#15#

Revisiones (todas) * Reviews (all)**

Cancer Pharmacogenomics.

Agosto - Septiembre 2013 / August - September 2013

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[1]

TÍTULO / TITLE: - Tumor necrosis factor inhibitors for inflammatory bowel disease.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - N Engl J Med. 2013 Aug 22;369(8):754-62. doi: 10.1056/NEJMct1209614.

●● Enlace al texto completo (gratuito o de pago) 1056/NEJMct1209614

AUTORES / AUTHORS: - Nielsen OH; Ainsworth MA

INSTITUCIÓN / INSTITUTION: - Department of Gastroenterology, Medical Section, Herlev Hospital, Faculty of Health and Medical Sciences, University of Copenhagen, Herlev, Denmark. ohn@dadlnet.dk

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[2]

TÍTULO / TITLE: - Antibody therapeutics in cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Science. 2013 Sep 13;341(6151):1192-8. doi: 10.1126/science.1241145.

●● Enlace al texto completo (gratuito o de pago) 1126/science.1241145

AUTORES / AUTHORS: - Sliwkowski MX; Mellman I

INSTITUCIÓN / INSTITUTION: - Genentech, Incorporated, 1 DNA Way, South San Francisco, CA 94080, USA. marks@gene.com

RESUMEN / SUMMARY: - In a relatively short period of time, monoclonal antibodies have entered the mainstream of cancer therapy. Their first use was as antagonists of oncogenic receptor tyrosine kinases, but today monoclonal antibodies have emerged as long-sought vehicles for

the targeted delivery of potent chemotherapeutic agents and as powerful tools to manipulate anticancer immune responses. With ever more promising results from the clinic, the future will likely see continued growth in the discovery and development of therapeutic antibodies and their derivatives.

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[3]

TÍTULO / TITLE: - NOX4 mediates cytoprotective autophagy induced by the EGFR inhibitor erlotinib in head and neck cancer cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Toxicol Appl Pharmacol. 2013 Jul 31;272(3):736-745. doi: 10.1016/j.taap.2013.07.013.

●● Enlace al texto completo (gratuito o de pago) 1016/j.taap.2013.07.013

AUTORES / AUTHORS: - Sobhakumari A; Schickling BM; Love-Homan L; Raeburn A; Fletcher EV; Case AJ; Domann FE; Miller FJ Jr; Simons AL

INSTITUCIÓN / INSTITUTION: - Interdisciplinary Graduate Program in Human Toxicology, The University of Iowa, Iowa City, IA, USA; Department of Pathology, The University of Iowa, Iowa City, IA, USA.

RESUMEN / SUMMARY: - Most head and neck squamous cell carcinomas (HNSCCs) overexpress epidermal growth factor receptor (EGFR) and EGFR inhibitors are routinely used in the treatment of HNSCC. However, many HNSCC tumors do not respond or become refractory to EGFR inhibitors. Autophagy, which is a stress-induced cellular self-degradation process, has been reported to reduce the efficacy of chemotherapy in various disease models. The purpose of this study is to determine if the efficacy of the EGFR inhibitor erlotinib is reduced by activation of autophagy via NOX4-mediated oxidative stress in HNSCC cells. Erlotinib induced the expression of the autophagy marker LC3B-II and autophagosome formation in FaDu and Cal-27 cells. Inhibition of autophagy by chloroquine and knockdown of autophagy pathway genes Beclin-1 and Atg5 sensitized both cell lines to erlotinib-induced cytotoxicity, suggesting that autophagy may serve as a protective mechanism. Treatment with catalase (CAT) and diphenylene iodonium (DPI) in the presence of erlotinib suppressed the increase in LC3B-II expression in FaDu and Cal-27 cells. Erlotinib increased NOX4 mRNA and protein expression by increasing its promoter activity and mRNA stability in FaDu cells. Knockdown of NOX4 using adenoviral siNOX4 partially suppressed erlotinib-induced LC3B-II expression, while overexpression of NOX4 increased expression of LC3B-II. These studies suggest that erlotinib may activate autophagy in HNSCC cells as a pro-survival mechanism, and NOX4 may play a role in mediating this effect.

TÍTULO / TITLE: - The expression of aldehyde dehydrogenase 1 in invasive primary breast tumors and axillary lymph node metastases is associated with poor clinical prognosis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Pathol Res Pract. 2013 Sep;209(9):555-61. doi: 10.1016/j.prp.2013.05.007. Epub 2013 Jun 14.

●● Enlace al texto completo (gratuito o de pago) 1016/j.prp.2013.05.007

AUTORES / AUTHORS: - Dong Y; Bi LR; Xu N; Yang HM; Zhang HT; Ding Y; Shi AP; Fan ZM

INSTITUCIÓN / INSTITUTION: - Department of Breast Surgery, First Hospital of Jilin University, Changchun, China.

RESUMEN / SUMMARY: - The enzyme aldehyde dehydrogenase 1 (ALDH1) has been reported as a biomarker for identifying cancer stem cells. Previous studies have shown that ALDH1 expression in primary breast cancers was associated with poor clinical prognosis. In this study, we aimed to determine whether ALDH1 expression in axillary lymph node metastases (ALNM) of breast cancer patients was also associated with poor prognosis. Expression of ALDH1, ER, PgR, HER2 and KI-67 was examined in primary tumors and ALNM of 161 patients with invasive breast cancer. Survival analysis and multivariate analysis were used to determine the relationship between ALDH1 expression and clinical prognosis. Patients with positive ALDH1 expression in primary tumors and in ALNM had significantly shorter relapse-free survival (RFS) times and overall survival (OS) times compared to those whose tissues were ALDH1 negative. ALDH1-positivity in primary tumors was significant both in univariate and multivariate analyses of RFS and OS. ALDH1 expression in ALNM was significant in a univariate analysis of RFS and OS but not in a multivariate analysis of RFS and OS. We conclude that the expression of ALDH1 in primary breast tumors or ALNM may be one potential risk factor for poor, long-term outcomes.

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[4]

TÍTULO / TITLE: - Overall survival for sorafenib plus interleukin-2 compared with sorafenib alone in metastatic renal cell carcinoma (mRCC): final results of the ROSORC trial.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Ann Oncol. 2013 Sep 24.

●● Enlace al texto completo (gratuito o de pago) 1093/annonc/mdt375

AUTORES / AUTHORS: - Procopio G; Verzoni E; Bracarda S; Ricci S; Sacco C; Ridolfi L; Porta C; Miceli R; Zilembo N; Bajetta E

INSTITUCIÓN / INSTITUTION: - Department of Medical Oncology, Unit 1, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan.

RESUMEN / SUMMARY: - BACKGROUND: The ROSORC trial, a randomised, phase II trial comparing sorafenib plus interleukin (IL-2) versus sorafenib alone as first-line treatment of metastatic renal cell carcinoma (mRCC) failed to demonstrate differences in progression-free survival (PFS). Updated overall survival (OS) results are reported. PATIENTS AND METHODS: In this study, 128 patients were randomised to receive sorafenib 400 mg twice daily plus subcutaneous IL-2 4.5 million international units (MIU) five times per week for 6 weeks every 8 weeks (arm A) or sorafenib alone (arm B). OS was estimated with the Kaplan-Meier method and compared with the two-sided log-rank test. RESULTS: After a median follow-up of 58

months (interquartile range: 28-63 months), the median OS was 38 and 33 months in arms A and B, respectively (P = 0.667). The 5-year OS was 26.3% [95% confidence interval (CI) 15.9-43.5) and 23.1% (95% CI 13.2-40.5) for the combination- and single-agent arm, respectively. Most of the patients who were refractory to first-line treatment were subsequently treated with different targeted agents; they had a median survival greater than expected. CONCLUSIONS: This outcome suggests a synergistic effect of the subsequent therapies following sorafenib failure. CLINICALTRIALS.GOV IDENTIFIER: NCT00609401.

TÍTULO / TITLE: - Activity ex vivo of cytotoxic drugs in patient samples of peritoneal carcinomatosis with special focus on colorectal cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - BMC Cancer. 2013 Sep 24;13(1):435.

●● Enlace al texto completo (gratuito o de pago) 1186/1471-2407-13-435

AUTORES / AUTHORS: - Mahteme H; Graf W; Karlsson H; Larsson R; Nygren P

RESUMEN / SUMMARY: - BACKGROUND: The optimal choice of cytotoxic drugs for intraperitoneal chemotherapy (IPC) in conjunction with cytoreductive surgery (CRS) for treatment of peritoneal carcinomatosis (PC) is poorly defined. We investigated drug sensitivity ex vivo in patient samples of various PC tumor types and correlated clinical outcome to drug sensitivity within the subset of PC from colorectal cancer (CRC). METHODS: PC tissue samples (n = 174) from mesothelioma, pseudomyxoma peritonei (PMP), ovarian cancer, CRC or appendix cancer were analyzed ex vivo for sensitivity to oxaliplatin, cisplatin, mitomycin C, melphalan, irinotecan, docetaxel, doxorubicin and 5-FU. Clinicopathological variables and outcome data were collected for the CRC subset. RESULTS: Mesothelioma and ovarian cancer were generally more drug sensitive than CRC, appendix cancer and PMP. Oxaliplatin showed the most favorable ratio between achievable IPC concentration and ex vivo drug sensitivity. Drug sensitivity in CRC varied considerably between individual samples. Ex vivo drug sensitivity did not obviously correlate to time-to-progression (TTP) in individual patients. CONCLUSIONS: Drug-sensitivity varies considerably between PC diagnoses and individual patients arguing for individualized therapy in IPC rather than standard diagnosis-specific therapy. However, in the current paradigm of treatment according to diagnosis, oxaliplatin is seemingly the preferred drug for IPC from a drug sensitivity and concentration perspective. In the CRC subset, analysis of correlation between ex vivo drug sensitivity and TTP was inconclusive due to the heterogeneous nature of the data.

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[5]

TÍTULO / TITLE: - The role of vascular epithelial growth factor receptor-tyrosine kinase inhibitors in the treatment of advanced breast cancer: a meta-analysis of 12 randomized controlled trials.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Curr Med Res Opin. 2013 Sep 23.

●● Enlace al texto completo (gratuito o de pago) 1185/03007995.2013.836080

AUTORES / AUTHORS: - Li J; Huang S; Zheng W; Ding H; Zhang Y; Huang S; Zhang Z; Chen B; Liang Z; He G; Xiao X; Li S; Xu T; Chen X

INSTITUCIÓN / INSTITUTION: - Department of Breast Surgery, Affiliated Hospital of Guangdong Medical College , Zhanjiang, Guangdong , China.

RESUMEN / SUMMARY: - Abstract Aim: To perform a systematic review and meta-analysis of randomized controlled trials to determine the efficacy and toxicity of approved vascular epithelial growth factor receptor-tyrosine kinase inhibitors (VEGFR-TKIs) in advanced breast cancer. Methods: A comprehensive literature search for studies published up to August 2013 was performed. The endpoints were overall survival (OS), progression-free survival (PFS), overall response rate (ORR) and grade 3 or 4 adverse event (AEs). The pooled hazard ratio (HR) or relative risk (RR), and 95% confidence intervals (CI) were calculated employing fixed- or random-effects models depending on the heterogeneity of the included trials. Results: Twelve randomized controlled trials involved 3256 patients were ultimately identified. The intention to treatment (ITT) analysis demonstrated that VEGFR-TKI therapy significantly improved ORR (RR 1.14, 95% CI: 1.03-1.28, p = 0.016), but it did not translate into benefits in PFS (HR 0.99, 95% CI: 0.81-1.22, p = 0.93) and OS (HR 1.11, 95% CI 0.99-1.24, p = 0.084) when compared to non-VEGFR-TKI therapy. Additionally, a higher incidence of grade 3 or 4 anemia, neutropenia, thrombocytopenia, diarrhea, hand-foot syndrome and fatigue was observed in VEGFR-TKI-based therapy. Conclusions: The VEGFR-TKI-based therapy offered a significant improvement in ORR in patients with advanced breast cancer but did not benefit PFS and OS. With present available data from randomized clinical trials, we were still unable to clearly set the role of VEGFR-TKIs in the treatment of metastatic breast cancer (MBC).

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[6]

TÍTULO / TITLE: - A systematic review and meta-analysis of adjuvant interferon therapy after curative treatment for patients with viral hepatitis-related hepatocellular carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Viral Hepat. 2013 Oct;20(10):729-43. doi: 10.1111/jvh.12096. Epub 2013 Apr 16.

●● Enlace al texto completo (gratuito o de pago) 1111/jvh.12096

AUTORES / AUTHORS: - Huang TS; Shyu YC; Chen HY; Yuan SS; Shih JN; Chen PJ

INSTITUCIÓN / INSTITUTION: - Department of General Surgery, Chang Gung Memorial Hospital, Keelung, Taiwan; Graduate Institute of Clinical Medicine, National Taiwan University College of Medicine, Taipei, Taiwan.

RESUMEN / SUMMARY: - The efficacy of adjuvant interferon treatment for the management of patients with viral hepatitis-related hepatocellular carcinoma (HCC) following curative treatment is controversial. We have conducted a systematic review with meta-analysis to assess the effects of adjuvant interferon therapy on survival outcomes. Randomized and nonrandomized studies (NRSs) comparing adjuvant interferon treatment with the standard of

care for viral hepatitis-related HCC after curative treatment were included. CENTRAL, Medline, EMBASE and the Science Citation Index were searched with complementary manual searches. The primary outcomes were recurrence-free survival (RFS) and overall survival (OS). Nine randomized trials and 13 NRSs were included in the meta-analysis. These nine randomized trials included 942 participants, of whom, 490 were randomized to the adjuvant interferon treatment group and 452 to the control group. The results of meta-analysis showed unexplained heterogeneity for both RFS and OS. The 13 NRSs included 2214 participants, of whom, 493 were assigned to the adjuvant interferon treatment group and 1721 to the control group. The results of meta-analysis showed that, compared with controls, adjuvant interferon treatment significantly improved the RFS [hazard ratio (HR) 0.66, 95% confidence interval (CI) 0.52-0.84, I(2) = 29%] and OS (HR 0.43, 95% CI 0.34-0.56, I(2) = 0%) of patients with hepatitis C virus-related HCC following curative treatment. There was little evidence for beneficial effects on patients with hepatitis B virus-related HCC. Future research should be aimed at clarifying whether the effects of adjuvant interferon therapy are more prominent in hepatitis C patients with sustained virological responses.

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[7]

TÍTULO / TITLE: - The Bcl-2 homology 3 (BH3)-only proteins Bim and Bid are functionally active and restrained by anti-apoptotic B-cell CLL/lymphoma 2 (Bcl-2) family proteins in healthy liver.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Biol Chem. 2013 Aug 28.

●● Enlace al texto completo (gratuito o de pago) 1074/jbc.M112.443093

AUTORES / AUTHORS: - Kodama T; Hikita H; Kawaguchi T; Saito Y; Tanaka S; Shigekawa M; Shimizu S; Li W; Miyagi T; Kanto T; Hiramatsu N; Tatsumi T; Takehara T

INSTITUCIÓN / INSTITUTION: - Osaka University Graduate School of Medicine, Japan.

RESUMEN / SUMMARY: - Background and Aim: An intrinsic pathway of apoptosis is regulated by the B-cell lymphoma-2 (Bcl-2) family proteins. We previously reported that a fine rheostatic balance between the anti- and pro-apoptotic multi-domain Bcl-2 family proteins controls hepatocyte apoptosis in the healthy liver. The Bcl-2 homology domain 3 (BH3)-only proteins set this rheostatic balance toward apoptosis upon activation in the diseased liver. However, their involvement in healthy Bcl-2 rheostasis remains unknown. In the present study, we focused on two BH3-only proteins, Bim and Bid, and we clarified the Bcl-2 network that governs hepatocyte life and death in the healthy liver. Methods: We generated hepatocyte-specific Bcl-xL- or Mcl-1-knockout mice, with or without disrupting Bim and/or Bid, and we examined hepatocyte apoptosis under physiological conditions. We also examined the effect of both Bid and Bim disruption on the hepatocyte apoptosis caused by the inhibition of Bcl-xL and Mcl-1. Results: Spontaneous hepatocyte apoptosis in Bcl-xL- or Mcl-1-knockout mice was significantly ameliorated by Bim deletion. The disruption of both Bim and Bid completely prevented hepatocyte apoptosis in Bcl-xL-knockout mice and weakened massive hepatocyte

apoptosis via the additional in vivo knockdown of mcl-1 in these mice. Finally, the hepatocyte apoptosis caused by ABT-737, which is a Bcl-xL/Bcl-2/Bcl-w inhibitor, was completely prevented in Bim/Bid double knockout mice. Conclusion: The BH3-only proteins Bim and Bid are functionally active but are restrained by the anti-apoptotic Bcl-2 family proteins under physiological conditions. Hepatocyte integrity is maintained by the dynamic and well-orchestrated Bcl-2 network in the healthy liver.

TÍTULO / TITLE: - Markers of angiogenesis (CD31, CD34, rCBV) and their prognostic value in low-grade gliomas.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Neurol Neurochir Pol. 2013 Jul-Aug;47(4):325-31.

AUTORES / AUTHORS: - Majchrzak K; Kaspera W; Szymas J; Bobek-Billewicz B; Hebda A; Majchrzak H

INSTITUCIÓN / INSTITUTION: - Katedra i Oddzial Kliniczny Neurochirurgii, Sosnowiec. wkaspera@wp.pl

RESUMEN / SUMMARY: - BACKGROUND AND PURPOSE: Antigens CD31 and CD34 and relative cerebral blood volume (rCBV) in gliomas reflect in different ways neoangiogenesis of the tumour. Thus, we decided: (1) to estimate the correlation between the values of CD31 and CD34 and the value of rCBV in low-grade gliomas (LGG), and (2) to establish the prognostic value of these markers. MATERIAL AND METHODS: The investigated group consisted of 53 patients with LGG who were operated on in the Neurosurgical Department at Sosnowiec between 2005 and 2011. On the basis of perfusion-weighted imaging (PWI-MRI) in the tumour texture, rCBV was calculated. The values of CD31 and CD34 were estimated on the basis of immunohistochemical investigation. Three outcome measures were assessed: (1) overall survival, (2) progression-free survival, and (3) malignant-free survival. Statistical analyses were done using the STATISTICA 9.0 program. RESULTS: Higher value of rCBV in the texture of LGG significantly correlated with higher CD31 ($p = 0.0006$) and CD34 values ($p = 0.0043$). Progression-free survival was significantly longer in patients with rCBV < 1.75 than for persons with rCBV > 1.75 ($p = 0.015$). Lower expression of CD31 correlated with probability of longer survival of the patients after the operation of LGG ($p = 0.068$). CONCLUSIONS: Density of microvessels as assessed immunohistochemically with CD31+ and CD34+ in LGG correlated with the value of rCBV in the tumour. The value of 1.75 for rCBV may be the threshold for better or poorer outcome of these patients. Expression of CD31 antigen is an important prognostic factor for the time of survival for patients with LGG.

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[8]

TÍTULO / TITLE: - Prognostic value of epidermal growth factor receptor in patients with gastric cancer: A meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Gene. 2013 Oct 15;529(1):69-72. doi: 10.1016/j.gene.2013.07.106. Epub 2013 Aug 13.

●● Enlace al texto completo (gratuito o de pago) 1016/j.gene.2013.07.106

AUTORES / AUTHORS: - Hong L; Han Y; Yang J; Zhang H; Jin Y; Brain L; Li M; Zhao Q

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Cancer Biology, Xijing Hospital of Digestive Diseases, Xijing Hospital, Fourth Military Medical University, Xi'an, 710032 Shaanxi Province, China. Electronic address: hongliu180@126.com.

RESUMEN / SUMMARY: - BACKGROUND: The epidermal growth factor receptor (EGFR) plays important roles in the development of gastric cancer. This study aims to analyze the prognostic value of EGFR in patients with gastric cancer. METHODS: A meta-analysis is performed by searching Cochrane Library, PubMed, EMBASE and Science Direct databases from Jan 1970 to May 2013. Data are extracted from studies evaluating the survival of gastric cancer patients with either positive or negative EGFR expression. Pooled hazard ratios (HRs) and 95% confidence intervals (CIs) are calculated. RESULTS: Totally 1600 cases of gastric cancer patients from five studies are subjected to final analysis. The HR of post-operational survival of patients with positive EGFR expression is 1.16 (95% CI: 0.94-1.43) as compared with those with negative expression, indicating that positive EGFR expression does not significantly predict the poor survival of gastric cancer. CONCLUSIONS: EGFR expression is not an independent predictor for the survival of gastric cancer patients.

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[9]

TÍTULO / TITLE: - Predictive effect of XRCC3 Thr241Met polymorphism on platinum-based chemotherapy in lung cancer patients: meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Tumour Biol. 2013 Aug 30.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-0987-5

AUTORES / AUTHORS: - Zhang W; Yan B; Jiang L

INSTITUCIÓN / INSTITUTION: - Department of Pulmonary Medicine, Shanghai Chest Hospital, Shanghai Jiaotong University, 241 West Huaihai Road, Shanghai, 200030, China.

RESUMEN / SUMMARY: - Previous published data on the association between X-ray repair cross-complementing group 3 (XRCC3) Thr241Met polymorphism and clinical outcome of platinum-based chemotherapy in patients with lung cancer reported conflicting results. A meta-analysis was performed to provide a systematic review of the published data. We retrieved the relevant studies from PubMed and Embase databases. The primary outcome was overall survival, and the hazard ratio (HR) with 95 % confidence interval (95 % CI) was estimated. Seven studies with a total of 1,514 patients were included into the meta-analysis. Overall, XRCC3 Thr241Met polymorphism had no influence on the overall survival of lung cancer patients receiving platinum-based chemotherapy (MetMet vs. ThrThr: HR = 0.82, 95 % CI 0.52-1.31, P = 0.410; MetThr vs. ThrThr: HR = 0.93, 95 % CI 0.79-1.10, P = 0.339; MetMet/MetThr vs. ThrThr: HR = 1.07, 95 % CI 0.88-1.31, P = 0.480). There was no obvious risk of publication

bias. Therefore, currently available data suggest that there is no predictive effect of XRCC3 Thr241Met polymorphism on platinum-based chemotherapy in lung cancer patients.

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[10]

TÍTULO / TITLE: - Responsiveness of neoadjuvant chemotherapy before surgery predicts favorable prognosis for cervical cancer patients: a meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Cancer Res Clin Oncol. 2013 Sep 11.

●● Enlace al texto completo (gratuito o de pago) 1007/s00432-013-1509-y

AUTORES / AUTHORS: - Ye Q; Yuan HX; Chen HL

INSTITUCIÓN / INSTITUTION: - Department of Obstetrics and Gynecology, Affiliated Hospital of Nantong University, Xi Si Road 20#, Nantong City, 226001, Jiangsu Province, People's Republic of China, pphss@126.com.

RESUMEN / SUMMARY: - BACKGROUND: Neoadjuvant chemotherapy (NAC) before surgery has already shown the therapy effectiveness in patients with cervical cancer. The present meta-analysis was conducted to determine whether the response to NAC predicts for prognosis. METHODS: Systematic computerized searches of the PubMed and Web of Knowledge were performed. Prognosis outcomes included progression-free survival (PFS), and overall survival (OS). The pooled odd ratio (OR) was estimated by using fixed-effect model or random-effect model according to heterogeneity between studies. RESULTS: Eighteen studies with 1,785 patients were included. Cisplatin-based NAC treatments were most commonly used. The clinical response rate ranged from 48.4 to 93.0 %, and the pathological response rate ranged from 27.6 to 30.6 %. The pooled ORs estimating the association of PFS with NAC response were 5.707 (95 % CI 3.564-9.137), 6.798 (95 % CI 4.716-9.799), 6.327 (95 % CI 4.398-9.102), and 5.214 (95 % CI 3.748-7.253) at 1-, 2-, 3-, and 5-year follow-up, respectively, and the pooled ORs estimating the association of OS with NAC response were 6.179 (95 % CI 3.390-11.264), 9.155 (95 % CI 5.759-14.555), 8.431 (95 % CI 5.667-12.543), and 5.785 (95 % CI 4.124-8.115) at 1-, 2-, 3-, and 5-year follow-up, respectively. No obvious statistical heterogeneity was detected. Funnel plots and Egger's tests did not reveal publication bias. Sensitivity analysis showed the results of meta-analysis were robust. CONCLUSION: This meta-analysis confirms that response to NAC is an indicator for PFS and OS, and suggests that patients-achieving response of NAC before surgery predicts favorable prognosis for cervical cancer patients.

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[11]

TÍTULO / TITLE: - Tumor necrosis factor alpha inhibitors in patients with Takayasu's arteritis refractory to standard immunosuppressive treatment: cases series and review of the literature.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Clin Rheumatol. 2013 Sep 1.

●● Enlace al texto completo (gratuito o de pago) 1007/s10067-013-2380-6

AUTORES / AUTHORS: - Novikov PI; Smitienko IO; Moiseev SV

INSTITUCIÓN / INSTITUTION: - Clinic of Nephrology, Internal and Occupational Diseases, University Clinical Hospital #3, First Moscow State Medical University, Moscow, Russia.

RESUMEN / SUMMARY: - The objective of this study was to report the long-term use of tumor necrosis factor (TNF) inhibitors in case series of patients with Takayasu's arteritis refractory to standard immunosuppressive treatment. Nine women (median age of 29 years) with refractory Takayasu's arteritis were treated with TNF inhibitors. Prior to TNF inhibitor administration, all patients received standard immunosuppressive treatment for 16 to 112 months including steroids and immunomodulators. All but one patient presented with high activity of disease (median ESR 80 mm/h, C-reactive protein level 16.8 mg/l, interleukin-6 level 7.2 pg/ml) that was confirmed with positron emission tomography (PET) with 18F-deoxyglucose. Eight patients were treated with infliximab and one was treated with adalimumab, respectively. The median duration of treatment was 36 months (12 to 84 months). For induction treatment, we used infliximab 200-300 mg every 4-6 weeks and adalimumab 40 mg every 2 weeks. The treatment resulted in complete remission in five (55.6 %) patients and incomplete remission in three (33.3 %) patients. We were able to taper the dose of prednisone to </=10 mg daily in all patients. Median levels of ESR, C-reactive protein, and interleukin-6 diminished to 20 mm/h, 1.0 mg/l, and 1.0 pg/ml, respectively. Repeated PET showed lower activity of vasculitis in six (85.7 %) of seven patients. The treatment was safe and well-tolerated. Only one patient developed allergic reactions after infusions of infliximab. Four patients developed relapse of vasculitis when we tried to increase the dosing interval of infliximab to 6-8 weeks. TNF inhibitors were highly effective and safe in patients with refractory Takayasu's arteritis.

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[12]

TÍTULO / TITLE: - Expression of thymidylate synthase predicts clinical outcomes of pemetrexed-containing chemotherapy for non-small-cell lung cancer: a systemic review and meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Cancer Chemother Pharmacol. 2013 Sep 26.

●● Enlace al texto completo (gratuito o de pago) 1007/s00280-013-2299-2

AUTORES / AUTHORS: - Liu Y; Yin TJ; Zhou R; Zhou S; Fan L; Zhang RG

INSTITUCIÓN / INSTITUTION: - Department of Comprehensive Medicine, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, 1095 Jie Fang Avenue, Wuhan, 430030, People's Republic of China.

RESUMEN / SUMMARY: - PURPOSE: Observational and preclinical studies suggested an association between the expression of thymidylate synthase (TS) and clinical effects of pemetrexed-based chemotherapy in non-small-cell lung cancer (NSCLC) patients. However, the predictive value of TS for pemetrexed-containing chemotherapy regimen remained

controversial. The aim of the study was to further appraise the association between the expression of TS and clinical efficacy pemetrexed-based chemotherapy in NSCLC patients. METHODS: We searched in MEDLINE (PubMed), EMBASE, and Cochrane Library from January 1945 to May 2013. Two authors independently extracted information from the characteristics of study participants. Primary outcomes included therapeutic response (TR; i.e., complete response + partial response vs. stable disease + progressive disease), progression-free survival (PFS), and overall survival (OS). Relative risk (RR) and hazard ratio (HR) were used for evaluating the risk or hazard. RESULTS: Eight studies were included in the meta-analysis. Better response usually appeared in NSCLC patients with a lower expression of TS [RR = 2.06 95 % confidence intervals (CI) 1.44, 2.96]. There was a significant association between TS expression and outcomes of pemetrexed-based chemotherapy for NSCLC (PFS: HR = 0.63 95 % CI 0.52, 0.76; OS: HR = 0.74, 95 % CI: 0.63, 0.88). In addition, no evidence of publication bias was observed. CONCLUSIONS: This meta-analysis evaluated the predictive value of TS and provided evidence that NSCLC patients with lower TS expression could significantly benefit from pemetrexed-based chemotherapy. This increased level of TS was probably an independent risk factor of potential resistance against pemetrexed.

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[13]

TÍTULO / TITLE: - The clinical significance of Ki-67 as a marker of prognostic value and chemosensitivity prediction in hormone-receptor-positive breast cancer: a meta-analysis of the published literature.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Curr Med Res Opin. 2013 Sep 11.

●● Enlace al texto completo (gratuito o de pago) 1185/03007995.2013.833088

AUTORES / AUTHORS: - Liu Y; Yin W; Yan T; Du Y; Shao Z; Lu J

INSTITUCIÓN / INSTITUTION: - Fudan University Shanghai Cancer Center , Shanghai , China.

RESUMEN / SUMMARY: - Abstract Objectives: Hormone-receptor (HR)-positive breast cancer is associated with a poor response to adjuvant chemotherapy. Thus, it is important to identify HR-positive patients who can benefit from chemotherapy and the Ki-67 index may help to predict chemotherapy efficacy in such populations. However, controversies exist regarding the prognostic and predictive role of Ki-67 and its exact cut-off value in HR-positive patients. Therefore, we conducted this study. Methods: The meta-analysis included 4512 patients in five trials. Due to different data formats provided by studies, we classified the trials into two groups to facilitate analysis. Group 1 included the PACS01, USON 01062, and IBCSG VIII and IX trials, while Group 2 included the BCIRG001, USON 01062, and IBCSG VIII and IX trials. Results: In Group 1, Ki-67 high patients had a worse prognosis in disease-free survival (DFS) than Ki-67 low counterparts (risk ratio [RR] = 1.62, 95% confidence index [CI] = 1.36-1.94, $P < 0.001$). In Group 2, Ki-67 high patients had a better prognosis in DFS (RR = 0.53, 95% CI = 0.45-0.61, $P < 0.001$) and overall survival (OS) (RR = 0.32, 95% CI = 0.25-0.42, $P < 0.001$). In Ki-67 high patients administered anthracycline/taxane-based chemotherapy, the experimental group

(FAC --> T, AC --> TX) achieved a better DFS than the control group (FAC, AC --> T, respectively) (RR = 0.60, 95% CI = 0.39-0.90, P = 0.014). With a cut-off point >/=19%, Ki-67 high patients achieved a worse DFS (RR = 1.49, 95% CI = 1.28-1.72, P < 0.001). Conclusion: This study had limitations due to its retrospective nature and the lack of standardized Ki-67 measurement methods. Nevertheless, our findings indicate that Ki-67 high patients have a worse prognosis and may be more sensitive to anthracycline/taxane-based regimens. The ideal Ki-67 cut-off point for predicting chemosensitivity may be a certain value among a range of values >/=19% in HR-positive patients.

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[14]

TÍTULO / TITLE: - Sustained virological response and baseline predictors in HIV-HCV coinfected patients retreated with pegylated interferon and ribavirin after failing a previous interferon-based therapy: systematic review and meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - HIV Clin Trials. 2013 Jul-Aug;14(4):127-39. doi: 10.1310/hct1404-127.

●● Enlace al texto completo (gratuito o de pago) 1310/hct1404-127

AUTORES / AUTHORS: - Basso M; Parisi SG; Mengoli C; Gentilini V; Menegotto N; Monticelli J; Nicole S; Cruciani M; Palu G

INSTITUCIÓN / INSTITUTION: - Department of Molecular Medicine, University of Padova, Padova, Italy.

RESUMEN / SUMMARY: - BACKGROUND: Published data on retreatment with pegylated interferon and ribavirin of previously failing HIV-HCV coinfected patients are sparse and limited to observational study. We aimed to evaluate efficacy and pretreatment predictors. METHODS: Systematic review and meta-analysis of observational studies. The overall and genotype-related success rate was investigated. A direct comparison was performed between genotypes ¼ and 2/3 by evaluating the sustained virological response (SVR) rate ratio (RR). The effect of study level variables on the effect size was investigated by meta-regression. Variables that were analyzed included age, gender, advanced hepatic fibrosis, pretreatment of HCV RNA and CD4, and successful antiretroviral treatment (ART). RESULTS: The available evidence was from 5 open-label, cohort studies (275 patients). The overall SVR rate was 0.280 (95% CI,0.171-0.425). The SVR rate in genotype ¼ infections was 0.174 (95% CI, 0.129-0.230), and in genotype 2/3 infections it was 0.474 (95% CI, 0.286-0.670). The pooled RR comparing the SVR of genotype ¼ to 2/3 was 0.369 (95% CI, 0.239-0.568), with a decreased probability of response for genotype ¼ (P < .001). HIV RNA suppression had a significant effect on SVR (P = .005). The other covariates had no effect on the overall SVR rate. CONCLUSIONS: The overall SVR rate was 28%, consistent with the rate reported in the retreatment of mono-infected patients with the same schedule. A substantial relative reduction in the SVR rate of about one-third, when treating genotypes ¼, was found, with a low SVR rate of 17%. Successful HIV suppression by ART predicted a higher rate of treatment success.

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[15]

TÍTULO / TITLE: - A new perspective on old drugs: non-mitotic actions of tubulin-binding drugs play a major role in cancer treatment.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Pharmazie. 2013 Jul;68(7):478-83.

AUTORES / AUTHORS: - Furst R; Vollmar AM

INSTITUCIÓN / INSTITUTION: - Institute of Pharmaceutical Biology, Biocenter, Goethe-University, Frankfurt am Main, Germany. fuerst@em.uni-frankfurt.de

RESUMEN / SUMMARY: - Microtubule-targeting agents (MTAs) are the most frequently used anti-cancer drugs. They can be divided into tubulin stabilizing and destabilizing agents. Their mode of action has been ascribed to their ability to interfere with the spindle apparatus and, thus, to block mitosis leading to tumor cell death. However, this view has been challenged in the last years and it became increasingly evident that non-mitotic actions of MTAs, i.e. their ability to affect the dynamics of interphase microtubules, are the most relevant mechanism underlying their efficacy. In this review we are presenting a distinct selection of examples of studies describing biological effects of MTAs in three areas: (i) mitosis-independent cell death and metastasis, (ii) tumor angiogenesis, and (iii) vascular-disrupting activity.

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[16]

TÍTULO / TITLE: - Antiestrogen-binding site ligands induce autophagy in myeloma cells that proceeds through alteration of cholesterol metabolism.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Oncotarget. 2013 Jun;4(6):911-22.

AUTORES / AUTHORS: - Sola B; Poirot M; de Medina P; Bustany S; Marsaud V; Silvente-Poirot S; Renoir JM

INSTITUCIÓN / INSTITUTION: - Normandie University, UNICAEN EA4652, Caen, France.

RESUMEN / SUMMARY: - Multiple myeloma (MM) is a malignancy characterized by the accumulation of clonal plasma cells in the bone marrow. Despite extensive efforts to design drugs targeting tumoral cells and their microenvironment, MM remains an incurable disease for which new therapeutic strategies are needed. We demonstrated here that antiestrogens (AEs) belonging to selective estrogen receptor modulators family induce a caspase-dependent apoptosis and trigger a protective autophagy. Autophagy was recognized by monodansylcadaverin staining, detection of autophagosomes by electronic microscopy, and detection of the cleaved form of the microtubule-associated protein light chain 3. Moreover, autophagy was inhibited by drugs such as bafilomycin A1 and 3-methyladenosine. Autophagy was mediated by the binding of AEs to a class of receptors called the antiestrogen binding site (AEBS) different from the classical estrogen nuclear receptors. The binding of specific ligands to the AEBS was accompanied by alteration of cholesterol metabolism and in particular accumulation of sterols: zymostenol or desmosterol depending on the ligand. This was due to

the inhibition of the cholesterol-5,6-epoxide hydrolase activity borne by the AEBS. We further showed that the phosphoinositide 3-kinase/AKT/mammalian target of rapamycin pathway mediated autophagy signaling. Moreover, AEBS ligands restored sensitivity to dexamethasone in resistant MM cells. Since we showed previously that AEs arrest MM tumor growth in xenografted mice, we propose that AEBS ligands may have a potent antimyeloma activity alone or in combination with drugs used in clinic.

TÍTULO / TITLE: - Simvastatin-induced up-regulation of gap junctions composed of connexin 43 sensitize Leydig tumor cells to etoposide: An involvement of PKC pathway.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Toxicology. 2013 Oct 4;312C:149-157. doi: 10.1016/j.tox.2013.08.013. Epub 2013 Aug 23.

●● Enlace al texto completo (gratuito o de pago) 1016/j.tox.2013.08.013

AUTORES / AUTHORS: - Wang L; Fu Y; Peng J; Wu D; Yu M; Xu C; Wang Q; Tao L

INSTITUCIÓN / INSTITUTION: - Department of Pharmacology, Zhongshan School of Medicine, Sun Yat-Sen University, Guangzhou 510080, People's Republic of China; Department of Anesthesia, The Second Affiliated Hospital, Guangzhou Medical University, Guangzhou 510260, People's Republic of China.

RESUMEN / SUMMARY: - Some of lipophilic statins have been reported to enhance toxicities induced by antineoplastic agents but the underling mechanism is unclear. The authors investigated the involvement of Cx43-mediated gap junction intercellular communication (GJIC) in the effect of simvastatin on the cellular toxicity induced by etoposide in this study. The results showed that a major component of the cytotoxicity of therapeutic levels of etoposide is mediated by gap junctions composed of connexin 43(Cx43) and simvastatin at the dosage which does not induce cytotoxicity enhances etoposide toxicity by increasing gap junction coupling. The augmentative effect of simvastatin on GJIC was related to the inhibition of PKC-mediated Cx43 phosphorylation at ser368 and subsequent enhancement of Cx43 membrane location induced by the agent. The present study suggests the possibility that upregulation of gap junctions may be utilized to increase the efficacy of anticancer chemotherapies.

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[17]

TÍTULO / TITLE: - Sulfotransferase genetic variation: from cancer risk to treatment response.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Drug Metab Rev. 2013 Sep 6.

●● Enlace al texto completo (gratuito o de pago) 3109/03602532.2013.835621

AUTORES / AUTHORS: - Daniels J; Kadlubar S

INSTITUCIÓN / INSTITUTION: - Department of Medical Genetics, College of Medicine, University of Arkansas for Medical Sciences , Little Rock, AR , USA.

RESUMEN / SUMMARY: - Abstract Cytosolic sulfotransferases (SULTs) are phase II detoxification enzymes that are involved in the biotransformation of a wide variety of structurally diverse endo- and xenobiotics. Single-nucleotide polymorphisms (SNPs) in SULTs can alter the phenotype of the translated proteins. SNPs in some SULTs are fairly uncommon in the population, but some, most notably for SULT isoform 1ª1, are commonly found and have been associated with cancer risk for a variety of tumor sites and also with response to therapeutic agents. SNPs in many SULTs vary by ethnicity, another factor that could influence SULT-associated disease risk and pharmacogenetics. This review surveys the current knowledge of SULT genetic variability in relation to cancer risk and response to therapy, focusing primarily on SULT1A1.

TÍTULO / TITLE: - Quantification of serum hepatitis B surface antigen in predicting the response of pegylated interferon alfa-2ª in HBeAg-positive chronic hepatitis B with prior lamivudine exposure.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Virol J. 2013 Sep 6;10(1):277.

●● Enlace al texto completo (gratuito o de pago) 1186/1743-422X-10-277

AUTORES / AUTHORS: - Weng M; Zeng WZ; Wu XL; Zhang Y; Jiang MD; Wang Z; Zhou DJ; He X

RESUMEN / SUMMARY: - AIMS: Majority of previous studies of pegylated interferon alpha-2ª (PegIFNalpha-2ª) forced on naive chronic hepatitis B (CHB) patients, and the data of PegIFNalpha-2ª in therapy of patients with prior exposure to nucleos(t)ide analogues is rare. This study aimed to investigate the predictive role of serum quantitative hepatitis B surface antigen (HBsAg) in predicting sustained response of PegIFNalpha-2ª in HBeAg-positive CHB patients with prior lamivudine exposure. METHODS: Forty-six patients with prior lamivudine exposure received PegIFNalpha-2ª for 12 months and followed-up for 6 months. The clinical features of responders and non-responders were compared, and the predictive role of quantitative HBsAg in predicting responders at the end of follow-up was evaluated. Responders were defined as an ALT normalization, HBeAg seroconversion and sustained virological response at the end of follow-up. RESULTS: In this cohort, only 26.1% (12/46) patients were responders. The baseline characteristics of the responders and non-responders were similar; however, the rates of ALT normalization, HBV DNA undetectability and HBeAg seroconversion were all significantly higher in responders than that in non-responders. During the treatment and follow-up, the HBsAg levels were all significantly lower in responders than that in non-responders. In predicting reponders, the serum HBsAg cutoff of 6000 IU/mL at months 6 had a positive predictive value of 73.3 and a negative predictive value of 96.8%, and with an area under the receiver operating characteristic curve of 0.869. CONCLUSION: The responders toward PegIFNalpha-2ª in CHB patients with prior lamivudine exposure is not high, and serum HBsAg <6000 IU/Ml at months 6 of on-treatment had a high value to predict long-term outcomes of treatment.

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[18]

TÍTULO / TITLE: - Prognostic role of epidermal growth factor receptor in nasopharyngeal carcinoma: A meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Head Neck. 2013 Aug 30. doi: 10.1002/hed.23481.

●● Enlace al texto completo (gratuito o de pago) 1002/hed.23481

AUTORES / AUTHORS: - Sun W; Long G; Wang J; Mei Q; Liu D; Hu G

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 1095 Jiefang Road, Hubei, Wuhan 430030, China.

RESUMEN / SUMMARY: - Background Various studies have assessed the prognostic value of epidermal growth factor receptor (EGFR) overexpression in nasopharyngeal carcinoma (NPC), but their results remain controversial. Methods Studies published up to January 2013 were collected. A total of 16 studies involving 1179 patients were reviewed. A meta-analysis was performed to clarify the prognostic role of EGFR in patients with NPC. The combined hazard ratio (HR) and 95% confidence interval CI were estimated using fi xed-effects or random-effects models. Results EGFR overexpression had significantly poor effect on overall survival (HR, 1.86; 95% CI, 1.25 to 2.77), disease-free survival (HR, 2.25; 95% CI, 1.66 to 3.04) and locoregional control (HR, 2.93; 95% CI, 1.71 to 5.02). However, the association between EGFR overexpression and distant metastasis-free survival was not statistically significant (HR, 1.39; 95% CI, 0.72 to 2.67). Conclusions EGFR overexpression can be a prognostic factor for patients with NPC. Head Neck, 2013.

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[19]

TÍTULO / TITLE: - Prognostic role of epidermal growth factor receptor in head and neck cancer: A meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - J Surg Oncol. 2013 Sep 13. doi: 10.1002/jso.23406.

●● Enlace al texto completo (gratuito o de pago) 1002/jso.23406

AUTORES / AUTHORS: - Zhu X; Zhang F; Zhang W; He J; Zhao Y; Chen X

INSTITUCIÓN / INSTITUTION: - Department of Otorhinolaryngology, Peking Union Medical College Hospital, Beijing, PR China.

RESUMEN / SUMMARY: - BACKGROUND AND OBJECTIVES: To evaluate the predicting value of the epidermal growth factor receptor (EGFR) for survival in patients with head and neck cancer (HNC). METHODS: Data were collected from studies comparing overall survival (OS) or progression-free survival (PFS) in patients with higher or lower EGFR levels. Studies were pooled and combined hazard ratios (HRs) of EGFR for survival were calculated. RESULTS: A total of 68 studies involving 6,781 patients were included for meta-analysis. Either EGFR protein expression or gene copy number had prognostic value in HNC patients. EGFR

overexpression could predict worse outcome, with HRs of 1.65 (95% CI: 1.45, 1.86) for OS and 1.27 (95% CI: 1.17, 1.37) for PFS. Increased EGFR copy number was also associated with reduced survival, with HRs of 1.5 (95% CI: 1.15, 1.96) for OS and 1.35 (95% CI: 1.14, 1.61) for PFS. Furthermore, EGFR overexpression could predict poorer OS in both eastern and western countries. Particularly, EGFR was considered a strong predictor in laryngeal squamous cell cancer (HR > 2). CONCLUSION: Elevated EGFR expression and gene copy number could predict poor survival in HNC patients. J. Surg. Oncol. © 2013 Wiley Periodicals, Inc.

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[20]

TÍTULO / TITLE: - Hepatitis C and interferon: fewer cases of liver cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Prescrire Int. 2013 Jul;22(140):191.

RESUMEN / SUMMARY: - Data on the risk of hepatocellular carcinoma in interferon-treated patients with chronic hepatitis C participating in placebo-controlled trials of interferon have been published after 3 to 9 years of follow-up. Among patients with chronic hepatitis C and either fibrosis or cirrhosis, interferon greatly reduced the risk of hepatocellular carcinoma after 8 years or more, especially when viral load was below the limit of detection.

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[21]

TÍTULO / TITLE: - Real-time nanoscale proteomic analysis of the novel multi-kinase pathway inhibitor rigosertib to measure the response to treatment of cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Expert Opin Investig Drugs. 2013 Aug 12.

●● Enlace al texto completo (gratuito o de pago) 1517/13543784.2013.829453

AUTORES / AUTHORS: - Fan AC; O'Rourke JJ; Praharaj DR; Felsher DW

INSTITUCIÓN / INSTITUTION: - Stanford University School of Medicine, Division of Oncology, Departments of Medicine and Pathology , Stanford, CA , USA afan@stanford.edu.

RESUMEN / SUMMARY: - Introduction: Rigosertib (ON01910.Na), is a targeted therapeutic that inhibits multiple kinases, including PI3K and PIk-1. Rigosertib has been found to induce the proliferative arrest and apoptosis of myeloblasts but not of other normal hematopoietic cells. Rigosertib has significant clinical activity as a therapy for patients with high-risk myelodysplastic syndrome who are otherwise refractory to DNA methyltransferase inhibitors. Moreover, rigosertib has potential clinical activity in a multitude of solid tumors. Areas covered: The objective of this review is to evaluate the mechanism of activity, efficacy and dosing of rigosertib. Furthermore, the challenge in the clinical development of rigosertib, to identify the specific patients that are most likely to benefit from this therapeutic agent, is discussed. A PubMed search was performed using the following key words: rigosertib and ON01910.Na. Expert opinion: We describe the application of a novel nanoscale proteomic assay, the nanoimmunoassay, a tractable approach for measuring the activity and predicting

the efficacy of rigosertib, in real-time, using limited human clinical specimens. Our strategy suggests a possible paradigm where proteomic analysis during the pre-clinical and clinical development of a therapy can be used to uncover biomarkers for the analysis and prediction of efficacy in human patients.

TÍTULO / TITLE: - Gold nanoparticle delivery-enhanced proteasome inhibitor effect in adenocarcinoma cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Expert Opin Drug Deliv. 2013 Oct;10(10):1345-52. doi: 10.1517/17425247.2013.827659. Epub 2013 Aug 13.

●● Enlace al texto completo (gratuito o de pago) 1517/17425247.2013.827659

AUTORES / AUTHORS: - Coelho SC; Rocha S; Juzenas P; Sampaio P; Almeida GM; Silva FS; Pereira MC; Coelho MA

INSTITUCIÓN / INSTITUTION: - University of Porto, Faculty of Engineering, Department of Chemical Engineering, LEPAE , Rua Roberto Frias, PT-4200-465 Porto , Portugal +351 225081679 ; +351 225081449 ; mcoelho@fe.up.pt.

RESUMEN / SUMMARY: - Background: Proteasome inhibition is a current therapeutic strategy used in the treatment of multiple myeloma. Drugs controlling proteasome activity are ideally suited for unidirectional manipulation of cellular pathways such as apoptosis. The first proteasome inhibitor approved in clinics was bortezomib. This drug is currently used in combination with other anticancer agents. Objectives : In this study, the enhancement of bortezomib activity was evaluated using gold nanoparticles coated with poly(ethylene glycol). The uptake mechanism of the gold nanoparticles in pancreatic cell lines, S2-013 and hTERT-HPNE, was assessed by laser scanning confocal microscopy (LSCM). Results: Pancreatic cancer cells internalized the nanoparticles together with the drug in few minutes through the formation of endocytic vesicles. This rapid uptake leads to an increase in the concentration and diffusion of bortezomib in the cytoplasm yielding an increased toxicity on the cells when compared to the drug alone. Conclusion: Gold nanoparticles can be used as effective delivery systems to increasing the permeation and retention of drugs in cancer cells.

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[22]

TÍTULO / TITLE: - Molecular mechanisms of the pro-apoptotic actions of melatonin in cancer: a review.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Expert Opin Ther Targets. 2013 Sep 14.

●● Enlace al texto completo (gratuito o de pago) 1517/14728222.2013.834890

AUTORES / AUTHORS: - Bizzarri M; Proietti S; Cucina A; Reiter RJ

INSTITUCIÓN / INSTITUTION: - University La Sapienza, Department of Experimental Medicine, Systems Biology Group , Rome , Italy mariano.bizzarri@uniroma1.it.

RESUMEN / SUMMARY: - Introduction: Compelling evidence has highlighted the complex pleiotropic functions elicited by the melatonin in cancer cells. Melatonin behaves as a 'smart killer', i.e., modulating anti-apoptotic processes in normal cells, and triggering pro-apoptotic signals in cancer cells. Areas covered: Melatonin induces programmed cell death in a wide range of different tumors (breast, gastro-intestinal, hematological, prostate, osteosarcoma, melanoma, kidney, etc..). Mechanisms of action and molecular pathways involved in pro-apoptotic processes under melatonin treatment are discussed. Expert opinion: Melatonin involvement in apoptotic processes is a new and relevant field of investigation. Even in tumor models unresponsive to melatonin alone, this hormone can significantly amplify the cytostatic and the cytotoxic effects triggered by other compounds or conventional drugs. We are far from having a satisfactory understanding about how and when melatonin exerts its beneficial effects. Melatonin in the nanomolar range activates the intrinsic and/or the extrinsic apoptotic pathway in cancer cells, namely through an increase in the p53/MDM2p ratio and downregulation of Sirt1. This finding is of great relevance since there is intense research ongoing to identify nontoxic feasible inhibitors of MDM2 and Sirt1. Melatonin should be evaluated for the management of those cancers where both of these are overexpressed and functionally strategic.

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[23]

TÍTULO / TITLE: - Predictive and Prognostic Roles of Ribonucleotide Reductase M1 in Patients with Pancreatic Cancer Treated with Gemcitabine: A Meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(7):4261-5.

AUTORES / AUTHORS: - Zhang X; Jin FS; Zhang LG; Chen RX; Zhao JH; Wang YN; Wang EF; Jiang ZD

INSTITUCIÓN / INSTITUTION: - Department of Laboratory Medicine, Hubei Wuchang Hospital, Wuhan, Hubei, China E-mail : wcyy_jzd@126.com.

RESUMEN / SUMMARY: - Increasing scientific evidence suggests that ribonucleotide reductase M1 (RRM1) may be a powerful predictor of survival in patients with pancreatic cancer treated with adjuvant gemcitabine-based chemotherapy after operative resection, but many existing studies have yielded inconclusive results. This meta-analysis aimed to assess the prognostic role of RRM1 in predicting survival in patients with pancreatic cancer treated with gemcitabine. An extensive literature search for relevant studies was conducted on PubMed, Embase, Web of Science, Cochrane Library, and CBM databases from their inception through May 1st, 2013. This meta-analysis was performed using the STATA 12.0 software and crude hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Eight clinical studies were included in this meta-analysis with a total of 665 pancreatic cancer patients treated with adjuvant gemcitabine-based chemotherapy, including 373 patients in the high RRM1 expression group and 292 patients in the low RRM1 expression group. Our meta-analysis revealed that high RRM1 expression was associated with improved overall survival (OS) of pancreatic cancer patients (HR=1.56, 95%CI=0.95-2.17, P<0.001). High RRM1 expression also

was linked to longer disease-free survival (DFS) than low RRM1 expression (HR=1.37, 95%CI=0.25-2.48, P=0.016). In conclusion, our meta-analysis suggests that high RRM1 expression may be associated with improved OS and DFS of pancreatic cancer patients treated with adjuvant gemcitabine-based chemotherapy. Detection of RRM1 expression may be a promising biomarker for gemcitabine response and prognosis in pancreatic cancer patients.

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[24]

TÍTULO / TITLE: - A meta-analysis and systematic review: adjuvant interferon therapy for patients with viral hepatitis-related hepatocellular carcinoma.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - World J Surg Oncol. 2013 Sep 24;11(1):240.

●● Enlace al texto completo (gratuito o de pago) 1186/1477-7819-11-240

AUTORES / AUTHORS: - Jiang S; Liu Y; Wang L; Duan C; Liu M

RESUMEN / SUMMARY: - OBJECTIVE: To evaluate the efficacy and safety of adjuvant IFN therapy for viral hepatitis-related hepatocellular carcinoma (HCC) after treatment with surgical resection or transarterial chemoembolization (TACE). METHODS: Controlled trials of adjuvant treatment with IFN for patients with HCC published between 2000 and 2012 were searched electronically in MEDLINE, PubMed, Cochrane Library, and EMBASE databases. According to the heterogeneity of the studies, two different models - the fixed-effect model and the random-effect model - were applied to analyze the results. RESULTS: Ten trials were screened according to inclusion and exclusion standards. Eight randomized, controlled trials and two non-randomized, controlled trials were included. These ten trials with a total of 1,029 subjects were eventually involved in the meta-analysis; 528 HCC patients were treated with adjuvant treatment with IFN and 501 patients with placebo. Compared to the control group, the recurrence rates of HCC in IFN group were significantly lower (odds ratio (OR) = 0.66; 95% confidence interval (CI) = 0.50 to 0.86;, P = 0.02), especially after TACE treatment according to subgroup analysis (OR = 0.73; 95% CI = 0.52 to 1.01; P = 0.06 for surgical resection; and OR = 0.54; 95% CI = 0.33 to 0.86, P = 0.01 for TACE). The death rates in the IFN group also significantly decreased according to not only total events analysis (OR = 0.42; 95% CI = 0.32 to 0.56; P < 0.00001) but also subgroup analysis (OR = 0.51; 95% CI = 0.36 to 0.72; P = 0.0002 for surgical resection; and OR = 0.33; 95% CI = 0.21 to 0.50; P < 0.00001 for TACE). CONCLUSIONS: Adjuvant IFN therapy may significantly reduce the recurrence rates of patients with viral hepatitis-related HCC and improve the survival of patients after surgical resection or TACE. The ideal dose mostly selected is 3 MIU/ml, three times per week, which can make patients tolerate the adverse reactions of IFN better and maintain effective concentrations for a long time.

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[25]

TÍTULO / TITLE: - Hypoxia-inducible Factor 1 Alpha (HIF-1alpha) as a Prognostic Indicator in Patients with Gastric Tumors: A Meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(7):4195-8.

AUTORES / AUTHORS: - Zhang ZG; Zhang QN; Wang XH; Tian JH

INSTITUCIÓN / INSTITUTION: - Evidence Based Medicine Center of Lanzhou University, Lanzhou, China E-mail : xhwanggs@126.com.

RESUMEN / SUMMARY: - Background and Objective: Though researched for years, the prognostic role of hypoxia-inducible factor 1 alpha (HIF-1alpha) in gastric cancer is still controversial. We thus undertook a systematic review to assess the relationship. Method: A systematically literature search of Pubmed, Embase, Web of Science, China Biological Medicine Disc and Cochrane Library was undertaken in February 2013, and the reference lists of articles were retrieved. Results: 12 trials (1,555 participants) were included to assess the association between HIF-1alpha expression and survival. Summary hazard ratios (HRs) were calculated. HIF-1alpha expression was significantly correlated with poor overall survival of gastric cancer patients (HR=1.34, 95%CI: 1.13-1.58; P=0.0009), but not with poor disease free survival of gastric cancer patients (HR=1.67, 95%CI: 0.99-2.82; P=0.06). Conclusion: HIF-1alpha was associated with poor OS, but not DFS, especially for Asian patients. But studies evaluating relationships of HIF- 1alpha with OS and DFS in non-Asian gastric cancer patients appear needed.

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[26]

TÍTULO / TITLE: - Novel mechanisms of regulation of IGF-1R action: functional and therapeutic implications.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Pediatr Endocrinol Rev. 2013 Jul;10(4):473-84.

AUTORES / AUTHORS: - Worralti C; Nedelcu D; Serly J; Suleymanova N; Oprea I; Girnita A; Girnita L

INSTITUCIÓN / INSTITUTION: - Department of Oncology and Pathology, Cancer Center Karolinska, Karolinska Institutet, Karolinska University Hospital, 17176 Stockholm, Sweden.

RESUMEN / SUMMARY: - The IGF-1R pathway is essential for the initiation and progression of many cancers. In contrast to other receptor tyrosine kinases involved in cancer, it is not frequently mutated or amplified. The classical model of signaling through the IGF-1R centers on ligand initiated kinase activation, allowing binding of adaptor molecules and downstream activation of the MAPK and PI3K pathways. The signaling is terminated through receptor ubiquitination and subsequent degradation. To date, therapies targeting IGF-1R have been designed solely aiming to block phosphorylation mediated signaling by preventing receptor-ligand interaction or by limiting kinase activation. Yet, the classical model is insufficient to explain receptor behavior induced by some IGF-1R inhibitors. This review advocates an updated model of IGF-1R signaling, accommodating the “classical” kinase signaling and the IGF-1R-kinase independent signaling thus providing the theoretical background for receptor

downregulation induced by IGF-1R inhibitors. This model should be considered for future design of effective therapies targeting the IGF-1R pathway.

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[27]

TÍTULO / TITLE: - Dysphagia in Head and Neck Cancer Patients: Pretreatment Evaluation, Predictive Factors, and Assessment during Radio-Chemotherapy, Recommendations.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Clin Exp Otorhinolaryngol. 2013 Sep;6(3):117-126. Epub 2013 Sep 4.

●● Enlace al texto completo (gratuito o de pago) 3342/ceo.2013.6.3.117

AUTORES / AUTHORS: - Denaro N; Merlano MC; Russi EG

INSTITUCIÓN / INSTITUTION: - Oncology Department, Azienda Ospedaliera Santa Croce e Carle, Cuneo, Italy.

RESUMEN / SUMMARY: - Progress in head and neck cancer (HNC) therapies has improved tumor response, loco-regional control, and survival. However, treatment intensification also increases early and late toxicities. Dysphagia is an underestimated symptom in HNC patients. Impairment of swallowing process could cause malnutrition, dehydration, aspiration, and pneumonia. A comprehensive literature review finalized in May 2012 included searches of electronic databases (Medline, Embase, and CAB abstracts) and scientific societies meetings materials (American Society of Clinical Oncology, Associazione Italiana Radioterapia Oncologica, Associazione Italiana di Oncologia Cervico-Cefalica, American Head and Neck Society, and European Society for Medical Oncology). Hand-searches of HNC journals and reference lists were carried out. Approximately one-third of dysphagia patients developed pneumonia requiring treatment. Aspiration pneumonia associated mortality ranged from 20% to 65%. Unidentified dysphagia caused significant morbidity, increased mortality, and decreased the quality of life. In this review we underline definition, causes, predictive factors of dysphagia and report on pretreatment and on-treatment evaluation, suggesting some key points to avoid underestimation. A multi-parameter assessment of swallowing problems may allow an earlier diagnosis. An appropriate evaluation might lead to a better treatment of both symptoms and cancer.

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[28]

TÍTULO / TITLE: - High-dose interleukin-2: is it still indicated for melanoma and RCC in an era of targeted therapies?

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Oncology (Williston Park). 2013 Jul;27(7):680-91.

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RESUMEN / SUMMARY: - Immunotherapy with interleukin-2 (IL-2) has been the mainstay of systemic therapy for advanced kidney cancer and melanoma. Although IL-2 treatment is limited to healthy patients, a select group of these patients have derived substantial, durable

benefit from it-in some translating into cures with no ongoing therapy or chronic toxicity. Over the past 10 years, insights into the biology of renal cell carcinoma and into key signaling mechanisms in melanoma, and growth in our understanding of immune checkpoints, have led to the development and approval of targeted and immune-modulatory therapeutic options with clinically relevant benefit. Our improved understanding of the relationship between the host environment, immune system, and malignancy has helped identify compounds and therapies that are changing the way we think about cancer and our approach to cancer therapeutics. While the newer options may be applicable to most patients, durable responses measured in years are rare. In this review, we examine the currently approved options available for these disease processes, including the newer agents and selected combinatorial approaches under investigation, and we attempt to identify the role of high-dose IL-2 in the context of current clinical practice.

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[29]

TÍTULO / TITLE: - Targeting proliferating cell nuclear antigen and its protein interactions induces apoptosis in multiple myeloma cells.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - PLoS One. 2013 Jul 31;8(7):e70430. doi: 10.1371/journal.pone.0070430. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0070430

AUTORES / AUTHORS: - Muller R; Misund K; Holien T; Bachke S; Gilljam KM; Vatsveen TK; Ro TB; Bellacchio E; Sundan A; Otterlei M

INSTITUCIÓN / INSTITUTION: - Department of Cancer Research and Molecular Medicine, Norwegian University of Science and Technology, Trondheim, Norway.

RESUMEN / SUMMARY: - Multiple myeloma is a hematological cancer that is considered incurable despite advances in treatment strategy during the last decade. Therapies targeting single pathways are unlikely to succeed due to the heterogeneous nature of the malignancy. Proliferating cell nuclear antigen (PCNA) is a multifunctional protein essential for DNA replication and repair that is often overexpressed in cancer cells. Many proteins involved in the cellular stress response interact with PCNA through the five amino acid sequence AlkB homologue 2 PCNA-interacting motif (APIM). Thus inhibiting PCNA's protein interactions may be a good strategy to target multiple pathways simultaneously. We initially found that overexpression of peptides containing the APIM sequence increases the sensitivity of cancer cells to contemporary therapeutics. Here we have designed a cell-penetrating APIM-containing peptide, ATX-101, that targets PCNA and show that it has anti-myeloma activity. We found that ATX-101 induced apoptosis in multiple myeloma cell lines and primary cancer cells, while bone marrow stromal cells and primary healthy lymphocytes were much less sensitive. ATX-101-induced apoptosis was caspase-dependent and cell cycle phase-independent. ATX-101 also increased multiple myeloma cells' sensitivity against melphalan, a DNA damaging agent commonly used for treatment of multiple myeloma. In a xenograft mouse model, ATX-101 was well tolerated and increased the anti-tumor activity of melphalan.

Therefore, targeting PCNA by ATX-101 may be a novel strategy in multiple myeloma treatment.

TÍTULO / TITLE: - Rebmab200, a humanized monoclonal antibody targeting the sodium phosphate transporter NaPi2b displays strong immune mediated cytotoxicity against cancer: a novel reagent for targeted antibody therapy of cancer.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - PLoS One. 2013 Jul 31;8(7):e70332. doi: 10.1371/journal.pone.0070332. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0070332

AUTORES / AUTHORS: - Lopes dos Santos M; Yeda FP; Tsuruta LR; Horta BB; Pimenta AA Jr; Degaki TL; Soares IC; Tuma MC; Okamoto OK; Alves VA; Old LJ; Ritter G; Moro AM

INSTITUCIÓN / INSTITUTION: - Lab. de Biofarmacos em Celulas Animais, Instituto Butantan, Sao Paulo, Brazil.

RESUMEN / SUMMARY: - NaPi2b, a sodium-dependent phosphate transporter, is highly expressed in ovarian carcinomas and is recognized by the murine monoclonal antibody MX35. The antibody had shown excellent targeting to ovarian cancer in several early phase clinical trials but being murine the antibody's full therapeutic potential could not be explored. To overcome this impediment we developed a humanized antibody version named Rebmab200, expressed in human PER.C6® cells and cloned by limiting dilution. In order to select a clone with high therapeutic potential clones were characterized using a series of physicochemical assays, flow cytometry, real-time surface plasmon resonance, glycosylation analyses, immunohistochemistry, antibody-dependent cell-mediated cytotoxicity, complement-dependent-cytotoxicity assays and quantitative PCR. Comparative analyses of Rebmab200 and MX35 monoclonal antibodies demonstrated that the two antibodies had similar specificity for NaPi2b by flow cytometry with a panel of 30 cell lines and maintained similar kinetic parameters. Robust and high producer cell clones potentially suitable for use in manufacturing were obtained. Rebmab200 antibodies were assessed by immunohistochemistry using a large panel of tissues including human carcinomas of ovarian, lung, kidney and breast origin. An assessment of its binding towards 33 normal human organs was performed as well. Rebmab200 showed selected strong reactivity with the tested tumor types but little or no reactivity with the normal tissues tested confirming its potential for targeted therapeutics strategies. The remarkable cytotoxicity shown by Rebmab200 in OVCAR-3 cells is a significant addition to the traits of stability and productivity displayed by the top clones of Rebmab200. Antibody-dependent cell-mediated toxicity functionality was confirmed in repeated assays using cancer cell lines derived from ovary, kidney and lung as targets. To explore use of this antibody in clinical trials, GMP production of Rebmab200 has been initiated. As the next step of development, Phase I clinical trials are now planned for translation of Rebmab200 into the clinic.

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[30]

TÍTULO / TITLE: - Bosutinib: a SRC-ABL tyrosine kinase inhibitor for treatment of chronic myeloid leukemia.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Pharmgenomics Pers Med. 2013 Aug 5;6:57-62.

●● Enlace al texto completo (gratuito o de pago) 2147/PGPM.S32145

AUTORES / AUTHORS: - Rassi FE; Khoury HJ

INSTITUCIÓN / INSTITUTION: - Division of Hematology, Department of Hematology and Medical Oncology, the Winship Cancer Institute at Emory University, Atlanta, Georgia, USA.

RESUMEN / SUMMARY: - Bosutinib is one of five tyrosine kinase inhibitors commercially available in the United States for the treatment of chronic myeloid leukemia. This review of bosutinib summarizes the mode of action, pharmacokinetics, efficacy and safety data, as well as the patient-focused perspective through quality-of-life data. Bosutinib has shown considerable and sustained efficacy in chronic myeloid leukemia, especially in the chronic phase, with resistance or intolerance to prior tyrosine kinase inhibitors. Bosutinib has distinct but manageable adverse events. In the absence of T315I and V299L mutations, there are no absolute contraindications for the use of bosutinib in this patient population.

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[31]

TÍTULO / TITLE: - Treating relapsed or refractory Philadelphia chromosome-negative acute lymphoblastic leukemia: liposome-encapsulated vincristine.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Int J Nanomedicine. 2013;8:3479-3488. Epub 2013 Sep 16.

●● Enlace al texto completo (gratuito o de pago) 2147/IJN.S47037

AUTORES / AUTHORS: - Davis T; Farag SS

INSTITUCIÓN / INSTITUTION: - Department of Internal Medicine, Division of Hematology and Oncology, Indiana University School of Medicine, Indianapolis, IN, USA.

RESUMEN / SUMMARY: - Acute lymphoblastic leukemia (ALL) remains a disease with poor outcomes in adults. While induction chemotherapy achieves a complete remission in almost 90% of patients, the majority will relapse and die of their disease. Relapsed ALL is associated with a high reinduction mortality and chemotherapy resistance, with allogeneic hematopoietic stem cell transplantation offering the only therapy with curative potential. However, there is no efficacious and well tolerated standard regimen accepted as a “bridge” to allogeneic stem cell transplantation or as definitive treatment for patients who are not transplant candidates. Vincristine is an active drug in patients with ALL, but its dose intensity is limited by neurotoxicity, and its full potential as an anticancer drug is thus not realized. Encapsulation of vincristine into sphingomyelin and cholesterol nanoparticle liposomes facilitates dose-intensification and densification to enhanced target tissues with reduced potential for toxicity. Vincristine sulfate liposome injection (VSLI) is associated with significant responses in clinically advanced ALL, and has recently been approved by the US Food and Drug Administration for treatment of relapsed and clinically advanced Philadelphia chromosome-negative ALL. This review provides an overview of the preclinical and clinical studies leading to the approval of

VSLI for the treatment of relapsed and refractory ALL, and suggests potential areas of future clinical development.

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[32]

TÍTULO / TITLE: - Effect and safety of interferon for hepatocellular carcinoma: a systematic review and meta-analysis.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - PLoS One. 2013 Sep 17;8(9):e61361. doi: 10.1371/journal.pone.0061361.

●● Enlace al texto completo (gratuito o de pago) 1371/journal.pone.0061361

AUTORES / AUTHORS: - Zhuang L; Zeng X; Yang Z; Meng Z

INSTITUCIÓN / INSTITUTION: - Department of Integrative Medicine, Fudan University Shanghai Cancer Center, Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China.

RESUMEN / SUMMARY: - BACKGROUND: The effect of interferon(IFN) in the management of hepatocellular carcinoma (HCC) remains controversial, and no clear recommendations have been proposed. OBJECTIVES: To evaluate the effect and safety of IFN for HCC. METHODS: PubMed, OvidSP, and Cochrane Library were searched from their establishment date until August 30, 2012. Studies that met the inclusion criteria were systematically evaluated and then subjected to meta-analysis. RESULTS: Thirteen randomized control trials (RCTs) involving 1344 patients were eligible for this study. When IFN was used as an adjuvant therapy for HCC patients after curative therapy, the meta-analysis showed that IFN reduced the 1-, 2-, 3-, 4-, and 5-year recurrence rates. Subgroup analysis showed that IFN reduced the 2-, 3-, 4-, and 5-year recurrence rates of hepatitis C viral (HCV)-related HCC. The effect of IFN for on hepatitis B virus(HBV)-related HCC patients could not be determined because of isufficient data. After surgical resection, adjuvant IFN therapy reduced the 4- and 5- recurrence rates. All studies reported that IFN could not improve the overall survival of HCV-realated HCC patients after curative therapies. Only one study showed that IFN was associated with better overall survival in HCC patients after curative therapy and subgroup of HCC patients after surgical resection. Thus, meta-analysis was not performed. Different treatment options were used as control to study the effect of IFN for intermediate and advanced HCC patients, thus meta-analysis was not appropriate. All included studies, except for one, reported that IFN treatment was well tolerated. CONCLUSIONS: After curative therapies, adjuvant IFN reduced the recurrence of HCC. IFN did not improve the survival of HCV-related HCC patients after curative therapy. Whether IFN is effective for intermediate and advanced HCC patients could not be determined because of insufficient data. The toxicity of IFN was acceptable.

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[33]

TÍTULO / TITLE: - Endogenous Retroviruses as Targets for Antitumor Immunity in Renal Cell Cancer and Other Tumors.

RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary

REVISTA / JOURNAL: - Front Oncol. 2013 Sep 17;3:243.

●● Enlace al texto completo (gratuito o de pago) 3389/fonc.2013.00243

AUTORES / AUTHORS: - Cherkasova E; Weisman Q; Childs RW

INSTITUCIÓN / INSTITUTION: - Hematology Branch, National Heart, Lung and Blood Institute, National Institutes of Health , Bethesda, MD , USA.

RESUMEN / SUMMARY: - Human endogenous retroviruses (HERVs), remnants of ancient germ-line infections with exogenous retroviruses, are estimated to comprise up to 8% of human genome. Most HERVs have accumulated mutations and deletions that prevent their expression as an infectious virus. Nevertheless, a growing number of HERV genes and proteins have been found to be expressed in different cancers, raising the possibility that HERV-derived antigens might represent excellent targets for tumor immunotherapy. Here, we review data showing HERV-encoded antigens are capable of eliciting humoral and T-cells specific antitumor immunity. We also describe a novel HERV-E that was recently found to be selectively expressed in over 80% of clear cell kidney cancer but not in normal tissues. Remarkably, the restricted expression of HERV-E in kidney tumors was found to occur as a consequence of inactivation of the von Hippel-Lindau tumor suppressor. Importantly, antigens derived from this provirus are immunogenic, stimulating cytotoxic T-cells that kill kidney cancer cells in vitro and in vivo. Taken altogether, these data suggest efforts aimed at boosting human immunity against HERV-derived antigens could be used as a strategy to treat advanced tumors including kidney cancer.
