P34 YOUTH INVOLVEMENT – AN OPTIMAL TECHNIQUE TO ERADICATE CANCER

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Background: Evidence that any delay in providing information results in lack of treatment or admission, which might result in death or irreversible harm to an individual, constitutes an emergency. Involving youth in the process could help avoid an unnecessary lack of information, and might contribute to the sustainable legacy of fighting cancer. Youth-development programmes and initiatives associated with awareness, education, and eradication of cancer could decrease unnecessary deaths caused by cancer. Ongoing youth-development projects and partnership campaigns could improve health awareness.

Methods: Analysis of 500 young people involved in a Rural Youth Health-Development programme (RYHD) conducted by Umvithi Youth Development and Department of Health in KwaZulu, Natal, showed an improved ability to care, teach, and prevent cancer. Through the RYHD, 2500 community members underwent training and tests to recognise symptoms, and others were diagnosed with cancer and related diseases that they were not aware of.

Findings: As a result of the RYHD, many individuals took positive action and full responsibility to decrease cancer risk, such as quitting smoking, eating healthy food, and exercising regularly.

Interpretation: Utilising youth for information distribution and involvement in the fight against cancer could propel communities towards sustainable improvement in health, and enhances the ability of individuals to take responsibility for their own health. Young people are founders and initiators of projects, groups, and organisations; they are lobbyists, decision-makers, and are a key element for building a successful and growing community.

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P35 PRELIMINARY STUDY OF *EGFR* MUTATION PROFILE IN CYTOLOGICAL SPECIMENS OF INDONESIAN LUNG-CANCER PATIENTS

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Background: Many lung-cancer studies have shown that female patients without a history of smoking and of Asian origin have a good response to tyrosine-kinase inhibitors (TKIs). Epidermal growth-factor receptor (EGFR) mutations are prevalent in these patients, which explains the promising response to TKIs. However, prevalence of mutations in the *EGFR* gene and response to TKIs in Indonesian patients with lung cancer has not been studied. We have begun preliminary work to collect cytological samples from 14 patients, to assess the prevalence of *EGFR* mutations and related clinicopathological parameters such as sex, age, stage, and response to TKIs.

Methods: Cytological slides were examined by pathologists and tumour cells were microdissected, to isolate total DNA, and sent to a certified reference laboratory in Jakarta. Direct DNA sequencing was done against exon 19 and 21 of the *EGFR* gene, which are the most frequent sites of mutation according to literature.

Findings: *EGFR* mutations were found in 50% of patients ($n = 14$); female patients had a higher frequency than male patients (71% [5 of 7] vs. 29% [2 of 7]). Deletion of exon 19 was more common than substitution mutations in exon 21, which contributed up to 71% and 29% to the overall mutation rate, respectively. *EGFR* mutation was not associated with age or other clinicopathological parameters. Response to TKIs in patients with and without *EGFR* mutations is currently being investigated.

Interpretation: *EGFR* mutations are more prevalent in Indonesian women than in men, and deletion of exon 19 being the most common mutation type. The preliminary response of patients to TKIs is being evaluated. Large prospective studies are needed to evaluate the response to TKIs among Indonesians with *EGFR* mutations.

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P36 DIAGNOSTIC AND PROGNOSTIC POTENTIAL OF CK20 GENE EXPRESSION IN PATIENTS WITH TRANSITIONAL-CELL CARCINOMA OF THE URINARY BLADDER

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Background: Bladder cancer is among the five most common malignancies worldwide, and recurrence of non-invasive tumours makes it one of the most prevalent cancers. Cystoscopy in conjunction with urine cytology is the gold standard for detection of bladder cancer; however, cystoscopy is invasive and expensive, with low accuracy for high-grade disease. Urine cytology has low sensitivity for detection of low-grade bladder cancer. The aim of study was to quantitate cytokeratin 20 (CK20) mRNA expression in exfoliated cells of urine in patients with transitional-cell carcinoma (TCC), by use of SYBR Green real-time PCR, which may be used as a non-invasive tool for follow-up of patients with bladder cancer.

Methods: Urine was collected from 78 bladder-cancer patients during follow-up, from 20 patients with benign urological disease, and from 20 healthy volunteers. RNA was isolated from exfoliated cells in urine by use of an RNA purification kit, and real-time PCR was performed with specific primers for the amplification of CK20, a marker for TCC urothelium.

Findings: A strong correlation was found between tumour grade and expression of CK20 in urine. All patients with grade III and IV tumours showed positive CK20 expression in the exfoliated cells, with 100% sensitivity. The sensitivity for lower grades was up to 83%. Out of 13 TCC patients, CK20 expression was found in nine patients who were previously diagnosed by biopsy and had a negative biopsy following treatment. These nine patients were followed up for 6 months, and TCC recurred in four patients.

Interpretation: Quantitative detection of CK20 in exfoliated cells of urine is a simple and non-invasive method for monitoring and follow-up of TCC in patients with bladder cancer. However, more information is needed regarding CK20 expression in non-malignant urological diseases to use it as a marker for routine screening.

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P37 ANTHRACYCLINE-BASED NEOADJUVANT CHEMOTHERAPY AND HYPERMETHYLATION OF A TUMOUR-SUPPRESSOR GENE IN LOCALLY ADVANCED BREAST CANCER

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Background: Anthracycline-based neoadjuvant chemotherapy kills cancer cells by inducing DNA double-strand breaks. In-vitro studies have shown that DNA damage leads to localised DNA methylation on CpG-rich sites found in promoter regions. Promoter methylation of some tumour-suppressor genes has been associated with poor prognosis. To determine whether neoadjuvant chemotherapy induces promoter methylation, we evaluated the promoter regions of the *SFRP1* and *CDH1* genes in locally advanced breast cancer, before and after treatment.

Methods: Paired FFPE blocks of 61 patients with locally advanced breast cancer before and after chemotherapy were collected and confirmed by pathologists. Patients had standard fluorouracil, doxorubicin (adriamycin), and cyclophosphamide (FAC) chemotherapy for three cycles. In a subset of 12 patients, epigenetic therapy (hydralazine and magnesium valproate) was added. DNA isolation and bisulfite conversion were performed to evaluate promoter methylation of *SFRP1* and *CDH1* genes using methyl-specific PCR (MSP).

Findings: Using *SFRP1* and *CDH1* as surrogate markers, 13 of 41 (32%) and 18 of 48 (38%) patients showed induction of promoter hypermethylation after chemotherapy ($p = 0.052$ and $p = 0.012$, McNemar test). However, the rate of demethylation of both markers was 10%. To explore the reversibility of chemotherapy-induced promoter hypermethylation, a subset of 12 patients were treated with a combination of epigenetic therapy and chemotherapy. Two of 12 patients (17%) showed hypermethylation and four of 12 (33%) had an increased rate of promoter demethylation. The dynamic status of promoter methylation is not associated with hormone-receptor status, *HER2* expression, age, or stage.

Interpretation: Neoadjuvant chemotherapy can induce promoter methylation of tumour suppressor genes in a significant proportion of patients, which may affect long-term clinical outcome. This trend of promoter hypermethylation of tumour-suppressor genes can be reversed using epigenetic therapy.

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P38 PHASE 1 DOSE-FINDING STUDY OF EPIRUBICIN, OXALIPLATIN, AND S-1 IN PATIENTS WITH PREVIOUSLY UNTREATED ADVANCED GASTRIC CANCER

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Background: To determine the recommended dose and dose-limiting toxicity (DLT) of epirubicin, oxaliplatin, and S-1 (EOS) combination in patients with previously untreated advanced gastric cancer (AGC).

Methods: Previously untreated patients with histologically proven metastatic or recurrent AGC and ECOG performance status 0–2 were enrolled. A fixed dose of epirubicin (50 mg/m^2) and oxaliplatin (130 mg/m^2) was administered intravenously on day 1. The dose of S-1 was escalated as follows: level 1, 30 mg/m^2; level 2, 40 mg/m^2; level 3, 45 mg/m^2; level 4, 50 mg/m^2. S-1 was administered orally twice a day on days 1–14. Each cycle was repeated every 21 days. DLTs were evaluated during the first two cycles of treatment.

Findings: 19 patients were enrolled: 13 patients in the dose-escalation phase and six patients in the extension at the recommended dose. The median age was 53 years (range, 40–71 years). At dose level 2, one DLT occured among six patients (grade 4 neutropenia lasting more than 5 days), and at dose level 3, two DLTs were observed among four patients (grade 3 diarrhoea and nausea). Therefore, dose level 2 was determined to be the recommended dose. Cumulative (all cycles) grade 3–4 toxicity included neutropenia (58%), leucopenia (32%), thrombocytopenia (11%), diarrhoea (11%), and nausea (5%). Of 13 patients with measurable lesions, eight achieved a partial response and three had stable disease, and the objective response rate was 62% (95% CI 36–88%). Median progression-free survival was 6.5 months (4.7–8.2).

Interpretation The recommended dose of the EOS regimen in patients with previously untreated AGC was epirubicin 50 mg/