about the myths concerning cancer. Cancer should not be taken as untreatable.

## Chemoprevention, Vaccination

### P23
### 4HPR: a new prevention trial in high risk women. Rationale, design and implementation

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Retinoids have been studied as chemopreventive compounds because of their role in regulating cell growth, differentiation and apoptosis in preclinical models. Induction of apoptosis is a unique feature of fenretinide (4-hydroxyphenylshy;retinamide, 4-HPR) the most studied retinoid in clinical trials of breast cancer (BC) prevention for its selective accumulation in the breast tissue and its low toxicity. Fenretinide is effective in inhibiting the growth of BRCA-1 mutated BC cell lines. Recent studies showed that it modulates gene expression in ovarian cells, with an up-regulation of expression of proapoptotic genes in OVCA433 cells and down-regulation of mutant BRCA genes in IOSE (premalignant) cells and OVCA433 cells.
The fifteen-year follow up of a randomized phase III trial of fenretinide to prevent second BC indicates that it induced a 17%, durable reduction of second BC incidence. When stratified by menopausal status, the analysis showed a 38%, statistically significant reduction of second BC in premenopausal women and this effect persisted for up to 15 years, i.e. 10 years after treatment cessation. Importantly, the younger were the women ($\leqslant$40 years), the greater was the trend of benefit of fenretinide. When considering the protective activity of fenretinide on second BC and a similar trend on ovarian cancer (OC) it appears that young women at high risk for both diseases such as carriers of gemiline BRCA-1 and BRCA-2 mutations or those with a high family risk may be ideal candidates for further investigation on this retinoid. Since a reduction of second BC might be a surrogate marker of primary prevention, a favourable effect of fenretinide provides strong rationale for a primary prevention trial in unaffected women at high risk for BC.
Based on all the above considerations the European Institute of Oncology (Milan, Italy) has promoted a multi-centric (15 centres) randomized phase III placebo-controlled study with fenretinide in healthy young women. 758 healthy women, 25–44 years old at increased BC risk (BRCA-1/2 mutation or at risk of mutation $\geqslant$20%, based on BRCAPRO program), will be randomized to 4-HPR 200 mg/day versus placebo for 5 years followed by a ten years follow up period.The aim of the trial is to assess the efficacy of fenretinide in reducing the incidence of invasive BC and ductal intraepithelial neoplasia (DIN). Secondary endpoints are the incidence of non-invasive breast disorders, OC, other cancers and various biomarkers of risk.

### P24
### Breast cancer prevention with calcium and vitamin D

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**Background:** Although some observational studies have associated higher calcium intake and especially higher vitamin D intake and 25-hydroxyvitamin D levels with lower breast cancer risk, no randomized trial has evaluated these relationships.
**Methods:** Postmenopausal women (N = 25,282) who were enrolled in a Women's Health Initiative clinical trial were randomly assigned to 1000 mg of elemental calcium with 400 IU of vitamin D3 daily or placebo for a mean of 6.0 years to determine the effects of supplement use on incidence of hip fracture. Mammograms and breast exams were serially conducted. Invasive breast cancer was a secondary outcome. Baseline serum 25-hydroxyvitamin D levels were assessed in a nested case–control study of 640 case patients and 640 control subjects. A Cox proportional hazards model was used to estimate the risk of breast cancer associated with random assignment to calcium with vitamin D3. Associations between 25-hydroxyvitamin D serum levels and total vitamin D intake, body mass index (BMI), recreational physical activity, and breast cancer risks were evaluated using logistic regression models. Statistical tests were two-sided.
**Results:** Invasive breast cancer incidence was similar in the two groups (398 supplement vs 410 placebo; hazard ratio = 0.96; 95% confidence interval = 0.84–1.02). In the nested case–control study, no effect of supplement group assignment on breast cancer risk was seen. Baseline 25-hydroxyvitamin D levels were modestly correlated with total vitamin D intake (diet and supplements) ($r = 0.18$, $P < 0.001$) and were higher among women with lower BMI and higher recreational physical activity (both $P < 0.001$). Baseline 25-hydroxyvitamin D levels were not associated with breast cancer risk in analyses that were adjusted for BMI and physical activity ($P_{trend} = 0.20$).
**Conclusions:** Calcium and vitamin D supplementation did not reduce invasive breast cancer incidence in postmenopausal women. In addition, 25-hydroxyvitamin D levels were not associated with subsequent breast cancer risk. These findings do not support a relationship between total vitamin D intake and 25-hydroxyvitamin D levels with breast cancer risk.

### P25
### Knowledge and attitudes about prevention of cervical cancer by human papilloma virus vaccine (HPV) or pap smears: a cross-sectional survey in France

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**Introduction:** The commercialisation of two vaccines which focus on the main types of human papilloma virus (HPV) has the potential to reduce approximately 70% of all cervical cancers. As these vaccines do not provide 100% protection, screening for cervical cancer needs to continue for many years. Yet little is known about knowledge and attitudes about HPV vaccine and prevention of cervical cancer in general population and particularly young women. The aim of this study was to measure information on attitudes about HPV vaccination as well as knowledge of HPV and other risk factors of cervical cancer and methods of screening for cervical cancers.
**Method:** 306 participants aged 14–77 years of age, in July 2008 were recruited from the unit for prevention of infectious diseases (AIDS, tuberculosis, ...) of the University Hospital of Amiens in France. They completed a self-administered questionnaire covering demographics, knowledge and attitudes about cervical cancer, pap-smears and HPV vaccination, the perceived risk for contracting HPV infection and/or for developing cervical cancer and the perceived benefits of a vaccination to prevent cervical cancer.
**Results:** The sex-ratio of the participants was 0.76. The mean age was 34.9 years and 81% were born in France. Thirty-six percent of the population was students and 44% were married. Sixty-six percent agreed that a pap-smear could detect cervical carcinoma. Eighty-three percent of women had undergone at least one pap-test in their life and 60% in

the last year. The causal relationship between HPV and cervical cancer was known by 71% of the participants.
From the participants, 43% had heard of the HPV vaccine, principally by mass media like newspapers, television, radio and 66% of these knew the correct age group for which the HPV vaccine was recommended in France. 98% were aware that only females were eligible for the HPV vaccine and 77% that the vaccine has to be administered before the onset of sexual activity. Only 4% of the participants had received at least one HPV vaccine dose. Fifty-two percent of the women, despite vaccination, knew that population-based screening for cervical neoplasia needs to be continued.
**Conclusion:** One year after introduction of the first two HPV vaccines in France, only 43% of women in our study knew HPV causes cervical cancer and that women can get vaccinated against it.

**P26**

**Modulation of mRNA and protein levels of CYP1A1, 1A2, and 1B1 in nontumorigenic breast epithelial cells (MCF10A) by cabbage juice and its active components**

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Epidemiological migrant studies have shown that consumption of raw or short cooked cabbage and sauerkraut is connected with significant reduction of breast cancer incidences. Concurrently, some of the active components of cabbage juices like indole-3-carbinol (I3C), 3,3′-diindolylmethane (DIM) – a major in vivo acid-catalyzed condensation product of I3C, and sulforaphane (SUL) were determined as potential anticancer agents.
Our previous study showed that cabbage juice and its isolated active ingredients affected the expression of the estrogen metabolism key enzymes including cytochrome P450 1A1/1A2 and 1B1 in MCF7 breast cancer cell line. The aim of the present study was to investigate the effect of cabbage and sauerkraut juices of different origins and I3C, DIM and SUL on the expression profile of CYP1A1, CYP1A2, CYP1B1 mRNA and proteins level in nontumorigenic human breast epithelial MCF10A cell line.
Cells were treated with the pure compounds at the concentrations relevant to those observed in human plasma. After 72 hours of incubation the screening of cDNA from total RNA was performed using real-time PCR assay with specific primers for CYPs and protein level was determined by Western blot analysis. The increased expression of CYP1A1 was found as a result of cabbage juices treatment. Sauerkraut juice has stronger effect than raw one. Similar effect was exerted by I3C and DIM. The CYP1A1 protein level was increased as result of I3C treatment at the dose of 30 μM. In contrast, a decreased level of protein was detected after treatment with lower dose of this compound (10 μM), both doses of DIM, and SUL at the dose of 5 μM. The decrease in CYP1B1 mRNA was observed after sauerkraut juice treatment. In contrast, expression of CYP1B1 was increased by both indoles and SUL at the concentration of 108 μM. CYP1B1 protein was decreased as result of DIM treatment at the dose of 5microM. Up-regulation of CYP1A1 and CYP1A results in the reduction of active estrogens and might prevent breast carcinoma development. Thus the increase of CYP1A1 and CYP1A2 mRNA levels as a result of treatment of MCF10A breast epithelial cells with indoles or CYP1A1 and CYP1A2 mRNA and protein levels with cabbage juices observed in this study, may explain in part the epidemiological observations linking the cabbage consumption with decreased risk of breast cancer development.

**P27**

**Purification and characterization of an N-acetyllactosamine specific lectin from tubers of *Arisaema utile* having anti-proliferative effect on human cancer cell lines**

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**Objective:** Lectins are defined as carbohydrate binding proteins other that enzymes and antibodies. Lectins have emerged as very important macromolecular tools to recognize carbohydrates on cell surfaces. The present work is designed to purify and characterize monocot lectins with interesting biological properties from Indian monocot plants.
**Methods:** On the basis of sugar specificity determined by hemagglutination, asialofetuin-linked affinity was used to purify monocot lectins. Anti-proliferative potential were determined through sulphorhodamine-B assays.
**Results:** *Arisaema utile* lectin (AUL) gave a single band in SDS-PAGE at pH 8.3 corresponding to subunit Mr 13.5 kDa. The native molecular mass of 54 kDa suggested a homotetrameric structure. Like other monocot lectins, AUL gave multiple bands in isoelectric focusing and in native PAGE at pH 8.3. AUL was inhibited by N-acetyl-D-lactosamine (LacNAc), a disaccharide and asialofetuin, a complex desialylated serum glycoprotein. When treated with denaturing agents, the lectin was stable in the presence of urea (3 M), thiourea (4 M) and guanidine HCl (4 M). The lectin had no requirement for divalent metal ions i.e. $Ca^{2+}$ and $Mn^{2+}$ for its activity. AUL was a glycoprotein with a carbohydrate content of 1.2%. Amino acid analysis revealed high content of aspartic acid, glutamic acid, glycine and threonine and a very low amount of methionine but complete absence of cysteine. Amino acid modification studies of AUL revealed the involvement of tryptophan and tyrosine residues involved in lectin–sugar interaction. AUL exhibited a fluorescence emission maximum (lambda max) at 340 nm upon excitation at 295 nm. Using Far UV CD spectra the estimated secondary structure was 37% alpha-helix, 25% beta-sheet and 38% random contributions. In vitro anti-proliferative activity of AUL was tested on eleven different human cancer cell lines viz. MCF-7 (Breast), SK-N-SH (CNS), 502713 (Colon), Colo-205 (Colon), HCT-15 (Colon), HT-29 (Colon), SW-620 (Colon), Hep-2 (Liver), IMR-32 (Neuroblastoma), DU-145 (Prostate) and PC-3 (Prostate). The concentrations of AUL which produced 50% inhibition (IC50) of cancer cell lines viz. SW-620, HCT-15, SK-N-SH, IMR-32, Colo-205 and HT-29 at 38, 42, 43, 49, 50 and 89 μg/ml, respectively.
**Conclusion:** The purified Arisaema utile lectin was found anti-proliferative on human cancer cell lines.

**P28**

**Breast cancer: Molecular mechanisms underlying resistance to chemotherapy**

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Breast cancer is the second leading cause of cancer deaths. This disease is estimated to be diagnosed in over one million people worldwide. Although chemotherapy is a successful treatment regime in many cases multidrug resistance (MDR) remains one of the main obstacles in treatment of these cancer patients. Several proteins have been identified that are able to prevent the intracellular accumulation of anticancer agents by efflux mechanism. Such drugs are exported in both ATP-dependent and -independent manners. To the ATP-dependent group belongs the ATP-binding cassette (ABC) transporter family, which includes P-gp, MRP, BCRP, etc. Another protein related to MDR, though not belonging