Evaluation of circulating tumor cells in patients with primary breast cancer
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Background: Circulating tumor cells (CTC) can be identified and characterized in blood of patients with many solid tumors, particularly breast cancer. The identification of CTC could potentially become an important prognostic factor in breast cancer patient. The aim of this prospective study is to detect CTC in the blood of breast cancer patients and to correlate between detection of CTC and other prognostic factors, disease free survival and overall survival.

Material and methods: The study was conducted at medical oncology department NCI, Cairo University during the period from August 2008 to August 2011. Forty two consecutive consenting female patients with non metastatic breast cancer who ended their adjuvant chemotherapy and radiotherapy at least 2 years were recruited. Detection of circulating tumor cells in the blood of our patients as well as 8 healthy donors was done by measuring the gene expression for mammaglobin by RT-PCR, and then the relative fold change was calculated relatively to normal samples using comparative Ct method.

Results: The median circulating tumor cells (CTC) fold changes was 9.3, ranging from 0 to 20.8 in the whole studied group while the CTC folds change were zero for the control group because the gene is not expressed in the serum of healthy adults. There was a highly statistically significant difference (p=0.001) between CTC folds of change for stage IIIA compared to stage II tumor, and a statistical significance (p = 0.070) in favor of higher CTC folds change in those with Her2-neu receptor positivity. There was no significant correlation between higher CTCs and other factors related to the patients or disease characteristics. There was also no relation between CTC fold changes and overall survival or disease free survival.

Conclusion: In this small study, mammaglobin is considered a sensitive marker for detection of CTC in breast cancer. Circulating tumor cells fold of changes is correlated with tumor stage and Her2 status. Further studies including larger number of patients and followed for longer period are recommended to evaluate this protocol more thoroughly.
Differences In Common Risk Factors For Breast Cancer Molecular Subtypes

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**Background:** Breast cancer is characterized by its molecular and clinical heterogeneity. The current study focuses on assessing how risk factors relate to molecular subtypes.

**Patients & methods:** A total of 507 female patients with breast cancer who have been followed up at NCI & Nasser institute during the period from July 2012 till February 2013 were included & categorized into 5 molecular subtypes by immunohistochemistry. Case-case odds ratios comparing risk factors across tumor subtypes using the luminal A tumors as the reference group were estimated.

**Results:** Three hundred and twenty one patients had luminal A, 73 had luminal B, 66 had Her2-overexpressing, 30 had basal like and 17 had unclassified breast cancers. We observed significant differences in biological subtypes for the distribution of residence (p=<0.001), age at diagnosis (P = 0.016), number of full term births (P =0.028) and history of contraception use (p=0.026). The age of ≤35 years was found to be a risk factor for unclassified tumors (OR: 5.16, 95% CI: 1.68-15.85; P = 0.008 compared with luminal A), similar to Luminal B and HER2 expressing cases (p=0.087 and 0.045 compared with Luminal A respectively). Rural residents were more likely to be unclassified cases (OR: 7.97, 95% CI: 2.53-25.07; P = <0.001 compared with luminal A). Nulliparous women had an increased risk of unclassified tumors (OR: 5.22, 95% CI: 1.53-17.83 p=0.008 compared with Luminal A), while women who had ≥ 2 children were found to be at high risk for Luminal B (OR: 3.241, 95 %CI: 1.48-7.09; P=0.003 compared to Luminal A). Premenopausal patients were associated with increased risk of unclassified breast cancer (OR: 3.43, 95% CI: 1.28-9.24; p=0.015 compared with Luminal A) whereas, no significant difference were found for other subtypes. Patients with history of combined estrogen and progesterone contraception use were associated with a significant increased risk of unclassified tumors (OR: 0.1, 95% CI: 0.02- 0.54; p= 0.004) while no protective association was seen against other biological subtypes.

**Conclusion:** Results from this study have shown that luminal A and unclassified tumors seem to have distinct sets of risk factors, suggesting etiologic, in addition to clinical, heterogeneity.
Adult Biphenotypic Acute Leukemia: The Egyptian National Cancer Institute Experience

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Background: Biphenotypic acute leukemia is a rare form of leukemia. Knowledge concerning the clinical and biological presentation, as well as the outcome of treatment, in adult is limited

Patients and methods: This is a retrospective analysis of the clinical, biological, and immunophenotypic features of 30 biphenotypic acute leukemias (BALs), fulfilling modified EGIL’s score, and treated in the medical oncology department at the National Cancer Institute (NCI-Cairo) between 2005 & 2010. Myeloid and T-lineage features were demonstrated by cytoplasmic myeloperoxidase and CD3; B-lineage features were demonstrated by CD19, CD22 and CD10.

Results: There were 18 men and 12 women; all were adults. Morphology was consistent with acute lymphoblastic leukemia (ALL; 8 patients), acute myeloid leukemia (AML; 14 patients), or inconclusive (8 patients). Immunophenotyping disclosed B + myeloid (66.6%), T + myeloid (16.6%), or trilineage (16.6%) combinations. Cytogenetic results were available for four patients 75% evidenced t(9;22)/(Ph+) and 2 of those patients were originally diagnosed and treated as chronic myeloid leukemia patients for several years before developing acute blastic crisis. There was no correlation between age, morphology, immunophenotype, or cytogenetics. Response to treatment and outcome were available for 18 patients. Eight received ALL, 14 AML and 8 were either unfit for chemotherapy or died during induction treatment. ALL treatment induced a response in 87.5%, AML therapy in 35.7%. Seventeen (56.6%) patients died, 4 of resistant disease. Overall survival was 10% of patients are alive at 3 years. Age, sex and low hemoglobin were predictors for poor outcome, though only low hemoglobin showed statistical significance (p=0.035).

Conclusion: Biphenotypic acute leukemia is confirmed to be a poor-risk disease. Although there are no uniform criteria about whether to treat these patients as ALL or AML, adult patients should be considered for transplantation in first remission.
Overall survival (OS) in the IMELDA randomized phase III trial of maintenance bevacizumab (BEV) with or without capecitabine (CAP) for HER2-negative metastatic breast cancer (mBC)

Prof. Rabab Gaafar

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BACKGROUND The open-label randomized phase III IMELDA trial demonstrated that adding CAP to maintenance BEV until disease progression (PD) after initial BEV–DOC provides statistically significant and clinically meaningful improvements in both progression-free survival (PFS [primary endpoint]; hazard ratio [HR]0.38 [95% CI 0.27–0.55]; p<0.001) and OS. We present OS in subgroups representing stratification factors and clinically important populations.

METHODS Patients (pts) with HER2-negative measurable mBC, ECOG PS <2, and no prior chemotherapy for mBC were eligible. After 3–6 cycles of BEV–DOC, pts without PD were randomized to BEV alone or BEV–CAP (BEV 15 mg/kg q3w; CAP 1000 mg/m² bid d1–14 q3w) until PD. Stratification factors were estrogen receptor (ER) status, visceral metastases, response status, and lactate dehydrogenase (LDH) concentration. OS from randomization was a secondary endpoint. The planned sample size of 360 enrolled pts (290 randomized) was calculated assuming a PFS HR of 0.70 (median PFS 5.8 → 8.3 months) with 80% power at 2-sided α=0.05 after 244 PFS events. Recruitment was stopped prematurely after regulatory withdrawal of the BEV–DOC combination but pts who had already been enrolled and randomized were followed as originally planned.

RESULTS Between Jun 2009 and Mar 2011, 284 pts were enrolled and treated. Of these, 99 withdrew from the study before randomization (most commonly due to PD [41%] or AEs/toxicity [31%]) and 185 (65%) were randomized. At the time of the primary PFS analysis, median follow-up (from randomization) was 20.0 months in the BEV arm and 26.9 months in the BEV–CAP arm. Median OS from randomization was 23.2 months in the BEV arm, but had not been reached in the BEV–CAP arm (events in 35% of pts). The HR for OS in the two randomized arms showed consistency between subgroups, favoring the BEV–CAP arm in all subgroups analyzed (Table).
<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of events/No. pts (%)</th>
<th>Unstratified HR (95% CI)</th>
<th>1-year OS rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BEV</td>
<td>BEV–CAP</td>
<td>BEV</td>
</tr>
<tr>
<td>All</td>
<td>53/94 (56)</td>
<td>32/91 (35)</td>
<td>0.42 (0.26–0.67)</td>
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<tr>
<td>&lt;65 years</td>
<td>46/81 (57)</td>
<td>26/77 (34)</td>
<td>0.50 (0.31–0.80)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>7/13 (43)</td>
<td>6/14 (43)</td>
<td>0.50 (0.16–1.60)</td>
</tr>
<tr>
<td>Triple negative</td>
<td>16/21 (76)</td>
<td>10/25 (40)</td>
<td>0.47 (0.21–1.07)</td>
</tr>
<tr>
<td>Hormone receptor positive</td>
<td>37/73 (51)</td>
<td>22/66 (33)</td>
<td>0.50 (0.29–0.84)</td>
</tr>
<tr>
<td>ER positive&lt;a&gt;b</td>
<td>36/69 (52)</td>
<td>22/64 (34)</td>
<td>0.50 (0.29–0.85)</td>
</tr>
<tr>
<td>ER negative&lt;a&gt;b</td>
<td>17/25 (68)</td>
<td>10/27 (37)</td>
<td>0.47 (0.21–1.06)</td>
</tr>
<tr>
<td>&lt;3 metastatic organ sites</td>
<td>17/40 (43)</td>
<td>16/48 (33)</td>
<td>0.71 (0.35–1.42)</td>
</tr>
<tr>
<td>≥3 metastatic organ sites</td>
<td>36/54 (67)</td>
<td>16/43 (37)</td>
<td>0.40 (0.22–0.73)</td>
</tr>
<tr>
<td>Visceral metastases&lt;a&gt;b</td>
<td>38/65 (59)</td>
<td>22/62 (35)</td>
<td>0.41 (0.24–0.70)</td>
</tr>
<tr>
<td>No visceral metastases&lt;a&gt;b</td>
<td>15/29 (52)</td>
<td>10/29 (34)</td>
<td>0.76 (0.34–1.70)</td>
</tr>
<tr>
<td>Complete or partial response&lt;a&gt;b</td>
<td>36/68 (53)</td>
<td>23/68 (34)</td>
<td>0.58 (0.35–0.99)</td>
</tr>
<tr>
<td>Stable disease&lt;a&gt;b</td>
<td>14/22 (64)</td>
<td>6/20 (30)</td>
<td>0.24 (0.08–0.66)</td>
</tr>
<tr>
<td>Non-measurable&lt;a&gt;b</td>
<td>3/4 (75)</td>
<td>3/3 (100)</td>
<td>0.30 (0.03–2.98)</td>
</tr>
<tr>
<td>LDH ≤1.5 x ULN&lt;a&gt;b</td>
<td>50/89 (56)</td>
<td>29/85 (34)</td>
<td>0.47 (0.30–0.75)</td>
</tr>
<tr>
<td>LDH &gt;1.5 x ULN&lt;a&gt;b</td>
<td>3/5 (60)</td>
<td>3/6 (50)</td>
<td>1.01 (0.20–5.00)</td>
</tr>
</tbody>
</table>
CONCLUSIONS. Combining maintenance BEV with CAP until PD after initial BEV–DOC provides a statistically significant and clinically meaningful improvement in OS, seen consistently irrespective of baseline characteristics.

Character count: 3349 [max 3400 characters (including title, body, table and spaces)]

Subject category [please select]:
- Advanced disease treatment
  - 605. Advanced chemotherapy
  - 607. Advanced therapy – targeted
- Therapeutic strategies
  - 616. Antiangiogenic therapy (adjuvant and metastatic)
  - 617. Antibody-based regimens
  - 621. New drugs and treatment strategies
IRREVOCIBLE ELECTROPORATION OF PERIHILAR HEPATOCELLULAR CARCINOMA: INITIAL EXPERIENCE

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Background: Local ablative therapies are being used increasingly to treat primary and metastatic hepatic tumors. The most common techniques include radiofrequency ablation (RFA) and microwave ablation (MWA). There is a high recurrence rate with these ablative techniques, ranging from 4% to 34% in hepatocellular carcinoma (HCC). Proximity to major portal veins has been associated with suboptimal ablation and high recurrence rates. Also, complications can be caused by thermal damage to major bile ducts or blood vessels. Irreversible electroporation (IRE) is a new ablative technique and has the advantages of non-thermal action, preventing damage to major portal veins and bile ducts. This initial experience study evaluated the safety and efficacy of IRE to ablate the perihilar HCC.

Patients and Methods: Ten patients having 10 perihilar HCC tumors were treated by IRE. The patients’ age ranged from 55 to 62 years (mean was 57 years). Patients were selected for IRE in the Multidisciplinary Team (MDT) when resection or other thermal ablation was not indicated due to tumor location. Five tumors were located in segment IV, 2 in segment V, 2 in segment VIII, and one in segment VII. The tumor size ranged from 3.5 cm to 5 cm (mean was 4.5 cm). All patients were treated percutaneously.

Results: Ten HCC tumors were treated by IRE. Nine patients (90%) show complete ablation. One patient (10%) shows residual disease. No major complications noted. One patient (10%) developed mild right lobe biliary radicle dilatation and one patient (10%) developed right portal vein thrombosis, which disappeared in the second follow-up. Follow-up ranged from 8 to 18 months (mean was 11 months). No tumor recurrence noted along this short-term follow-up.

Conclusion: IRE appears to be safe and effective ablation technique for treatment of perihilar HCC. However, larger studies with longer follow-up are required to confirm these results.
Modified percutaneous radiologic gastrostomy technique without endoscopic or nasogastric access

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National Cancer Institute - Cairo University, Egypt

Aims and Objectives: Gastrostomy is required to provide enteral nutrition to dysphagic patients with esophageal and neck cancers during combined chemotherapy and radiotherapy treatment due to an obstructed upper digestive tract [1]. Percutaneous endoscopic gastrostomy (PEG) and radiologic percutaneous gastrostomy (RPG) are two currently established methods to provide enteral feeding to this group of patients [2]. However, high grade narrowing or obstruction of the upper digestive tract precludes the passage of the endoscope for PEG and the nasogastric tube for the conventional fluoroscopic-guided RPG [3].

The aim of this study is to evaluate the effectiveness and safety of a modified percutaneous radiologic gastrostomy (MPRG) technique under ultrasound and fluoroscopic guidance without endoscopic or nasogastric access.

Methods and Materials: Twenty-four oncology patients were recruited in this study. Ten patients were males and 14 were females with the age ranged from 44 to 80 years old. Fourteen patients had oesophageal cancer and 10 patients had neck cancer. The neck cancers were; 1 cancer tongue, 2 post-cricoid cancer, 2 recurrent post-cricoid cancer, 3 cancer larynx, 3 thyroid cancer, and 3 recurrent thyroid cancer.

Twenty-five modified percutaneous radiologic gastrostomy (MPRG) techniques were attempted for all patients. Percutaneous endoscopic gastrostomy (PEG) and conventional percutaneous radiologic gastrostomy (PRG) were not feasible in 12 patients because of the complete upper digestive tract obstruction. The modified technique was attempted in 13 patients without the trial with the PEG of conventional PRG techniques.

Ultrasound-guided gastric puncture was done using the 21G needle of the gastrostomy set, then air insufflation was done using 50 mL syringes through a connecting tube. Through the needle, stiff guide wire was introduced to the gastric lumen then the needle was withdrawn. The peel-way sheath was advanced to the gastric lumen over the guide wire, which then removed with the trocar of the peel-way sheath. The gastrostomy tube was introduced through the peel-way sheath, which was removed. Finally, the gastrostomy tube is fixed to the skin.

Results: Technical success was achieved in 23 out of the 25 procedures (92%). Two procedures were failed (8%) and converted to the conventional technique by using the nasogastric tube. No major complications were reported. Minor complications were observed in 6 patients (24%): intraperitoneal air and contrast leakage in 4 patients; Focal mucosal dissection by the contrast in 1 patient; and dislodgment of the gastrostomy tube in 1 patient after month.

Conclusion: The modified percutaneous radiologic gastrostomy technique has high technical success rate, is safe with no major complications, and is most feasible when endoscopic or nasogastric access cannot be performed.
Is interim $^{18}$F-FDG-PET/CT has prognostic role during management of pediatric Hodgkin’s Lymphoma (pHL)? Qualitative and semi-quantitative analysis

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Introduction: Positron emission tomography using $^{18}$F-fluorodeoxyglucose (FDG-PET) is considered an excellent tool for staging and monitoring disease status in patients with lymphoma.

Aim of the study: To assess the prognostic role of interim $^{18}$F-Fluorodeoxyglucose ($^{18}$F-FDG)-PET/CT in pediatric patients with Hodgkin lymphoma (PHL)

Patients and Methods: prospective analysis of 195 patients presented in CCHE with pathologically proven pediatric HL, they underwent interim PET/CT after 2 cycles of ABVD with or without baseline study, analysis of interim PET was done visually according to the Deauville score (5-point score) with cut-off 3-4 between MRU and positive result as well as semi-quantitative analysis using maximum standardized uptake value (SUVmax), average SUV (SUVmean2.5 and SUVmean40%), metabolic tumor volume (MTV) measured after thresholding to a threshold SUV value of 2.5(MTV2.5) and at 40% of SUVmax (MTV40%) and total lesion glycolysis (TLGs) corresponding to MTVs (TLG2.5and TLG40%). The parameters were calculated as absolute values and as percentage of difference between the initial and the interim’s hottest residual lesion. Follow-up was done for period of 2.9 years (range, 0.9 to 5.2 years, Clinical outcomes were obtained from medical records.

Results: Univariate analysis showed that the risk group, visual analysis and qualitative analysis of interim PET were significant predictors for OS and PFS. Among the semi-quantitative parameters, SUVmean (2.5) has the highest hazard ratio. In multivariate analysis, using the significant prognostic factors found in univariate analysis as covariates we found that the three are important prognostic factor that can predict OS and PFS. However, SUVmean (2.5) when tested against the visual assessment of interim PET failed to show independent prognostic properties.

Conclusion: assessment of early interim PET/CT after 2 cycles of ABVD in PHL shows potential value in prediction of OS and PFS both qualitatively and quantitatively, however, the qualitative assessment shows better performance than the semi-quantitative analysis.

Key words: FDG-PET/CT, pediatric HL, Early response, prognosis, interim PET, MTV, TLG.
The Egyptian Clinical Trials' registry profile: analysis of three trial registries

(International Clinical Trials Registry Platform, Pan-African Clinical Trials Registry and clinicaltrials.gov)

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Abstract

Registering clinical trials (CTs) in public domains enhances transparency, increases trust in research, improves participation and safeguards against publication bias. This work was done to study the profile of clinical research in Egypt in three CT registries with different scopes; the WHO International CT Registry Platform (ICTRP), the continental Pan-African CT Registry (PACTR) and the US clinicaltrials.gov (CTGR). In March 2014, ICTRP, PACTR and CTGR were searched for clinical studies conducted in Egypt. It was found that the number of studies conducted in Egypt (percentage) was 686 (0.30%) in ICTRP, 56 (11.3%) in PACTR and 548 (0.34%) in CTGR. Most studies were performed in universities and sponsored by university/organization, industry or individual researchers. Inclusion of adults from both genders predominated. The median number of participants per study was 63-155. The conditions researched differed among the three registries Study purpose was mostly treatment followed by prevention. Endpoints were mostly Efficacy followed by safety. Observational: Interventional studies (i.e. clinical trials) represented 15.5%:84.5% in ICTRP, 0%:100% in PACTR and 16.4%: 83.6% in CTGR. Most interventions were drugs or procedures. Observational studies were mostly prospective and cohort studies. Most CTs were phase 3 and tested drugs or procedures. Parallel group assignment and random allocation predominated. Blinding was implemented in many of trials and was mostly double-blind. We conclude that CTs from Egypt in trial registries is apparently low and does not accurately reflect clinical research conducted in Egypt or its potential. Development of an Egyptian CT registry is eagerly needed. Registering all Egyptian CTs in public domains is highly recommended.

Key words: Clinical trial registry; design; interventional studies; observational studies; Egypt
Solitary loco-regional abdominal lymph-adenopathy is a challenging surgical situation. It is easier to have a lymph nodes biopsy to confirm pathology & the cause of generalized lymphadenopathy. We had developed our techniques for approaching abdominal exploration, taking lymph nodes as well as tissue biopsies by laparoscopy. We will present our experience by videos & show our results. Discussion of the benefit and draw backs of this technique will be also presented.
Prognostic Effect of Drug Resistance of Glutathione-S-Transferase in Non Small Lung Cancer

Dr. Hala Aziz

Abstract:

Background And Objective: It has been known that the expression levels GST were correlated with tumorigenesis and prognosis. The aim of this study is to investigate the relationship between expression levels of GST in tissue & serum level, and clinicopathologic parameters, survival & response to platinum containing regimen used in treatment of patients with lung cancer.

METHODS: The expression levels of GST were detected by immunohistochemical staining on tissue micro-array sections made of 64 cases of lung cancer and serum samples were collected from 68 cases pre-treatment, post 2nd Cycle & post 4th as such. 10 control cases serum samples were also examined. The results were compared with relevant clinical and pathologic data.

RESULTS: There were 50 males (73.6%) and 18 females (26.4%), their ages ranged from 30 to 69 years with a median of 55 years. The pathology included 24 patients had squamous cell carcinoma and 44 non squamous cell carcinomas. PS was I in 36 (52.9%) cases while PS was II in the remaining 32 cases (47.1%). Sixty cases were presented with either stage IIIB or IV. Serum samples pre-treatment could express tissue expression of GST (P<0.001). We also found that GST in serum rose markedly in progressive disease compared to minor rise in stable disease in post 2nd & 4th cycle samples compared to pre-treatment level, while it decreased in disease responding cases (PR) p<0.001 and 0.015 consecutively. A strong correlation between early & late stages disease and both OS (p=0.03) & PFS (p=0.003) was found. There were no significant correlations between tissue expression of GST and either overall survival (P = 0.66) nor progression free survival. (P =0.34), same as serum GST pre-treatment level (p=0.68 & 0.106). Multivariate analysis using Cox regression model showed that expression levels of GST & serum level pretreatment were not the important independent prognostic factors for survival.

Conclusion: Serum GST pretreatment level in non small cell lung cancer could predict tissue expression of GST. Changes in this level, whether rising or declining, could predict response to platinum containing regimen.
Primary Ovarian Non-Hodgkin’s Lymphoma: A Clinico-pathologic Study of Eight Cases

hala A. Shokralla, Ahmed E. Fathalla; National Cancer Institute, Garden City Cairo/Egypt

Abstract

Introduction
Primary non-Hodgkin’s lymphoma (PONHL) of the ovary is rare.

Objectives
To analyze, to report & to better understand the clinico-pathologic features and results of treatment and prognostic factors of these tumors.

Material & methods
Eight cases of primary ovarian non Hodgkin lymphoma (PONHL) treated in National Cancer Institute-Cairo University from January 2010 till December 2015. All available medical data of the patients were analyzed.

Results
The patients ranged in age from 14 to 55 years (mean 28 years). Pelvic pain was the most common symptom (62.5%); however, three of eight neoplasms were presented with either menstrual abnormalities or abdominal distension. Five cases were bilateral and Ann Arbor stage IV-E. The remaining three cases were right-sided & stage I-E. Size of tumors ranged from 5 to 24 cm (mean 13.1). Tumors were classified according to the World Health Organization as follows: diffuse large B-cell lymphoma (four cases), Burkitt’s lymphoma (three cases) and B-lymphoblastic lymphoma/leukemia (one case). All tumors were of B-cell lineage. All cases were CD20 positive. All Burkitt’s lymphoma cases showed higher Ki67 index (2 cases were 100% and the last one was 88%). B-lymphoblastic lymphoma/leukemia case was positive for TDT & CD 10. LDH was elevated in all cases (mean 644U/L).

Patients were treated by various combinations of surgery and chemotherapy.
Follow-up period ranged from 3 months to 5 years (mean 31 months). Five patients were alive without disease at last follow-up while apart of one. We had three died cases, one of them died during treatment.

Conclusion
We conclude that most patients with primary ovarian NHL present with symptoms attributable to an ovarian mass. More studies will be needed to better define & treat this rare entity. Routine addition of rituximab to CHOP regimen for CD-20 positive disease should be advocated.

Key words: Ovary-NHL-Reporting-NCI-Egypt
Forty eight hours hospital stay after fast track laparoscopic colorectal surgery, RCT

Mostafa A. MD, DeBakey Y. Bsc

Abstract

Introduction: To date, laparoscopic colorectal surgery is still fighting to become the standard treatment for elective colorectal resection. In recent years, there has been a renewed interest in evaluating fast track laparoscopic colorectal surgery intending to shorten hospital stay with low morbidity and low readmission rates.

Aim of work: The aim of this work is to examine the safety and feasibility of a two-day hospital stay after laparoscopic colorectal surgery in a referral center.

Patients and methods: This randomized controlled trial (RCT) including 22 patients who underwent laparoscopic colorectal surgical intervention from June 2014 to May 2015. Patients were classified into two groups; group A: fast track laparoscopic colorectal surgery and group B: conventional laparoscopic colorectal surgery. Baseline demographics, body mass index (BMI), previous abdominal surgeries, preoperative diagnosis, operation performed, postoperative outcomes, and readmission and reoperation rates were analyzed.

Results: Group A represented 59% of this series (13 patients). There were no differences regarding age, gender, BMI, ASA, previous abdominal surgeries and reoperation rate between the two groups. Group A had a lower overall morbidity rate than group B (7.7 vs. 22.2%; p = 0.004) and the overall conversion rate was 13.6% (only one patient in group A required conversion), Group A had a higher readmission rate (7.7% vs. 0%; p = 0.067).

Conclusion: A two-day hospital stay after LCR is safe and feasible under an ERAS pathway, without compromising the readmission or complication rate. Patients fulfilling standardized criteria can be safely discharged after 48 hours with a low readmission and complication rate.
Prognostic value of neutrophil lymphocyte ratio in second line advanced malignant pleural mesothelioma

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Background:

Malignant pleural mesothelioma is a lethal disease and hence the strong need for identifying new prognostic factors.

Methods:

This is a retrospective study including all eligible patients with advanced malignant pleural mesothelioma (MPM) presenting to National Cancer Institute, Cairo University. Neutrophil lymphocyte (N/L) ratio was assessed before second line chemotherapy. 2.5 was used as the cutoff point. Endpoints were assessment of correlation between N/L ratio and clinical response (CR), progression free survival (PFS) and overall survival (OS).

Results:

52 patients (19 stage III and 33 stage IV) MPM were included and followed up during the period from July 2009 till November 2012 with a median follow up period of 2.6 months. 87.5% of patients with N/L ratio > 2.5 showed progressive disease versus 91.7% in patients with N/L ratio < 2.5. (P-value = 0.66). 6 months PFS was 11% for patients with N/L ratio > 2.5 versus 14% for patients with N/L ratio < 2.5. (P-value = 0.001). 6 months OS was 72% for patients with N/L ratio > 2.5 versus 66% for patients with N/L ratio < 2.5. (P-value = 0.4).

Conclusion:

N/L ratio is a potential prognostic marker for advanced MPM treated with second line chemotherapy.
Granulosa Cell Tumors of the Ovary, Retrospective Analysis Of 17 Cases

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Abstract

**Background:** Granulosa cell tumors (GCTs) are rare neoplasms with a relatively favorable prognosis. They are characterized by a prolonged history and a tendency to late recurrences. It is the most common type of sex cord-stromal tumors.

**Aims:** To analyze, to report & to better understand the clinico-pathologic features and results of treatment, and prognostic factors of these tumors.

**Materials and methods:** 17 cases of GCTs treated in National Cancer Institute-Cairo University from January 2010 till December 2014. All available medical data of the patients were analyzed.

**Results:** data from 17 patients were obtained. The median age was 54 years (range; 14-72). Abdominal pain was the most common presentation (64.7%). The mean tumor size was 14cm (range; 7-23 cm). The majority of our patients were stage I (n=11; 64.7%), while (n=3; 17.6%) had stage III and (n=2, 11.8%) were stage IV. Only one case (5.9%) had an unknown stage (explored outside NCI). The majority of cases were of adult type disease (n=14) & low grade pathology (n=10). In follow-up period (median = 42 months; ranging 9-60) three patients relapsed; the median overall survival time was not reached yet, however, the estimated 3-year survival was 72.5%.

**Conclusion:** Granulosa cell tumors are rare neoplasms of the ovaries. They progress slowly and often are diagnosed in an early stage. Surgery is the main line of treatment. Prolonged post-therapeutic follow-up is necessary. Definition of proper prognostic factors is mandatory.

**Keywords:** Granulosa cell tumors; Ovary; Outcomes.
Clinicopathologic features and pattern of care of renal cell carcinoma: A retrospective study from Egypt.

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Background: Worldwide, renal cell carcinoma (RCC) accounts for 2%-3% of all adult malignancies, In Egypt renal cancers represent 1%-1.7% of all cancer types. Limited data are available on renal cell carcinoma in Egypt, hence this study was undertaken to analyze the patterns of renal cell carcinoma at four oncology centers in Egypt.

Methods: The study included of 65 consecutive patients with pathologically proven renal cell carcinoma presented to Medical Oncology Department, Clinical Oncology Department, Zagazig University, El-Mabara Hospital, Zagazig and Damietta Cancer Institute, Damietta from January 2012 to December 2014. Patients’ files were evaluated for clinic-pathologic features and treatment approaches by surgeons and oncologists.

Results: Out of 65 patients, 63.1 % were males and 36.9% were females. The age ranged between 21 to 83 years (mean ± SD: 54.9 ± 11.7: median = 58 years). The tumor size ranged from 4 to 21 cm (mean ± SD: 7.5 ± 3.4: median 7 cm). One case had bilateral RCC (1.5%), 53.8% (35/65 patients) had right RCC while, 44.6% (29/65 patients) had left RCC. Histopathologically, 55.4% of the patients had organ confined RCC (T1-2 N0 M0), 4.6% of the patients had regional lymph node involvement, 40% of the patients presented as metastatic RCC. After nephrectomy 14 patients had distant metastasis (21.5% of total)

The most common pathological type was clear cell in 55.4% followed by papillary renal cell carcinoma in 13.8 %, chromophobe renal cell carcinoma in 10.8 %, and renal cell carcinoma, unclassified in 9.2 %. Fuhrman’s nuclear grade 2 was found in 61.5%. All patients had undergone radical nephrectomy except for 16 patients were not operated for metastatic RCC, out of which one patient had, bilateral RCC and the other 15 patients were surgically unfit.

Among the 40 metastatic RCC patients, due to tolerability or financial causes only 22 patients received sunitinib as first line therapy, 3 patients received palliative chemotherapy which was stopped after 1 cycle due to poor tolerance, 8 patients received palliative radiotherapy and the other 7 patients were under best supportive care.

Regarding sunitinib response, CR was achieved in 13.6% (3/22), PR in 18.2% (4/22), SD in 31.8% % (7/22), and PD in 13.6% % (3/22) of patients. Five patients (22.7%) were non-evaluable due to loss of follow up.
Conclusion
In Egypt, RCC is more common in males. The most common pathological type was clear cell RCC, grade 2 and right side RCC were more predominant. Radical nephrectomy was not done to all our patients; and targeted therapy was not available for all eligible patients.

KEY WORDS
Renal cell carcinoma, clinicopathologic features, pattern of care, Egypt.
Plasma Vascular endothelial growth factor 165(VEGF 165) in advanced Non-small cell lung cancer

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Background:

Lung cancer is the leading cause of death among malignant tumors worldwide therefore it is important to develop novel diagnostic techniques.

Methods:

This is a prospective case control study including two groups of patients: Group I: healthy volunteers as control. Group II: Patients with advanced non-small cell lung cancer (NSCLC). Plasma VEGF 165 levels were measured at baseline by ELISA before first line Gemcitabine-Cisplatin regimen. High VEGF 165 cutoff taken was >703 pg/ml. Primary end point was comparison of plasma VEGF 165 levels in cases and controls. Secondary endpoint was correlation between High VEGF 165 and clinical response (CR), Progression free survival (PFS) and overall survival (OS) in advanced NSCLC patients.

Results:

35 patients with advanced NSCLC and 34 age and sex matched normal subjects as control were included and followed up during the period from 10/2009 to 10/2012 with median follow up of 10.5 months. Median plasma VEGF 165 level was 707 pg./ml in cases versus 48 pg./ml in controls, (p < 0.001). No significant correlation was found between plasma VEGF 165 level and clinical response(p < 0.5). No significant correlation was found between plasma VEGF 165 level and Median PFS and OS (p=1 and 0.7 respectively.

Conclusion:

Plasma VEGF 165 is a potential diagnostic marker in advanced NSCLS.
Small biopsies and heterogeneity give erroneous molecular leads in small cell lung cancer – a molecular study.


Abstract:

Background and Aim:

Molecular biomarkers have been investigated in non-small cell lung cancer (NSCLC) and targeted treatments in advanced disease are established. However, there are no established targeted therapies at the moment for small cell lung cancer (SCLC). The aim of this study was to examine for the presence of known molecular targets in patients with SCLC and their prognostic effect.

Patients and Methods:

A panel of histopathologically proven FFPE specimens of SCLC were analysed for EGFR, KRAS, NRAS, BRAF mutations, ALK gene rearrangements and MET amplification. EGFR and KRAS testing were done using real time-polymerase chain reaction (RT-PCR cobas®), BRAF and NRAS using Multiplex PCR and capillary electrophoresis-single strand conformation analysis (CE-SSCA) and ALK and MET using fluorescent in situ hybridization (FISH). Any positive results were repeated for confirmation. Any inconsistent results were sequenced using the direct Sanger sequencing.

Results:

Sixty samples were suitable for molecular testing, with 25 successfully examined for all 6 markers. No mutations in EGFR were detected in the 31 cases suitable for analysis. KRAS and NRAS mutational analysis was successful in 35 and 37 cases respectively; all of which were wild type. Fifty eight cases were assessed for ALK gene rearrangements and 42 cases for MET gene amplifications; no rearrangements or amplifications were detected. Forty seven samples were successfully analysed for BRAF mutations, with one V600E mutation (2.1% of cases). This patient was a 55 years old Caucasian male smoker diagnosed with lung cancer, treated with lobectomy and his post-lobectomy pathology revealed SCLC with squamoid and glandular features (positive BRAF mutation and negative for the rest of the markers).
Conclusion

EGFR, KRAS, NRAS, ALK and MET were not detected in the examined panel of SCLC patients. One BRAF mutation was identified in a patient with a diagnosis of combined SCLC; the mutation was probably in the squamoid component. We think that this panel of biomarkers should no longer be explored in SCLC. Small heterogeneous samples of often poor quality in SCLC give erroneous leads in the biology of SCLC.

**Key Words:** Small cell lung cancer, molecular biomarkers, EGFR, KRAS, BRAF, NRAS, ALK, MET, heterogeneity, DNA sequencing, real time PCR, FISH, single strand conformation analysis.
SOX2 IN INFLAMMATORY BREAST CANCER: DID WE EVENTUALLY HAVE AN ANSWER?

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Background: inflammatory breast cancer (IBC) is the most aggressive type of breast cancer and continuous research to identify its nature is of utmost importance.

Patients and methods: This is a retrospective case control study including all eligible cases of advanced IBC compared to a control group of stage comparable locally advanced breast cancer (LABC) cases presenting to the National Cancer Institute (NCI), Cairo University in the period between November 2007 and February 2011. SOX2, as a stem cell marker, was assessed in both arms by quantitative RT-PCR. All patients received standard FEC10. Assessment of clinical response (CR) was done after 4 cycles. Primary endpoints were 1-assessment of SOX2 expression in IBC and LABC. 2-Assessment of correlation between SOX2 expression and CR in both arms. Secondary endpoints were assessment of correlation between SOX2 expression and PFS & OS in both arms.

Results: 30 cases of IBC and 19 cases of LABC were included with a median follow up period of 31.3 months. SOX2 was highly expressed in IBC compared to LABC (p-values: 0.03). SOX2 expression was significantly correlated with clinical response in IBC where 100% of the SOX2 -ve cases had good overall clinical response (Complete and partial remission) compared to 64.7% of the SOX2 +ve cases (P-value: 0.042). SOX2 expression was significantly correlated with PFS in IBC where 1 and 2 year PFS were 72.7% and 45.5% in SOX2 negative versus 36.8% and 5.3% in SOX2 positive (p-value = 0.045). SOX2 expression showed a trend towards significant correlation with OS in IBC where 1 and 2 year OS were 100% and 90.4% in SOX2 negative versus 95.2% and 73.7% in SOX2 positive (p-value = 0.087).

Conclusion: SOX2 expression, as a Stem cell marker, is significantly expressed in IBC and is well correlated with clinical outcome.

Key words: SOX2 – stem cell phenotype– Inflammatory breast cancer
Phase 3 trial (NGR015) with NGR-hTNF plus best investigator choice (BIC) versus placebo plus BIC in previously treated patients with advanced malignant pleural mesothelioma (MPM)

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Background: Currently, there are no standard options for MPM patients who failed a pemetrexed-based chemotherapy (CT). NGR-hTNF, a tumor-targeted antivascular agent, displays antitumor activity through a vessel normalization that improves intratumor CT uptake and T-cell infiltration

Methods: MPM patients who progressed on or after a front-line pemetrexed-based regimen, stratified for performance status (PS) and CT agent, were randomly assigned to receive weekly NGR-hTNF 0.8 μg/m\textsuperscript{2} (arm A; n=200) or placebo (arm B; n=200), both given with BIC (gemcitabine [G], vinorelbine [V], doxorubicin [D] or supportive care). Primary endpoint was overall survival (OS). Hypothesis testing: hazard ratio (HR)=0.72, 1-β=0.80, α=0.05

Results: Baseline characteristics were balanced between arms (A vs B): median age (65 vs 67 years); men (76% vs 74%); PS ≥1 (72% vs 69%); non epithelial histology (15% vs 19%); poor EORTC score (30% vs 23%); prior treatment-free interval (TFI)< median of 4.8 months (47% vs 53%). Investigator-selected CT (n=381, 95%): G 55%, V42%, D3%. Patients completing six CT cycles: 41% vs 32% (p=0.08). Most common grade 3/4 toxicity: neutropenia (17% vs 19%) and fatigue (5% vs 8%). After a median follow-up of 18.9 months, OS did not differ significantly between arms in ITT analysis (median 8.4 vs 7.9 months; HR=0.94 p=0.61). By predefined OS analyses, there was a significant interaction only between treatment group and TFI (p=0.008). In 198 patients with TFI shorter than 4.8 months after first-line therapy, median OS for NGR-hTNF vs placebo was 9.0 vs 6.3 months and 1-year OS was 39% vs 23%, respectively (HR=0.69 p=0.02; stratified HR=0.65 p=0.01). By CT agent, median OS for NGR-hTNF plus G vs placebo plus G was 9.0 vs 6.2 months and for NGR-hTNF plus V vs placebo plus V was 9.7 vs 6.9 months. A significant treatment-by-TFI interaction was also observed for PFS (p=0.009), with 6-month rates in the short TFI subset of 25% for NGR-hTNF and 12% for placebo (HR=0.71 p=0.03).

Conclusion: Though the primary endpoint was not met, OS and PFS benefit reported with NGR-hTNF plus CT in patients with short TFI deserves a confirmatory first-line phase 3 trial.

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Prognostic impact of 25-Hydroxyvitamin D Levels in Egyptian patients with breast cancer

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Abstract

Background: According to the literature, vitamin D (Vit D) deficiency is a risk factor for developing breast cancer with lack of information on its direct prognostic effects in breast cancer.

Patients and Methods: A total of 168 women with proven breast cancer diagnosed in Zagazig University Hospitals-Egypt were enrolled in the study. Serum level of 25(OH) Vit D was measured in stored blood. Hydroxy vit D level classified into three groups: deficient :< 10ng/dl; insufficient: 10-30 ng/dl; and sufficient :> 30ng/dl. Clinical and pathological data were accessed to examine prognostic effects of vitamin D.

Results: median age was 51.5 (26- 77) years, Metastasis was present in 13.1% of the cases. Stage of tumor was I, II, III and IV in 15.5%, 34.5%, 36.9% and 13.1% of patients, respectively. The tumor grade was low in 11.9% of cases, intermediate in 63.3% of cases, and high in 26.8% of cases. The Ki-67, HER2, ER and PR were positive in 35.7%, 32.7%, 69%, and 64.3% of the patients, respectively. The median serum level of 25(OH) Vit D was 20 (5-98) ng/ml; it was deficient in 39.3% of patients, insufficient in 32.1% of patients, and sufficient in 31% of patients. serum level of 25(OH)D levels decreased significantly with increasing body mass index( BMI) (P=0.00), also the relation of 25 (OH) Vit D level with the number of positive lymph nodes, tumor size, tumor stage and KI 67 level was statistically significant (p= 0.01, p=0.011, p=0.002, p= 0.001 respectively). The level of 25 (OH) vitamin D was significantly lower in metastatic patients compared to non metastatic patients (p=0.01).

Conclusion: There may be an association between deficiency in the serum level of 25(OH) Vit D and prognosis of breast cancer.

Keywords: Breast cancer - vitamin D - prognosis - Egypt
Rituximab-Induced Hepatitis C Virus Reactivation in HCV-positive patients with diffuse large B-cell lymphoma

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Background: The clinical outcome and hepatic toxicity occurrence of diffuse large B-cell lymphoma (DLBCL) patients with hepatitis C virus (HCV) infection in the rituximab era remains controversial.

Methods: To elucidate the characteristics of DLBCL patients in relation to HCV infection status, we retrospectively analyzed DLBCL patients diagnosed and treated with chemo- or immunochemotherapy at our institutes and at a private hospital during the last decade. Of the 132 patients, 64(48.5%) and 68 (51.5%) patients received RCHOP and CHOP, respectively.

Results: In all, HCV infection was identified in 35(26.5%) of 132 DLBCL patients. Except for being more likely to present with B symptoms and splenic involvement, patients with HCV infection were demographically indistinguishable from HCV-negative patients.

Multivariate analysis of the whole group showed 3 factors found to independently predict an inferior OS including extra-nodal involvement (≤1 vs. >1; HR=4.5, 95% CI = 1.6-12.6, p=0.012), splenic involvement (presence vs. absence; HR=0.5, 95% CI = 0.33-0.82, p=0.0008), and performance status (0-1 vs. >1; HR=2.9, 95% CI = 1.6-12.6, p=0.04). Adverse effects on DFS was significant only with splenic involvement (presence vs. absence; HR=0.6, 95% CI = 0.45-0.9, p=0.04).

Among the HCV-infected patients, the incidence of hepatitis flares was 40%; (14/35) patients vs. 9.3% (9/97) patients among the HCV-uninfected individuals (P=<0.001).

Of the 35 HCV-positive patients, 14 (40%) received R-CHOP and 21 (60%) received CHOP. HCV reactivation occurred in 34.2% (11/35 patients) without any relation to treatment regimen (7 (11%) for RCHOP and 5(7.3%) for CHOP; p=0.3). No hepatic toxicity related deaths had been reported.

In conclusion, our study results demonstrated that HCV infection did not influence the clinical outcome of DLBCL patients, and its reactivation has no relation to the type of treatment.

Keywords: DLBCL, Hepatitis C virus, Immunochemotherapy, Reactivation
"Role of Colonoscopy in Diagnosis and Treatment of early malignant colo-rectal tumors"

Tamer Saber

ABSTRACT

Colonoscopic screening in developed countries allows detection and resection of a great number of early colorectal cancers. There is a strong controversy to decide when endoscopic treatment is enough or when surgical resection is necessary. To this contributes the diverse names to define the lesions, the wide number of classifications and the different criteria of each author. We perform an extensive literature review, aiming to clarify concepts and unify criteria that can be used as a guide for the treatment of early colorectal cancer. We conclude that in early colorectal cancer arising in pedunculated polyps (0-Ip), mucosal endoscopic resection would be indicated as only treatment in Haggitt levels 1, 2 and 3, tumors smaller than 2 cm, well- or moderately differentiated, without vascular or lymphatic affection, with submucosal infiltration lower than 1 μm from the muscularis mucosae and maximal submucosal width lower than 4 μm, and undergoing en bloc resection. In sessile polyps (0-Iṣ) or non-polypoidal elevated (0-IIa) or plain (0-IIb) lesions, recommendations will be similar, without applicability of Haggitt levels.

INTRODUCTION

Adenomas of the gastrointestinal tract may present malignant transformation following the histopathological sequence adenoma-carcinoma. Most colonic adenomas are considered as precursors of colorectal carcinomas. It is described in literature that between 2-10% of adenomas will develop an invasive carcinoma that can achieve up to 85% when considering villous adenomas.

Screening with test for fecal occult blood and, specially, with colonoscopy, recently introduced in Western countries, has permitted the detection and resection of a great number of elevated adenomatous polyps in early stages of malignant transformation, avoiding their progression to invasive carcinoma.

Historically, most colorectal adenomas were considered polypoid structures, allowing an easy endoscopic resection. Notwithstanding, the number of flat or depressed colorectal lesions has increased in the last decades, representing up to 38% of colonic adenomas.

Those polyps with a size bigger than 3 cm, affecting more than one third of circumference or two colonic haustras, or with flat or depressed morphology are more difficult to be resected with the conventional endoscopic polypectomy, thus with the new endoscopic approaches, such
as endoscopic mucosal resection, the number of resected polyps has increased, avoiding the surgical act in many cases.

There is still a strong controversy around the indications of endoscopic or surgical resection, but with the advance of endoscopic techniques, the indications of endoscopic resection are growing and in fewer cases surgical treatment is necessary.

**Conclusions**

New methods of endoscopic diagnosis and treatment have been recently developed.

Patients with early-stage colorectal carcinoma can be diagnosed by colonoscopy. Endoscopic treatment facilitates healing, and the method is less invasive, more cost-effective, and less time-consuming for patients.

Endoscopic apparatuses, devices, and techniques must be further improved in the near future. Endoscopy for colorectal carcinoma will remain important in medical education and practice.
Endoscopic mucosal resection for high-grade dysplasia and intramucosal carcinoma in Barrett’s esophagus

Tamer Saber

Abstract

AIM: To evaluate endoscopic mucosal resection (EMR) in patients with high-grade dysplasia (HGD) and/or intramucosal cancer (IMC) in Barrett’s esophagus (BE).

METHODS: Between June 2010 and December 2013, 20 consecutive patients with HGD (18) and/or IMC (2) underwent EMR. BE >30 mm was present in 13 patients. In three patients with short segment BE, HGD was detected in a normal appearing BE. Lesions had a mean diameter of 14.8±10.3 mm. Mucosal resection was carried out using the cap method.

RESULTS: The average size of resections was 19.7± 9.4×14.6±8.2 mm. Histopathologic assessment post resection revealed 3 low-grade dysplasia (LGD) (15%), 14 HGD (70%), 2 IMC (10%), and 1 SMC 5%). EMR changed the pre-treatment diagnosis in 5 patients (25%). One patient with SMC underwent surgery. Histology of the surgical specimen revealed T1N0 lesion. A metachronous lesion was detected after 25 mo in one patient with HGD. Intra-procedural bleeding, controlled at endoscopy, occurred in four patients (20%). After a median follow up of 34.9 mo, all patients remained in remission.

CONCLUSION: In the medium term, EMR is effective and safe to treat HGD and/or IMC within BE and is a valuable staging method. It could become an alternative to surgery.
Validation of an IGF-CTP scoring system for assessing hepatic reserve in Egyptian hepatocellular carcinoma Patients

Reham Abdel Wahab

Background: The Child-Turcotte-Pugh score (CTP) is the standard tool for assessment of hepatic reserve in hepatocellular carcinoma (HCC), although it has several limitations. Recently, we reported that integrating plasma insulin-like growth factor-1 (IGF-1) level into the CTP score, creating the IGF-CTP (Kaseb-Morris) score, was associated with better patient risk stratification as compared to CTP score in two independent cohorts (training and validation) from the U.S. Our current study aimed to internationally validate the IGF-CTP score in patients who have different demographics, geographical location, and HCC risk factors.

Methods: We prospectively recruited 100 Egyptian patients and their blood samples for IGF-1 analysis. We calculated their IGF-CTP scores and compared them to CTP score. The log-rank test was used to detect statistical significance. Harrell's C-index was used to compare the prognostic significance of the two scoring systems. Finally, we compared our results with the previous published data from the U.S. cohorts.

Results: IGF-CTP score showed statistically significant better patient stratification as compared to CTP score in the international validation cohort, similar to our previous cohorts (P = 0.003). Among CTP class A patients, the group that is usually considered for active treatment and clinical trial enrollment, 32.5% were reclassified as IGF-CTP class B; they had a statistically significantly shorter OS than did patients classified as class A using both scoring systems with hazard ratio [HR] = 6.15, 95% confidence interval [CI] = 2.18 to 17.37, and P = .001.

Conclusions: The IGF-CTP scoring system showed significantly better patient stratification and survival prediction not only in the U.S. population originally tested but also in this first international validation population, who had different demographics, geographical location, and HCC risk factors.

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Background: Assessment of multiple prognostic and/or predictive biomarkers in breast cancer patients with good reliability and reproducibility utilizing material obtained by fine needle aspiration (FNA) can be of significant clinical value.

Objective: To assess the reliability of Ki-67, p53 and HER-2/neu expression by immunohistochemistry (IHC) on cell blocks (CB) prepared from agarose-embedded FNAs of primary breast cancer patients.

Material and methods: FNAs samples were obtained from fifty female patients presenting with primary breast carcinoma. To prepare cell blocks (cytoblocks), cells were fixed in 10% neutral formalin for 6-12 h, embedded in 2% agarose gel, processed using standard laboratory protocol for biopsy tissue and paraffin embedded. The expression of Ki-67, p53 and HER-2/neu was evaluated by IHC on cytoblocks and their corresponding formalin-fixed, paraffin-embedded (FFPE) histological resection specimens.

Results: H&E sections from FNA cytoblocks revealed stromal invasion by malignant cells in 46% (23/50) of BC cases. High Ki67 expression (≥ 20%) was observed in 62% (31/50) of breast carcinomas analyzed with the use of FNA cytoblocks and in 72% (36/50) on corresponding tissue specimens. Forty-six percent of breast carcinomas were positive for p53 immunoreactivity (≥ 10%) on FNA cytoblocks compared to 52% in tissue sections. The concordance rate between cytoblocks and tissue sections was 86% and 94% for Ki-67 and p53 expression, respectively. HER-2/neu gene overexpression was detected in 18% (9/50) of breast carcinoma FNA cytoblocks and showed a concordance rate of 75% with HER-2/neu protein expression on tissue sections.

Conclusion: In invasive breast carcinoma, the expression of Ki67 and p53 proteins could be determined with good reliability and on agar cell blocks prepared from FNA using standard IHC however HER-2/neu expression assessment was moderately reliable.
Key words: Agar cell block, breast cancer, HER-2/neu, CISH

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Efficacy and safety of Cladribine: Subcutaneous versus Intravenous administration in Hairy Cell Leukemia

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Abstract

Background:

Hairy cell leukemia (HCL) is rare B-cell lymphoproliferative disorder. Its treatment has evolved from splenectomy with time to failure (TTF) of 19 months to Cladribine that increased complete remission (CR) rate to 90%, with only small percentage of patients relapsing at 30 months. Cladribine (CDA) is originally administered intravenously as continuous infusion for 7 days; subsequently, it was administered subcutaneously. This study aims at comparing efficacy and toxicity of Subcutaneous (SC) versus Intravenous (IV) administration of CDA in treatment of HCL.

Patients and methods:

This retrospective study included HCL patients presented to National Cancer Institute and Nasser Institute, Cairo, Egypt, during period 2004-2010. Included patients received CDA as 1st or 2nd line with minimum follow up of 12 months. All files were reviewed for baseline clinical & laboratory parameters, route of administration, response, adverse events and survival.

Results:

This study included 49 eligible patients, 41 patients received CDA as 1st line treatment, while 8 patients as 2nd line. Eighteen patients were treated by continuous IV infusion whereas 31 patients by SC injections. Both groups were comparable regarding baseline clinical and laboratory parameters with no statistically significant difference. At median follow up period of 33.5 months, complete remission rate was 94% in IV group versus 97% in SC group (p=0.691); median TTF for IV group was 52.9 months while that for SC group was not reached (p=0.035). The median time to achieve CR in both arms was similar. By analyzing different factors affecting TTF using multivariate analysis, route of administration proved to be the only statistically significant factor (P=0.006). Regarding adverse events, there was no difference between both groups in hematological toxicities. IV route was associated with a significant higher incidence of mucositis (p=0.02) and viral infections (p=0.01). Hepatotoxicity and neurotoxicity were higher in SC group but difference was not statistically significant.
Conclusion:

SC administration of cladribine is an alternative route to IV in treatment of HCL with similar response rate, longer time to treatment failure and better tolerability.

Key words: hairy cell leukemia, cladribine, subcutaneous, intravenous.
Role of epigenetic changes in Chronic Myeloid leukaemia

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Background: Epigenetics are heritable changes in gene expression that are not a consequence of changes in DNA sequence and very commonly altered in cancer and pharmacologically reversible. The Hox family of homeodomain transcription factors plays an important role in regulating definitive hematopoiesis. In this study we will reveal the relation between epigenetics (DNA methylation, Histone modification) and Chronic Myeloid leukemias.

Materials and Methods:
Genomic DNA was extracted from peripheral blood samples of 55 CML patients (25 good responders and 30 resistant) and 15 normal controls.

The patients selected were Philadelphia chromosome positive CML patients in chronic, accelerated, or blast phase.

HOXA5, HOXA4 and TWIST2 expression were studied in sequential samples of patients with CML using RT-PCR. All samples were bisulfite treated and analysed by methylation-specific high-resolution melt analysis.

Results: HOXA5 (34%) and HOXA4 (59%) hypermethylation common in chronic phase, correlates with progression to blast crisis (p=0.00004 (HOXA5), p=0.005 (HOXA4)), correlates with other factors known to be associated with increased risk of progression (p=0.002), correlates with poor response to imatinib (p=0.0014) HOXA4 re-expression induces apoptosis. TWIST2 inhibits proliferation and increases sensitivity to cytotoxic agents.
**Conclusions:** Epigenetic changes (DNA methylation) are highly prevalent in leukaemias especially myeloid leukemias, it allows identification of functionally relevant genes (HOXA4, A5 and TWIST2). They are potentially prognostic markers and also they allow identification of new therapeutic approaches.

**Keywords:** CML: Chronic Myeloid Leukemia
High expression of the ALK gene is associated with unfavorable prognosis in human neuroblastomas

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Statement Of Translation Research

Neuroblastoma in advanced stages is one of the most difficult paediatric cancers, even with recent advances in therapy. Neuroblastoma harbours many genetic changes. Patients were diagnosed clinically as well as pathologically and tested for DNA ploidy, MYCN amplification and TrkA expression. The patients were treated by the Pediatric Oncology Group for Treatment of Advanced Neuroblastoma protocols. The clinical follow-up ranged from 3 to 93 months, with a median of 42 months. RNA extraction and semi-quantitative RT-PCR Total mRNA was prepared from Fresh-frozen tissues of primary neuroblastomas. The purpose of our study was to examine ALK expression level in human NBL tissue samples and tumor cell lines to evaluate its role in disease progression and prognosis.

Findings suggested that high expression of ALK is associated with poor prognosis indicating that such cases need further aggressive management and suggesting that ALK might have function in cell growth and differentiation in neuroblastoma.

Abstract

Background: The mutated Anaplastic lymphoma kinase (ALK) gene has been identified as a potential oncogene in human neuroblastomas (NBLs). However, the frequency of mutation is only 5-8%.

Purpose: The present study was performed to examine the level of ALK mRNA gene expression in primary neuroblastoma and to assess its relation to other prognostic factors of neuroblastoma.

Methods: Quantitative real-time RT-PCR was applied to examine the expression level of ALK mRNA, and its prognostic value in primary neuroblastoma patients. Immunohistochemical staining was used to check the expression level of ALK proteins.

Results:

In analysis of 79 patients with sporadic primary neuroblastoma, we found that high expression level of ALK mRNA was significantly associated with Shimada's pathological classification (p<0.001), patient's age (p<0.001), MYCN amplification status (p<0.001), tumor stage (p<0.001) and low TrkA expression level (p=0.0390), all these factors are known to be associated with poor prognosis in neuroblastoma. Of interest, immunohistochemical study revealed positive ALK in ALK-amplified tissues.
**Conclusion:** Our findings suggested that, high expression of *ALK* is associated with poor prognosis of NBL and that the expression level of *ALK* gene might also have some function in cell growth as well as differentiation in neuroblastoma.
Management of Thymic Neoplasm: Egyptian NCI Experience

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Background

Thymic tumors are rare entity with little information regarding outcomes after therapy with curative intent. We undertook a prospective analysis of all patients who underwent resection of thymic tumors at NCI hospitals. The optimal treatment includes surgical resection, chemotherapy, and radiotherapy.

Methods

From 2008 to 2014, 13 patients (8 men, 5 women) underwent surgical resection of thymic tumor at a mean age of 47 years. Patient demographics, extent of surgical resection, and outcomes were compiled. Use of chemotherapy or radiotherapy, perioperative variables, recurrence rates, and long-term survival were analyzed retrospectively. The Masaoka stage and tumor diameter were recorded along with other variables that potentially influenced survival such tumor grade, site & number of metastatic disease.

Results

Masaoka stage at presentation was I in 6 cases (47%), II in 3 cases (23%), III in only one cases (7%), and IV in 3 cases (23%). Neoadjuvant chemotherapy was administered to three patients (23%) whose tumors were deemed to be more locally invasive, two of them received neoadjuvant concomittant chemo-radiotherapy. Of the 13 patients in the surgical cohort, 8 (61.5%) were men. Mean age was 47 years (range: 21 to 58 years). No patient demonstrated an associated immunologic disorder such as myasthenia gravis. In all patients pathologic confirmation of thymic tumor was by CT guided fine needle aspiration/biopsy as part of the diagnostic workup. Preoperatively, three patients (23%) received chemotherapy and two (15.5%) received radiotherapy. The decision to administer chemotherapy or radiotherapy preoperatively was individualized in each patient and based on the extent of tumor invasion. Complete tumor resection with pathologically confirmed negative resection margins (R0) was achieved in twelve patients (92.3%). The other 1 patient had microscopic residual disease (R1). The
most common approach to surgical resection was sternotomy, used in 11 patients (84.5%). Mean tumor size was 9.5 cm (range: 4.5 to 16 cm) for the 13 patients. Pulmonary wedge resection was done for two cases, pleural resection for 5 cases & lobectomy in only one case. No perioperative deaths occurred nor patients required tracheostomy for postoperative respiratory failure. The two patients who had unilateral phrenic nerve resection as part of their operation none of these patients underwent a diaphragmatic plication early in the postoperative course to improve respiratory insufficiency. Four patients received adjuvant chemotherapy or radiotherapy or both. Of those whose tumors were completely resected, a patient experienced a local recurrence. Survival Mean length of survival in the entire group was 22.7 months (range: 14 to 36 months). At the last follow-up, 8 patients (61.5%) were alive without disease, 1 (7.5%) was alive with disease, and 4 (31%) had died.

Conclusion

Thymic tumors are amenable to surgical therapy, with increased use of computed tomography imaging, patients with early stage disease are being identified more frequently, complete surgical resection appears to have favorable cure rates in these patients. Patients with locally advanced disease can experience long-term survival with a multimodality approach.
THE PREDICTIVE VALUE OF FATS (FRAGILE-SITE ASSOCIATED TUMOR SUPPRESSOR) GENE EXPRESSION ON THE SENSITIVITY OF CISPLATIN IN ADVANCED NON-SMALL CELL LUNG CANCER


Abstract

**Background:** Cisplatin based chemotherapy regimens have been the standard of care for the treatment of advanced stage non-small cell lung cancer but not all patients respond adequately to the treatment. We therefore assessed the expression of FATS (Fragile-site associated tumor suppressor) gene and the response to cisplatin and gemcitabine.

**Patients and methods:** A prospective longitudinal study has been conducted in NCI (National Cancer Institute) medical oncology department in outpatient setting, in the period between June 2012 and July 2014. The study included 70 patients with pathologically proven advanced (stage IIIB and IV) non-small cell lung cancer (NSCLC) treated with cisplatin and gemcitabine. FATS gene expression was measured before starting the treatment. The primary end point was overall response rate (ORR) while the secondary end point was progression free survival (PFS) and overall survival (OS).

**Results:** Seventy patients were assessed and included in the trial. Thirteen patients achieved partial response while 13 patients achieved stable disease and the rest had a progressive disease. The overall response rate was statistically significant (p-value 0.031) for the high FATS expression group. The median PFS was 4.1 months (95% CI 2.1-6.2) in the low expression group and 3.8 months (95% CI 3.3-4.3) in the high expression group (p-value 0.442) while median OS was 6.9 months (95% CI 5.4-8.3) in the high expression group and 4.5 months (95% CI 3.7-5.3) in the low expression group (p-value 0.031)

**Conclusion:** The expression of the FATS gene can have an implication on the response to cisplatin and the overall survival. This opens the opportunity that FATS gene can be used as a predictive marker for NSCLC patients receiving cisplatin and gemcitabine chemotherapy.

**Keywords:** NSCLC, FATS, Cisplatin
Management of Ovarian Sex Cord Stromal Tumors: NCI Study

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Abstract

Background: Ovarian sex cord-stromal tumors are a heterogeneous group of benign or malignant neoplasms that develop from the dividing cells that normally produce cells that support and surround the oocytes, including the cells that produce ovarian hormones (the non-germ cell and nonepithelial components of the gonads). Ovarian sex cord-stromal tumors are rare, comprising only 1.2 percent of all primary ovarian cancers.

Objective: to review the management of ovarian sex cord stromal tumors in the NCI Cairo university during a period of 5 years (2005 till 2010).

Material and Methods: retrospective study including 114 patients who diagnosed and treated with ovarian sex cord stromal tumor (2005 to 2010). Data were collected from the biostatistics and cancer epidemiology department. Results: Out of 114 patients; 25(21.9%) were benign and 25 (21.9%) were borderline malignant; 55 (48.2%) were malignant and 9 (7.89%) of them were unpredicted biologic behavior; the median age of the study population was 49.7 years (range 14_83years). Panhysterectomy was done in 77(67.5%) of the patients; ovariectomy and debulking were done in 22(19.3%); salpingo-oophorectomy was done in 10(8.8%) 0f patients and cystectomy was done in 3(2.6%) and 2 cases underwent biopsy.

Conclusion: Total abdominal hysterectomy and bilateral salpingo-oophorectomy for women with granulosa cell tumors who have completed childbearing period. Conservation of a contralateral ovary or the uterus if they have no evidence of disease is possible in some women who wish to preserve fertility, but the feasibility varies by tumor histology. For recurrent localized disease, surgical resection is suggested to be done, if feasible. Chemotherapy rather than surgery alone for patients with metastatic or suboptimally cytoreduced disease.

Keywords: sex cord stromal tumor; granulosa cell tumors.
Normal Pregnancy and Lactation in a Cat after Treatment of Mammary Gland Tumor When Using Photothermal Therapy with Gold Nanorods: A Case Report

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Abstract

Background: Breast cancer therapy, which includes surgery, radiotherapy, chemotherapy and/or systemic therapy can have a profound impact on reproductive functions, leading to loss of fertility. To our knowledge, this is the first report on cancer photothermal therapy using gold nanorods on the mammary gland treatment of a cat, and the safe effect of the treatment on the reproductive function after tumor remission.

Case presentation: A seven years old Shirazi cat (Toatoa) was evaluated because of a 2-week history of progressive dyspnea, signs of depression, and loss of appetite. The cat has a large tumor mass at the left caudal mammary gland. The diameter of the tumor mass was measured using caliper with the dimensions of 14 × 12 × 10.5 cm for length, width and depth, respectively. This was confirmed with ultrasonography. Biopsy samples were taken and fixed in 10% formalin for histopathological investigation, and it was diagnosed as mammary gland adenocarcinoma Grade II. Toatoa was injected intratumoral (IT) with 75 µg gold nanorods (GNRs)/kg body weight followed by exposure to 808 nm laser light for 10 min. GNRs were injected twice, with 15 days apart. After 15 days from the first GNRs injection, there was 60% ablation of the tumor size, while, after 17 days from the second GNRs dose, there was a complete tumor remission. Ultrasound scanning revealed complete ablation of the tumor mass. Complete blood picture (CBC), liver and kidney function analyses showed no changes in any of the tested parameters and indicated that GNRs photothermal treatment is safe and have no immediate toxic effects. After complete remission of the mammary gland tumor, the cat restores all the biological activities including the reproductive function. After 2 months from complete tumor remission, the cat was pregnant after mating with a fertile male, and 62 days later she delivered 3 kittens of normal morphology and growth rate. Breast feeding was found to be normal from all the nipples including the previously affected nipple.

Conclusion: Photothermal therapy with gold nanorods can be used for the treatment of mammary gland tumor with apparently no impairments of reproductive functions in cats.
Management of phyllodes tumors of the breast; NCI study

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Abstract

Background: The frequency of mesenchymal breast tumors is very low, being represented mostly by tumors with biphasic proliferation (phyllodes tumors) and less by other types of non-epithelial tumors. From clinical point of view, phyllodes tumors (PT) can mimic a breast carcinoma.

Objective: To review the Management of phyllodes tumors of the breast in the NCI Cairo university during a period of 5 years (2005 till 2010).

Material and Methods: retrospective study including 32 patients who diagnosed and treated with phyllodes tumors of the breast between (2005 to 2010).Data were collected from the biostatistics and cancer epidemiology department.

Results: Out of 32 patients; 19 (59.3%) were benign and 8 (25%) were borderline and 5 (15.6%) were malignant; the median age of the study population was 44.5 years (range 18-71 years). The radiological tool of diagnosis was breast US and mammography 93.7%. Preoperative fine needle aspiration (FNA) was performed in 12(37.5%) cases for cytodiagnosis but true cut biopsy was done in 8 (25%) cases only. Lumpectomy was done in 78.1%, simple mastectomy was done in 9.3% and modified radical mastectomy was done only in 12.5% of all cases. Oncoplastic breast reconstruction was done in one case only.

Conclusion: different surgical modalities are considered the main line for management of phyllodes breast tumors. Local recurrence can be avoided with wide local excision from the frist surgery. Axillary LN dissection is not a role in management of breast PT.

Keywords: phyllodes tumor (PT), breast, fine
Evaluation of the etiological spectrum of malignant obstructive jaundice in the NCI Cairo University

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Abstract

Background: Obstructive jaundice is a common problem in the medical and surgical gastroenterological practice. Malignant obstructive jaundice can be caused by cancer head of pancreas, periampullary carcinoma, carcinoma of the gall bladder and cholangiocarcinomas.

Objective: to review the etiological spectrum of malignant obstructive jaundice in NCI Cairo university during a period of 3 years (2008 till 2010).

Patients and methods: retrospective study including 232 patients who presented with malignant obstructive jaundice between (2008 to 2010).Data were collected from the biostatistics and cancer epidemiology department.

Results: out of 232 patients; 156 (67.2%) were male and 76 (32.8%) were female; the median age of the study population was 49 years (range 19_80years).

The commonest cause of malignant obstructive jaundice was pancreatic head cancer, 72% (167/232), followed by the ampullary carcinoma 15% (36/232).The last cause was cholangiocarcinoma12.5% (29/233).Regarding the commonest symptom; clay colored stools (98.7%) was more frequent in patients with malignant disease whereas abdominal pain (97.7%) was 2nd common symptom.

Conclusion: Obstructive jaundice is more common among males and cancer head of pancreas is the commonest malignancy.US, ERCP and CT-Scan are important diagnostic modalities for evaluation of patient with obstructive jaundice with ERCP having the additional advantage of being therapeutic as well.

Keywords: Obstructive jaundice, ERCP, Ca Head of pancreas, Ca gall bladder.
Introduction: Hepatocellular carcinoma HCC is resistant to many combination chemotherapy without any survival benefits. This mandates the search for biomarker that may predict the response and or prognosis in this dull disease. We conduct this study to evaluate the relation between Topoisomerase II alpha level in the liver tissue and response to therapy.

Methods: The study included 50 unresectable HCC patients, who were diagnosed and treated in the NCI, Cairo University. The mean age was 54.5 years; 47 of them were males and 3 females. Doxorubicin 50 mg/ m2 every 3 weeks was given for 3 cycles and the response was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST).

Results: Over expression of TopoIIα was found in 19/50 (38%) and was negative in 31/50 (62%). No CR was seen after treatment with doxorubicin, while PR was 8/50 (16%), SD 21/50 (42%) and PD 21/50 (42%). There was a significant correlation between TopoIIα and the response to the chemotherapy (P = 0.001) (Table1). The study showed significant correlation between TopoIIα and OS; 8 months for over expression compared to 14 months in negative expression (figs1).

Conclusion: Detection of Topoisomerase IIα level in liver tissue showed a significant correlation to both response to therapy and survival in 50 HCC patients. TopoIIα is a promising prognostic and predictive factor that may reflect an aggressive behavior as seen with less survival in positive group but it represents a good response to therapy. With further studies in the near future Topoisomerase II alpha together with others factors as tumor size, pathological grade may help for more personalized therapy in f HCC.
Prevalence and chemotherapy-induced reactivation of occult hepatitis B virus among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma: Significance of hepatitis B core antibodies screening

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Abstract Background: Occult hepatitis B infection (OBI) is characterized by negative hepatitis B surface antigen (HBsAg) and detectable hepatitis B virus (HBV)-DNA in the liver and/or serum, with or without hepatitis B core antibody (anti-HBc). Anti-HBc is the most sensitive marker of previous HBV. HBV reactivation in patients under immunosuppressive treatment is life-threatening, occurring in both overt and occult HBV especially in hematological malignancies.

Aim of the work: To evaluate the prevalence and chemotherapy-induced reactivation of OBI among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma (DLBCL) patients and to determine the significance of anti-HBc screening among this group of patients before receiving chemotherapy.

Patients and methods: This cross-sectional study included 72 DLBCL patients negative for HBsAg, HBsAb and hepatitis C virus antibodies (anti-HCV). Patients were subjected to investigations including anti-HBc. All patients underwent alanine transaminase (ALT) monitoring before each cycle of chemotherapy and monthly for 12 months after the end of chemotherapy. Patients with suspected OBI were tested for HBV-DNA using real-time polymerase chain reaction (PCR).

Results: Anti-HBc was detected in 10 of 72 HBsAg negative sera (13.89%) (95% confidence interval 6.9–22.2%). Five of the 10 anti-HBc positive patients in this study had OBI reactivation.

Conclusion: The study concluded that anti-HBc screening is mandatory before chemotherapy. HBsAg-negative/anti-HBc-positive patients should be closely observed for signs of HBV reactivation through the regular monitoring of ALT. Prophylaxis lamivudine is recommended for anti-HBc positive patients before chemotherapy.
Sequential Sorefinib and TACE in unresectable Hepatocellular Carcinoma

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Abstract:

**Background and Aims**: Combination of Antiangiogenic therapy for a short duration before Transarterial Chemoembolization (TACE) for the treatment of unresectable Hepatocellular carcinoma (HCC) is a matter of debate in recent years. This study presents small number of patients treated with sorefinib and TACE at Assiut University Hospital, introducing the steps, results for the challenging combination trial in terms of Progression Free Survival (PFS) and Overall Survival (OS).

**Methods**: In a prospective trial of 60 patients with Sorefinib and TACE at Assiut University Hospital from 2013 till 2015. Outcomes of interest included progression free survival and overall survival (PFS and OS), tumor response, and toxicities.

**Results**: Sixty patients were treated with combination of TACE and Sorefinib given throughout 30 days, depending on preliminary results, but off-protocol prior to TACE procedure and in a duration not more than one week separation, with median follow-up 19.8 months. The median time to progression and overall survival are 18.6 and 33 months respectively, 1 year and 2 year survival were 100% and 75% respectively, demonstrating objective response (CR+PR) is 60% and SD is 10%. The most common toxicity is grade 3-4 adverse event is diarrhea (40%) which necessitates hospital stay 12 days in 10%.

**Conclusions**: Combination therapy may bring benefits for unresectable HCC patients in terms of PFS and OS. Further well-designed randomized controlled studies are needed to confirm the efficacy of combination therapy. However, such sorafenib-based combination cannot be recommended for routine practice outside the setting of clinical trials.

**Keywords**: TACE: Trans-Arterial Chemoembolization, TTP: Time To Progression, OS: Overall Survival, CR: Complete Response, PR: Partial Response, SD: Stable Disease.