

<b>CANCER</b> <b>85/3 FEBRUARY 1 1999</b>	
<b>EDITORIAL</b>	
<p>Transforming Growth Factor <math>\beta</math>1: A Useful Tumor Marker in Patients with Colorectal Carcinoma?  Alan D. Langerak and Harinder S. Garewal  Although transforming growth factor-<math>\beta</math>1 may prove to be an important new tumor marker in colorectal carcinoma, larger, prospective studies are needed to confirm this theory. See also pages 554-61</p>	517
<b>ORIGINAL ARTICLE</b>	
Anatomic Site	
Esophagus (C15.9)	
<p>Pathologic Prognostic Factors in Barrett's-Associated Adenocarcinoma: A Follow-Up Study of 96 Patients  Carlos Torres, Jerrold R. Turner, Helen H. Wang, William Richards, David Sugarbaker, Ali Shahsafaei, and Robert D. Odze  A retrospective study of morphologic prognostic features in 96 cases of resected Barrett's-associated adenocarcinoma, either with (61 cases) or without (35 cases) preoperative neoadjuvant chemoradiotherapy, found that older patient age, higher pathologic stage, absence of peritumoral lymphoid infiltrate, and most likely perineural invasion were associated with shortened survival by multivariate analysis. The effect of chemoradiotherapy, as assessed by the degree of residual tumor, did not correlate with survival in this patient group.</p>	520
Stomach (C16.9)	
<p>Successful Intraperitoneal Hyperthermic Chemoperfusion for the Prevention of Postoperative Peritoneal Recurrence in Patients with Advanced Gastric Carcinoma  Shigeru Fujimoto, Makoto Takahashi, Takaaki Mutou, Kokuriki Kobayashi, and Tadashi Toyosawa  Seventy-one gastric carcinoma patients with serosal invasion were treated with intraperitoneal hyperthermic chemoperfusion combined with surgery. The survival rate of these 71 patients was significantly higher than that of the control group of 70 patients who were treated with surgery alone.</p>	529
Colon and Rectum (C19.9)	
<p>5-Fluorouracil and Levofolinic Acid with or without Recombinant Interferon-2b in Patients with Advanced Colorectal Carcinoma: A Randomized Multicenter Study with Stratification for Tumor Burden and Liver Involvement by the Southern Italy Oncology Group  Giuseppe Colucci, Evaristo Maiello, Vittorio Gebbia, Francesco Giuliani, Giuseppe Serravezza, Giorgio Lelli, Silvana Leo, Gianfranco Filippelli, Giampaolo Nicoletta, and Mario Brandi, for the Southern Italy Oncology Group (G.O.I.M.).  A Phase III trial was performed to evaluate the impact of interferon on the efficacy of levofolinic acid and 5-fluorouracil against metastatic colorectal carcinoma, as well as the role of tumor burden and liver involvement as prognostic factors. Interferon did not appear to have a positive influence on patient outcome, although liver</p>	535

involvement and tumor burden were found to be important prognostic factors.	
<p>Amplified CDK2 and cdc2 Activities in Primary Colorectal Carcinoma  Jong Hun Kim, Min Jeong Kang, Chul Uhng Park, Hee Jin Kwak, Yong Hwang, and Gou Young Koh</p> <p>The results of this study indicate that significant activation of CDK2 and cdc2 occurs in primary colorectal carcinoma.</p>	546
<p>Elevated Serum Levels of Transforming Growth Factor- <math>\beta</math>1 in Patients with Colorectal Carcinoma: Its Association with Tumor Progression and Its Significant Decrease after Curative Surgical Resection  Kang Sup Shim, Kwang Ho Kim, Woon Sup Han, and Eung Bum Park</p> <p>Serum levels of transforming growth factor-<math>\beta</math>1 (TGF- <math>\beta</math>1) in patients with colorectal carcinoma were significantly higher than those in normal control subjects and these levels decreased significantly after curative surgical resection. These results suggest that the serum level of TGF- <math>\beta</math>1 might be a useful biomarker in the management of colorectal carcinoma. See also pages 517-9.</p>	554
Liver (C22.0)	
<p>Epithelioid Hemangioendothelioma of the Liver: A Clinicopathologic Study of 137 Cases  Hala R. Makhlof, Kamal G. Ishak, and Zachary D. Goodman</p> <p>To the authors' knowledge, this series of 137 cases is the largest series reported from one institution. Epithelioid hemangioendothelioma is of unknown etiology and only one histologic parameter, tumor cellularity, is predictive of outcome.</p>	562
Pancreas (C25.9)	
<p>Analysis of Paraaortic Lymph Node Involvement in Pancreatic Carcinoma: A Significant Indication for Surgery?  Masato Kayahara, Takukazu Nagakawa, Tetsuo Ohta, Hirohisa Kitagawa, Keiichi Ueno, Hidehiro Tajima, Ayman Elnemr, and Koichi Miwa</p> <p>Paraaortic lymph node involvement in invasive ductal carcinoma of the pancreas is common and highly significant for prognosis. Therefore the resected specimen should include the paraaortic lymph nodes.</p>	583
Larynx (C32.9)	
<p>Spontaneous Apoptosis in Laryngeal Squamous Cell Carcinoma Is Independent of bcl-2 and bax Protein Expression  Martin C. Jäckel, Mansur A. Dorudian, Dagmar Marx, Ulrich Brinck, Alfred Schauer, and Wolfgang Steiner</p> <p>In this study, the rate of spontaneous apoptosis occurring in laryngeal carcinoma was closely associated with mitotic activity but appeared to be unrelated to protein expression of bcl-2 and bax. Elevated bcl-2 and reduced bax levels were correlated with adverse prognostic parameters.</p>	591
Lung (C34.9)	
<p>Genetic Changes in the Spectrum of Neuroendocrine Lung Tumors  Naoyoshi Onuki, Ignacio I. Wistuba, William D. Travis, Arvind K. Virmani, Kazuo Yashima, Elizabeth Brambilla, Phillip Hasleton, and Adi F. Gazdar</p> <p>The authors studied the molecular changes present in 59 cases representing all 4 types of pulmonary neuroendocrine tumors. Their findings support the</p>	600

<p>clinicopathologic concept that neuroendocrine tumors of the lung represent a spectrum ranging from low grade typical carcinoids to highly malignant neuroendocrine carcinomas.</p>	
<p>Blood/Bone Marrow (C42.1)</p>	
<p>Extramedullary Tumors of Myeloid Blasts in Adults as a Pattern of Relapse following Allogeneic Bone Marrow Transplantation Yener Koc, Kenneth B. Miller, David P. Schenkein, Philip Daoust, Kellie Sprague, and Eugene Berkman Solitary extramedullary myeloid sarcoma as a pattern of recurrence following allogeneic bone marrow transplantation in patients with acute or chronic myeloid leukemia is rare. The prognosis for this group of patients is very poor, as in any case of posttransplantation leukemic relapse, with the exception of patients with chronic myeloid leukemia.</p>	608
<p>Breast (C50.9)</p>	
<p>Predictors of Local Recurrence after Treatment of Ductal Carcinoma In Situ: A Meta-Analysis John Boyages, Geoff Delaney, and Richard Taylor Patient tumor and treatment factors as potential predictors for local recurrence after surgery for ductal carcinoma in situ are reviewed. This meta-analysis shows that various pathologic factors and conservative surgery alone are predictors for higher incidence of local recurrence.</p>	616
<p>Male Breast Carcinoma: A Review of 229 Patients Who Presented to the Princess Margaret Hospital during 40 Years: 1955-1996 Paul E. Goss, Caroline Reid, Melania Pintilie, Ruth Lim, and Naomi Miller This single-institution review of 229 male breast carcinoma patients who presented during the years 1955-1996 describes clinical presentation, some changes in treatment practices, and no improvement in outcome over the 4-decade period. Collection of detailed, prospective data on male breast carcinoma patients may optimize clinical management.</p>	629
<p>Cognitive Deficits after Postoperative Adjuvant Chemotherapy for Breast Carcinoma Sanne B. Schagen, Frits S. A. M. van Dam, Martin J. Muller, Willem Boogerd, Jaap Lindeboom, and Peter F. Bruning Breast carcinoma patients treated with adjuvant cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) chemotherapy have a significantly higher risk of late cognitive impairment than breast carcinoma patients not treated with chemotherapy. This cognitive impairment is unaffected by anxiety, depression, fatigue, and time since treatment, and is not related to patients' reports of cognitive dysfunction.</p>	640
<p>Cervix (C53.9)</p>	
<p>Vascularity Index as a Novel Parameter for the In Vivo Assessment of Angiogenesis in Patients with Cervical Carcinoma Wen-Fang Cheng, Chien-Nan Lee, Jan-Show Chu, Chi-An Chen, Tzer-Ming Chen, Wen-Yi Shau, Chang-Yao Hsieh, and Fon-Jou Hsieh In vivo vascularity index was found to correlate well with in vitro microvessel density. The authors believe the in vivo vascularity index would help to predict lymph node metastasis in patients with cervical carcinoma.</p>	651

Ovary (C56.9)	
<p>Altered Expression of Transforming Growth Factor-<math>\beta</math> Ligands and Receptors in Primary and Recurrent Ovarian Carcinoma</p> <p>Robert E. Bristow, Rae Lynn Baldwin, S. Diane Yamada, Murray Korc, and Beth Y. Karlan</p> <p>Enhanced expression of transforming growth factor- <math>\beta</math>TGF- <math>\beta</math>1 and TGF- <math>\beta</math>3 mRNA, as well as loss of expression of TGF-<math>\beta</math> receptors T <math>\beta</math>R-I and T <math>\beta</math>R-III, were observed in ovarian carcinoma specimens, suggesting a role for alterations in TGF-<math>\beta</math>-mediated pathways in ovarian tumorigenesis.</p>	658
<p>Clear Cell Carcinoma Has an Expression Pattern of Cell Cycle Regulatory Molecules that Is Unique among Ovarian Adenocarcinomas</p> <p>Motohiko Shimizu, Toshio Nikaido, Toshihiko Toki, Tanri Shiozawa, and Shingo Fujii</p> <p>Clear cell carcinoma exhibits higher expression of cyclin E and p21 and lower expression of p53 and cyclin A than any other histologic subtype of ovarian adenocarcinoma.</p>	669
Prostate (C61.9)	
<p>Late Side Effects Unchanged 4-8 Years after Radiotherapy for Prostate Carcinoma: A Comparison with Age-Matched Controls</p> <p>Per Fransson and Anders Widmark</p> <p>Changes in complications between 4 and 8 years after radiotherapy were prospectively assessed among prostate carcinoma patients who received a self-assessment questionnaire, and these changes were compared with those found in an age-matched population.</p>	678
Kidney (C64.9)	
<p>Impact of Tumor Size on the Clinical Outcomes of Patients with Robson Stage I Renal Cell Carcinoma</p> <p>Toshiaki Kinouchi, Shigeru Saiki, Norio Meguro, Osamu Maeda, Masao Kuroda, Michiyuki Usami, and Toshihiko Kotake</p> <p>The tumor size cutoff of 5.5 cm, rather than 7.0 cm, in the TNM system (fifth edition, 1997) for classifying renal cell carcinoma was most significantly predictive of the survival of Robson Stage I patients after radical nephrectomy. The tumor size cutoff of 5.5 cm was also shown to be significant in univariate and multivariate analyses.</p>	689
Thyroid (C73.9)	
<p>Incidence of Breast Carcinoma in Women with Thyroid Carcinoma</p> <p>Rena Vassilopoulou-Sellin, Lynn Palmer, Sarah Taylor, and Catherine S. Cooksley</p> <p>Breast carcinoma developing after thyroid carcinoma was diagnosed more frequently than expected in young adult women. This potential association and plausible mechanisms should be evaluated in larger cohorts of patients.</p>	696
Lymph Node (C77.9)	
<p>The Management of Unicentric and Multicentric Castleman's Disease: A Report of 16 Cases and a Review of the Literature</p> <p>Wilbur B. Bowne, Jonathan J. Lewis, Daniel A. Filippa, Ruben Niesvizky, Ari D. Brooks, Michael E. Burt, and Murray F. Brennan</p>	706

<p>The authors report on the responses to therapy and clinical outcomes of patients with the clinical and histopathologic features of unicentric and multicentric Castleman's disease treated at a single institution. The current understanding of the pathogenesis of this disease in regard to possible treatment strategies is discussed.</p>	
<p>p53 Gene Mutations and Rearrangements in Non-Hodgkin's Lymphoma Po-Min Chen, Tzeon-Jye Chiou, Ruey-Kuen Hsieh, Frank S. Fan, Chiau-Jun Chu, Ching-Zong Lin, Hung Chiang, Chueh-Chuan Yen, Wei-Shu Wang, and Jin-Hwang Liu</p> <p>Point mutations and rearrangements of the p53 gene were found in 9 (10.8%) of 84 non-Hodgkin's lymphomas. Patients who carried these alterations had worse outcomes than other patients. Of three patients with gene rearrangements, the two with one abnormal p53 allele had a more favorable prognosis than the one with two abnormal alleles.</p>	718
<p>GENERAL TOPIC PEDIATRIC ONCOLOGY</p>	
<p>Extraskeletal Ewing's Sarcoma Rick Ahmad, Brian R. Mayol, Mary Davis, and Bruce T. Rougraff</p> <p>Combination therapy with chemotherapy, radiation, and attempted surgical resection of the tumor mass in patients younger than 16 years with extraskeletal Ewing's sarcoma was associated with a better survival than that for older patients or those treated without surgical resection.</p>	725
<p>Military Service of Male Survivors of Childhood Malignancies Päivi M. Lähteenmäki, Heikki A. Salmi, Toivo T. Salmi, Hans Helenius, Anne Mäkipernaa, Marjatta Lanning, Mikko Perkkiö, and Martti A. Siimes</p> <p>Childhood cancer survivors are less likely to meet the requirements for military service in Finland, but enlisted survivors cope with the service well if their treatment sequelae are evaluated carefully at the time of military enlistment. The survivors who are eligible for duty are well motivated for training and use the medical services of the garrison physician less than controls, and, as a whole, their service is comparable to that of the general population.</p>	732
<p>The RNA Component of Telomerase as a Marker of Biologic Potential and Clinical Outcome in Childhood Neuroblastic Tumors Anirban Maitra, Kazuo Yashima, Asha Rathi, Charles F. Timmons, Beverly Barton Rogers, Jerry W. Shay, and Adi F. Gazdar</p> <p>Neuroblastic tumors are characterized by unpredictable biologic behavior. In this study, the expression of the RNA component of human telomerase (hTR) was examined in archival material from neuroblastic tumors by an in situ hybridization assay, and hTR expression was correlated with prognosis and outcome of therapy.</p>	741
<p>Childhood Melanoma Survival Nicholas C. Saenz, Judit Saenz-Badillos, Klaus Busam, Michael P. LaQuaglia, Martin Corbally, and Mary S. Brady</p> <p>Like adults, children with melanoma are at significant risk of dying of the disease. The survival of children is similar to that of adults and is related to stage at presentation. The survival advantage observed for adult females is not seen among children.</p>	750

CORRESPONDENCE	
Serum CA 125 Is of Clinical Value in the Staging and Follow-Up of Patients with Non-Hodgkin's Lymphoma: Correlation with Tumor Parameters and Disease Activity	755
<b>VOLUME 85 NUMBER 4 FEBRUARY 15, 1999</b>	
Immunohistochemical Study of the Expression of Human Chorionic Gonadotropin- $\beta$ in Oral Squamous Cell Carcinoma Kanokporn Bhalang, Abdel H. Kafrawy, and Dale A. Miles Human chorionic gonadotropin- $\beta$ (hCG $\beta$ ) was immunohistochemically detected in 64% of oral squamous cell carcinoma cases. The presence of hCG $\beta$ immunoreactive cells may reflect a potentially higher malignant behavior of oral squamous cell carcinoma.	757
Esophagus (C15.9)	
The Quality of Swallowing for Patients with Operable Esophageal Carcinoma: A Randomized Trial Comparing Surgery with Radiotherapy Rajendra A. Badwe, Vinay Sharma, Mehul S. Bhansali, Ketayun A. Dinshaw, Prakash K. Patil, Neelima Dalvi, Srinivas G. Rayabhattanavar, and Prafulla B. Desai The quality of swallowing among patients with operable esophageal carcinoma improved after surgery as well as after radiation. The improvement was marginally superior for patients in the surgery arm compared with the radiotherapy arm at 6 months after treatment. While surgery was twice as likely to result in improvement in swallowing than radiotherapy, the small number of patients was a limitation.	763
The Prognostic Significance of Lymph Node Micrometastasis in Patients with Esophageal Carcinoma Jonathan N. Glickman, Carlos Torres, Helen H. Wang, Jerrold R. Turner, Aliakbar Shahsafaei, William G. Richards, David J. Sugarbaker, and Robert D. Odze Occult microscopic lymph node metastasis may be detected by cytokeratin immunohistochemistry in a significant proportion of apparent lymph node negative esophageal carcinoma (adenocarcinoma and squamous cell carcinoma) patients undergoing esophagectomy. However, the presence of micrometastasis did not correlate with poorer survival rates in this cohort of patients.	769
Colon and Rectum (C19.9)	
Validation and Simplification of Bethesda Guidelines for Identifying Apparently Sporadic Forms of Colorectal Carcinoma with Microsatellite Instability Marilia L. Cravo, Paulo O. Fidalgo, Pedro A. Lage, Cristina M. Albuquerque, Paula P. Chaves, Isabel Claro, Teresa Gomes, Claudia Gaspar, Jorge O. Soares, and Carlos Nobre-Leitão In the current study the authors applied the Bethesda guidelines, which were developed to identify colorectal tumors with microsatellite instability (MSI), to a population of 62 patients with apparently sporadic forms of colorectal carcinoma. Although the guidelines were highly specific, their sensitivity and positive predictive value in the identification of tumors with MSI at > 3 loci were only 43% and 27%, respectively. The authors propose a simplification of the Bethesda guidelines that increases the sensitivity to 85% and the positive predictive value to 46%.	779
A Multicenter, Phase II Trial of Weekly Irinotecan (CPT-11) in Patients with Previously Treated Colorectal Carcinoma	786

Mace L. Rothenberg, John V. Cox, Russell F. DeVore, John D. Hainsworth, Richard Pazdur, Saul E. Rivkin, John S. Macdonald, Charles E. Geyer, Jr., John Sandbach, Daniel L. Wolf, J. Scott Mohrland, Gary L. Elfring, Langdon L. Miller, and Daniel D. Von Hoff A large, multicenter Phase II trial confirms the activity of irinotecan (CPT-11) as second-line therapy for patients with metastatic colorectal carcinoma.	
Markedly Elevated Cell Turnover Is Characteristic of Small, Deeply Invasive Carcinomas of the Colorectum Hiroyuki Takahashi, Hiroyuki Mitomi, Masahiro Igarashi, Tomoe Katsumata, and Isao Okayasu The small, deeply invasive colorectal carcinoma can be considered a distinct tumor entity, and presents with accelerated tumor cell turnover.	796
Rectum (C20.9)	
The Effect of Preoperative Radiation Therapy on Glucose Utilization and Cell Kinetics in Patients with Primary Rectal Carcinoma Christiaan Schiepers, Karin Haustermans, Karel Geboes, Ludo Filez, Guy Bormans, and Freddy Penninckx Preoperative radiation therapy of patients with locally invasive rectal carcinoma resulted in tumor reduction. Tumor glucose metabolism measured with positron emission tomography decreased accordingly. Cell cycling slowed, but the viable cell fraction maintained its proliferative rate.	803
Liver (C22.0)	
Measurement of Serum Levels of Des- $\gamma$ -Carboxy Prothrombin in Patients with Hepatocellular Carcinoma by a Revised Enzyme Immunoassay Kit with Increased Sensitivity Hiroaki Okuda, Toshimi Nakanishi, Kazuko Takatsu, Akiko Saito, Naoaki Hayashi, Keisuke Watanabe, Naoki Magario, Takeshi Yokoo, and Toru Naraki The revised des- $\gamma$ -carboxy prothrombin (DCP) kit described in this report is more useful than the conventional DCP kit as a tumor marker for hepatocellular carcinoma and should be used in combination with $\alpha$ -fetoprotein.	812
Acquisition of Glutamine Synthetase Expression in Human Hepatocarcinogenesis: Relation to Disease Recurrence and Possible Regulation by Ubiquitin-Dependent Proteolysis Takuya Osada, Michiie Sakamoto, Hirokazu Nagawa, Junji Yamamoto, Yoshihiro Matsuno, Akihiro Iwamatsu, Tetsuichiro Muto, and Setsuo Hirohashi Expression of glutamine synthetase increases during the progression of hepatocellular carcinoma (HCC), and this enzyme activity seems to be regulated by a ubiquitin-dependent proteolytic system. Moreover, glutamine synthetase might play a role in promoting the metastatic potential of HCC.	819
Pancreas (C25.9)	
Characterization of Six Cell Lines Established from Human Pancreatic Adenocarcinomas Masayuki Kato, Yutaka Shimada, Hisashi Tanaka, Ryo Hosotani, Gakuji Ohshio, Kanji Ishizaki, and Masayuki Imamura Six human pancreatic carcinoma cell lines, designated as KMP-1 to KMP-6, have	832

been established. The biologic and molecular properties of the KMP cell lines are described.	
Nasal Cavity (C30.0)	
Basaloid Squamous Cell Carcinoma of the Sinonasal Tract Jacqueline A. Wieneke, Lester D. R. Thompson, and Bruce M. Wenig Primary sinonasal basaloid squamous cell carcinomas are uncommon tumors that share the light microscopic and immunohistochemical features, as well as aggressive biologic behavior characteristics, of basaloid squamous cell carcinomas occurring in more common head and neck mucosal sites. Multimodality therapy is indicated.	841
Lung (C34.9)	
Increasing Dose Intensity of Cisplatin-Etoposide in Advanced Nonsmall Cell Lung Carcinoma: A Phase III Randomized Trial of the Spanish Lung Cancer Group Albert Font, Alfredo J. Moyano, Jose M. Puerto, Alejandro Tres, Carlos Garcia-Giron, Isidoro Barneto, Antonio Anton, Jose J Sanchez, Ana Salvador, and Rafael Rosell This randomized Phase III trial assessed the impact on advanced nonsmall cell lung carcinoma of increasing the dose intensity of a cisplatin-etoposide combination. Dose intensification achieved by shortening the period between cycles did not correlate with significant improvements in response rate or survival.	855
Five-Year Survivors with Resected pN2 Nonsmall Cell Lung Carcinoma Motoyasu Sagawa, Akira Sakurada, Shigefumi Fujimura, Masami Sato, Satomi Takahashi, Katsuo Usuda, Chiaki Endo, Hirokazu Aikawa, Takashi Kondo, and Yasuki Saito Even in the presence of pN2 disease, lung carcinoma patients with T1 tumors, skip metastasis, or single level mediastinal lymph node involvement are expected to have a relatively favorable prognosis and may be candidates for primary resection.	864
Bone (C41.9)	
Pelvic Ewing Sarcoma: A Retrospective Analysis of 241 Cases Christiane Hoffmann, Susanne Ahrens, Jürgen Dunst, Axel Hillmann, Winfried Winkelmann, Alan Craft, Ulrich Göbel, Christian Rube, Paul A. Voûte, Dieter Harms, and Herbert Jürgens Combined modality treatment has resulted in definitive improvement in prognosis for patients with localized pelvic Ewing sarcoma. Tumor load, responsiveness to chemotherapy, and adequate surgical margins are the major factors influencing prognosis.	869
The Surgical Management of Sacrococcygeal Chordoma Tsukasa Yonemoto, Shin-ichiro Tatezaki, Toshinao Takenouchi, Takeshi Ishii, Tetsuzo Satoh, and Hideshige Moriya Accurate assessment of sacrococcygeal chordoma infiltration by magnetic resonance imaging and excision with appropriate surgical margins are vital for complete tumor removal and favorable prognosis.	878
Skin (C44.9)	
Lymphoepithelioma-Like Carcinoma of the Skin with Apparent Origin in the Epidermis—A Pattern or an Entity?: A Case Report Anne C. Lind, Wayne A. Breer, and Mark R. Wick	884

<p>This case report documents another facet of lymphoepithelioma-like carcinoma of the skin (LELCS), namely, its apparent ability to arise from the surface integument. This observation, along with others made previously, further supports the conclusion that LELCS is a shared phenotypic pattern rather than a tumor entity in the skin.</p>	
<p><b>Breast (C50.9)</b></p>	
<p><b>Prognostic Value of Plasma Prostate Specific Antigen after Megestrol Acetate Treatment in Patients with Metastatic Breast Carcinoma</b>  Eleftherios P. Diamandis, Svein I. Helle, He Yu, Dimitrios N. Melegos, Steinar Lundgren, and Per E. Lonning</p> <p>The measurement of plasma prostate specific antigen (PSA) in patients with metastatic breast carcinoma treated with megestrol acetate has prognostic significance. A subset of patients with increases in plasma PSA after treatment has an unfavorable prognosis.</p>	891
<p><b>Long Term Follow-Up of Women Treated with 16-Week, Dose-Intensive Adjuvant Chemotherapy for High Risk Breast Carcinoma</b>  Bahar Mikhak, Marianna Zahurak, Martin D. Abeloff, John H. Fetting, Nancy E. Davidson, Ross C. Donehower, William Waterfield, and M. John Kennedy</p> <p>Long term follow-up is reported for a cohort of women with breast carcinoma and <math>\geq 10</math> involved axillary lymph nodes treated with a 16-week, dose-intensive, doxorubicin-based adjuvant combination chemotherapy regimen. Patients underwent intensive staging prior to study entry. However, despite this, the results of the current study are similar to those of previous reports for standard dose chemotherapy and appear inferior to those reported for high dose therapy.</p>	899
<p><b>Ovary (C56.9)</b></p>	
<p><b>The Current Status of Surgical Staging of Ovarian Serous Borderline Tumors</b>  Paul S. Lin, David M. Gershenson, Michael W. Bevers, Kristin R. Lucas, Thomas W. Burke, and Elvio G. Silva</p> <p>Despite extensive educational efforts, intraoperative frozen-section analysis of ovarian masses and surgical staging of ovarian serous borderline tumors remain suboptimal in the United States.</p>	905
<p><b>Testis (C62.9)</b></p>	
<p><b>The Management of Inferior Vena Cava Obstruction Complicating Metastatic Germ Cell Tumors</b>  Bass Hassan, Ken Tung, Richard Weeks, and Graham M. Mead</p> <p>Inferior vena cava obstruction is a poorly characterized complication of metastatic germ cell tumors. Approximately one-third of patients can develop thromboembolism, either as a presenting feature or during treatment. Brief prophylactic anticoagulation is recommended in cases of metastatic germ cell tumor with features of inferior vena cava obstruction.</p>	912
<p><b>Bladder (C67.9)</b></p>	
<p><b>Telomerase Activity in Patients with Transitional Cell Carcinoma: A Preliminary Study</b>  Michal A. Rahat, Nitza Lahat, Haifa Gazawi, Murray B. Resnick, Yanina Sova, Gad Ben-Ari, Michael Cohen, and Avi Stein</p> <p>Telomerase activity was detected in almost all malignant tumors and in a high</p>	919

incidence of cup biopsies and urine samples taken from transitional cell carcinoma (TCC) patients. Although no correlation was found between the grade and stage of the tumor and telomerase activity, the finding that telomerase activity can be detected in a urine sample with high sensitivity indicates that it might be a good diagnostic marker for the identification and follow-up of TCC patients.	
Brain (C71.9)	
Final Report on the University of California-San Francisco Experience with the Bromodeoxyuridine Labeling Index as a Prognostic Factor for the Survival of Glioma Patients Kathleen R. Lamborn, Michael D. Prados, Sarah B. Kaplan, and Richard L. Davis The bromodeoxyuridine labeling index (LI) was found predictive of the survival of glioma patients considered separately according to tumor grade and whether surgery was performed at the time of initial diagnosis or recurrence. Usual proportional hazards modeling assumptions were not met for some patient groups, and more advanced statistical methods were used to evaluate the usefulness of this LI.	925
Peritumoral Brain Edema Associated with Meningioma: Influence of Vascular Endothelial Growth Factor Expression and Vascular Blood Supply Hiroyuki Yoshioka, Seiji Hama, Eiji Taniguchi, Kazuhiko Sugiyama, Kazunori Arita, and Kaoru Kurisu The expression of vascular endothelial growth factor induces meningioma-associated peritumoral brain edema under the condition of existence of a cerebral-pial blood supply.	936
Thyroid (C73.9)	
Surveillance of Patients to Detect Recurrent Thyroid Carcinoma Perry W. Grigsby, Kathy Baglan, and Barry A. Siegel A single negative iodine-131 scintigraphic study after complete ablation has a lower predictive value for relapse free survival than do two consecutive annual negative studies. Annual iodine-131 imaging is recommended for surveillance until two consecutive annual negative studies are obtained, after which repeat imaging at 3-5 years appears to be satisfactory.	945
Head and Neck (C76.0)	
A Phase II Trial of Cisplatin, Methotrexate, Levofolinic Acid, and 5-Fluorouracil in the Treatment of Patients with Locally Advanced, Metastatic Squamous Cell Carcinoma of the Head and Neck Francesco Caponigro, Pasquale Comella, Paolo Marcolin, Francesco Russo Spena, Maria Biglietto, Giacomo Carteni, Luigi De Lucia, Antonio Avallone, Adriano Gravina, and Giuseppe Comella Cisplatin, methotrexate, levofolinic acid, and 5-fluorouracil is an active, moderately toxic, cost-effective regimen for therapy of patients with advanced squamous cell carcinoma of the head and neck.	952
Expression of Thymidine Phosphorylase and Vascular Endothelial Cell Growth Factor in Human Head and Neck Squamous Cell Carcinoma and Their Different Characteristics Tatsuya Fukuiwa, Yuji Takebayashi, Suminori Akiba, Tsutomu Matsuzaki, Yutaka Hanamure, Kazutaka Miyadera, Yuji Yamada, and Shin-ichi Akiyama	960

Vascular endothelial growth factor is involved in angiogenesis in head and neck squamous cell carcinoma. Thymidine phosphorylase may have effects on tumor growth other than angiogenic activity in head and neck squamous cell carcinoma.	
Lymph Node (C77.9)	
Hodgkin Disease with Subsequent Transformation to CD30 Positive Non-Hodgkin Lymphoma in Six Patients Naoyoshi Mori, Kazuko Watanabe, Yoriko Yamashita, Atsuo Nakayama, Yasushi Yatabe, Michihiko Narita, Toshitaka Kobayashi, Yuuichi Hasegawa, Hiroshi Kojima, and Toshiro Nagasawa Six patients who were diagnosed initially as having Hodgkin disease subsequently developed anaplastic large cell lymphoma (ALCL) features. These patients had intermediate phenotypes between Hodgkin disease and ALCL and had a worse prognosis than ALCL patients.	970
GENERAL TOPIC CHEMOTHERAPY: INTRATUMORAL INJECTION	
An Early Phase II Study of Intratumoral P-32 Chromic Phosphate Injection Therapy for Patients with Refractory Solid Tumors and Solitary Metastases Nosrat Firusian and Wolfram Dempke Intratumoral P-32 chromic phosphate injection deserves consideration as a new treatment modality for patients with refractory solid cancers or solitary metastases. The response rate found in this Phase II study was 71%.	980
GERM CELL TUMOR	
Treatment Outcome of Patients with Brain Metastases from Malignant Germ Cell Tumors Sophie D. Fosså, Carsten Bokemeyer, Arthur Gerl, Stephane Culine, William G. Jones, Graham M. Mead, José R. Germa-Lluch, Jörg Pont, Hans J. Schmoll, and Sergei Tjulandin In a retrospective, multicenter analysis cerebral radiotherapy given in combination with chemotherapy was not associated with increased survival of patients presenting with brain metastases at the time of initial diagnosis of a germ cell malignancy. Cerebral irradiation was found to be an independent predictor of good prognosis for patients who developed brain metastases after cisplatin-based chemotherapy.	988
PALLIATIVE CARE	
Outcome of Palliative Urinary Diversion in the Treatment of Advanced Malignancies Bijan Shekarriz, Hodjat Shekarriz, Jyoti Upadhyay, Mousumi Banerjee, Herman Becker, J. Edson Pontes, and David P. Wood, Jr. Endourologic management of malignant ureteral obstruction has a high surgical failure and complication rate. Furthermore, palliative urinary diversion is associated with poor prognosis in terms of survival and performance status after diversion, regardless of the type of malignancy.	998
STAGING: MAGNETIC RESONANCE IMAGING	
Magnetic Resonance Imaging of Bone Marrow Metastases in the Initial Staging of Small Cell Lung Carcinoma and Breast Carcinoma Guenter Layer, Andreas Steudel, Heinrich Schüller, Gerhard van Kaick, Frank Grünwald, Maximilian Reiser, and Hans H. Schild	1004

Screening magnetic resonance imaging (MRI) bone marrow examinations of the spine and pelvis led to different results in patients with small cell lung carcinoma (SCLC) and female breast carcinoma (FBC), although both have a high incidence of bone marrow metastases. Due to its superiority compared with biopsy and bone scan, MRI should become an integral part of the initial staging procedures in patients with SCLC. When staging patients with FBC, MRI should be applied only in clinically selected cases.	
Information Item	
Erratum Article FOOTNOTES AND ACKNOWLEDGMENTS	1010
<b>VOLUME 85 NUMBER 6 MARCH 15, 1999</b>	
Anatomic Site Esophagus (C15.9)	
Phase II Clinical Trial of 13-Cis-Retinoic Acid and Interferon- $\alpha$ -2a in Patients with Advanced Esophageal Carcinoma Peter C. Enzinger, David H. Ilson, Leonard B. Saltz, Lisa K. Martin, and David P. Kelsen The combination of interferon- $\alpha$ -2a and 13-cis-retinoic acid previously has been shown to have antitumor activity in squamous cell carcinoma. A Phase II trial of this combination in patients with esophageal squamous cell carcinoma and adenocarcinoma did not reveal any significant antitumor activity.	1213
Colon (C18.9)	
Iodine-125 Brachytherapy in the Treatment of Colorectal Adenocarcinoma Metastatic to the Liver Rafael Martinez-Monge, Subir Nag, Carol A. Nieroda, and Edward W. Martin Iodine-125 brachytherapy can be recommended for patients with unresectable or incompletely resected solitary liver metastases from colorectal adenocarcinoma.	1218
Anus (C21.0)	
Overexpression of p53 Protein and Outcome of Patients Treated with Chemoradiation for Carcinoma of the Anal Canal: A Report of Randomized Trial RTOG 87-04 Steven R. Bonin, Thomas F. Pajak, Anthony H. Russell, Lawrence R. Coia, Kristie J. Paris, Marshall S. Flam, and Ed R. Sauter This randomized study suggests that the p53 staining pattern may have prognostic significance for patients treated with chemoradiation for carcinoma of the anal canal. More aggressive treatment may overcome this detrimental effect.	1226
Liver (C22.0)	
Expression of the MAGE Gene Family in Human Hepatocellular Carcinoma Kouichirou Tahara, Masaki Mori, Noriaki Sadanaga, Yoshihiro Sakamoto, Seigo Kitano, and Masatoshi Makuuchi MAGE gene expression is frequent in hepatocellular carcinoma (HCC), suggesting that HCC may be a good candidate for MAGE specific immunotherapy.	1234
Ampulla of Vater (C24.1)	
Carcinoid Tumors of the Ampulla of Vater: A Comparison with Duodenal Carcinoid	1241

<p>Tumors</p> <p>Hala R. Makhlof, Allen P. Burke, and Leslie H. Sobin</p> <p>Carcinoid tumors of the ampulla differ clinically, histologically, and immunohistochemically from carcinoid tumors elsewhere in the duodenum.</p>	
<p>Pancreas (C25.9)</p>	
<p>Loss of p27Kip1 Expression Independently Predicts Poor Prognosis for Patients with Resectable Pancreatic Adenocarcinoma</p> <p>Cai-De Lu, Shinsho Morita, Takashi Ishibashi, Hitoshi Hara, Hiroshi Isozaki, and Nobuhiko Tanigawa</p> <p>As a universal cyclin-dependent kinase inhibitor, p27Kip1 expression was reduced drastically in patients with pancreatic adenocarcinoma. Patients with resectable tumors displaying &gt;1% p27Kip1 positive tumor cells survived significantly longer than those with p27Kip1 negative tumors.</p>	1250
<p>An Investigational New Drug Treatment Program for Patients with Gemcitabine: Results for Over 3000 Patients with Pancreatic Carcinoma</p> <p>Anna Maria Storniolo, Nathan H. Enas, Cheryl A. Brown, Maurizio Voi, Mace L. Rothenberg, and Richard Schilsky</p> <p>In this series (which, to the authors' knowledge, was the largest series of pancreatic carcinoma patients ever presented in a typical clinical setting), notable disease-related symptom improvement and survival were demonstrated with gemcitabine, and these findings support those of earlier registration trials.</p>	1261
<p>Lung (C34.9)</p>	
<p>Phase I/II Trial of Paclitaxel by 1-Hour Infusion, Carboplatin, and Gemcitabine in the Treatment of Patients with Advanced Nonsmall Cell Lung Carcinoma</p> <p>John D. Hainsworth, Howard A. Burris III, Joan B. Erland, Lisa H. Morrissey, Anthony A. Meluch, Leonard A. Kalman, Jeremy K. Hon, Daniel C. Scullin, Jr., Steven W. Smith, and F. Anthony Greco</p> <p>In this Phase I/II trial, a third active drug, gemcitabine, was added to a standard paclitaxel/carboplatin regimen for the treatment of patients with advanced nonsmall cell lung carcinoma. This regimen was feasible and active, with a 44% response rate and actuarial 45% 1-year survival in a multicenter study.</p>	1269
<p>Breast (C50.9)</p>	
<p>Estrogen Replacement Therapy in Women with a History of Proliferative Breast Disease</p> <p>William D. Dupont, David L. Page, Fritz F. Parl, W. Dale Plummer, Jr., Peggy A. Schuyler, Masako Kasami, and Roy A. Jensen</p> <p>Estrogen replacement therapy does not significantly elevate the risk of invasive breast carcinoma in women with a history of different types of histologically defined benign breast disease. This therapy is not contraindicated in these women.</p>	1277
<p>A Randomized Trial of Tamoxifen Alone or Combined with Octreotide in the Treatment of Women with Metastatic Breast Carcinoma</p> <p>James N. Ingle, Vera J. Suman, Carl G. Kardinal, James E. Krook, James A. Mailliard, Michael H. Veeder, Charles L. Loprinzi, Robert J. Dalton, Lynn C. Hartmann, Cheryl A. Conover, and Michael N. Pollak</p> <p>A randomized trial of tamoxifen alone or combined with octreotide revealed no</p>	1284

indication that the combination was substantially more efficacious in the treatment of postmenopausal women with metastatic breast carcinoma.	
Prostate (C61.9)	
<p>p53 Protein Overexpression Is Associated with Increased Cell Proliferation in Patients with Locally Recurrent Prostate Carcinoma after Radiation Therapy Liang Cheng, Thomas J. Sebo, John C. Cheville, Thomas M. Pisansky, Jeff Slezak, Erik J. Bergstralh, Anna Pacelli, Roxann M. Neumann, Horst Zincke, and David G. Bostwick</p> <p>Patients selected for salvage prostatectomy had recurrent prostate carcinoma that remained biologically aggressive after radiation therapy. Increased p53 nuclear accumulation correlated with cellular proliferative activity, both of which were found in a high proportion of study patients.</p>	1293
<p>Predictors of Cancer Progression in T1a Prostate Adenocarcinoma Liang Cheng, Erik J. Bergstralh, Beth G. Scherer, Roxann M. Neumann, Michael L. Blute, Horst Zincke, and David G. Bostwick</p> <p>The clinical course of patients with T1a prostate adenocarcinoma is variable. If left untreated, a small but significant proportion of patients are at risk for cancer progression and death. Patients with a transurethral resection tissue weight <math>\geq 30</math> g have an excellent prognosis and can be managed conservatively.</p>	1300
<p>Demographics, Family Histories, and Psychological Characteristics of Prostate Carcinoma Screening Participants Kathryn L. Taylor, Joanne DiPlacido, William H. Redd, Karen Faccenda, Linda Greer, and Aaron Perlmutter</p> <p>Among a sample of men seeking prostate carcinoma screening, the authors investigated the association of family history of prostate carcinoma with 1) the reasons men seek screening, and 2) their levels of psychological distress and perceived risk. The findings suggested that self-referral was the most common reason for seeking screening. Perceived risk for prostate carcinoma was higher among men with a family history, and psychological distress was greater among men with a family history only among those who also reported elevated perceived risk.</p>	1305
Testis (C62.9)	
<p>Short Term Pretreatment with Medroxyprogesterone and Testosterone May Potentiate Irradiation Damage to Spermatogenesis in Rats Samira Es-slami, Sébastien Charcellay, Ghislaine Pinon-Lataillade, and Jean-Claude Soufir</p> <p>It has been claimed that a short period of steroid pretreatment protects the testis from irradiation damage. However, we show here that this pretreatment may exacerbate the effects of irradiation on germ cells, especially the survival and genomic alteration of stem cells.</p>	1313
<p>Expression of Vascular Endothelial Growth Factor in Patients with Testicular Germ Cell Tumors as an Indicator of Metastatic Disease Souichirou Fukuda, Tsutomu Shirahama, Yoshiharu Imazono, Tomoyasu Tsushima, Hiroyuki Ohmori, Tsuneyoshi Kayajima, Saburo Take, Kenryu Nishiyama, Suguru Yonezawa, Suminori Akiba, Shin-ichi Akiyama, and Yoshitada Ohi</p> <p>Expression of vascular endothelial growth factor is a hallmark of testicular germ cell</p>	1323

tumor development, and is related to angiogenesis and metastatic disease.	
<p>Resection of Small, Residual Retroperitoneal Masses after Chemotherapy for Nonseminomatous Testicular Cancer: A Decision Analysis</p> <p>Ewout W. Steyerberg, Phillip B. Marshall, H. Jan Keizer, and J. Dik F. Habbema</p> <p>According to a decision analysis model, surgical resection resulted in a greater survival benefit than observation for patients with small, retroperitoneal residual masses after chemotherapy for metastatic, nonseminomatous testicular cancer. The benefit, however, depended on clinical characteristics and the prognosis of unresected residual malignancy, which supports an individualized approach to decision-making regarding resection.</p>	1331
Urinary System (C68.9)	
<p>Unusual Clinical Presentation of Upper Urothelial Carcinoma in Taiwan</p> <p>Yii-Her Chou and Chun-Hsiung Huang</p> <p>The gender incidence (showing a slight female predominance) and ratio of renal pelvic transitional cell carcinoma to all renal carcinomas (40%) were found to be different in Taiwan in contrast to the majority of other reports.</p>	1342
Thyroid (C73.9)	
<p>Unusual Features of Thyroid Carcinomas in Japanese Patients with Werner Syndrome and Possible Genotype-Phenotype Relations to Cell Type and Race</p> <p>Yuichi Ishikawa, Haruo Sugano, Takehisa Matsumoto, Yasuhiro Furuichi, Robert W. Miller, and Makoto Goto</p> <p>Thyroid carcinomas in Japanese patients with Werner syndrome, as compared with those in the general Japanese population, were more often follicular in type, were associated with less female predominance, and occurred at a younger age. The increase only among Japanese may be due to a different mutational spectrum than that in whites with the syndrome.</p>	1345
Lymph Node (C77.9)	
<p>A Case-Control Study of Non-Hodgkin Lymphoma and Exposure to Pesticides</p> <p>Lennart Hardell and Mikael Eriksson</p> <p>In this case-control study on non-Hodgkin lymphoma (NHL), increased risk was found for subjects exposed to herbicides and fungicides. The herbicide 4-chloro-2-methyl phenoxyacetic acid was significantly associated with NHL. For several categories of herbicides, it was noted that only exposure during the most recent decades before diagnosis of NHL was associated with an increased risk of NHL.</p>	1353
<p>Outcome of Advanced Stage Low Grade Follicular Lymphomas in a Population-Based Retrospective Cohort</p> <p>Lori A. Wood, Robert W. Coupland, Scott A. North, and Martin C. Palmer</p> <p>To the authors' knowledge this is the first study to describe the outcome of patients with advanced stage follicular lymphoma in a population-based cohort. The median overall survival of 5.9 years offers a less positive perspective on the outcome of these patients than in previous nonpopulation-based reports.</p>	1361
GENERAL TOPIC CALCIUM CHANNEL BLOCKER AND CANCER RISK	
<p>Incidence of Cancer in Postmyocardial Infarction Patients Treated with Short-Acting Nifedipine and Diltiazem</p> <p>Ken Kanamasa, Akio Kimura, Masaru Miyataka, Toshihiko Takenaka, and Kinji</p>	1369

Ishikawa, on behalf of the Secondary Prevention Group The incidence of cancer was found to be slightly higher in patients receiving nifedipine compared with patients who were not receiving a calcium antagonist, but the increase was not statistically significant.	
<b>COMPLICATIONS OF THERAPY: INTERFERON CARDIOTOXICITY</b>	
The Effect of Interferon on Mouse Myocardial Capillaries: An Ultrastructural Study Hertzel Salman, Michael Bergman, Hanna Bessler, Svetlana Alexandrova, and Meir Djaldetti Two groups of mice treated with interferon- $\alpha$ -2a at a dose of 400 U per g of body weight for 3 and 5 months, respectively, showed significantly increased thickness of their myocardial capillary walls. The observed subsequent decrease in the size of the myocardial lumen may serve as one explanation for the cardiac complications observed in patients treated with interferon.	1375
<b>PEDIATRIC ONCOLOGY</b>	
Parental Cigarette Smoking and the Risk of Acute Leukemia in Children Jack Brondum, Xiao-Ou Shu, Michael Steinbuch, Richard K. Severson, John D. Potter, and Leslie L. Robison In two large case-control studies, no association was found between paternal or maternal cigarette smoking and risk of acute myeloid leukemia or acute lymphocytic leukemia in children.	1380
Genomic Imprinting of H19 and Insulin-Like Growth Factor-2 in Pediatric Germ Cell Tumors Julie A. Ross, Peter T. Schmidt, John P. Perentesis, and Stella M. Davies The authors found variable patterns of imprinting of H19 and insulin-like growth factor-2 in pediatric tumors of ovarian and extragonadal origin, whereas loss of imprinting of both genes occurred in tumors of testicular origin. This may indicate differences in the timing of carcinogenesis in germ cells at these sites.	1389
Induction Failure in Acute Lymphoblastic Leukemia of Childhood Lewis B. Silverman, Richard D. Gelber, Mary L. Young, Virginia Kimball Dalton, Ronald D. Barr, and Stephen E. Sallan There is variability regarding the precise definition of induction failure in acute lymphoblastic leukemia of childhood. The results of the current study demonstrate that patients with persistent leukemia at the end of 1 month of induction therapy have a dismal prognosis, regardless of when they subsequently achieve remission.	1395
<b>COMMUNICATION</b>	
The International Union Against Cancer (UICC) TNM/Prognostic Factors Project Committee	
Frequently Asked Questions regarding the Application of the TNM Classification Leslie H. Sobin This communication from the International Union Against Cancer (UICC) TNM/Prognostic Factors Project Committee answers some questions that are frequently asked on the organization's Internet TNM "helpdesk."	1405
Thanks to Authors and Peer Reviewers	1407