of the impact of expression of hENT1, dCK, HuR and HuR cytoplasmic/nuclear ratio on overall survival in patients with intestinal type tumours

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **Number (events)** | **OS HR (95% CI)** | | ***P for interaction*** |
|  |  | *unadjusted* | adjusted |  |
| **hENT1** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 31 (18) | 1.00 | 1.00 |  |
| High | 30 (12) | 0.57 (0.28–1.19) | 0.49 (0.22–1.11) |  |
| *No adjuvant* |  |  |  | *NS* |
| Low | 23 (15) | 1.00 | 1.00 |
| High | 20 (9) | 0.51 (0.22–1.18) | **0.33 (0.12–0.85)** |
| *Adjuvant* |  |  |  |
| Low | 8 (3) | 1.00 |  |
| High | 10 (3) | 0.82 (0.16–4.11) | † |
| **dCK** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 30 (17) | 1.00 | 1.00 |  |
| High | 31 (13) | 0.78 (0.38–1.61) | 1.09 (0.50–2.33) |  |
| *No adjuvant* |  |  |  | *\** |
| Low | 21 (11) | 1.00 | 1.00 |
| High | 22 (13) | 1.28 (0.57–2.86) | 1.54 (0.65–3.64) |
| *Adjuvant* |  |  |  |
| Low | 9 (6) |  |  |
| High | 9 (0) | \* | \* |
| ***HuR*** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 32 (23) | 1.00 | 1.00 |  |
| High | 29 (7) | **0.21 (0.09–0.49)** | **0.26 (0.11–0.64)** |  |
| *No adjuvant* |  |  |  | *NS* |
| Low | 23 (18) | 1.00 | 1.00 |
| High | 20 (6) | **0.22 (0.09–0.56)** | **0.23 (0.09–0.60)** |
| *Adjuvant* |  |  |  |
| Low | 9 (5) | 1.00 |  |
| High | 9 (1) | 0.18 (0.02–1.51) | † |
| ***HuR C/N ratio*** |  |  |  |  |
| *All* |  |  |  |  |
| Low | 32 (20) | 1.00 | 1.00 |  |
| High | 29 (10) | **0.42 (0.20–0.91)** | **0.42 (0.19–0.93)** |  |
| *No adjuvant* |  |  |  | *NS* |
| Low | 24 (16) | 1.00 | 1.00 |
| High | 19 (8) | 0.50 (0.21–1.18) | 0.40 (0.16–1.01) |
| *Adjuvant* |  |  |  |
| Low | 8 (4) | 1.00 |  |
| High | 10 (2) | 0.31 (0.05–1.83) | † |

The multivariable model included age (continuous), T-stage (1–2 vs 3–4), N-Stage, differentiation grade (well-moderate vs poor), lymphatic invasion, vascular invasion, perineural growth, and in the analysis including all cases also adjuvant treatment (yes/no). C/N ratio= cytoplasmic/nuclear ratio. Bold text indicates significant values. NS= non-significant. Asterisk (\*) indicates non-computable HR and interaction, due to no events in one stratum. Dagger (†) indicates that multivariable analysis was not performed due to few cases and events.