#15#

Revisiones (todas) * Reviews (all)**

Cancer Pharmacogenomics.

Julio - Agosto 2013 / July - August 2013

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[1]

TÍTULO / TITLE: - Advances in the development of nucleoside and nucleotide analogues for cancer and viral diseases.

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

REVISTA / JOURNAL: - Nat Rev Drug Discov. 2013 Jun;12(6):447-64. doi: 10.1038/nrd4010.

●● Enlace al texto completo (gratuito o de pago) 1038/nrd4010

AUTORES / AUTHORS: - Jordheim LP; Durantel D; Zoulim F; Dumontet C

INSTITUCIÓN / INSTITUTION: - Anticancer Antibody Team, Institut National de la Sante et de la Recherche Medicale U1052, Centre National de la Recherche Scientifique UMR 5286, Cancer Research Center of Lyon, Faculte Rockefeller, 8 Ave Rockefeller, 69008 Lyon, France. lars-petter.jordheim@univ-lyon1.fr

RESUMEN / SUMMARY: - Nucleoside analogues have been in clinical use for almost 50 years and have become cornerstones of treatment for patients with cancer or viral infections. The approval of several additional drugs over the past decade demonstrates that this family still possesses strong potential. Here, we review new nucleoside analogues and associated compounds that are currently in preclinical or clinical development for the treatment of cancer and viral infections, and that aim to provide increased response rates and reduced side effects. We also highlight the different approaches used in the development of these drugs and the potential of personalized therapy.

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[2]
TÍTULO / TITLE: - MDR1 mRNA expression and MDR1 gene variants as predictors of response to chemotherapy in patients with acute myeloid leukaemia: a meta-analysis.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Biomarkers. 2013 Aug;18(5):425-35. doi: 10.3109/1354750X.2013.808263. Epub 2013 Jun 27.

●● Enlace al texto completo (gratuito o de pago) 3109/1354750X.2013.808263

AUTORES / AUTHORS: - Doxani C; Voulgarelis M; Zintzaras E
INSTITUCIÓN / INSTITUTION: - Department of Biomathematics, University of Thessaly School of Medicine , Larissa , Greece .
RESUMEN / SUMMARY: - Abstract Data from 30 pharmacogenomic studies that investigated MDR1 mRNA expression or gene variants (C3435T, G2677TA, C1236T) and response to therapy in acute myeloid leukaemia (AML) were synthesized. Anthracycline-based regimens were mainly used. MDR1 mRNA overexpression was associated with poor response to therapy [odds ratio (OR) = 2.49 95% confidence interval (CI) 1.38-4.50]. The gene variants were not associated with response to treatment; the generalized ORs, a genetic model-free approach, for the variants C3435T, G2677TA and C1236T were ORG = 0.86 (95% CI 0.55-1.37), ORG = 0.97 (95% CI 0.58-1.64) and ORG = 1.17 (95% CI 0.75--1.83), respectively. There is indication that MDR1 mRNA expression may be considered as a potential marker for response to chemotherapy in AML patients.

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[3]
TÍTULO / TITLE: - A meta-analysis of gene expression-based biomarkers predicting outcome after tamoxifen treatment in breast cancer.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Breast Cancer Res Treat. 2013 Jul;140(2):219-32. doi: 10.1007/s10549-013-2622-y. Epub 2013 Jul 9.

●● Enlace al texto completo (gratuito o de pago) 1007/s10549-013-2622-y

AUTORES / AUTHORS: - Mihaly Z; Kormos M; Lanczky A; Dank M; Budczies J; Szasz MA; Gyorffy B
INSTITUCIÓN / INSTITUTION: - 1st Department of Pediatrics, Semmelweis University, Budapest, Hungary.
RESUMEN / SUMMARY: - To date, three molecular markers (ER, PR, and CYP2D6) have been used in clinical setting to predict the benefit of the anti-estrogen tamoxifen therapy. Our aim was to validate new biomarker candidates predicting response to tamoxifen treatment in breast cancer by evaluating these in a meta-analysis of available transcriptomic datasets with known treatment and follow-up. Biomarker candidates were identified in Pubmed and in the

2007-2012 ASCO and 2011-2012 SABCS abstracts. Breast cancer microarray datasets of endocrine therapy-treated patients were downloaded from GEO and EGA and RNAseq datasets from TCGA. Of the biomarker candidates, only those identified or already validated in a clinical cohort were included. Relapse-free survival (RFS) up to 5 years was used as endpoint in a ROC analysis in the GEO and RNAseq datasets. In the EGA dataset, Kaplan-Meier analysis was performed for overall survival. Statistical significance was set at $p < 0.005$. The transcriptomic datasets included 665 GEO-based and 1,208 EGA-based patient samples. All together 68 biomarker candidates were identified. Of these, the best performing genes were PGR (AUC = 0.64, p = 2.3E-07), MAPT (AUC = 0.62, p = 7.8E-05), and SLC7A5 (AUC = 0.62, p = 9.2E-05). Further genes significantly correlated to RFS include FOS, TP53, BTG2, HOXB7, DRG1, CXCL10, and TPM4. In the RNAseq dataset, only ERBB2, EDF1, and MAPK1 reached statistical significance. We evaluated tamoxifen-resistance genes in three independent platforms and identified PGR, MAPT, and SLC7A5 as the most promising prognostic biomarkers in tamoxifen treated patients.

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[4]

TÍTULO / TITLE: - Meta-analysis of transcriptome reveals let-7b as an unfavorable prognostic biomarker and predicts molecular and clinical subclasses in high-grade serous ovarian carcinoma.

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

REVISTA / JOURNAL: - Int J Cancer. 2013 Jul 3. doi: 10.1002/ijc.28371.

●● Enlace al texto completo (gratuito o de pago) 1002/ijc.28371

AUTORES / AUTHORS: - Tang Z; Ow GS; Thiery JP; Ivshina AV; Kuznetsov VA

INSTITUCIÓN / INSTITUTION: - Bioinformatics Institute, A*STAR, Singapore.

RESUMEN / SUMMARY: - High-grade serous ovarian carcinoma (HG-SOC) is a heterogeneous, poorly classified, lethal disease that frequently exhibits altered expressions of microRNAs. Let-7 family members are often reported as tumor suppressors; nonetheless, clinicopathological functions and prognostic values of individual let-7 family members have not been addressed in HG-SOC. In our work, we performed an integrative study to investigate the potential roles, clinicopathological functions and prognostic values of let-7 miRNA family in HG-SOC. Using microarray and clinical data of 1,170 HG-SOC patients, we developed novel survival prediction and system biology methods to analyze prognostic values and functional associations of let-7 miRNAs with global transcriptome and clinicopathological factors. We demonstrated that individual let-7 members exhibit diverse evolutionary history and distinct regulatory characteristics. Statistical tests and network analysis suggest that let-7b could act as a global synergistic interactor and master regulator controlling hundreds of protein-coding genes. The elevated expression of let-7b is associated with poor survival rates, which suggests an unfavorable role of let-7b in treatment response for HG-SOC patients. A novel let-7b-defined 36-gene prognostic

survival signature outperforms many clinicopathological parameters, and stratifies HG-SOC patients into three high-confidence, reproducible, clinical subclasses: low-, intermediate- and high-risk, with 5-year overall survival rates of 56-71%, 12-29% and 0-10%, respectively. Furthermore, the high-risk and low-risk subclasses exhibit strong mesenchymal and proliferative tumor phenotypes concordant with resistance and sensitivity to primary chemotherapy. Our results have led to identification of promising prognostic markers of HG-SOC, which could provide a rationale for genetic-based stratification of patients and optimization of treatment regimes.

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[5]

TÍTULO / TITLE: - Interferon alpha for the adjuvant treatment of cutaneous melanoma.

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

REVISTA / JOURNAL: - Cochrane Database Syst Rev. 2013 Jun 18;6:CD008955. doi: 10.1002/14651858.CD008955.pub2.

●● Enlace al texto completo (gratuito o de pago)

1002/14651858.CD008955.pub2

AUTORES / AUTHORS: - Mocellin S; Lens MB; Pasquali S; Pilati P; Chiarion Sileni V

INSTITUCIÓN / INSTITUTION: - Meta-Analysis Unit, Department of Surgery, Oncology and Gastroenterology, University of Padova, Via Giustiniani 2, Padova, Veneto, Italy, 35128.

RESUMEN / SUMMARY: - BACKGROUND: Interferon alpha is the only agent approved for the postoperative adjuvant treatment of high-risk cutaneous melanoma. However, the survival advantage associated with this treatment is unclear, especially in terms of overall survival. Thus, adjuvant interferon is not universally considered a gold standard treatment by all oncologists. OBJECTIVES: To assess the disease-free survival and overall survival effects of interferon alpha as adjuvant treatment for people with high-risk cutaneous melanoma. SEARCH METHODS: We searched the following databases up to August 2012: the Cochrane Skin Group Specialised Register, CENTRAL in The Cochrane Library (2012, issue 8), MEDLINE (from 2005), EMBASE (from 2010), AMED (from 1985), and LILACS (from 1982). We also searched trials databases in 2011, and proceedings of the ASCO annual meeting from 2000 to 2011. We checked the reference lists of selected articles for further references to relevant trials. SELECTION CRITERIA: We included only randomised controlled trials (RCTs) comparing interferon alpha to observation (or any other treatment) for the postoperative (adjuvant) treatment of patients with high-risk skin melanoma, that is, people with regional lymph node metastasis (American Joint Committee on Cancer (AJCC) TNM (tumour, lymph node, metastasis) stage III) undergoing radical lymph node dissection, or people without nodal disease but with primary tumour thickness greater than 1 mm (AJCC TNM

stage II). DATA COLLECTION AND ANALYSIS: Two authors extracted data, and a third author independently verified the extracted data. The main outcome measure was the hazard ratio (HR), which is the ratio of the risk of the event occurring in the treatment arm (adjuvant interferon) compared to the control arm (no adjuvant interferon). The survival data were either entered directly into Review Manager (RevMan) or extrapolated from Kaplan-Meier plots and then entered into RevMan. Based on the presence of between-study heterogeneity, we applied a fixed-effect or random-effects model for calculating the pooled estimates of treatment efficacy. MAIN RESULTS: Eighteen RCTs enrolling a total of 10,499 participants were eligible for the review. The results from 17 of 18 of these RCTs, published between 1995 and 2011, were suitable for meta-analysis and allowed us to quantify the therapeutic efficacy of interferon in terms of disease-free survival (17 trials) and overall survival (15 trials). Adjuvant interferon was associated with significantly improved disease-free survival (HR (hazard ratio) = 0.83; 95% CI (confidence interval) 0.78 to 0.87, P value < 0.00001) and overall survival (HR = 0.91; 95% CI 0.85 to 0.97; P value = 0.003). We detected no significant between-study heterogeneity (disease-free survival: I(2) statistic = 16%, Q-test P value = 0.27; overall survival: I(2) statistic = 6%; Q-test P value = 0.38).Considering that the 5-year overall survival rate for TNM stage II-III cutaneous melanoma is 60%, the number needed to treat (NNT) is 35 participants (95% CI = 21 to 108 participants) in order to prevent 1 death. The results of subgroup analysis failed to answer the question of whether some treatment features (i.e. dosage, duration) might have an impact on interferon efficacy or whether some participant subgroups (i.e. with or without lymph node positivity) might benefit differently from interferon adjuvant treatment.Grade 3 and 4 toxicity was observed in a minority of participants: In some trials, no-one had fever or fatigue of Grade 3 severity, but in other trials, up to 8% had fever and up to 23% had fatigue of Grade 3 severity. Less than 1% of participants had fever and fatigue of Grade 4 severity. Although it impaired quality of life, toxicity disappeared after treatment discontinuation. AUTHORS' CONCLUSIONS: The results of this meta-analysis support the therapeutic efficacy of adjuvant interferon alpha for the treatment of people with high-risk (AJCC TNM stage II-III) cutaneous melanoma in terms of both disease-free survival and, though to a lower extent, overall survival. Interferon is also valid as a reference treatment in RCTs investigating new therapeutic agents for the adjuvant treatment of this participant population. Further investigation is required to select people who are most likely to benefit from this treatment.

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[6]

TÍTULO / TITLE: - Low rates of adherence for tumor necrosis factor-alpha inhibitors in Crohn's disease and rheumatoid arthritis: Results of a systematic review.

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

REVISTA / JOURNAL: - World J Gastroenterol. 2013 Jul 21;19(27):4344-50. doi: 10.3748/wjg.v19.i27.4344.

●● Enlace al texto completo (gratuito o de pago) 3748/wjg.v19.i27.4344

AUTORES / AUTHORS: - Fidder HH; Singendonk MM; van der Have M; Oldenburg B; van Oijen MG

INSTITUCIÓN / INSTITUTION: - Herma H Fidder, Maartje MJ Singendonk, Mike van der Have, Bas Oldenburg, Martijn GH van Oijen, Department of Gastroenterology and Hepatology, University Medical Center Utrecht, 3508 GA Utrecht, The Netherlands.

RESUMEN / SUMMARY: - AIM: To investigate adherence rates in tumor necrosis factor-alpha (TNF-alpha)-inhibitors in Crohn's disease (CD) and rheumatoid arthritis (RA) by systematic review of medical literature. METHODS: A structured search of PubMed between 2001 and 2011 was conducted to identify publications that assessed treatment with TNF-alpha inhibitors providing data about adherence in CD and RA. Therapeutic agents of interest where adalimumab, infliximab and etanercept, since these are most commonly used for both diseases. Studies assessing only drug survival or continuation rates were excluded. Data describing adherence with TNF-alpha inhibitors were extracted for each selected study. Given the large variation between definitions of measurement of adherence, the definitions as used by the authors where used in our calculations. Data were tabulated and also presented descriptively. Sample size-weighted pooled proportions of patients adherent to therapy and their 95%CI were calculated. To compare adherence between infliximab, adalimumab and etanercept, the adherence rates where graphed alongside two axes. Possible determinants of adherence were extracted from the selected studies and tabulated using the presented OR. RESULTS: Three studies on CD and three on RA were identified, involving a total of 8147 patients (953 CD and 7194 RA). We identified considerable variation in the definitions and methodologies of measuring adherence between studies. The calculated overall sample size-weighted pooled proportion for adherence to TNF-alpha inhibitors in CD was 70% (95%CI: 67%-73%) and 59% in RA (95%CI: 58%-60%). In CD the adherence rate for infliximab (72%) was highercompared to adalimumab (55%), with a relative risk of 1.61 (95%CI: 1.27-2.03), whereas in RA adherence for adalimumab (67%) was higher compared to both infliximab (48%) and etanercept (59%), with a relative risk of 1.41 (95%CI: 1.3-1.52) and 1.13 (95%CI: 1.10-1.18) respectively. In comparative studies in RA adherence to infliximab was better than etanercept and etanercept did better than adalimumab. In three studies, the most consistent factor associated with lower adherence was female gender. Results for age, immunomodulator use and prior TNF-alpha inhibitors use were conflicting. CONCLUSION: One-third of both CD and RA patients treated with TNF-alpha inhibitors are non-adherent. Female gender was consistently identified as a negative determinant of adherence.

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[7]
TÍTULO / TITLE: - Quantification of circulating Epstein-Barr virus DNA in NK/T-cell lymphoma treated with the SMILE protocol: diagnostic and prognostic significance.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Leukemia. 2013 Jul 11. doi: 10.1038/leu.2013.212.
●● Enlace al texto completo (gratuito o de pago) 1038/leu.2013.212
AUTORES / AUTHORS: - Kwong YL; Pang AW; Leung AY; Chim CS; Tse E
INSTITUCIÓN / INSTITUTION: - Department of Medicine, Queen Mary Hospital, Hong Kong, China.
RESUMEN / SUMMARY: - Circulating Epstein-Barr virus (EBV) DNA is a biomarker of EBV-associated malignancies. Its significance in natural killer/T-cell lymphoma treated with the novel regimen SMILE was investigated. EBV DNA was quantified with a World Health Organization EBV standard in 910 plasma samples collected during 230 courses of SMILE in 56 patients. Median presentation EBV DNA was 1900 (0-1.4 x 107) IU/ml. Presentation EBV DNA was significantly associated with tumor load and treatment response. To examine lymphoma chemosensitivity, EBV DNA changes after SMILE were evaluated. EBV DNA after SMILE (I) significantly correlated with tumor load and treatment response. Two dynamic parameters were further analyzed: negative EBV DNA after SMILE (I) and EBV DNA change patterns during treatment (A: persistently undetectable; B: persistently detectable<presentation; C: persistently detectable>presentation). Negative EBV DNA after SMILE (I) and pattern A EBV DNA change significantly correlated with lower tumor load and superior outcome. Multivariate analysis involving presentation features, international prognostic index (IPI), Korean prognostic score and EBV DNA parameters showed that negative EBV DNA after SMILE (I) had the most significant impact (P<0.001) on overall survival and pattern A EBV DNA change had the most significant impact (P=0.002) on disease-free survival. Presentation EBV DNA, IPI and Korean prognostic scores were not independent prognostic factors.Leukemia advance online publication, 9 August 2013; doi:10.1038/leu.2013.212.

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[8]
TÍTULO / TITLE: - Complement factor H-derived short consensus repeat 18-20 enhanced complement-dependent cytotoxicity of Ofatumumab on chronic lymphocytic leukemia cells.
RESUMEN / SUMMARY: - Enlace al Resumen / Link to its Summary
REVISTA / JOURNAL: - Haematologica. 2013 Jul 12.
●● Enlace al texto completo (gratuito o de pago)
3324/haematol.2013.089615
AUTORES / AUTHORS: - Horl S; Banki Z; Huber G; Ejaz A; Mullauer B; Willenbacher E; Steurer M; Stoiber H

INSTITUCIÓN / INSTITUTION: - Austria;

RESUMEN / SUMMARY: - Antitumor activity of monoclonal antibodies for the treatment of chronic lymphocytic leukemia is mediated mainly by antibody-dependent cellular cytotoxicity and complement- dependent-cytotoxicity. Unfortunately, the efficacy of complement-dependent-cytotoxicity is strongly restricted due to the expression and acquisition of regulators of complement activation by lymphocytic leukemia cells. Whereas the role of membrane regulators of complement activation like CD55 and CD59 has been investigated in detail in chronic lymphocytic leukemia, the involvement of soluble regulators of complement activation like complement factor-H has not yet been reported. Propidium iodide staining was performed to investigate the efficacy of ofatumumab and factor-H-derived short-consensus-repeat 18-20 in the induction of complement-dependent-cytotoxicity on primary chronic lymphocytic leukemia cells from 20 patients. Deposition of complement C3 fragments was monitored by Western blot analysis. Expression of CD20, CD55 or CD59 was determined by FACS analysis. Replacement of factor-H with short-consensus-repeat 18-20 significantly increased the susceptibility of primary chronic lymphocytic leukemia cells to ofatumumab-induced complement-dependent-cytotoxicity. More importantly, addition of short-consensus-repeat 18-20 was able to overcome complement- resistance occurring during treatment with OFA alone. Use of short-consensus-repeat 18-20 is likely to prolong the turnover time of active C3b fragments generated on the target cells following ofatumumab-induced complement activation, thereby improving specific killing of chronic lymphocytic leukemia cells by complement-dependent-cytotoxicity. The relative contribution of factor-H to the protection of chronic lymphocytic leukemia cells against complement-dependent-cytotoxicity was comparable to that of CD55. Our data suggest that by abrogating factor-H function short-consensus-repeat 18-20 may provide a novel approach that improves the complement- dependent-efficacy of therapeutic monoclonal antibodies.

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[9]

TÍTULO / TITLE: - Interferon after surgery for women with advanced (Stage II-IV) epithelial ovarian cancer.

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

REVISTA / JOURNAL: - Cochrane Database Syst Rev. 2013 Jun 6;6:CD009620. doi: 10.1002/14651858.CD009620.pub2.

●● Enlace al texto completo (gratuito o de pago)

1002/14651858.CD009620.pub2

AUTORES / AUTHORS: - Lawal AO; Musekiwa A; Grobler L

INSTITUCIÓN / INSTITUTION: - Centre for Evidence-based Health Care, Faculty of Medicine and Health Sciences, Stellenbosch University, PO Box 19063, Tygerberg, Cape Town, Western Cape, South Africa, 7505.

RESUMEN / SUMMARY: - BACKGROUND: Epithelial ovarian cancer (EOC) is a life-threatening disease. Most often women become symptomatic only in the advanced stages of the disease, increasing the difficulty of treatment. Whilst the disease responds well to surgery and chemotherapy, the relapse rate is high. New treatments to prevent disease recurrence or progression, prolong survival, and increase the quality of life are needed. OBJECTIVES: To assess the effectiveness and safety of interferon after surgery in the treatment of advanced (stage II-IV) EOC. SEARCH METHODS: The Cochrane Gynaecological Cancer Review Group Specialized Register, Cochrane Central Register of Controlled Trials (CENTRAL) Issue 1, 2012, MEDLINE and EMBASE were searched to January 2012. Handsearching of conference proceedings was also undertaken. Reference lists of reviews and included trials were screened and experts in the field were contacted for additional trials. Clinical trials registers were searched for ongoing trials. SELECTION CRITERIA: Randomised controlled trials (RCTs) involving participants with advanced EOC that compared post-operative chemotherapy alone with post-operative interferon therapy in combination with chemotherapy or post-operative chemotherapy followed by interferon or observation alone DATA COLLECTION AND ANALYSIS: Two review authors (AL and AM) independently screened the search results for relevant trials and extracted pre-specified information from each included trial. Data were managed using Review Manager 5.1. Hazard ratios (HR) were calculated for time-to-event outcomes and risk ratios (RR) for dichotomous outcomes, with corresponding 95% confidence intervals (CI). MAIN RESULTS: Five trials, including 1476 participants, were included in the review. Two trials compared interferon with observation alone and three trials compared interferon plus chemotherapy with chemotherapy alone. A meta-analysis of two trials involving 370 participants found no significant difference in both overall survival (HR 1.14, 95% CI 0.84 to 1.55) and progression free survival (HR 0.99, 95% CI 0.79 to 1.24) between the interferon and observation alone groups in post-surgical women who had undergone first-line chemotherapy for advanced EOC. One trial with 293 participants found that while no significant difference was observed in incidence of nausea or vomiting between the two treatment groups, significantly more flu-like symptoms (RR 2.25, 95% CI 1.73 to 2.91) and fatigue (RR 1.54, 95% CI 1.27 to 1.88) were reported in the interferon group. For the second comparison, a meta-analysis of two trials comprising 244 participants found that although there was no significant difference in overall survival between the interferon plus chemotherapy and the chemotherapy alone group (HR 1.14, 95% CI 0.74 to 1.76), women in the interferon plus chemotherapy group had worse progression free survival than those in the chemotherapy alone group (HR 1.43, 95% CI 1.02 to 2.00). Compared to chemotherapy alone, adding interferon to chemotherapy did not alter the incidence of adverse events in post-surgical women with advanced EOC. AUTHORS' CONCLUSIONS: Implications for practiceBased on low quality evidence, the addition of interferon to first-line chemotherapy did not alter the overall survival in post-surgical

women with advanced EOC compared with chemotherapy alone. There is low quality evidence to suggest that interferon in combination with chemotherapy worsened the progression free survival in post-surgical women with advanced EOC compared with chemotherapy alone. There is not enough evidence that interferon therapy alone alters overall survival or progression free survival compared to observation alone in post-surgical women who have undergone first-line chemotherapy. Implications for researchThree of the five trials included in this review were stopped early and were, therefore, underpowered to detect any true effect of the intervention. The trials did not report the results of important outcomes in a uniform manner, preventing statistical aggregation of the results. Trial methodology was poorly reported resulting in unclear risk of bias. For clear recommendations to be made regarding the effectiveness of interferon in the treatment of advanced EOC, long-term, well conducted and adequately powered RCTs would be needed. However, the available data do not suggest that interferon has an adequately advantageous effect to warrant further investigation.

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[10]

TÍTULO / TITLE: - Prognostic value of cyclin E expression in breast cancer: a meta-analysis.

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

REVISTA / JOURNAL: - Tumour Biol. 2013 Jun 18.

●● Enlace al texto completo (gratuito o de pago) 1007/s13277-013-0915-8

AUTORES / AUTHORS: - Gao S; Ma JJ; Lu C

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Reproductive Medicine, Department of Breast Surgery, Nanjing Maternity and Child Health Care Hospital Affiliated to Nanjing Medical University, Nanjing, 210004, China.

RESUMEN / SUMMARY: - Cyclin E is an important regulator of cell cycle progression. Various studies examined the relationship between cyclin E overexpression with the clinical outcome in patients with breast cancer but yielded conflicting results. Electronic databases updated to May 2013 were searched to find relevant studies. A meta-analysis was conducted with eligible studies which quantitatively evaluated the relationship between cyclin E overexpression and survival of patients with breast cancer. Survival data were aggregated and quantitatively analyzed. We conducted a final analysis of 7,759 patients from 23 eligible studies and evaluated the correlation between cyclin E overexpression and survival in patients with breast cancer. Combined hazard ratios suggested that cyclin E overexpression had an unfavorable impact on overall survival (OS) (hazard ratio (HR) = 1.30, 95 % confidence interval (CI), 1.12-1.49) and breast cancer-specific survival (BCSS) (HR = 1.48, 95 % CI, 1.03-1.93), but not disease-free survival (HR = 1.11; 95 % CI, 0.96-1.27) in patients with breast cancer. Significantly, risks were found among stage I-II

breast cancer for (HR = 1.75; 95 % CI, 1.30-2.19). Cyclin E overexpression is associated with poor OS and BCSS in breast cancer.

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[11]

TÍTULO / TITLE: - Recent advances in melanoma systemic therapy. BRAF inhibitors, CTLA4 antibodies and beyond.

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

REVISTA / JOURNAL: - Eur J Cancer. 2013 Jul 16. pii: S0959-8049(13)00502-9. doi: 10.1016/j.ejca.2013.06.027.

●● Enlace al texto completo (gratuito o de pago) 1016/j.ejca.2013.06.027

AUTORES / AUTHORS: - Menzies AM; Long GV

INSTITUCIÓN / INSTITUTION: - Melanoma Institute Australia, Sydney, Australia; The University of Sydney, Sydney, Australia.

RESUMEN / SUMMARY: - Metastatic melanoma has a poor prognosis and until recently systemic therapy was ineffective. Advances in the understanding of tumour biology and immune regulation have led to the development of targeted agents that have changed clinical practice, with further improvements expected with new compounds and combinations. The first major advance was the development of selective mitogen-activated protein (MAP) kinase inhibitors (BRAF and MEK inhibitors) and immune checkpoint blockade with a CTLA4 antibody (ipilimumab). These drugs proved vastly superior to conventional chemotherapy, however response, resistance and toxicity were limitations. The second major advance is the development of other immune checkpoint blocking agents, including PD-1 and PD-L1 antibodies, and the use of BRAF and MEK inhibitors in combination, with a higher proportion of durable responses coupled with less toxicity. In an effort to improve outcomes for patients with melanoma further, trials are underway examining the combination of MAPK inhibitors, immunotherapies and other pathway inhibitors and adjuvant studies of many of these agents have commenced.

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[12]

TÍTULO / TITLE: - Circulating C-peptide level is a predictive factor for colorectal neoplasia: evidence from the meta-analysis of prospective studies.

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

REVISTA / JOURNAL: - Cancer Causes Control. 2013 Jul 12.

●● Enlace al texto completo (gratuito o de pago) 1007/s10552-013-0261-6

AUTORES / AUTHORS: - Chen L; Li L; Wang Y; Li P; Luo L; Yang B; Wang H; Chen M

INSTITUCIÓN / INSTITUTION: - The Emergency Department, The Chinese PLA General Hospital, Beijing, People’s Republic of China.

RESUMEN / SUMMARY: - PURPOSE: C-peptide, a hormone secreted by the pancreas, is a marker for insulin production and hyperinsulinemia. Epidemiological studies have suggested an association between circulating C-peptide level and colorectal neoplasia risk; however, the results were not always consistent. Herein, we conducted a systematic review and meta-analysis study to evaluate the association between circulating C-peptide level and the colorectal neoplasia risk. METHODS: The PubMed database was searched for the eligibility studies updated to May 2013, which prospectively evaluated the association between circulating C-peptide level and colorectal neoplasia risk. The summary estimates and 95 % confidential intervals (95 % CIs) for those with the highest quantile C-peptide level in contrast to the lowest quantile were estimated with the random-effects model. Heterogeneity between the studies was assessed with the Q test and the I 2 statistic. Potential publication bias was evaluated with the Egger's test. RESULTS: We identified 9 nested case-control studies that have recruited a total of 3,109 cases and 4,285 controls met the criteria. From the meta-analysis, we found that subjects with high circulating C-peptide were associated with a 37 % increased colorectal neoplasia risk [pooled odds ratios (OR) 1.37, 95 % CI 1.09-1.72] under the random-effects model. In the stratification studies, we found the association was more prominent in the men (pooled OR 2.34, 95 % CI 1.36-4.04) compared to women (pooled OR 1.41, 95 % CI 0.89-2.25). Significant association between circulating C-peptide level and colon cancer risk was found (pooled OR 1.72, 95 % CI 1.26-2.36), but not for rectal cancer (pooled OR 1.14, 95 % CI 0.75-1.73). No significant publication bias was found for any meta-analysis study. CONCLUSION: In conclusion, the results of the meta-analysis studies suggested that higher circulating C-peptide could be a predictive factor for higher colorectal neoplasia susceptibility.

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[13]

TÍTULO / TITLE: - Overexpression of thymidylate synthetase confers an independent prognostic indicator in nasopharyngeal carcinoma.

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

REVISTA / JOURNAL: - Exp Mol Pathol. 2013 Aug;95(1):83-90. doi: 10.1016/j.yexmp.2013.05.006. Epub 2013 May 28.

●● Enlace al texto completo (gratuito o de pago)

1016/j.yexmp.2013.05.006

AUTORES / AUTHORS: - Lee SW; Chen TJ; Lin LC; Li CF; Chen LT; Hsing CH; Hsu HP; Tsai CJ; Huang HY; Shiue YL

INSTITUCIÓN / INSTITUTION: - Department of Radiation Oncology, Chi-Mei Medical Center, Liouying, Tainan, Taiwan.

RESUMEN / SUMMARY: - Data mining on public domain identified that thymidylate synthetase (TYMS) and dihydrofolate reductase (DHFR) transcripts were significantly higher expressed in nasopharyngeal carcinoma (NPC). In the folate

pathway, TYMS catalyzes the methylation of deoxyuridylate to deoxythymidylate using 5,10-methylenetetrahydrofolate [5,10-CH2=THF, derived from tetrahydrofolate (THF)], as a cofactor. This function maintains the thymidine-5-prime monophosphate pool critical for DNA replication and repair and, THF is generated from dihydrofolate (DHF) through the activity of DHFR. Immunoexpression of TYMS and DHFR were retrospectively assessed in biopsies of 124 consecutive NPC patients without initial distant metastasis and treated with consistent guidelines. The outcome was correlated with clinicopathological features and patient survivals. Results indicated that high TYMS (50%) expressions were correlated with primary tumor (p=0.008) and AJCC stage (p=0.006), and high DHFR (50%) expression were correlated with nodal status (p=0.039) and AJCC stage (p=0.029) (7th American Joint Committee on Cancer), respectively. In multivariate analyses, high TYMS expression emerged as an independent prognosticator for worse disease-specific survival (p<0.001), distal metastasis-free survival (p=0.002) and local recurrence-free survival (p<0.001), along with AJCC stage. Therefore, TYMS expression is common and associated with adverse prognosticators and might confer tumor aggressiveness through dysregulation of the nucleotide biosynthetic process.

TÍTULO / TITLE: - Activation of Rac1 GTPase promotes leukemia cell chemotherapy resistance, quiescence and niche interaction.

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

REVISTA / JOURNAL: - Mol Oncol. 2013 May 15. pii: S1574-7891(13)00080-X. doi: 10.1016/j.molonc.2013.05.001.

●● Enlace al texto completo (gratuito o de pago)

1016/j.molonc.2013.05.001

AUTORES / AUTHORS: - Wang JY; Yu P; Chen S; Xing H; Chen Y; Wang M; Tang K; Tian Z; Rao Q; Wang J

INSTITUCIÓN / INSTITUTION: - State Key Laboratory of Experimental Hematology, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, 288 Nanjing Road, Tianjin 300020, PR China.

RESUMEN / SUMMARY: - Leukemia stem cells (LSCs) reside in bone marrow niche and receive important signals from the microenvironment that support self-renewal, maintain quiescence and endow LSC with the ability of chemotherapy resistance. Rac1 belongs to the small GTP-binding protein superfamily and is implicated in the interactions of hematopoietic progenitors and bone marrow niche. Our previous studies have shown that Rac1 is over-expressed in leukemia patients and activation of Rac1 GTPase is closely associated with the efficient migration of leukemia cells. However, the potential functions for Rac1 GTPase in LSCs behaviors and in the residence of leukemia cells in niche remain unknown. In this study, by forced expression of a

dominant-negative form of Rac1 GTPase in a CD34+ myeloid leukemia cell line, as well as bone marrow cells from leukemia patients, we show that inactivation of Rac1 GTPase causes impaired migration and enhances chemotherapeutic sensitivity. Inactivation of Rac1 in leukemia cells also lead to a reduction in the frequency of cells in quiescent state and inhibition of homing to bone marrow niche. Gene expression analysis shows that inactivation of Rac1 down-regulates the expression of several cell intrinsic cell cycle inhibitors such as p21, p27, and p57, as well as the extrinsic molecules that mediated the interaction of LSC with osteoblastic niche. Furthermore, we show that Rac1 mediated the localization in niche is further attributed to the maintenance of quiescence. Our results provide evidence for the critical role of Rac1 GTPase in leukemia cell chemotherapy resistance, quiescence maintenance and the interaction with bone marrow microenvironment.

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[14]

TÍTULO / TITLE: - Adjuvant treatment in resected non-small cell lung cancer: Current and future issues.

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

REVISTA / JOURNAL: - Crit Rev Oncol Hematol. 2013 Jun 25. pii: S1040-8428(13)00120-0. doi: 10.1016/j.critrevonc.2013.05.017.

●● Enlace al texto completo (gratuito o de pago)

1016/j.critrevonc.2013.05.017

AUTORES / AUTHORS: - Remon J; Lianes P; Martinez S; Velasco M; Querol R; Zanui M

INSTITUCIÓN / INSTITUTION: - Medical Oncology Department, Hospital de Mataro, Carretera de la Cirera, s/n, 08304 Mataro, Barcelona, España. Electronic address: jremon@csdm.cat.

RESUMEN / SUMMARY: - The cornerstone of treatment for early-stage non-small cell lung cancer (NSCLC) has been surgical resection. In the last five years two phase III trials have provided evidence of adjuvant platinum-based chemotherapy for completely resected stage II-IIIA patients. We review the evidence supporting adjuvant therapy in early-stage NSCLC; we discuss new issues surrounding adjuvant therapy such as treatment in the elderly-unfit population, treatment toxicity and its influence on outcomes, the importance of histology and gender in adjuvant treatment; and we discuss the future landscape of early-stage NSCLC research, namely, therapeutic strategies exploiting pharmacogenomic and gene-expression profiling, in an attempt to customize the treatment.

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[15]

TÍTULO / TITLE: - Efficacy and safety profile of combining agents against epidermal growth factor receptor or vascular endothelium growth factor receptor

with gemcitabine-based chemotherapy in patients with advanced pancreatic cancer: A meta-analysis.

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

REVISTA / JOURNAL: - Pancreatology. 2013 Jul-Aug;13(4):415-22. doi: 10.1016/j.pan.2013.04.195. Epub 2013 Apr 28.

●● Enlace al texto completo (gratuito o de pago) 1016/j.pan.2013.04.195

AUTORES / AUTHORS: - Tian W; Ding W; Kim S; Xu X; Pan M; Chen S

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, No. 1665, Kongjiang Road, Yangpu District, Shanghai 200092, PR China.

RESUMEN / SUMMARY: - OBJECTIVES: Several clinical trials have been published on gemcitabine-based chemotherapy with or without addition of agents against epidermal growth factor receptor (EGFR) or vascular endothelium growth factor receptor (VEGFR) in patients with advanced pancreatic cancer, however, with diverse results. The objective of this study was to perform a meta-analysis of the published trials. METHODS: The database of CENTRAL, MEDLINE and EMBASE were searched. Eligible studies were randomized clinical trials (RCTs) that evaluated the efficacy and safety profile of adding targeted agents against EGFR or VEGFR to gemcitabine-based chemotherapy in patients with advanced pancreatic cancer. The primary outcome was overall survival (OS) while secondary outcomes included progression free survival (PFS) and overall response rate (ORR). Toxicity profiles were also assessed. Review Manager 5.1 was used to perform the analysis. RESULTS: Results reported from 6 RCTs involving 2733 patients were included in the analysis. Compared to gemcitabine-based chemotherapy alone, addition of an agent against EGFR resulted in significant longer OS [Hazard ratios (HR) 0.89 (0.79-0.99), p = 0.04] and longer PFS [HR 0.87 (0.79-0.97), p = 0.01], but no significant difference in ORR [RR 1.18 (0.82-1.70), p = 0.36]. The addition of an agent against VEGFR resulted in higher ORR [RR 1.54 (1.03-2.30), p = 0.04], but no advantage in OS [HR 0.95 (0.83-1.09), p = 0.47] or PFS [HR 0.97 (0.77-1.23), p = 0.82]. CONCLUSIONS: Addition of an agent against EGFR to gemcitabine-based chemotherapy improved OS compared to gemcitabine-based chemotherapy alone in patients with advanced pancreatic cancer, while addition of an agent against VEGFR showed a modest improvement in ORR but not PFS and OS.

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[16]

TÍTULO / TITLE: - Incidence of chemotherapy-induced neutropenia and current practice of prophylaxis with granulocyte colony-stimulating factors in cancer patients in España: a prospective, observational study.

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

REVISTA / JOURNAL: - Eur J Cancer Care (Engl). 2013 Jul;22(4):513-21. doi: 10.1111/ecc.12057. Epub 2013 Jun 3.

●● Enlace al texto completo (gratuito o de pago) 1111/ecc.12057

AUTORES / AUTHORS: - Jolis L; Carabantes F; Pernas S; Cantos B; Lopez A; Torres P; Funes C; Caballero D; Benedit P; Salar A

INSTITUCIÓN / INSTITUTION: - Oncology Unit, Hospital General de Granollers, Granollers, España.

RESUMEN / SUMMARY: - We aimed to describe the incidence of neutropenia in breast cancer and lymphoma patients and granulocyte colony-stimulating factors (G-CSF) use in clinical practice. We conducted a multicentre, prospective, observational study including breast cancer and lymphoma patients initiating chemotherapy (>/= 10% febrile neutropenia risk). We included 734 patients with breast cancer and 291 with lymphoma. Over the first four chemotherapy cycles, patients had an incidence of 11.0% grade 3-4 neutropenia (absolute neutrophil count <1.0 x 10(9) /L) and 4.3% febrile neutropenia (absolute neutrophil count <0.5 x 10(9) /L and fever >/= 38 degrees C) in the breast cancer cohort, and 40.5% and 14.8% in the lymphoma cohort. Full dose on schedule (>85% of planned chemotherapy dose and </= 3 days delay) was achieved by 85.6% of breast cancer and 68.9% of lymphoma patients. Hospitalisation due to febrile neutropenia was required in 2.0% and 12.0% of breast cancer and lymphoma patients respectively. G-CSF was administered to 70.0% of breast cancer and 83.8% of lymphoma patients, and initiated from the first chemotherapy cycle (primary prophylaxis) in 60.6% and 64.2% of cases. Severe neutropenia affects approximately one in 10 breast cancer patients and one in two lymphoma patients receiving chemotherapy with moderate or greater risk of febrile neutropenia. Most patients received treatment with G-CSF in Spanish clinical practice.

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[17]

TÍTULO / TITLE: - Epidermal growth factor receptor tyrosine kinase inhibitor versus placebo as maintenance therapy for advanced non- small-cell lung cancer: a meta-analysis of randomized controlled trials.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(4):2413-9.

AUTORES / AUTHORS: - Alimujiang S; Zhang T; Han ZG; Yuan SF; Wang Q; Yu TT; Shan L

INSTITUCIÓN / INSTITUTION: - Department of Chemotherapy, Tumor Hospital Affiliated to Xinjiang Medical University, Urumqi, China.

RESUMEN / SUMMARY: - BACKGROUND: Use of epidermal growth factor receptor inhibitors (EGFR-TKIs) is now standard for non- small-cell lung cancer (NSCLC). However, the effects of EGFR-TKIs in maintenance therapy for advanced NSCLC patients are still unclear. The preent meta-analysis was performed to examine pooled data of randomized control trials (RCT) where EGFR-TKIs were compared against placebo in maintenance regimens for patients with advanced NCSLC to quantify potential benefits and determine

safety. METHODS: Several data bases were searched, including PubMed, EMBASE and CENTRAL, and we performed an internet search of conference literature. The endpoints were objective response rates (ORR), progression-free survival (PFS) and overall survival (OS). We performed a meta-analysis of the published data, using Comprehensive Meta Analysis software (Version 2.0). with a fixed effects model and an additional random effects model, when applicable. The results of the meta-analysis are expressed as hazard ratios (HRs) or risk ratios (RRs), with their corresponding 95% confidence intervals (95%CIs). RESULTS: The final analysis included six trials, covering 3,758 patients. Compared with placebo, EGFR-TKIs maintenance therapy improved ORR and PFS for patients with advanced NSCLC, the difference being statistically significant (P<0.05), but proved unable to prolong patients' OS. The main adverse reactions were diarrhea and rashes. CONCLUSION: EGFR-TKIs demonstrated encouraging efficacy, safety and survival when delivered as maintenance therapy for patients with advanced NSCLC after first-line chemotherapy, especially for the patients who had adenocarcinomas, were female, non-smokers and patients with EGFR gene mutations.

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[18]

TÍTULO / TITLE: - Lack of Association between Cytotoxic T-Lymphocyte Antigen-4 -318C/T Polymorphism and Cancer Risk: A Meta-analysis of Case-Control Studies.

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

REVISTA / JOURNAL: - Technol Cancer Res Treat. 2013 Jun 6.

●● Enlace al texto completo (gratuito o de pago) 7785/tcrt.2012.500350

AUTORES / AUTHORS: - Xia W; Shi R; Zheng WL; Ma WL

INSTITUCIÓN / INSTITUTION: - Institute of Genetic Engineering, Southern Medical University, Guangzhou, People's Republic of China. weneli0626@126.com.

RESUMEN / SUMMARY: - Cytotoxic T-lymphocyte antigen-4 (CTLA-4) is important for the down regulation of T-cell activation. Number of studies assessed the association between CTLA-4 -318C/T polymorphisms and cancer in different populations. However, the studies have provided conflicting results. We performed a meta-analysis to examine the association between CTLA-4 -318C/T polymorphisms and cancer susceptibility. Eligible studies were identified by searching several databases for relevant reports published up to September 30, 2012. Sixteen eligible studies with a total of 6190 patients and 6560 controls were included to summarize the association between CTLA-4 -318C/T polymorphisms and the risk of cancer. Odds ratios (ORs) with 95% confidence intervals (CIs) were used to assess the strength of associations. Overall, no significant associations were found in all genetic models when all studies were pooled into the meta-analysis (for -318C/T polymorphisms as estimated using a fixed effect model: TT vs. (CC + CT), OR = 1.02, 95% CI = 0.83-1.24; (TT + CT) vs. CC, OR = 1.20, 95% CI = 1.00-1.44; TT vs. CC, OR = 1.09, 95% CI = 0.74-

1.59; CT vs. CC, OR = 1.21, 95% CI = 1.00-1.46). In further subgroup analyses for the -318C/T polymorphisms, stratified by design of ethnicity, cancer types, solid tumors to non-solid tumors, epithelial tumors to non-epithelial tumors, no significant associations were found in any subgroup of the population. This meta-analysis strongly suggests that -318C/T polymorphisms in CTLA-4 are not associated with an increased risk of cancer.

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[19]

TÍTULO / TITLE: - Prognostic Role of Human Epidermal Growth Factor Receptor in Gastric Cancer: A Systematic Review and Meta-analysis.

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

REVISTA / JOURNAL: - Arch Med Res. 2013 Jul 16. pii: S0188-4409(13)00145-8. doi: 10.1016/j.arcmed.2013.07.001.

●● Enlace al texto completo (gratuito o de pago)

1016/j.arcmed.2013.07.001

AUTORES / AUTHORS: - Chen C; Yang JM; Hu TT; Xu TJ; Yan G; Hu SL; Wei W; Xua WP

INSTITUCIÓN / INSTITUTION: - Institute of Clinical Pharmacology, Anhui Medical University, Key Laboratory of Antiinflammatory and Immunopharmacology of Education Ministry, Hefei, China.

RESUMEN / SUMMARY: - BACKGROUND AND AIMS: Human epidermal growth factor receptor (EGFR) and HER2 (ErbB2) both belong to EGFR family, which are overexpressed in a significant proportion of cases of gastric cancer (GC). Various studies have evaluated the prognostic value of EGFR or HER level in GC. However, the overall test performance remains unclear. We undertook this study to perform a systematic review and meta-analysis of prognostic cohort studies evaluating the use of EGFR or HER2 as a predictor of survival time in patients with GC. METHODS: Eligible studies were identified through multiple search strategies. Studies were assessed for quality using the Newcastle-Ottawa Tool. Data were collected comparing overall survival (OS) in patients with high and low EGFR or HER2 level. Studies were pooled and summary hazard ratios were calculated. RESULTS: Studies were listed twice if they provided overall survival data for both EGFR and HER2. Eight studies (seven for EGFR and eight for HER2) were included. Two distinct groups were pooled for analysis and revealed that high EGFR, HER2 levels predicted poor overall (HR = 1.66, 95% CI: 1.35-2.02) and (HR = 1.43, 95% CI: 1.09-1.88) survival. No publication bias was found. CONCLUSIONS: This meta-analysis result suggested that EGFR or HER2 should have significant predictive ability for estimating overall survival in GC patients and may be useful for defining prognosis of GC patients.

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[20]

TÍTULO / TITLE: - Tissue inhibitor of metalloproteinase 1 (TIMP-1) as a biomarker in gastric cancer: a review.

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

REVISTA / JOURNAL: - Scand J Gastroenterol. 2013 Aug;48(8):899-905. doi: 10.3109/00365521.2013.812235. Epub 2013 Jul 8.

●● Enlace al texto completo (gratuito o de pago)

3109/00365521.2013.812235

AUTORES / AUTHORS: - Grunnet M; Mau-Sorensen M; Brunner N

INSTITUCIÓN / INSTITUTION: - Department of Oncology, Rigshospitalet , Copenhagen , Denmark.

RESUMEN / SUMMARY: - Abstract Objective. The value of Tissue Inhibitor of MetalloProteinase-1 (TIMP-1) as a biomarker in patients with gastric cancer (GC) is widely debated. The aim of this review is to evaluate available literature describing the association between levels of TIMP-1 in tumor tissue and/or blood and the prognosis of patients suffering from GC. Material and methods. Using the search words 'TIMP-1', 'Gastric Cancer' and 'Tumor marker', a search was carried out on PubMed. Exclusion criteria were articles never published in English, articles from before 1995 and articles evaluating tumor markers other than TIMP-1 in GC. Results. Of initially 50 articles, 17 were found to fulfill the selection criteria and relevant for this study. The 17 articles evaluated the usefulness of TIMP-1 levels in tumor tissue or blood, respectively, as a prognostic marker in patients with GC. Conclusions: A literature search showed that elevated protein levels of TIMP-1 in either tumor tissue extracts or in plasma from patients suffering from GC associates with poor patient outcome.

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[21]

TÍTULO / TITLE: - Meta-analysis of Associations of the Ezrin Gene with Human Osteosarcoma Response to Chemotherapy and Prognosis.

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

REVISTA / JOURNAL: - Asian Pac J Cancer Prev. 2013;14(5):2753-8.

AUTORES / AUTHORS: - Wang Z; He ML; Zhao JM; Qing HH; Wu Y

INSTITUCIÓN / INSTITUTION: - Graduate School of Guangxi Medical University, Nanning, Guangxi, China E-mail : zhaojinmin@hotmail.com.

RESUMEN / SUMMARY: - Various studies examining the relationship between Ezrin overexpression and response to chemotherapy and clinical outcome in patients with osteosarcoma have yielded inconclusive results. We accordingly conducted a meta-analysis of 7 studies (n = 318 patients) that evaluated the correlation between Ezrin and histologic response to chemotherapy and clinical prognosis (death). Data were synthesized in receiver operating characteristic curves and with fixed-effects and random-effects likelihood ratios and risk ratios. Quantitative synthesis showed that Ezrin is not a prognostic factor for the response to chemotherapy. The positive likelihood ratio was 0.538 (95%

confidence interval [95% CI], 0.296- 0.979; random-effects calculation), and the negative likelihood ratio was 2.151 (95% CI, 0.905- 5.114; random-effects calculations). There was some between-study heterogeneity, but no study showed strong discriminating ability. Conversely, Ezrin positive status tended to be associated with a lower 2-year survival (risk ratio, 2.45; 95% CI, 1.26-4.76; random-effects calculation) with some between-study heterogeneity that disappeared when only studies that employed immunohistochemistry were considered (risk ratio, 2.97; 95% CI, 2.01- 4.40; fixed-effects calculation). To conclude, Ezrin is not associated with the histologic response to chemotherapy in patients with osteosarcoma, whereas Ezrin positivity was associated with a lower 2-year survival rate regarding risk of death at 2 years. Expression change of Ezrin is an independent prognostic factor in patients with osteosarcoma.

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[22]

TÍTULO / TITLE: - Ultrasound-mediated drug/gene delivery in solid tumor treatment.

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

REVISTA / JOURNAL: - J Healthc Eng. 2013;4(2):223-54. doi: 10.1260/2040-2295.4.2.223.

●● Enlace al texto completo (gratuito o de pago) 1260/2040-2295.4.2.223

AUTORES / AUTHORS: - Zhou Y

INSTITUCIÓN / INSTITUTION: - School of Mechanical and Aerospace Engineering, Nanyang Technological University, Singapore. yfzhou@ntu.edu.sg

RESUMEN / SUMMARY: - Ultrasound is an emerging modality for drug delivery in chemotherapy. This paper reviews this novel technology by first introducing the designs and characteristics of three classes of drug/gene vehicles, microbubble (including nanoemulsion), liposomes, and micelles. In comparison to conventional free drug, the targeted drug-release and delivery through vessel wall and interstitial space to cancerous cells can be activated and enhanced under certain sonication conditions. In the acoustic field, there are several reactions of these drug vehicles, including hyperthermia, bubble cavitation, sonoporation, and sonodynamics, whose physical properties are illustrated for better understanding of this approach. In vitro and in vivo results are summarized, and future directions are discussed. Altogether, ultrasound-mediated drug/gene delivery under imaging guidance provides a promising option in cancer treatment with enhanced agent release and site specificity and reduced toxicity.

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[23]

TÍTULO / TITLE: - The impact of chemokine receptor CXCR4 on breast cancer prognosis: A meta-analysis.

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

REVISTA / JOURNAL: - Cancer Epidemiol. 2013 Jun 10. pii: S1877-7821(13)00080-5. doi: 10.1016/j.canep.2013.04.017.

●● Enlace al texto completo (gratuito o de pago)

1016/j.canep.2013.04.017

AUTORES / AUTHORS: - Xu TP; Shen H; Liu LX; Shu YQ

INSTITUCIÓN / INSTITUTION: - Department of Oncology, The First Affiliated Hospital of Nanjing Medical University, No. 300 Guangzhou Road, Nanjing 210029, People's Republic of China. Electronic address: tongpeng_xu@yahoo.cn.

RESUMEN / SUMMARY: - Background: C-X-C chemokine receptor type 4 (CXCR4) has been implicated in the invasiveness and metastasis of diverse cancers. However, the published data remain controversial on the correlation between CXCR4 expression level, as well as its subcellular distribution in tumor cells, and the clinical outcome of patients with breast cancer. Methods: To identify the precise role of CXCR4 in the clinical outcome of breast cancer, we performed a meta-analysis including 15 published studies. Original data included the hazard ratios (HRs) of overall survival (OS) and disease-free survival (DFS) in breast cancer with high CXCR4 expression versus low expression. We pooled hazard ratios (HRs) with 95% confidence intervals (CIs) to estimate the hazard. Results: A total of 15 published studies (including 3104 patients) were eligible. Overall survival (OS) and disease-free survival (DFS) of breast cancer were found to be significantly related to CXCR4 expression level, with the HR being 1.65 (95%CI: 1.34-2.03; P<0.00001) and 1.94 (95%CI: 1.42-2.65; P<0.00001) respectively. Stratified analysis according to subcellular distribution of CXCR4 showed that high expression in whole cells, cytoplasm and nucleus could predict unfavorable OS, with the HR of 2.02 (95%CI: 1.43-2.85; P<0.0001), 1.57 (95%CI: 1.13-2.18; P=0.007), and 1.47 (95%CI: 1.19-1.81; P=0.0004) respectively. As for DFS, elevated expression level of CXCR4 both in whole cells and cytoplasm predicted a poor outcome, with the HR being 2.23 (95%CI: 1.48-3.37; P=0.0001) and 1.76 (95%CI: 1.11-2.80; P=0.02), while high expression in the nucleus had no statistical significance, with HR 1.15 (95%CI: 0.52-2.55; P=0.73). Conclusions: Increased CXCR4 expression, especially in whole cells and cytoplasm, may serve as a poor prognostic indicator in patients with breast cancer. Future studies are warranted to investigate the relationship between CXCR4 expression and survival of patients with breast carcinoma, which could help predict the clinical outcome and guide clinical decision-making for therapy.

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[24]

TÍTULO / TITLE: - Prognostic significance of vascular endothelial growth factor expression in esophageal carcinoma: a meta-analysis.

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

REVISTA / JOURNAL: - J BUON. 2013 Apr-Jun;18(2):398-406.

AUTORES / AUTHORS: - Peng J; Shao N; Peng H; Chen LQ

INSTITUCIÓN / INSTITUTION: - West China Medical School, Sichuan University, Chengdu, Sichuan, China.

RESUMEN / SUMMARY: - Purpose: The purpose of this study was to comprehensively and quantitatively review eligible published studies to explore the prognostic significance of vascular endothelial growth factor (VEGF) expression in patients with esophageal carcinoma (EC). Methods: PubMed and Embase databases were searched until September 11, 2011. A meta-analysis was performed to demonstrate any relationship between VEGF and 5-year overall survival (OS) in EC patients. Results: The ?nal analysis included 1453 patients from 19 studies. The studies were grouped by patient source, histology, VEGF isoform and cutoff value. The estimated risk of death suggested that VEGF positivity had negative impact on prognosis of patients with EC, esophageal squamous cell carcinoma (ESCC) and Asian patients. The risk ratios (RR) and 95% con?dence interval (95% CI) were 1.26 (1.16-1.37) in EC patients, 1.28 (1.16-1.40) in ESCC patients and 1.35 (1.24-1.48) in Asian patients. Furthermore, when the cutoff value was set at 10% in 6 studies, the RR (95% CI) was 1.48 in the VEGF positive group (1.27-1.73). In addition, VEGFC was also correlated with patient poor prognosis with a RR (95% CI) of 1.30 (1.15-1.48). However, EC patients from non-Asian countries and cutoff value at 30% showed no significant correlation with survival. Data were not suf?cient to determine the prognostic value of VEGF expression in esophageal adenocarcinoma (EA) patients and VEGFD expression. Conclusions: VEGF positivity indicated poor prognosis in patients with EC, ESCC and of Asian origin. Cutoff value at 10% may be a more appropriate standard to define VEGF positivity. VEGFC also correlated with poor prognosis in EC patients.

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[25]

TÍTULO / TITLE: - Hepatitis B and C reactivation with tumor necrosis factor inhibitors: synopsis and interpretation of screening and prophylaxis recommendations.

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

REVISTA / JOURNAL: - Isr Med Assoc J. 2013 Jun;15(6):303-7.

AUTORES / AUTHORS: - Fuchs I; Abu-Shakra M; Sikuler E

INSTITUCIÓN / INSTITUTION: - Pediatric Infectious Disease Unit, Soroka University Medical Center, Israel.

RESUMEN / SUMMARY: - Information on reactivation of chronic viral hepatitis infection in patients who are candidates for tumor necrosis factor alpha inhibitors (TNFi) is in a constant state of flux. We retrieved the most updated guidelines (in English) of prominent rheumatological and gastroenterological professional socienties for the mangement of chronic hepatitis B (HBV) and hepatitis C virus (HCV) infection in the context of treatment with TNFi. Subsequently, the major areas of uncertainty and absence of consensus in the guidelines were located and a secondary search for additional studies addressing those areas was performed. Based on our search we formulated a

personal interpretation applicable to health care settings with virological laboratories capable of performing viral load measurements, and health systems that can support use of potent nucleoside/tide analogues in well-defined patient populations.

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[26]

TÍTULO / TITLE: - Endometrial tumour BRAF mutations and MLH1 promoter methylation as predictors of germline mismatch repair gene mutation status: a literature review.

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

REVISTA / JOURNAL: - Fam Cancer. 2013 Jul 24.

●● Enlace al texto completo (gratuito o de pago) 1007/s10689-013-9671-6

AUTORES / AUTHORS: - Metcalf AM; Spurdle AB

INSTITUCIÓN / INSTITUTION: - Department of Genetics and Computational Biology, Queensland Institute of Medical Research, Herston, QLD, 4006, Australia.

RESUMEN / SUMMARY: - Colorectal cancer (CRC) that displays high microsatellite instability (MSI-H) can be caused by either germline mutations in mismatch repair (MMR) genes, or non-inherited transcriptional silencing of the MLH1 promoter. A correlation between MLH1 promoter methylation, specifically the 'C' region, and BRAF V600E status has been reported in CRC studies. Germline MMR mutations also greatly increase risk of endometrial cancer (EC), but no systematic review has been undertaken to determine if these tumour markers may be useful predictors of MMR mutation status in EC patients. Endometrial cancer cohorts meeting review inclusion criteria encompassed 2675 tumours from 20 studies for BRAF V600E, and 447 tumours from 11 studies for MLH1 methylation testing. BRAF V600E mutations were reported in 4/2675 (0.1 %) endometrial tumours of unknown MMR mutation status, and there were 7/823 (0.9 %) total sequence variants in exon 11 and 27/1012 (2.7 %) in exon 15. Promoter MLH1 methylation was not observed in tumours from 32 MLH1 mutation carriers, or for 13 MSH2 or MSH6 mutation carriers. MMR mutation-negative individuals with tumour MLH1 and PMS2 IHC loss displayed MLH1 methylation in 48/51 (94 %) of tumours. We have also detailed specific examples that show the importance of MLH1 promoter region, assay design, and quantification of methylation. This review shows that BRAF mutations occurs so infrequently in endometrial tumours they can be discounted as a useful marker for predicting MMR-negative mutation status, and further studies of endometrial cohorts with known MMR mutation status are necessary to quantify the utility of tumour MLH1 promoter methylation as a marker of negative germline MMR mutation status in EC patients.

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[27]

TÍTULO / TITLE: - Leuprolide acetate 1-, 3- and 6-monthly depot formulations in androgen deprivation therapy for prostate cancer in nine European countries: evidence review and economic evaluation.

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

REVISTA / JOURNAL: - Clinicoecon Outcomes Res. 2013 Jun 24;5:257-69. doi: 10.2147/CEOR.S44855. Print 2013.

●● Enlace al texto completo (gratuito o de pago) 2147/CEOR.S44855

AUTORES / AUTHORS: - Wex J; Sidhu M; Odeyemi I; Abou-Setta AM; Retsa P; Tombal B

INSTITUCIÓN / INSTITUTION: - PharmArchitecture Limited, London, UK.

RESUMEN / SUMMARY: - OBJECTIVE: Leuprolide is an established luteinizing hormone-releasing hormone (LHRH) agonist used as first-line treatment in advanced prostate cancer. As different formulations and dosing schedules are likely to have economic implications, we aimed to evaluate their efficacy, safety, and costs in nine European countries: Austria, Belgium, Czech Republic, Hungary, Italy, Latvia, Netherlands, Poland, and Portugal. METHODS: Database searches identified 13 clinical trials of leuprolide 1- (1 M), 3- (3 M) and 6-monthly (6 M). Only data on leuprolide with Atrigel were compared for all three formulations, which had the same efficacy, safety, and adherence. Cost-minimization analysis accounting for cost of Eligard®, specialist consultations, and diagnostics during up to 12 months follow-up was conducted. The perspective was that of public payers. RESULTS: No significant differences were observed in the percentages of intention-to-treat patients achieving testosterone levels </= 50 ng/dL following treatment with Eligard® 1 M (93.3%), 3 M (98.3%), and 6 M (97.3%) (P > 0.05), and adverse event profiles of the three formulations were comparable. Overall, 6 M was the least expensive, with average total annual costs from euro788 (Belgium) to euro1839 (Portugal). The 3 M option was between 2.5% (Hungary) and 37.6% (Belgium) more expensive than 6 M; 1 M formulation was the most expensive, with costs 15.5% and 151.6% more expensive than 6 M for those countries, respectively. The 3 M option was 11.2%-45.3% less expensive than 1 M. Total costs were associated with frequency of visits for injection and monitoring. The 1 M required twelve visits, 3 M 4.4-4.8 visits, and 6 M 2.1-2.3 visits. Up to 50% additional visits could be funded with the savings resulting from switching eligible patients from 1 M and 3 M to 6 M. Results were stable in univariate and probabilistic sensitivity analyses. CONCLUSION: Eligard® formulations offer comparable efficacy and safety, but different dosing schedules require different number of visits. The 6 M formulation offers the greatest cost savings and should be considered the treatment of choice in eligible patients in Europe.

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TÍTULO / TITLE: - Use of azacitidine for myelodysplastic syndromes: controversial issues and practical recommendations.

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

REVISTA / JOURNAL: - Blood Res. 2013 Jun;48(2):87-98. doi: 10.5045/br.2013.48.2.87. Epub 2013 Jun 25.

●● Enlace al texto completo (gratuito o de pago) 5045/br.2013.48.2.87

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RESUMEN / SUMMARY: - Azacitidine is recommended for patients with higher-risk myelodysplastic syndromes (MDS) who are not eligible for intensive therapy or for patients with lower-risk MDS who have thrombocytopenia or neutropenia or have anemia that is unresponsive to other therapies. However, standard treatment with azacitidine has not been optimized and many issues about the use of azacitidine remain unresolved. The use of azacitidine is expanding rapidly, but limited comparative clinical trial data are available to (i) define the optimal use of azacitidine in patients with higher-risk MDS or around the time of allogeneic hematopoietic stem cell transplantation, (ii) identify those patients with lower-risk MDS who may benefit from treatment, and (iii) guide physicians on alternative therapies after treatment failure. Increasing evidence suggests that the clinical features, prognostic factors, and cytogenetic profiles of patients with MDS in Asia differ significantly from those of patients in Western countries, so the aim of this review is to summarize the evidence and provide practical recommendations on the use of azacitidine in patients with MDS in the Republic of Korea. Evidence considered in this review is based on published clinical data and on the clinical experience of an expert panel from the acute myeloid leukemia/MDS Working Party of the Korean Society of Hematology.
