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| Supplementary Table 1Treatment patterns |
| Characteristic | GC-4w*n* = 251 | GC-3w*n* = 455 | *P*-value |
| Median number of cycles (range)Mean number of cyclesNo. of cycles1234No. of treatment-occasions with cisplatin delivered of total planned (%)No. of treatment-occasions with gemcitabine delivered of total planned (%) | 3 (1–3)2.718 (7)33 (13)200 (80)-9180 | 4 (1–4)3.348 (11)55 (12)81 (18)271 (60)8278 |  |
| 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 prematurelyReason 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)04 (2)5 (2)5 (2)8 (3)8 (3)5 (2)2 (1)0013 (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 delayaReason for dose delayb Anaemia Neutropenia Thrombocytopenia Neutropenic fever Infection  Decreased kidney function Other reasons | 14 (6)1 (0)1 (0)01 (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 doseaNo. of patients with omitted gemcitabine day 8a Reasonomitted day 8b Anaemia  Neutropenia Thrombocytopenia Neutropenic fever Infection Decreased kidney function Other reasonNo. 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)010 (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)034 (7) 5 (1) 1 (0) 12 (3) 13 (3) 47 (10) - | < 0.0050.332 |
| No. of patients with any dose reductionaNo. 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 reasonNo. 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)05 (2)5 (2)006 (2)6 (2)34 (14)016 (6)18 (7)005 (2)6 (2)75 (30)1 (0)19 (8)64 (25)004 (2)4 (2) | 73 (16)63 (14)1 (0) 17 (4) 7 (2) 4 (1) 05 (1) 32 (7) 56 (12)1 (0) 27 (6) 8 (2) 5 (1) 01 (0) 19 (4) - | < 0.0050.0050.637 |
| Data are *n* (%), except where indicated.aIn at least one cycle.bMore than one reason per patient possible. |

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| Supplementary Table 2Multivariable analysis of factors predicting pathologic response  |
|  |  | pT0N0 |  |  | < pT2N0 |  |
|  | OR (95% CI) | *P*-value | OR (95% CI) | *P*-value |
| Chemotherapy regimen GC-4w GC-3w | 11.80 (1.16–2.80) | 0.009 | 11.08 (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 | 10.86 (0.60–1.22) | 0.398 | 10.67 (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 3Relapse |
|  | 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 4Multivariable 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. |