CANCER DE OVARIO

CANCER DE OVARIO – CARCINOGENESIS Y BIOLOGIA MOLECULAR

F Buttitta et al (JCO 2003;21:1320-5). N=59. HTERT (PCR-RT) in patients treated with CDDP. 28/59 had low TERT (47%). High TERT was associated to CR (75%). 18/20 patients with a rsidual tumor >2cm and low TERT were PR/P while 11/12 patients with <2cm residual disease and high TERT were CR. Predictor of OR to CDDP.

R Schmandt et al (Cancer 2003;98:758-64). c-Abl is universally expressed in normal ovary and in 71% serous carcinoma, 65% in high grade tumors; PDGFR-B is expressed in 93% normal ovary, 81% serous carcinoma and no expression found in high grade; c-kit undetectable in normal ovary, no expression in low grade and 26% expression in high grade. Interest for Imatinib?.

V Hess et al Royal Marsden Sutton(JCO 2004;22:1040-4). Mucinous epithelial ovarian cancer was compared to other histological subtypes. N=81 (27 cases and 51 controls). OR 26.3% vs 64.9%; MPFS 5.7 mo vs 14.1 mo; MOS 12 mo vs 36.7 mo. Poor results, require new approach.

J Dupont et al (JCO 2004; 22:3330-9). YKL-40 secreted glycoprotein was compared to Ca125 and ca 15.3 in early ovarian cancer. YKL-40 median 28 ng/mL healthy women, 36 ng/mL high risk without cancer, 44.5 ng/mL high risk and prior breast cancer, 38 ng/mL benign gyn processes. In ovarian cancer preoperative level was 94 ng/mL. YKL-40 was elevated in 72% ovarian cancer cases and Ca125 in 35%. Deserves further study.

E Stevens et al (Vcancer 2005;103:2313-9). Expression of XPA (Xeroderma pigmentosum A, nucleotide excission repair of DNA adducts) present in 96% ovarian cancer cells in effuxion specimiens. When expression was >25% of the cells correlated with better OS/PFS (paradoxically). Could it be a marker of CDDP/Alkyl agent response?

LY Han et al MDACC (JCO 2006; 24:755-61). N=150. Seric Tissue factor level : Median 82.5 pg/mL preop in maligant tumors and median 12.8-30-7 pg/mL in bening and borderline lesions. Level >190 pg/mL associated to poor survival (HR 3.4).

J Lacey et al (JNCI 2006;98:1397-405). NIH-AARP Diet & Health Study Cohort (97.638 women) reviewed SEER Data and found excess of ovarian cancer associated with HRT. >10 y unoppossed estrogen in previous hysterectomy RR=1.7; >10 y unoppossed estrogen in previous hysterectomy RR=1.7; >10 y unoppossed estrogen in all women RR=1.89; >5y sequnetial estrogen-progestin RR=3.09; and > 5y continuous estrogen/progestin RR=1.82. Significant risk association.

C Diefenbach et al (Cancer 2006;107:1511-9). Lysophosphatidic acid acyltransferase B (LPAAT-B) tumor expression (new marker for ovarian cancer) is overexpressed in 57% of 158 tumors and it ia associated to high grade, papillary-serous histology, advanced stage, short PFS (5yPFS 32% vs 60%) and low OS (5 yOS 54% vs 74%).

H Dressman et al (JCO 2007;25:517-25). Gene expression arrays for discovery and validation of a set (primary N=119 and cell lines=12) to improve ChX Platinum sensitivity prediction. Resistance identified with >80% accuracy with activation of src and Rb/E2F pathways.

**5568. ERCC1 negative ovarian cancer OR 63.5% vs ERCC1 positive 35.6%. ERCC-1 present in 37.7% of cases. ASCO 2007

CANCER DE OVARIO – CANCER BORDERLINE

G Zanetta et al (JCO 2001;19:2651-64). N=339 borderline tumors. 83% Stage I. Only 2% progression to invasive (serous or mucinous) carcinoma.

R Bristow (Cancer 2002;95:791-800). N=21. Distinguish micropapillary serous ovarian carcinoma from serous brderline tumors becuase of bilaterality, recurrence rate and inferior survival... MST 61% after debulking for recurrence; OR 25% to ChX.

CANCER DE OVARIO – HEREDITARIO

K Bergfeldt et al (Lancet 2002;360:8891-4). Ovarian cancer in relatives of breast cancer <50 yo SIR=5.6; in relatives of ovarian cancer SIR=17. Family history of ovarian cancer carried 10% risk of ovarian cancer and justify oophorectomy at menopause...

T Pal et al (Cancer 2005;104:2807-16). N=209 women with ovarian cancer had BRCA1-2 germ line sequenced and 15.3% had mutation (58% outside the ovarian cancer cluster region).

D Ehrmann et al (NEJM 2005;352:1223-6). Polycystic ovary syndrome: Genetic, hereditary, frequent in Ashkenazim. Associated to Obesity-Metabolic syndrome; Diabetes-Intolerance to/resistance to insulin; Amenorrhea-Hypogonadism-Hirsutism-Acne; Increased risk of endometrial carcinoma (perfor biopsy if amenorrhea > 1y after measuring ultrasound endometyrial thickness. Treatment with: Antiandrogens, antiestrogens, Glucocorticoids, Spironolactone. ADO-weight reduction: Metformin, Thiazolidinediones.

C Bethan Powell et al (JCO 2005;23:127-32). BSO in BRCA1-2 patients: Serial sectioning detected cancer in 7/67 additional patients in addition to the origuinal 2.5% found at first report.

A Chetrit et al (JCO 2007;26:20-5). BRCA1-2 mut in Israel: Ashkenazi BRCA1 185delAG, 5382insC & BRCA2 6174delT) found in 213/605 ovarian cancers (35.2%). 5 y OS 39%; MST carriers 53.7 mo vs 37.9 mo. All carriers had stages III-IV and poor grade. Improved survival remained significant after age, grade and morphology controls

**5513. Overexpression of BRCA1 IRIS gene in ovarian cancer families without BRCA mutation. ASCO 2007

CANCER DE OVARIO – ESTADIO PRECOZ

I Vergote et al (Lancet 2001;357:176-82). N=1545. Stage I. Prognostic factors were degree of differentiation HR=3.13, and rupture during surgery HR=1.64. Other factors had no effect (histology, extracapsular growth, ascitis and tumor size).

D Kolomainen et al Royal Marsden Sutton (JCO 2003;21:3113-8). N=194. Stage I, no adjuvant chemotherapy and treated with Pt based ChX at relapse time. 31% relapsed and 55/61 treated → 24% 5yPFS., 10yOS 72% (N=192) and 10 yDFS 80%.

J B Trimbos et al EORTC-ACTION TRIAL (JNCI 2003;95:113-25). N=448, M F up 5.5y. Surgery →Randomized to control vs CDDP. OS HR =0.69, RFS HR=0.63. Optimal staging had better OS HR=2.31. The CDDP effect is limited to non-optimal staging...

ICON-1 (EU) (JNCI 2003;95:125-32). N=447. Surgery → Randomized to control 5yOS 70%, 5yRFS 62%) vs ChX-Pt based (5yOS 79%, 5yRFS 73%), OS HR=0.66

Meta-analysis ICON-1 + ACTION TRIALS: ChX 5yOS 82%, 5yRFS 76%; control 5yOS 74%, 5yRFS 65%.

R Young et al (JCO 2003;21:4350-5). N=251, 229 eligible, Stages Ia & Ib grade 3, stage Ic and Stage II no residual macro. Randomized to CDDP (10 y recurrence rate 28%, stage I 27% and Stage II 44%) or P32 intraperitoneal (10 y recurrence 35%(. Considered CDDP preferred treatment.

PB Panici et al (JNCI 2005;97:560-6). Optimal resection of eatrly ovarian cancer randomized to aortic + pelvic lymphadenectomy . MF up 68.4 mo. (N=216, 5yPFS 31.2%, MPFS 29.4 mo, 5yOS 48.5%, MOS 58.7 mo, operative morbidity 28%) vs resection of bulky lymph nodes (N=211, 5yPFS 21.6%, MPFS 22.4 mo, 5yOS 47%, MOS 56.3 mo, operative morbidity 28%)

L Eliot et al (Cancer 2004;101:1926-35). Review 13 randomized trials of adjuvant chemotherapy in Stage I Ovarian cancer. All showed benefit for adj Chemotherapy with RR recurrence =.70 and RR survival 0.74. CDDP based chemotherapy gave a 5 yOS advantage fo 8%.

SC Crawford et al (JCO 2005;23:8802-11). SCOTROC-1 compared TXT+CBDCA vs TXL+CBDCA and found no differences, except for UK treated patients who had lymphadenectomy only in 6% respect to 30% in the rest of patients and indicated that better debulking aasociated with less chemotherapy benefit.

C Trope and J Kaern (JCO 2007;25:2909-20). Adjuvant chemotherapy guidelines: Completely resected and staged patients require adjuvant chemotherapy when in Stage IB, IC and aneuploid tumors. Incompletely staged patients recommendation is careful selection for a surgical restaging.

BA Goff et al (Cancer 2007;109:221-7). Ovarian Cancer Symptom Index: Presence of >12d/month & <1y of pelvic/abdominal pain, increased abdominal size and bloating, or difficulty in eating/ feeling well. Sensitivity 56.7% early stage and 79.5% advanced stage; specificity 90% in >50yo & 86.7% in <50yo...

*5580. Early ovarian cancer size 10.7 cm and advanced ovarian cancer size 4.8 cm in a series of 110 operated cases (Univ Utah) indicating different biologic types and early seeding for aggressive type.
ASCO 2007

CANCER DE OVARIO – QUIMIOTERAPIA

W McGuire et al (JCO 2000; 18:1062-7). N=48, 1st line salvage CDDP sensitive disease. TPTC 1.5 mg/m2 30 min iv x 5 d q 3 wk. OR 33%,(2CR, 13 PR), MDR 11.2 mo. Fatigue 30%.

G Aravantiun et al (Ann Oncol 2000; 11:607-12). N=51 resistant to CDDP, prior TXL, Med interval from Chemotherapy 3.9 mo, M number lines 2. IFX 2.25 g/m2 x 2 d + VP 100 mg po qd d 1-10. OR 26% (CR 12%). MF up 18 mo: MTTP 3 mo, MDR 9 mo, MST 13 mo. ANC 41%, WBC 29%).

S Pignata et al (Ann Oncol 2000; 11:613-6). Pt resistant, refractory. GEM 1000 mg/m2 d 1&8 + EPI 60 mg/m2 d 1 x 4-6 cycles q 3wk. OR 23.1% (3 PR).

M Gore et al (JCO 2001; 19:1893-900). Second line therapy: Randomized to TPTC 1.5 mg/m2/d x 5 q 3 wk (OR 3%, Cross over 13%, MST 40 wk, MTTP 9 wk) vs TXL 175 mg/m2 3 h iv q 3 wk (OR 14% crossover 10%, MST 48 wk, MTTP 9 wk). Lack crossresistance.

A Gordon et al (A Lacave) (JCO 2001;19:3312-22). N=474 CDDP resistant. Randomized to TPTC 1.5 mg/m2/d x 5 q 3 wk (OR 17%, MST 56 wk, OS 108 wk) vs Liposomal DOX 50 mg/m2 q 3 wk (OR 19.7%, MST 60 wk, OS 71 wk). Similar activity.

*C Papadimitrious et al (Cancer 2001;92:1856-63). N=35, bulky disease, M F up 46 mo. TXL 175 mg/m2 3 h iv d 1 + CDDP 75 mg/m2 d 2 + IFX 1.5 g/m2 d 1-3 (Mesna). OR 85% (15 CR + 7 PR), MST 52.8 mo,MTTP 22 mo, Hematol toxicity 42%.

T Meyer et al (Ann Oncol 2001;12:1705-9). N=42, prior Pt. CDDP 60 mg/m2 d 1, 8, 15, 29, 36, & 43 + VP 50 d 1-4 po & d 29-43 & then 2 wk on-off. OR 44% (57% & 40% according to prior ChX lines).

M Van der Berg et al (BJC 2002;86:19-25). N=107, prior Pt. CDDP 60 mg/m2 wkly x 6 + VP po 50 mg qd x 14 q 4 wk. OR 92% (CR 63%) for >12 mo interval from prior Pt ChX, MST 26 mo; OR 91% for 1-12 mo interval, MST 16 mo, and OR 46% (CR 29%) in Pt refractory, MST 13 mo.

ICON 3 (Lancet 2002:360:505-15). N=2070, 130 centres, M F up 51 mo. Randomized to TXL + CBDCA vs CAP or CBDCA alone. HR=0.98 for OS; MOS 36.1 mo vs 35.4 mo; MPFS 17.3 mo vs 16.1 mo.

R Bristow et al JHU (JCO 2002;20:1248-59). Meta-analysis of cytoreductive surgery: For each 10% increase in maximal cytoreduction there is a 5.5% increase in MST. Cohorts with a <25% maximal cytoreduction MST 22.7 mo; Cohorts with >75% maximal cytoreduction MST 33.9%. Platinum dose, age, stage were not significant factors.

ICON4 – AGO – OVAR 2.2 TRIALS (Lancet 2003;361:2099-106). N=802, CDDP sensitive and >6mo interval to relapse. Randomized to TXL + CDDP (2 y OS 57%, 1 y PFS 50%) vs CDDP (2 y OS 50%, 1 y PFS 40%).

***R Ozols et al (JCO 2003;21:3194-2000). N=792, prior surgery and residuum<1 cm. Randomized to CDDP 75 mg/m2 + TXL 135 mg/m2 24 h iv civi (MPFS 19.4 mo, MOS 48.7 mo) vs CBDCA AUC 7.5 + TXL 175 mg/m2 in 3 h iv (MPFS 20.7 mo, MOS 57.4 mo). Last group less toxic and non inferior RR 0.88 for Progression and RR=0.84 for death.

AGO (JNCI 2003;95:1320-30). N=798 stages IIB-IV. Randomized to CDDP 75 mg2 + TXL 185 mg/m2 (MPFS 1º7.2 mo, MOS 43.3 mo) vs CCBDCA AUC 6 + TXL 185 mg/m2 (MPFS 19.1 mo , MOS 44.1 mo). Similar efficacy.

P Vasey et al Scottish SOCOTROC trial (JCO 2003;21:136s-44s). N=1077, M F up 23 mo. Randomizwed to TXL 175 3 h iv/m2 + CBDCA AUC 5 q 3 wk x 6 (Neurotoxicity, 2 y OS 69.8%), vs TXT 75 mg/m2 1 h iv + CBDCA equal (Hemtotoxicity, 2 y OS 65.5%). NO differences except for toxicity, perhaps better for TXT...

P Rose et al GOG (NEJM 2004;351:2489-97). N=550, primary surgery < 6wk + 2 cycles Chemotherapy. Randomized to secondary cytoreductive surgery →ChX x 3 (PFS HR=1.07, OS HR=0.99) vs ChX x 3. Nodifferences. Previous EORTC study indicated better MPFS (18 vs 13 mo) andMST (26 vs 20 mo) using CPA+CDDP. Current protocols used CDDP+TXL and improved MST (36.2 vs 35.7 mo).

G Dark et al (JCO 2005;23:1859-66). N=81 relapsed after 1-2 lines. Liposomal lurtotecan 1.8 mg/m2 /d 30 min iv d 1-3 q 3 wk (Toxicity +++, hemetologic 51%, OR 15.4%) vs Liposomal Lurtotecan 2.4 mg/m2/d in 30 min d 1 & 8 q 3 wk (Toxicity ++, hemotlogic 22%, OR 4.9%).

***C Sessa et al (JCO 2005;23:1867-74). Trabectedin 1.300 ug/m2 3 h iv. N=59: 12 PR in sPT sensitive patients (OR 43%) and 2 PR in resistant. MTTP 7.9 mo. Quite active.

G Bolis et al (JCO 2004;22:686-90). N=502. Randomized study CBDCA AUC=6 + TXL 175 mg/m2 (CR 63.8%, 4 y PFS 41%, 4 yOS 46.2%) vs CBDCA same + TXL 225 g/m2 (CR 55.7%, 4 yPFS 39%, 4yOS 47.3%.

AK Sood et al (Clin Ca Res 2004;10:6080-5). N=22, median prior ChX 1.5. Treatment: ip TPTC 1 mg/m2 d 1-5 + po VP 100 mg/m2 d 6-9 (plasma peak 1.9-6.9 ug/mL, mean 3.6 ug/ml) q 4 wk x 6. Results: OR 38% (3 CR + 5 PR), 7 NC. Neutropenia IV 36%, thrombopenia IV 18%. Active.

D Mirchandani et al (Clin Ca Res 2005;11:5912-9). N=57. Randomized Doxil 30-40 mg/m2 d 1 + po TPTC 0.4 mg/m2 bid x 14 d q 4 wk (erratic absorption) vs Doxil 30.40 mg/m2 d 1 + iv TPTC 0.3-0.4 mg/m2/d x 14-21 d q 4 wk. 2 CR + 2 PR/ 23 patients. The maximum dose was tolerated.

AN Gordon et al (Gyn Oncol 2004;95:1-8). Caelyx 50 mg/m2 q 4 wk (MOS 62.7 wk, PT sensitive MOS 107.9 wk) vs TPTC 1.5 mg/m2 x 5d q 3wk (MOS 59.7 wk, PT sensitive MOS 70.1 wk).

S Madhusudan et al (JCO 2005;23:5950-9). Phase IB recurrent ovarian cancer. ETANERCEPT 25 mg bi qwk/TI wk until PD. N=30. After 12 wk treatment 6 NC and minor decrerase Ca125. Increase in TNFalfa, fall in IL6 and CCL2. Signs of biological activity.

*******M Kyrgionet al (JNCI 2006;98:1655-63). Metanalysis published trials of ChX, Montecarlo analysis looking for improvements in survival: 198 randomized trials. PT + TXn non intraperitoneal reduced mortality 42%. Pt + Txn intraperuitoneal reduced mortality 55%. Represents a 3 y survival gain (overall 5.5%).

J Pfisterer et al (JNCI 2006;98:1036-45). N=1308 AGO-OVAR-GINECO gorpus. Randomized to TXL + CBDCA x 6 (MPFS 18.5 mo, MOS 44.5 mo, 3 y OS 57%, OR 76.2%) vs TXL+CBDCA x 6 then →TPTC x 4 (MPFS 18.2 mo, MOS 43.1 mo, 3yOS 57%, OR 69%)

J Smyth et al (Clinn Ca Res 2007; 3:3617-22). Letrozole in ER+ tumors. N=42. Ca 125 OR 17% and NC at 6 mo 26%, measurable disease OR 9%, NC 42%.

R Bukowski et al (Sem Oncol 2007:34:1s-15s). Review BV trials: OR single agent 16-28%, PFS 27-57% All 6 trials were positive. Pertuzumab OR 4%, NC 7%; Trastuzumab OR 7%, NC 39%; Erlotinib OR 6% NC 42%; Gefitinib OR 3%, NC 15%.

RA Burger et al (JCO 2007; 25:5165-71). BV Phase II 15 mg/kg q 3 wk. N=62, 2 prior linesChX, 42% Pt resistant. OR 21% (2 CR + 11 PR) MDR 10 mo, 6 moPFS 40.3%, MPFS 4.7 mo, MOS 17 mo. Active single agent data.

S Cannistra et al (JCO 2007;25:5180-6). BV Phase II 15 mg/kg q 3 wk. N=44, 84% Pt resistant and 48% prior ChX. OR 15.9%, MPFS 4.4 mo, MOS 10.7 mo, GI perforation 11.4%.

*5521. Ovarian ca: CBDCA AUC 6 d 1 + TXL 60 mg/m2 d 1, d 8 and d 15, repeated q 3 wk x 6. N=40. All achieved a cCR. At second look 145 negative, 4 positive. PCR 78%. Completed therapy 82% (MGH, DFCI). ASCO 2007

**5522. Ovarian cancer. Icodextrin 4% for CBDCA AUC up to 8 (DLT) have PK advantages. ASCO 2007

**5525. Nano-Alb-TXL 260 mg/m2 in 30 min q 3 wk in ovarian cancer. N=44. OR 50% (13 CR + 9 PR). ASCO 2007

*5505. Ovarian cancer: 6 cycles TXL after a pCR (TXL-CBDCA) do not add to cure. MPFS 34.4 mo; 3 y OS 87% vs 79%. ASCO 2007

*LBA5506. GEM similar to Caelyx in recurrent ovarian cancer. ASCO 2007

*5507 Pertuzumab + GEM > GEM in platinum resistant ovarian/fallopian/primary peritoneal carcinoma. N=130. ASCO 2007

*5508. VEGF-Trap (VEGFR fused to Fc of IgG) 2-4 mg/kg q 2 wk randomized study. OR 11% in heavily pretreated ovarian cancer. ASCO 2007
**5515. Ovarian cancer. Mannan-MUC1 fusion protein (DC-MFP, Loveland et al Clin Ca Res 2006;12:869) cultured DC(IL4-GMCSF) on d 5 and injected d 6 intradermally 5x10e6DC q 4 wk x 3 and then q 10 wk x 1 y. N=28. Results: 4/21 (19%) ca125 OR, 2 PR, 2 NC (88% tumors were MUC1+ on IHC).

*5527. Ovarian ca. Epothilone ZK-EPO 16 mg/m2 in 3 h iv, in Platinum resistant N=63. Results: 4/13 initial patients had a PR... ASCO 2007

**LBA5529. Canfosfamide (glutathione analog activated by glutathione S Transferase P1-1 + CBDCA in ovarian cancer resistant to 2 platinum lines. OR 31.6% (Randomized to lisomal DOX, OR 10%). MST not reached (Caelyx 11 mo). ASCO 2007

**5561. Pazopanib (GW786034, inhibitor of VEGFR 11-3, PDGFR a/b, cKit) 800 mg q d in Pt resistant ovarian cancer. N=17. Ca125 OR 7 (47%) NC 4 (27%).
ASCO 2007

**5566. Ovarian ca. Gefitinib 500 mg/d + CBDCA + TXL (2^{nd} line > 6 mo interval). N=68 /26 resistant and 42 sensitive) ORR 19.2% and 69.2% respectively. 2 MDS and 1 AML. OS 16 mo and 25 mo. MDR 6 mo and 7.5 mo. ASCO 2007

**5579. Relapsed ovarian cancer. Trabectedin 1.3 mg/m2- 1.5 mg/m2 or wkly 0.58 mg/m2. ORR 33% and 16% in platinum sensitive and platinum resistant cases respectively. MTTP 6.3 mo and 25 mo. Now in Phase III. Availability?. ASCO 2007

L Downs et al (Cancer 2008;112:331-9). N=69. Randomized TPTC 1.25 mg/m2 d 1-5 q 3 wk (OR 21%, CR18%), MPFS 4 mo, MOS 15 mo) vs TPTC + Thalidomide 200 mg po (OR 47% CR 30%, MPFS 6 mo, MOS 19 mo). Improved survival.

AA Garcia et al (JCO 2008;26:76-82). Phase II BV 10 mg/kg q 2 wk + CPA 50 mg/d. N=70. PR 24%, 6 moPFS 56%, MTTP 7.23 mo, MOS 16.9 mo. Active as BV single agent.

J Silber et al (JCO 2007;25:1169-75). SEER Data 1991-2001 identified patients treated by agynecologist (N=344, Med treatment time 12.1 wk; 5 yOS 35%) or by a medical oncologist (N=344; Med treatment time 16.51 wk; 5 yOS 34%). NO differences.

CANCER DE OVARIO – TRATAMIENTO INTRAPERITONEAL

R Morgan et al (Clin Ca Res 2003;9:5896-901). Txt IP mtd 100 MG/M2 IP Q 3 WK.

P Sabattini et al (Clin Ca Res 2004;10:2962-7). N=30, complete cytoreduction, 2nd look persistant disease & all with epritoneal catheter. CDDP 75 mg/m2 ip d 1 + GEM 500-1250 mg/m2 d 1, d 8 & d 15. MTTP 15.9 mo, MOS 43.5 mo (Optimal debulking TTF 25.2 mo, non optimal 10.2 mo). Fibrotic changes severe in 17%, all requiring surgery.

*******D Armstrong et al GOG (NEJM 2006;354:34-43). Randomized TXL 135 mg/m2 d 1 24 h iv + CDDP 75 mg/m2 d2q 3wk x 3 (Completed all, MPFS 18.3 mo, MOS 49.7 mo) vs TXL 135 mg/m2 24h d1 + CDDP ip 100 mg/m2 d 2 + TXL 60 mg/m2 ip d 8 q 3 x 6 (Completed 42%, MPFS 23.8%, MOS 65.6 mo, optimal results arm).

S Kusamura et al NCI Milan, (Cancer 2006;106:1144-53). N=205, 50 mesothelioma, 49 pseudomyxoma, 41 ovarian ca, 32 sarcoma, 13 colon, 12 gastric, 8 another primary tumors. Procedures 209, cytoreductive surgery + ip hyperthermia perfusion 44º x 60-90 min, (closed technique) CDDP 25 mg/m2/L + Mito C 3.3 mg/m2/L or CDDP 43 mg/L perfusate + Dox 15.25 mg/L perfusate. Morbidity 30%, Mortality 5-8%. Similar open and closed techniques.

PM Hanlon et al (Clin Can Res 2006;12:2517-25). Ip photodynamic therapy PHOTOPHRIN Phase II.. 2.5 mg/kg iv 48 h before debulking + laser light therapy. N=100 (33 ovary, 37 GI, 30 sarc): MFFS 2.1 mo MOS 20.1 mo (Ovar); MFFS 1.8, MOS 11.1 (GI); MFFS 3.7 mo, MOS 21.9 mo (Sarc). Post-op deaths 2...

SM Hahn et al (Clin Ca Res 2006;12:5464-70). Photophrin uptake 2.5 mg/jkg 48 h prior tyo devulking. Samples intestine normal 2.7 ng/mg- 3.4 ng/mg; tumors 3.32-5.31 ng/mg ovaruian, gastric, small bowel; 2.09-2.45 ng/mg sarcoma, appendix tumorm CRC; 0.93 pseudomyxoma. Narrow window with a drug level ratio tumor/intestine only <2.3.

**********C Marth et al (Cancer 2007;109:645-9). Full consensus by international panel on ip/iv ChX for ovarian cancer: Optimal debulking follwed by TXL-CDDP. Approved in the USA and with Cochrane analysis results support...

RJ Morgan ety al (Clin Ca Res 2007;13:1232-6). Peritonela carcinomatosis of different origins GEM 40-160 mg/m2 in 2 L saline d 1, 4, 8, & 12 q 4 wk. N=30. DLT N&V, diarrhea, dyspnea, GOT. N=19 evaluable: 10 NC and 9 PD. At 120 mg/m2 AUC 82.612 ng/mLxh; Mean peritoneal advantage 847 (AUC peritoneal/AUC plasma). Interest in ovarian cancer.

DS Alberts and A Delforge (Sem Oncol 2006;33:8s-17s). Guidelines ip therapy: Day 1: TXL 135 mg/m2 3 h iv in 0.5 L (non PVC catheter) associate DXMTS, Granisetron, Loazepam, Famotidine. Portacath/Bardport iserted laparoscopically. Day 2: Intraperitoneally CDDP 100 mg/m2 in 1 L warm NaCl solution folloew by 1 L normal saline in 1-2 hr and Intravenously 1 L

saline solution + DXMTS, Apprepitant, Lorazepam, x 3-4 d. Day 8: TXL 60 mg/m2 in 1L warm NaCl solution + 1 L saline solution ip + DXMTS, Granisetron, Lorazepam, Famotidine, Diphenhyderamine

CANCER DE OVARIO – BIOTERAPIA E INMUNOTERAPIA

J Berek et al (JCO 2004;17:3507-16). Consolidation after OR with MoAb B43.13 (murine MoAb against Ca 125) Randomized Oregovomab (TTR 13.3 mo) vs Placebo (TTR 10.3 mo) NO differences.

P Sabbatini et al (Clin Ca Res 2006;12:5503-10). Abagovomab (mimics Ca 125 MoAb) Randomized 2 mg x 4 im vs o.2 mg x 4 q 2 subcutaneously and studied correlation of appearance of Ab3 with MOS.N=42. Side effects: pain, myalgia, fever in local asite. Ab3= All patients. No differences according to dose o route. HAMA not present at baseline and walwways positive at wk 16. Proposal?

A Burges et al (Clin Ca Res 2007;13:3899-905). Catumaxomab (anti EPCAM x anti CD3, trifunctional antibody to redirect T cells & Fc gamma receptorT/III+ accesory cells to tumor site in malignant ascites EpCAM+). Treatment>: 5 ip infusions 5-200 ug in 1-2 wk. N=23. Side effects: fever, nausea and vomiting grade 1-2, reversible at higher doses. No furtehr paracentesis in 22/23 in 5 wks and reduction of 5 logs in tyhe number of EPCAM+ cell counts.

PJ Sabattini et al (Clin Ca Res 2007;13:4170-7). Heptavalent vaccine (GM2, GloboH, LewisY,Tn, STn, TF & TnMUC-1) + KLH + QS21 wks 1, 2, 3, 7 &15. N=11. Mild side effects at site of injection. 8/9 Ab response to >3 Antigen.

I Kryczet et al (Ca Res 2007;67:8900-5). B7H4 costimulatory molecules expressed by tumor nad macrophages interact with T reg cells and suppress immunity in ovarian cancer.