OP3 COST-EFFECTIVENESS OF EPIDERMAL GROWTH-FACTOR RECEPTOR MUTATION TESTING AND FIRST-LINE TREATMENT WITH GEFITINIB FOR ADVANCED NON-SMALL-CELL LUNG CANCER

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Background: Epidermal growth-factor receptor (EGFR) testing and first-line therapy with gefitinib is becoming the standard treatment for advanced non-small-cell lung cancer (NSCLC). Yet, to date, no study has quantified the cost-effectiveness of this approach within an Asian population, where the prevalence of activating mutations is higher than among western populations.

Methods: A decision-analytic model was developed to determine the cost-effectiveness of EGFR testing and first-line treatment with gefitinib for patients with activating EGFR mutations, versus standard care, which includes first-line treatment with chemotherapy followed by gefitinib as second-line treatment. The model uses clinical and outcomes data from three randomised clinical trials, and societal (non-subsidised) costs from three cancer treatment centres in Singapore. Health effects were expressed as quality-adjusted life-years (QALY) gained. Costs include relevant costs for prescription medications, physician visits, laboratory tests, scans, hospitalisations, and treatment of adverse events. All costs and cost-effectiveness ratios were expressed in 2010 Singapore dollars. Sensitivity analyses were done to identify the extent to which results were robust to key model assumptions.

Findings: EGFR testing and first-line treatment with gefitinib was found to be a dominant strategy (lower costs and greater effectiveness) compared with standard care. Because the primary savings in the testing group did not result from not providing gefitinib to patients who do not benefit, this finding holds regardless of the percentage of patients who test positive for EGFR mutation. In a secondary analysis, first-line treatment with gefitinib was also dominant compared with first-line chemotherapy in patients with activating EGFR mutations.

Interpretation: Based on these data, EGFR testing and first-line treatment with gefitinib for patients with activating mutations should become a standard treatment in advanced NSLC.

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OP4 SALVAGE CHEMOTHERAPY IN PRIMARY RESISTANT OR RELAPSING STAGE III–IV NEUROBLASTOMA

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Background: Neuroblastoma is the most common extracranial tumour, accounting for 8–10% of childhood malignancies and 15% of deaths from cancer in the paediatric age group. Approximately half of newly diagnosed children are at high risk for treatment failure. The aim of this study was to evaluate the response rate of salvage chemotherapy with ifosfamide, carboplatin, and etoposide (ICE) when given to previously treated patients with primary refractory or progressive high-risk neuroblastoma.

Methods: Sixty-six patients from NCI and CCHE received salvage chemotherapy (ICE) for primary resistance ($n = 51$, 77.2%) or disease progression on primary chemotherapy ($n = 15$ 22.8%). Forty male patients (60.6%) and 26 females (39.4%), between 3 months and 12.5 years of age, were included.

Findings: The most common tumour site was suprarenal, followed by retroperitoneal mass. Two patients (3%) died from chemotherapy toxicity during ICE administration. Evaluation of tumour response in the remaining 64 patients showed the following: complete or partial response in 24 patients (36.5%), stable disease in 11 patients (16.6%), and progressive disease in 29 patients (43.9%). 14 patients (21.2%) were considered eligible for an autologous bone-marrow transplant, and 50 patients (78.8%) failed second-line (salvage) chemotherapy and had palliative lines of therapy. By the end of the study (May 2010), 47 of 66 (71.2%) of patients were still alive, and 19 of 66 (28.8%) were dead. Two of 14 patients (14.2%) who underwent haematopoietic stem-cell transplantation died from post-transplantation disease progression, and 12 of 14 (85.8%) were in complete cytogenic remission (CCR).

Interpretation: Chemotherapy with ICE for primary resistant or progressive stage III–IV neuroblastoma seems well tolerated. With a 36.6% response rate, 18% CCR, and 3.0% treatment mortality rate, it can be considered a good salvage therapy for patients in whom palliation is appropriate.

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OP5 DIFFERENCE IN HORMONE-RECEPTOR STATUS OF BREAST CANCERS IN VIETNAMESE AND SWEDISH WOMEN

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Background: The aim of this study was to compare oestrogen-receptor (ER) and progesterone-receptor (PgR) status of operable breast cancers in Vietnamese and Swedish patients.

Methods: Primary breast-cancer tissues were randomly selected from 249 Vietnamese patients treated in Hanoi, Vietnam, and 1257 Swedish patients treated in Stockholm, Sweden, between 2002 and 2003. Clinical information was available for

all patients in the study. For tumours from Vietnamese patients, hormone-receptor status was analysed by immunohistochemistry, using an automated slide stainer (Bench MarkXT, Ventana) in combination with anti-ER (SP1 250) and anti-PgR (clone 1E2) rabbit monoclonal antibodies. Tumours with 10% or more stained nuclei were considered receptor positive. Tumours from Swedish patients were analysed with an enzyme immunoassay, with a cut-off point of 0.10 fmol/μg DNA as positive. The hormone-receptor frequencies between populations were compared according to clinicopathologic features.

Findings: Compared with Swedish patients with similar menopausal status, the ER-positive rate was higher in premenopausal Vietnamese patients (71% vs. 58%, $p = 0.007$) and lower in postmenopausal Vietnamese patients (45% vs. 72%, $p < 0.001$). PgR-positive tumours were found in 58% of premenopausal and 25% of postmenopausal Vietnamese patients. The corresponding figures for Swedish patients were 73% and 66%, respectively.

Interpretation: ER positivity in Vietnamese patients decreased gradually with rising patient age, by contrast with the trend observed for Swedish patients, who showed a gradual increase with age. PgR positivity was lower for Vietnamese than for Swedish patients, regardless of age or menopausal status. Our findings suggest that a high percentage of young patients could benefit from endocrine therapy, and indicate a limited benefit among postmenopausal Vietnamese patients.

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OP6 CLINICAL SIGNIFICANCE OF DOWN-REGULATED SPARCL1 IN HUMAN GASTRIC CANCER

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Background: SPARC-like protein 1 (SPARCL1) is an extracelluar matrix glycoprotein involved in many physiological functions. Studies have shown an important role for SPARCL1 in cancer development and progression.

Methods: Tissue microarray blocks were constructed based on 1072 Chinese patients, containing gastric-cancer tissue and adjacent normal-mucosa tissue. We analysed expression of SPARCL1 from mRNA and at the protein level, using real-time quantitative polymerase chain reaction (qRT-PCR), semi-quantitative PCR, immunohistochemistry (IHC), and Western blotting. We analysed loss of heterozygosity at the SPARCL1 gene locus, using ten tumour and matched normal-tissue pairs.

Findings: SPARCL1 mRNA was substantially lower in tumour specimens than in normal tissues. Down-regulation of SPARCL1 protein was detected in 413 (38.7%) of 1072 primary gastric-tumour tissues. Significant differences in expression were found according to histological type, tumour size, depth of invasion, regional lymph-node involvement, TNM stage, and differentiation. Low expression of SPARCL1 was more common in poorly differentiated and undifferentiated tumour tissues (51.1%) than in well and moderately differentiated tumours (29.9%). Kaplan–Meier survival curves showed that SPARCL1-positive patients had longer median survival than SPARCL1-negative patients (59 months vs. 28 months, $p = 0.001$). Our data also showed significantly lower 5-year survival for patients with reduced expression of SPARCL1 (37.8%) than for patients with high expression (49.7%; $p < 0.001$). The incidence of loss of heterozygosity for each individual marker was 12.5% (1 of 8) for D4S2462, 20% (2 of 10) for D4S2929 and 33.3% (3 of 9) for SPARCL1.

Interpretation: Our study revealed the clinical significance of SPARCL1 expression, providing a basis for a novel negative biomarker in gastric-cancer progression and prognosis. Furthermore, SPARCL1 protein might be considered a potential differentiation marker.

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OP7 BRACHYTHERAPY VERSUS EXTERNAL-BEAM BOOST IN NEOADJUVANT RADIATION THERAPY OF LOCALLY ADVANCED RECTAL CANCER – WITHDRAWN

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OP8 VIDEO-ASSISTED THORACIC SURGERY LOBECTOMY FOR NON-SMALL-CELL LUNG CANCER—PROPENSITY-SCORE ANALYSIS BASED ON A MULTI-INSTITUTIONAL REGISTRY

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Background: We did a multi-institutional propensity-matched study comparing video-assisted thoracic surgery (VATS) with

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