

**Conclusions:** Significant differences in the incidence of cancer reported from countries of Central Asia and the Caspian Region necessitate conducting a series of epidemiologic investigations in the region to identify factors associated with these differences for various types of cancers.

## Publication

### Epidemiology, prevention and public health

593

PUBLICATION

#### Cadmium concentration in men' urine base to smoking

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226 urine samples of 6–74 years old men, smoking and non-smoking from Tehran gathered. To determine the concentration of cadmium in participants' body, all samples standardized to microgramme of creatinine in urine. samples were analysed with GFAAS. The amount of concentrations in smoking and non-smoking men's urine were compared with T-test and logistic regression method was used to determine the relation between cadmium concentration in urine, smoking habit and age. In this investigation found that the smoking men had more concentrations of cadmium in their urine (OR = 0.01, 95%CI: 0.35) than non-smoking men (OR = 0.01, 95%CI: 0.29) and the cadmium concentration in urine, in both smoking and non-smoking men increase with age. The group of 51–60 of smoking men had the highest concentration of cadmium in urine. Findings demonstrate an independent relation between smoking habit and age in cadmium concentration.

594

PUBLICATION

#### Cancer literacy in Iran: knowledge, attitudes and perceived causes of cancer

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**Background:** Knowledge, attitudes and perceptions towards cancer and its treatment vary dramatically based on an individual's cultural backgrounds. Those in resources poor countries such as Iran often view a cancer diagnosis as guaranteed suffering and death.

**Material and methods:** This cross sectional study examines cancer literacy among the general population in Tehran, Iran. Five hundred and six (n = 506) adults age 15 and over participated in the study and were surveyed using a 16-item questionnaire. Five of the questions were related to demographics, five to knowledge, five to attitudes, and one to perceived causes of cancer.

**Results:** The mean age of respondents was 27.7 years (SD = 9.1). Most were male (68%), never married (59%), employed (63%) with a secondary education (60%). It appeared that the respondents were fairly knowledgeable about cancer based on their correct answers ranging from 39% to 81%. Eighty-nine percent of the respondents either agreed or strongly agreed with the statement that cancer patients and their family should receive special support. Only 40% either agreed or strongly agreed that patients should be told about their cancer diagnosis. Seventy-nine percent either disagreed or strongly disagreed with the statement that cancer cannot be cured. Fifty-two percent indicated the diagnosis and treatment process related to cancer in developing countries was inferior to that of developed nations. Finally, 195 respondents admitted they were uncertain about cancer causes while the remaining 311 indicated that they perceived causes to be related to: diet (19%), genetics (16%), environmental factors (14%), stress (13%), smoking (11%), and new life styles (10%). Those with lower education were more likely to be uncertain about cancer causes (P = 0.001).

**Conclusions:** Study results suggest that cancer literacy in Iran is fairly good. The findings are encouraging and may contribute to the future efforts to create highly effective cancer prevention and treatment educational materials in Iran and other similar developing countries.

595

PUBLICATION

#### The role of genetic factors for detection of ovary cancer risk persons

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**Background.** The early diagnosis of ovary cancer usually is rather difficult because of lack of clear symptoms. Very often it is recognized as a locally

widespread disease in it's III or IV stage, when the successful treatment is doubtful.

The death rate from ovarian cancer in Latvia takes the high third place. Some progress promises the information about risk groups. One of these groups could be the BRCA1 mutation carriers, as well as patients with positive family or personal oncological anamnesis. In this study we tried to analyse: 1) The occurrence of BRCA1 mutations between the patients of ovary cancer. 2) The importance of oncological anamnesis of patients and/or families

**Material and methods:** At the beginning of our research (1996–2001) we clarified BRCA1 mutation spectrum for the patients with breast and ovary cancer. We established, that in 90% cases three prevalent mutations (300T > A in exon 5, 4154delA in exon 11 and 5382insC in exon 20) were detected in our patients. 115 voluntary ovary cancer patients were included in the study (2002–2004), three prevalent BRCA1 mutations were detected to each participant followed by a questionnaire and the genealogical tree analysis.

**Results:** We clarified that patients without BRCA1 mutations in 39.1% cases had no family history of cancer, but in the cases of positive mutations only 4.4% of patients had not cancer in their families. The first and second stage of disease were recognized for 34% of BRCA1 negative patients and 17.4% for the mutations carrier, but the third stage of disease for 45.7% BRCA1 negative patients and 70% BRCA1 positive patients.

	BRCA1 negative	BRCA1 positive
Number of patients	92	23
Middle age of affection	48 (24–72)	47 (34–57)
<b>Family history of cancer</b>		
1 breast or ovary	15	9
2 breast or/and ovary	10	5
3 breast or/and ovary		2
4 breast or/and ovary	1	
Other oncological disease	30	6
Without cancer history	36	1
<b>Patient history of cancer</b>		
Bilateral breast cancer	1	
Breast cancer	8	6
Colorectal cancer	2	
Hodgkin disease	1	
Renal cancer	1	

**Conclusion:** The most important role to discover the ovary (and breast) cancer risk persons has the family (and personal as well) breast and/or ovary cancer history, particularly the cancer cases at the early age. The determination of BRCA1 3 prevalent mutations in Latvia is suggested for all the ovary cancer patients in the reproductive age, it would help to locate the potential ovary (or breast) cancer patient risk group between the relatives. Patients with negative family oncological anamnesis were quite reserved regarding the genetic examination and usually refused from it, therefore 68% of the study participants had positive family history.

596

PUBLICATION

#### Technologies Augmenting Clinical Insight: transforming TACIT knowledge into explicit knowledge in the domain of cancer care

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Healthcare, and especially cancer care relies on knowledge. Indeed, one of the challenges today is the effective management of clinical knowledge, or more specifically, expertise. Efforts to share it have so far focused on explicit knowledge, mainly data, while tacit knowledge remains in the mind of the expert, only to be accessed by training or practice.

The paper presents the TACIT (Technologies Augmenting Clinical Insight) project [1], which vision is to unlock the tacit knowledge of Europe's senior clinicians both by linguistically analysed multimedia recording, and by expert location and communications. TACIT aims at developing a software solution that combines these elements with explicit knowledge from heterogeneous information sources (such as clinical systems, Publication onlins, or research reports) into a user friendly Clinical Expertise Browser. The TACIT project focuses on the clinician needs and on breast cancer care processes. The user requirements analysis revealed that the TACIT solution should be a knowledge-based system to support the clinician's decision making process in the diagnosis, prognosis and treatment of patients affected by breast cancer. The clinician will inquire the system to monitor and better assess a given patient's pattern, or to define the next steps in the patient's clinical pathway.

Therefore, the TACIT system will be able to:

- Record patient episode data and associated applied Tacit Knowledge used by Consultant Oncologists during the clinical management of patients diagnosed with advanced breast cancer
  - Provide a knowledge resource for oncologists in the domain of advanced breast cancer
  - Propose similar episodes of patient care for patients attending outpatient clinics
  - Provide an 'ask the expert' service where junior oncologists can provide anonymous patient data and request advice from acknowledged experts. It will be fully prototyped and experimented within the key clinical process of cancer care, addressing the substantial problems of bridging clinical expertise between secondary (hospital) care and after care led by the general practitioner and supporting specialist community nurses.
- Thus the innovations arising from the project will be piloted and fully validated in two European hospitals, leading to a strong set of case studies and results which will be disseminated to the healthcare and Information and Communication Technologies communities, and to the wider European research area.
- This project has been partially funded by the European Commission under the IST initiative.

## References

[1] <http://oncology.fecs.be>

## Gastrointestinal Tumours

Oral presentations (Wed, 2 Nov, 9.15–11.15)

### GI – metastatic colon cancer

597

ORAL

**A randomised phase III multicenter trial comparing irinotecan in combination with either the Nordic bolus 5FU and folinic acid (5FU/FA) schedule (FLIRI) or the bolus/infused de Gramont schedule (FOLFIRI), in patients with metastatic colorectal cancer**

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**Background:** Irinotecan with FU/FA is an established regimen in metastatic colorectal cancer, however, with major uncertainties related to the mode of administration of FU. In the US, a weekly bolus schedule, the Saltz regimen, was used extensively, whereas in Europe, infused 5FU is preferred. We have compared irinotecan in combination with either the Nordic fortnightly 5FU/FA bolus schedule (FLIRI) or the fortnightly Lv5FU2 schedule (FOLFIRI).

**Methods:** Between August 2001 and March 2004, 567 previously untreated patients with metastatic colorectal cancer at 27 centres in the Nordic countries were randomized to either FLIRI (irinotecan 180 mg/m<sup>2</sup> day 1, 5FU 500 mg/m<sup>2</sup> bolus iv day 1,2, FA 60 mg/m<sup>2</sup> day 1,2) or FOLFIRI (irinotecan 180 mg/m<sup>2</sup> day 1, FA 200 mg/m<sup>2</sup> day 1,2, 5FU bolus 400 mg/m<sup>2</sup> day 1,2 and infused 5FU 1200 mg/m<sup>2</sup> per 48 hour). The dose of irinotecan, found in a preceding phase II study with the Nordic schedule (210 mg/m<sup>2</sup>) was lowered after the first 100 randomized patients to 180 mg/m<sup>2</sup> because of a slight excess of toxicity (any grade 3–4, 49 vs 38 instances, 60 day mortality 3 vs 2) and concerns seen using the Saltz regimen in two American trials. The primary endpoint was progression-free survival with the aim to show non-inferiority (at the most 20% worse or from median 6.7 to 5.4 months,  $\alpha = 0.05$ ,  $1 - \beta = 0.80$ ).

**Results:** Patient characteristics were well balanced between groups. In the entire patient material, including the first 100 patients, toxicity did not differ between groups (grade 3/4 nausea/vomiting 20 vs 37, diarrhea 23 vs 31, neutropenia 19 vs 8, fever 11 vs 14). The 60 day mortality was 2.4% vs 2.3% (6 patients each in both groups). The primary endpoint, time to progression, did not differ between groups (median 9.1 months in both groups,  $p = 0.34$ ).

**Conclusions:** Irinotecan with the bolus FU/FA Nordic schedule (FLIRI) is a convenient treatment with efficacy and toxicity comparable to the 'infused'

FOLFIRI regimen. Response rates and overall survival will be presented at the meeting.

The work was supported in part by Aventis.

598

ORAL

**Randomised comparison of 5-FU/folinic acid plus irinotecan (FOLFIRI) and irinotecan plus oxaliplatin (IROX) in first-line therapy of metastatic colorectal cancer (CRC): the fire-trial**

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**Objective:** This randomised trial compares the 1st-line efficacy and toxicity of infusional 5-FU/FA (AIO regimen) plus irinotecan (FOLFIRI) to the combination of irinotecan plus oxaliplatin (IROX).

**Methods:** 488 patients (pts) from 56 centres were enrolled between July 2000 and the end of study in September 2004. In the FOLFIRI arm, pts received FA 500 mg/m<sup>2</sup> plus 5-FU 2000 mg/m<sup>2</sup> (24h) and irinotecan 80 mg/m<sup>2</sup> given weekly for 6 times. In the IROX arm pts were treated with oxaliplatin 85 mg/m<sup>2</sup> (d1, 15, 29) and irinotecan 80 mg/m<sup>2</sup> weekly times 6. Treatment cycles were repeated on day 50 in both treatment arms. Patients were stratified according to LDH, adjuvant pretreatment, and Karnofsky performance status (KPS) showing LDH >240 U/ml in 42% vs 39%, adjuvant pretreatment in 31% vs 29%, and a KPS = 100% in 48% vs 47%, in the FOLFIRI- and IROX-arm respectively. The primary end-point of the trial was progression-free survival. At disease progression, pts were offered to switch to the comparator regimen.

**Results:** Treatment efficacy was evaluable in 478 pts (240 FOLFIRI, 238 IROX). Second-line therapy according to the cross-over protocol was FOLFIRI of patients. The IROX and 29% (IROX documented in 33% (FOLFIRI complete remission rate (CR) was 7.9% vs 8.3%, the partial remission rate (PR) 36.7% vs 39.5% for an overall remission rate (CR+PR) of 44.6% vs 47.8% in the FOLFIRI- and IROX-arm, respectively. Stable disease (SD) was documented in 44.2% vs 30.7%. Median progression-free survival was 8.2 months vs 7.0 months ( $p = 0.377$ ) with a hazard ratio of 1.093 (95%CI: 0.897–1.330), while median overall survival was 21.9 months vs 19.3 months ( $p = 0.249$ ) with a hazard ratio of 1.159 (95%CI: 0.902–1.49). 60-day mortality was 6.3% and 4.2% (FOLFIRI vs IROX).

**Conclusions:** FOLFIRI and IROX are comparably effective with regard to response, progression-free survival, and overall survival. Toxicity is similarly acceptable in both treatment arms.

599

ORAL

**Improved activity with irinotecan, oxaliplatin and infusional 5-FU/LV (FOLFOXIRI) compared with FOLFIRI in metastatic colorectal cancer (MCR): results of a randomized Phase III trial by the Gruppo Oncologico Nord Ovest (G.O.N.O.)**

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**Background:** The FOLFOXIRI regimen has demonstrated promising antitumor activity coupled with manageable toxicities in Phase II trials in MCR.

**Patients and methods:** 244 patients (pts) with measurable, not resectable MCR and previously untreated with chemotherapy (CT) for advanced disease, were randomly assigned to receive: irinotecan 180 mg/sqm d1, I-LV 100 mg/sqm d1+d2, 5FU 400 mg/sqm bolus d1+d2, 5-FU 600 mg/sqm 22-h infusion on d1+d2 (FOLFIRI, arm A, n = 122) or irinotecan 165 mg/sqm d1, oxaliplatin 85 mg/sqm d1, I-LV 200 mg/sqm d1, 5FU 3200 mg/sqm 48-h infusion starting on d1 (FOLFOXIRI, arm B, n = 122). Both treatments were repeated every 2 weeks and after progression to FOLFIRI an oxaliplatin containing regimen was recommended.