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| Supplementary Table 1  Treatment patterns | | | |
| Characteristic | GC-4w  *n* = 251 | GC-3w  *n* = 455 | *P*-value |
| Median number of cycles (range)  Mean number of cycles  No. of cycles  1  2  3  4  No. of treatment-occasions with cisplatin delivered of total planned (%)  No. of treatment-occasions with gemcitabine delivered of total planned (%) | 3 (1–3)  2.7  18 (7)  33 (13)  200 (80)  -  91  80 | 4 (1–4)  3.3  48 (11)  55 (12)  81 (18)  271 (60)  82  78 |  |
| Time, median (range), weeks  start chemotherapy to cystectomy  stop chemotherapy to cystectomy | 13.9 (4.1–31.1)  4.7 (1.1–26.1) | 14.4 (3.0–36.1)  5.0 (1.9–26.1) |  |
| No. of patients who stopped treatment prematurely  Reason to stop treatment prematurelyb  Anaemia  Neutropenia  Thrombocytopenia  Febrile neutropenia  Infection  Decreased kidney function  Thromboembolic event  Impaired hearing  Peripheral neuropathy  Heart failure  Progressive disease  Other reasons | 51 (20)  0  4 (2)  5 (2)  5 (2)  8 (3)  8 (3)  5 (2)  2 (1)  0  0  13 (5)  14 (6) | 184 (40)  4 (1)  21 (5)  6 (1)  4 (1)  6 (1)  42 (9)  10 (2)  28 (6)  14 (3)  3 (1)  7 (2)  8 (2) | < 0.005 |
| No. of patients with dose delaya  Reason for dose delayb  Anaemia  Neutropenia  Thrombocytopenia  Neutropenic fever  Infection  Decreased kidney function  Other reasons | 14 (6)  1 (0)  1 (0)  0  1 (0)  9 (4)  1 (0)  2 (1) | 125 (27)  1 (0)  91 (20)  10 (2)  4 (1)  7 (2)  6 (1)  15 (3) | < 0.005 |
| No. of patients with G-CSFa | 20 (8) | 122 (27) | < 0.005 |
| No. of patients with any omitted dosea  No. of patients with omitted gemcitabine day 8a  Reasonomitted day 8b  Anaemia  Neutropenia  Thrombocytopenia  Neutropenic fever  Infection  Decreased kidney function  Other reason  No. of patients with omitted gemcitabine day 15a  Reason omitted day 15b  Anaemia  Neutropenia  Thrombocytopenia  Neutropenic fever  Infection  Decreased kidney function  Other reason | 132 (53)  50 (20)  0  10 (4)  4 (2)  1 (0)  13 (5)  7 (3)  30 (12)  119 (47)  6 (2)  55 (22)  70 (28)  4 (2)  16 (6)  5 (2)  26 (10) | 105 (23)  105 (23)  0  34 (7)  5 (1)  1 (0)  12 (3)  13 (3)  47 (10)  - | < 0.005  0.332 |
| No. of patients with any dose reductiona  No. of patients with cisplatin dose reduction day 1a  Reason for cisplatin dose reduction day1b  Anaemia  Neutropenia  Thrombocytopenia  Neutropenic fever  Infection  Decreased kidney function  Other reason  No. of patients with gemcitabine dose reductionday 8a  Reason for gemcitabine dose reduction day 8b  Anaemia  Neutropenia  Thrombocytopenia  Neutropenic fever  Infection  Decreased kidney function  Other reason  No. of patients with gemcitabine dose reductionday 15a  Reason for gemcitabine dose reduction day 15b  Anaemia  Neutropenia  Thrombocytopenia  Neutropenic fever  Infection  Decreased kidney function  Other reason | 92 (37)  17 (7)  0  5 (2)  5 (2)  0  0  6 (2)  6 (2)  34 (14)  0  16 (6)  18 (7)  0  0  5 (2)  6 (2)  75 (30)  1 (0)  19 (8)  64 (25)  0  0  4 (2)  4 (2) | 73 (16)  63 (14)  1 (0)  17 (4)  7 (2)  4 (1)  0  5 (1)  32 (7)  56 (12)  1 (0)  27 (6)  8 (2)  5 (1)  0  1 (0)  19 (4)  - | < 0.005  0.005  0.637 |
| Data are *n* (%), except where indicated.  aIn at least one cycle.  bMore than one reason per patient possible. | | | |

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| Supplementary Table 2  Multivariable analysis of factors predicting pathologic response | | | | | | | | |
|  |  | pT0N0 | |  |  | < pT2N0 | |  |
|  | OR (95% CI) | | *P*-value | | OR (95% CI) | | *P*-value | |
| Chemotherapy regimen  GC-4w  GC-3w | 1  1.80 (1.16–2.80) | | 0.009 | | 1  1.08 (0.70–1.66) | | 0.743 | |
| Treatment calendar period  2010–2012 | 1 | |  | | 1 | |  | |
| 2013–2015 | 0.83 (0.46–1.47) | | 0.517 | | 1.31 (0.74–2.29) | | 0.355 | |
| 2016–2018 | 0.53 (0.29–0.97) | | 0.038 | | 0.92 (0.51–1.66) | | 0.781 | |
| Age interval  34–59 years | 1 | |  | | 1 | |  | |
| 60–69 years | 1.01 (0.68–1.51) | | 0.959 | | 1.00 (0.67–1.49) | | 0.994 | |
| 70–80 years | 1.29 (0.83–2.00) | | 0.261 | | 1.30 (0.84–2.03) | | 0.244 | |
| Sex  Male  Female | 1  0.86 (0.60–1.22) | | 0.398 | | 1  0.67 (0.48–0.96) | | 0.027 | |
| ECOG performance status  0 | 1 | |  | | 1 | |  | |
| 1 | 0.68 (0.41–1.24) | | 0.145 | | 0.57 (0.35–0.94) | | 0.028 | |
| Missing data | 0.90 (0.45–1.79) | | 0.755 | | 1.33 (0.63–2.80) | | 0.454 | |
| GFR  < 60 ml/min | 1 | |  | | 1 | |  | |
| ≥ 60 ml/min | 2.23 (0.86–5.76) | | 0.098 | | 2.38 (1.02–5.57) | | 0.045 | |
| cTNM  cT2N0 | 1 | |  | | 1 | |  | |
| cT3N0 | 0.65 (0.42–1.01) | | 0.054 | | 0.44 (0.29–0.67) | | < 0.005 | |
| cT4N0 | 0.33 (0.13–0.83) | | 0.019 | | 0.26 (0.11–0.60) | | < 0.005 | |
| cTxN0 | 0.91 (0.61–1.37) | | 0.657 | | 1.10 (0.72–1.68) | | 0.661 | |
| ECOG, Eastern Cooperative Oncology Group; GFR, glomerular filtration rate; OR, odds ratio; CI, confidence interval. | | | | | | | | |

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| Supplementary Table 3  Relapse | | | | | | |
|  | GC-4w | GC-3w |  |  |  |  |
|  | *n* (%) | *n* (%) | OR (95% CI) | *P*-value | aORa (95% CI) | *P***-**value |
| Relapse | 85 (34) | 129 (28) | 0.77 (0.56–1.08) | 0.127 | 1.38 (0.86–2.21) | 0.177 |
| Relapse during year 1 | 45 (53) | 68 (54) |  |  |  |  |
| Relapse during year 2 | 25 (29) | 41 (33) |  |  |  |  |
| Relapse during year 3 | 7 (8) | 9 (7) |  |  |  |  |
| Relapse after year 3 | 8 (9) | 7 (6) |  |  |  |  |
|  |  |  |  |  |  |  |
| Time from chemo start  to relapse, months |  |  |  |  |  |  |
| Median (range) | 11.4 (2.5–65.2) | 11.3 (2.3–66.9) |  |  |  |  |
| Time from relapse to  death, months |  |  |  |  |  |  |
| Median (range) | 6.2 (0.03–39.0) | 5.1 (0.2–28.0) |  |  |  |  |
| Data are *n* (%), except where indicated.  aAdjusted for calendar period, age, sex, ECOG, GFR, and clinical stage.  OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval. | | | | | |  |

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| Supplementary Table 4  Multivariable analysis of factors predicting survival | | | |
|  | All-cause survival | Bladder-cancer-specific survival | Relapse-free survival |
|  | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| Chemotherapy regimen |  |  |  |
| GC-4w | 1 | 1 | 1 |
| GC-3w | 1.36 (0.89–2.07) | 1.30 (0.82–2.04) | 1.24 (0.84–1.84) |
| Treatment calendar period |  |  |  |
| 2010–2012 | 1 | 1 | 1 |
| 2013–2015 | 0.87 (0.53–1.43) | 0.86 (0.51–1.46) | 0.70 (0.44–1.09) |
| 2016–2018 | 0.79 (0.47–1.35) | 0.81 (0.46–1.43) | 0.72 (0.45–1.16) |
| Age interval |  |  |  |
| 34–59 years | 1 | 1 | 1 |
| 60–69 years | 1.00 (0.68–1.45) | 0.93 (0.63–1.38) | 0.82 (0.58–1.15) |
| 70–80 years | 0.90 (0.59–1.37) | 0.79 (0.50–1.24) | 0.73 (0.50–1.08) |
| Sex |  |  |  |
| Male | 1 | 1 | 1 |
| Female | 1.66 (1.22–2.26) | 1.77 (1.27–2.46) | 1.81 (1.36–2.42) |
| ECOG performance status |  |  |  |
| 0 | 1 | 1 | 1 |
| 1 | 1.24 (0.79–1.93) | 1.22 (0.76–1.96) | 1.30 (0.86–1.95) |
| missing | 1.12 (0.59–2.10) | 0.82 (0.38–1.79) | 0.83 (0.42–1.66) |
| GFR |  |  |  |
| < 60 ml/min | 1 | 1 | 1 |
| ≥ 60 ml/min | 0.58 (0.32–1.04) | 0.60 (0.32–1.13) | 0.54 (0.31–0.94) |
| cTNM |  |  |  |
| cT2N0 | 1 | 1 | 1 |
| cT3N0 | 1.48 (1.01–2.18) | 1.62 (1.07–2.45) | 1.37 (0.95–1.96) |
| cT4N0 | 2.13 (1.18–3.85) | 2.41 (1.29–4.49) | 1.97 (1.13–3.44) |
| cTxN0 | 0.87 (0.57–1.33) | 1.04 (0.66–1.62) | 0.90 (0.60–1.34) |
| HR, hazard ratio; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; GFR, glomerular filtration rate. | | | |