Material and methods: Prostate cancer cells (PC-3) were treated with either 2–20 Gy of ^{60}Co gamma-IR or 0.5–50 μM 8-Cl-cAMP alone or as an adjuvant immediately after 10 Gy IR. The antiproliferative and cytotoxic effect of these treatments was followed by trypan-blue exclusion assay, MTT assay and BrdU incorporation, while cell cycle distribution and death were analyzed by flow-cytometry of PI stained cells. The combination index value (CI) was calculated by the Calcu syn software.
Results: Both 8-Cl-cAMP and IR showed significant inhibition of PC-3 cell proliferation with IC_{50} of 12.5 μM and 11.9 Gy, respectively, according to BrdU test. The TBE assay showed that the number of viable cells in treated *vs.* control cells (*i.e.* Viability index) decreased, with IC_{50} values of 15 μM and 10.4 Gy, respectively. The Viability index was further decreased when combined treatment was applied, demonstrating synergism (CI 0.5–0.7). Also, CI value for the same combination in BrdU assay demonstrated synergism (CI 0.4–0.9), suggesting that combined treatment significantly enhance either of single treatments of PC-3 cells. Cell cycle analysis showed S and G2/M arrest after all three applied treatments. However, combined tratment also demonstrated significant increase in hypodiploid cell population (18% in treated *vs.* 4% in control cells), suggesting possible induction of apoptosis.
Conclusions: This *in vitro* study indicates that, when used in combination with IR, 8-Cl-cAMP may be effective at concentrations that are lower than those required for efficiency as a single agent. Further preclinical tests should be introduced to confirm if 8-Cl-cAMP in combination with IR could successfully control growth of hormone-refractory prostate-cancer *in vivo*.

901 PUBLICATION

The preferred treatment for stage I seminoma: a survey of Canadian radiation oncologists

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Purpose: To evaluate the preferences for managing stage I seminoma patients post orchiectomy among Canadian radiation oncologists.
Methods: In February 2005 an electronic survey with questions related to the management of stage I seminoma post orchiectomy patients was sent, via email, to Canadian radiation oncologists who treat genitourinary malignancies. The preferences of the respondents with regards to treatment were analyzed and are presented.
Results: Of 119 oncologists surveyed, 93 responded (78% response rate). Fourteen responders did not manage seminoma patients, and one declined to complete the survey. Therefore, the survey completion rate was 74% of the 105 eligible responders. Among the respondents, 89% were male, 11%, female with the median age being 43 years. The median number of years in practice was 13, and 80% worked in academic centres. Responses to questions on the most appropriate and preferred treatment options are presented in table.

Question	Surveillance	Adjuvant radiation	Adjuvant chemotherapy	Unsure
The most appropriate treatment for most stage I seminoma patients	56%	31%	1%	12%
If I had Stage I seminona, I would prefer . . .	52%	27%	8%	13%

There was a strong association between what respondents thought was the best treatment for their patients and what they would choose for themselves ($p < 0.001$). Older oncologists are more likely to choose radiotherapy for themselves ($p = 0.05$) and there is a trend (non-significant) for older oncologist to choose radiotherapy for their patient ($p = 0.07$). Years in practice, type of practice (academic vs. community) and provincial location did not appear to influence management choices.
Conclusions: There remains considerable variation in the opinions of Canadian radiation oncologists regarding the optimal treatment approach for stage I seminoma patients although currently the majority seem to favour surveillance post orchiectomy.

Gynaecological Cancer

Oral presentations (Tue, 1 Nov, 9.15–11.15)
Gynaecological cancer

902 ORAL

Paclitaxel-carboplatin-gemcitabine (TCG) versus paclitaxel-carboplatin (TC) as first line treatment in women with ovarian cancer: A randomized phase III GCIG Intergroup study (AGO-OVAR 9, GINECO-TCG, NSGO-OC-0102)

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Background: Despite major progress achieved in the last decades, epithelial ovarian cancer is still not curable in the majority of patients. Addition of non cross-resistant drugs to standard TC is a potential option for improvement of efficacy. In phase II trials the addition of gemcitabine to TC resulted in high compliance and manageable toxicity. Therefore, a prospectively randomized phase III Intergroup study comparing TCG to standard TC was initiated within the GCIG network.
Patients and methods: This protocol started in 8/02 and recruitment was completed in 04/04. Patients were 18 years or older, had epithelial ovarian cancer FIGO stages IC-IV, and were randomized within 6 weeks after primary surgery. Two-fold stratification was based on centre and disease characteristics: stratum I = FIGO stages IC-IIA, stratum II = FIGO stages IIB-IIC and residual tumor 0–1 cm, and stratum III = FIGO stage IV or residual tumor >1 cm. Patients were randomized to either TC (T 175 mg/m^2 3h iv d1+C AUC 5 iv d1) or TCG (TC as above+G 800 mg/m^2 iv d1+8) for at least 6 cycles every 21 days.
Results: This first interim analysis was based on data from 1,724 patients receiving at least one cycle of study medication, 5.257 cycles of TC and 5,111 cycles of TGC. The strata distribution showed 175, 891, and 676 patients in strata I, II, and III respectively. Most patients received 6+ cycles (87.5% TC, 87.1% TCG). Dose reductions on d1 occurred in <10% in both arms and G d8 was omitted in 37% of cycles. Hematologic toxicity and need for support with G-CSF, blood products and antibiotics occurred significantly more frequent in the TCG arm, but neutropenic fever was rare with 2.1% and 6.5% ($p < 0.0001$). Fatigue was the only non-hematological toxicity showing a significant difference favouring TC (Grade 3/4: 6.6% versus 10.4%, $p = 0.005$). Until 04/05 166 deaths were observed of whom 142 were related to ovarian cancer. The other 24 deaths were equally distributed among patients in both arms and included 5 events possible related to study medication.
Conclusion: TCG was feasible but induced more haematological toxicity. Further follow-up will show if addition of G to TC will provide a meaningful benefit in women with ovarian cancer.
(This study was supported by Eli Lilly & Co).

903 ORAL

Clinical activity of single agent pertuzumab (rhuMab 2C4), a HER dimerization inhibitor, in advanced ovarian cancer (OC): potential predictive relationship with tumor HER2 activation status

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Background: Ovarian cancers (OC) frequently have activation of HER2 even in the absence of HER2 overexpression. Pertuzumab (P), a humanized HER2 antibody, represents a new class of targeted agents called HER dimerization inhibitors (HDIs) that inhibit dimerization of HER2 with EGFR, HER3 and HER4, and inhibit signaling through MAP and PI3 kinases. A phase I trial has demonstrated activity in OC.
Methods: 123 pts. with relapsed OC were treated with P, administered intravenously with a loading of 840 mg followed by 420 mg every 3 weeks to 61 pts. in cohort 1, while 62 pts. in cohort 2 received 1050 mg of P intravenously every 3 weeks. Response rate (RR) by RECIST was the primary endpoint, assessed after cycles 2, 4, 6, 8, 12 and 16. Fresh tumor biopsies were mandatory for cohort 1 in order to assay for HER2 phosphorylation (pHER2) status.