Supplementary material

Supplementary Table 1. Drugs with potentially interactions with chemotherapy.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Chemotherapy | ATCa number | Drug | Grade | Side effects | Potential effect on chemotherapy |
| Cisplatin | | | | | |
|  | A02B C02 | Pantoprazole | Mb | Hypomagnesemi | - |
| A02B C05 | Esomeprazole | M | Palpitations, spasm, seizures | - |
| C10A A03 | Pravastatin | M | Muscle weeknes | - |
| D07A A02 | Hydrocortisone | M | Pain, cramps, dizzines | - |
| HO2A B02 | Dexamethason | M | Muscle weeknes, pain, dizzines | - |
| H02A B04 | Methylprednisolone | M | Dizzines | - |
| H02A B06 | Prednisolone | M | Low potassium | - |
| L03A A13 | Pegfilgrastim | M | Effect on myeloid cellproliferation | - |
| N05A D02 | Haloperidol | M | Hearth arytmia, dizzines, nausea | - |
| Paclitaxel | | | | | |
|  | A04A A55 | Netupidant | M | Inhibition CYP450 2C8/3A4 diarrhea, mucositis,myelosup., peripheral neuropathy | Increase |
| A04A D12 | Aprepitant | M | Inhibition CYP450 3A4 | Increase |
| C10A A01 | Simvastatin | M | Peripheral neuropathy | - |
| C10A A03 | Pravastatin | M | Peripheral neuropathy | - |
| C08C A05 | Nifedipine | M | Inhibition CYP450 2C8/3A4 | Increase |
| HO2A B02 | Dexamethason | M | Increased CYP450 2C8/3A4 | Decrease |
| J01E A01 | Trimethoprim | M | Inhibition CYP450 2C8/3A4 | Increase |
| L01X A01 | Cisplatin | M | Peripheral neuropathy | - |
| L03A A02 | Pegfilgrastim | M | Effect on myeloid cellproliferation | - |
| Trabectedin | | | | | |
|  | A04A A55 | Netupidant | M | Inhibition CYP450 2C8/3A4 diarrhea, mucositis,myelosup., Peripheral neuropathy | Increase |
| A04A D12 | Aprepitant | M | Inhibition CYP450 3A4 | Increase |
| C09A A02 | Enalapril | M | Hepatotoxicity | - |
| H03A A13 | Dexamethasone | M | Induce CYP450 3A4, muscle Weeknes, pain, dizzines | Decrease |
| M01A E01 | Ibuprofen | M | Hepatotoxicity | - |
| N02B E01 | Actaminophen | M | Hepatotoxicity | - |
| N06A X21 | Duloxetine | M | Hepatotoxicity | - |
| PLDc | | | | | |
|  | A04A A01 | Ondansetron | M | QT interval prolongation | - |
| A04A A05 | Palonosetron | M | QT interval prolongation | - |
| A04A D12 | Aprepitant | M | Inhibition CYP450 3A4 | Increase |
| A06A B08 | Sodium picosulfate | M | ventricular arrhythmia | - |
| A07D A03 | Loperamide | M | Syncope, cardiac arrest, arrhythmia, QT interval prolongation |  |
| H03A A13 | Dexamethasone | M | Induce CYP450 3A4, muscle weeknes, pain, dizzines | Decrease |
| N06A A09 | Amitriptyline | M | QT interval prolongation | - |
| R03A L07 | Formoterol | M | Irregular heart rhythm | - |
| R03C C02 | Albuterol | M | QT interval prolongation, potassium loss | - |

aAnatomical Therapeutic Chemical.

bModerate.

cPegylated liposomal doxorubicin.

Supplementary Table 2. Characteristics before and during trabectedin and cisplatin hypersensitivity treatment (n = 39).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Charactristics | | | All patients  n = 39 (100%) | T-cohorta  n = 16 (41%) | C-cohortb  n = 23 (59%) | *p*-valuec |
| Secondary cytoreductive surgery before trabectedin or cisplatin treatment | | | | | | |
|  | Yes | | 10 (26) | 5 (31) | 5 (22) | 0.50 |
| No | | 29 (74) | 11 (69) | 18 (78) |  |
| Secondary residual disease (cm)b | | | | | | |
|  | Median | | 0 |  |  |  |
| Mean | | 0.2 |  |  |  |
| 0 | | 9 | 4 | 5 |  |
| >0 | | 1 | 1 | 0 |  |
| Location of radiation Therapy before and after Trabectedin or Cisplatin treatment | | | | | | |
|  | No radiation | | 27 (69) | 10 (63) | 17 (74) | 0.40 |
| Pelvic | | 3 (8) | 2 (13) | 1 (4) |  |
| LN inguinal | | 1 (3) | 1 (6) | 0 |  |
| LN paraaortal | | 1 (3) | 1 (6) | 0 |  |
| LN neck/axille | | 2 (5) | 0 | 2 (9) |  |
| Lung | | 1 (3) | 1 (6) | 0 |  |
| Brain | | 4 (10) | 1 (6) | 3 (13) |  |
| Radiation therapy before and after trabectedin or cisplatin treatment | | | | | | |
|  | Radiation before | | 4 (31) | 2 (33) | 2 (29) | 0.70 |
| Radiation after | | 9 (69) | 4 (67) | 5 (71) |  |
| Cross over after trabectedin or cisplatin treatment | | | | | | |
|  | Yes | | 5 (13) | 1 (6) | 4 (17) | 0.30 |
| No | | 34 (87) | 15 (94) | 19 (83) |  |
| Cross over indications | | | | | | |
|  | Hypersensitivity to platinum | | 2 | 1 | 1 | 0.60 |
| Headache/tinnitus | | 1 | 0 | 1 |  |
| Nephropathy | | 1 | 0 | 1 |  |
| Nevropathy | | 1 | 0 | 1 |  |
| Total numbers of cycles trabectedin or cisplatin treatment | | | | | | |
|  | 2 | | 2 (5) | 2 (13) | 0 | 0.30 |
| 3 | | 2 (5) | 1 (6) | 1 (4) |  |
| 5 | | 5 (13) | 1 (6) | 4 (17) |  |
| 6 | | 30 (77) | 12 (75) | 18 (78) |  |
| Interactions | | | | | | |
|  | Potentially decreased chemo effect | | 5 (13) | 3 (19) | 2 (9) | 0.01 |
| Potentially increased chemo effect | | 17 (44) | 2 (13) | 15 (65) |  |
| No | | 17 (44) | 11 (69) | 6 (26) |  |
| Site of recurrence before trabectedin or cisplatin treatment | | | | | | |
|  | Pelvic only | | 8 (21) | 5 (31) | 3 (13) | 0.20 |
| Pelvic with LN | | 3 (8) | 2 (13) | 1 (4) |  |
| Carcinomatosis upper abd. without LN | | 6 (15) | 3 (19) | 3 (13) |  |
| Carcinomatosis upper abd. with LN | | 5 (13) | 3 (19) | 2 (9) |  |
| Extra abdominal lesions only | | 7 (18) | 2 (13) | 5 (22) |  |
| Extra abd. lesions | | 10 (26) | 1 (6) | 9 (39) |  |
| Response | |  |  |  |  |
| Complete response | | 11 (28) | 6 (38) | 5 (22) | 0.04 |
| Partial response | | 20 (51) | 4 (25) | 16 (70) |  |
| Stationary disease | | 4 (10) | 2 (13) | 2 (9) |  |
| Progresive disease | | 3 (8) | 3 (19) | 0 |  |
| Not evaluable disease | | 1 (3) | 1 (6) | 0 |  |
| CA125 before first trabectedin or cisplatin treatment | | | | | | |
|  | Range 5–2278 | |  |  |  |  |
| Mean 284 | |  |  |  |  |
| Median 102 | |  |  |  |  |
| CA125 three weeks after last trabectedin or cisplatin treatment (IU/L) | | | | | | |
|  | Range 6–2396 | |  |  |  |  |
| Mean 161.5 | |  |  |  |  |
| Median 21 | |  |  |  |  |
| Residual disease after end of trabectedin or cisplatin treatment (maximal diameter in cm)b | | | | | | |
|  | Median | | 0.2 |  |  |  |
| Mean | | 1.39 |  |  |  |
| 0 | | 10 (37) | 4 (33) | 6 (40) | 0.70 |
| 0–0.9 | | 5 (19) | 3 (25) | 2 (13) |  |
| ≥1 | | 12 (44) | 5 (42) | 7 (47) |  |
| Treatment free interval before Trabectedin or Cisplatin treatment | | | | | | |
|  | <6 months | | 5 (13) | 2 (13) | 3 (13) | 0.90 |
| 6–11 months | | 7 (18) | 3 (19) | 4 (17) |  |
| 12–23 months | | 12 (31) | 4 (25) | 8 (35) |  |
| ≥24 months | | 15 (39) | 7 (44) | 8 (35) |  |
| Bevacizumab treatment before T or CH treatment | | | | | | |
|  | Bevacizumab before T or CH | | 2 (5) | 1 (6) | 1 (4) | 0.50 |
| Bevacizumab after T or CH | | 10 (26) | 3 (19) | 7 (30) |  |
| No Bevacizumab treatment | | 27 (69) | 12 (75) | 15 (65) |  |
| PARPi | | | | | | |
|  | After Trabectedin or Cisplatin | | | | | |
|  | treatment | 9 (23) | 3 (19) | 6 (26) | 0.60 |
| No | 30 (77) | 13 (81) | 17 (74) |  |
| Antioestrogen treatment | | | | | | |
|  | Before Trabectedin or Cisplatin | | | | | |
|  | treatment | 5 (13) | 2 (13) | 3 (13) | 0.10 |
| After Trabectedin or Cisplatin | | | | | |
|  | treatment | 15 (38) | 3 (19) | 12 (52) |  |
| No | 19 (49) | 11 (69) | 8 (35) |  |
| ECOG status 0–4 weeks before trabectedin or cisplatin treatment | | | | | | |
|  | 0 | | 12 (31) | 3 (19) | 9 (39) | 0.20 |
| 1 | | 16 (41) | 9 (56) | 7 (30) |  |
| 2 | | 8 (21) | 4 (25) | 4 (17) |  |
| 3 | | 0 | 0 | 0 |  |
| Unknown | | 3 (8) | 0 | 3 (13) |  |
| ECOG status 0–4 weeks after trabectedin or cisplatin treatment | | | | | | |
|  | 0 | | 7 (18) | 3 (19) | 4 (17) | 0.30 |
| 1 | | 17 (44) | 4 (25) | 13 (57) |  |
| 2 | | 6 (15) | 3 (19) | 3 (13) |  |
| 3 | | 4 (10) | 3 (19) | 1 (4) |  |
| Unknown | | 5 (13) | 3 (19) | 2 (9) |  |
| BMI before trabectedin or cisplatin treatment | | | | | | |
|  | Underweight BMI <18.5 | | 2 (5) | 0 | 2 (9) | 0.09 |
| Normal BMI 18.5–25 | | 16 (41) | 8 (50) | 8 (35) |  |
| Overweight 25–30 | | 10 (26) | 2 (13) | 8 (35) |  |
| Obese 30–40 | | 8 (21) | 6 (38) | 2 (9) |  |
| Very severely obese >40 | | 2 (5) | 0 | 2 (9) |  |

aTrabectedin and pegylated liposomal doxyrubicin (PLD).

bCispaltin and paclitaxel.

cPearson Chi-Square comparison between the chemotherapeutic groups.

Supplementary Table 3. Adverse effects of trabectedin and cisplatin hypersensitivity treatment (n = 39).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Charactristics | | | All patients  n = 39 (100%) | T-cohort  n = 16 (41%) | C-cohort  n = 23 (59%) | *p*-valuea |
| Age trabectedin or cisplatin treatment | | | | | |  |
|  | Median | | 60.9 | 59.9 | 61.0 |  |
| Mean | | 59.4 | 58.9 | 59.7 |  |
| Range | | 37.2–79.5 | 37.2–79.5 | 43.3–74.1 |  |
| Side effects | | | | | | |
|  | | None | 1 (3) | 1 (6) | 0 | 0.08 |
| Neurotoxic | 8 (22) | 0 | 8 (38) |  |
| Neutrophelia | 1 (3) | 0 | 1 (5) |  |
| Trombocytopenia | 1 (3) | 0 | 1 (5) |  |
| Diarrhea | 1 (3) | 0 | 1 (5) |  |
| Weight loss | 3 (8) | 2 (13) | 1 (5) |  |
| Nausea/vomiting | 8 (22) | 4 (25) | 4 (19) |  |
| Fatique | 23 (59) | 11 (69) | 12 (52) |  |
| Liver toxic | 7 (18) | 7 (44) | 0 |  |
| Allergic reaction | 1 (3) | 1 (6) | 0 |  |
| Dermatotoxic | 4 (11) | 2 (13) | 2 (9) |  |
| Other reactions | 9 (24) | 3 (19) | 6 (26) |  |
| Change of treatment because of side effects | | | | | | |
|  | | Dose reduction one level | 1 (3) | 0 | 1 (5) | 0.50 |
| Withdrawal | 3 (8) | 2 (13) | 1 (5) |  |
| Shift to trabectedin | 1 (3) | 0 | 1 (5) |  |
| Delay >5 days | 1 | 0 | 1 (5) |  |
| No | 33 (85) | 14 (88) | 19 (83) |  |
| Granulocyte colony stimulating factors | | | | | | |
|  | | Yes | 4 (11) | 1 (6) | 3 (14) | 0.50 |
| No | 34 (90) | 15 (94) | 19 (86) |  |

aPearson Chi-Square comparison between the chemotherapeutic groups.

Supplementary Table 4. Adverse effects from trabectedin/PDL and cisplatin hypersensitivity/paclitaxel treatment (n = 39).

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Side effects  Grade | No side effects (%)  0 | Mild  1 | Moderate  2 | Serve  3 | Life threatening  4 | Unknown |
| Neurotoxic | 29 (74) | 1 (3)b | 6 (15)b | 2 (5)b | 0 | 1 (3) |
| Neutrophilia | 35 (90) | 1 (3)b | 1 (3)b | 1 (3) b | 0 | 1 (3) |
| Trombocytopenia | 37 (95) | 1 (3)b | 0 | 0 | 0 | 1 (3) |
| Diarrhea | 37 (95) | 1 (3)b | 0 | 0 | 0 | 1 (3) |
| Weight loss | 33 (85) | 1 (3)a | 1 (3)b | 1 (3)a | 0 | 3 (8) |
| Nausea | 24 (62) | 7 (18)a,b | 3 (8)a,b | 3 (8)a,b | 1 (3)b | 1 (3) |
| Vomiting | 31 (80) | 2 (5)b | 5 (13)a,b | 0 | 0 | 1 (3) |
| Fatique | 15 (40) | 11(28)a,b | 8 (21)a,b | 4 (10)a | 0 | 1 (3) |
| Liver toxic | 31 (80) | 4(10)a | 2 (5)a | 1 (3)a | 0 | 1 (3) |
| Allergical reaction | 37 (95) | 0 | 0 | 1 (3)a | 0 | 1 (3) |
| Dermatotoxic | 34 (87) | 4 (10)a,b | 0 | 0 | 0 | 1 (3) |
| Other reactions | 29 (74) | 6 (15)a,b | 1 (3)b | 1 (3)a | 1 (3)b | 1 (3) |

aTrabectedin-PDL cohort.

bCisplatin-Paclitaxel cohort.