Semantic MEDLINE: An Advanced Information Management Application for Biomedicine

Thomas C. Rindflesch, Ph.D.
Lister Hill National Center for Biomedical Communications
Access to online text

- Document retrieval systems
  - Document retrieval systems
  - PubMed for biomedical information
- Technology: Manipulate text strings
  - Technology: Manipulate text strings
  - Frequency of occurrence
Access to online text

- Document retrieval systems
  - Google
  - PubMed for biomedical information
- Technology: Manipulate text strings
  - Frequency of occurrence
  - Distribution patterns
  - No access to meaning
Emerging applications

- Text mining
  - Task-driven extraction of facts
  - Observe trends
- Connect text and structured data
- Question answering
- Literature-based discovery
  - Research assistance
Emerging applications

- Text mining
  - Task-driven extraction of facts
  - Observe trends
- Connect text and structured data
- Question answering
- Literature-based discovery
  - Research assistance
- Require more effective language processing
Augment document retrieval systems
Manipulate information
  - Not just documents
Bridge the gap between
  - Language (text)
  - Meaning
Summarize and visualize information
  - In the biomedical domain
Automatic semantic interpretation

- Augment document retrieval systems
- Manipulate information
  - Not just documents
- Bridge the gap between
  - Language (text)
  - Meaning
- Summarize and visualize information
  - In the biomedical domain
Semantic MEDLINE
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PubMed
MEDLINE citations
Natural language processing
Semantic relationships
Automatic summarization
Graphical summary

Enhanced access to biomedical research literature
Tamoxifen has long been considered the hormonal therapy of choice for patients with estrogen-responsive breast cancer, accumulating clinical data suggest the new generation of aromatase inhibitors (AIs) is more effective and less toxic. With the availability of new information, guidelines have been updated and reformulated regarding the use of AIs as first-line hormonal therapy in postmenopausal women with ER-positive breast cancer. This paper, a product of the ongoing advances in oncology, incorporates two distinct, yet important, features of oncology: first, clinical concepts related to hormone-dependent breast cancer and second, pharmacoeconomic outcomes. The antiestrogen tamoxifen and the new generation of aromatase inhibitors for post-menopausal women with advanced breast cancer. AB - Adjuvant trastuzumab in the treatment of HER-2-positive early breast cancer: a meta-analyses of published randomized trials. ABSTRACT: BACKGROUND: Breast cancer is the most common cancer in women in the U.S. and western Europe. Amplification of the her-2/neu gene occurs in approximately 25% of invasive ductal carcinomas of the breast. The first HER-2/neu-targeted approach to reach the clinic was trastuzumab, a humanized monoclonal antibody directed against the extracellular domain of the HER-2/neu protein. Trastuzumab therapy prolongs the survival of patients with metastatic HER-2/neu-overexpressing breast cancer when combined with chemotherapy and has recently been demonstrated to lead to dramatic improvements in disease-free survival when used in the adjuvant therapy setting in combination with or following chemotherapy. Here, we performed a meta-analyses of completed clinical trials of adjuvant trastuzumab in the treatment setting. Survival, recurrence, brain metastases, cardiotoxicity and directions for future research are discussed. METHODS: A meta-analysis of randomized controlled trials (RCT) was performed comparing adjuvant trastuzumab treatment for HER2-positive early breast cancer (EBC) to observation. The MEDLINE, EMBASE, CANCERLIT and Cochrane Library databases, and abstracts published in the annual proceedings were systematically searched for evidence. Relevant results were reviewed independently and the references from these reports were searched for additional trials, using guidelines set by QUOROM statement criteria. RESULTS: Pooled results from that five randomized trials of adjuvant Trastuzumab showed a significant reduction of mortality (p0.00001), recurrence (p0.00001), metastases rates (p0.00001) and second tumors other than skin or brain (2.07) as compared with observation (95% CI 1.89 - 2.25) versus no treatment. The likelihood of cardiac toxicity was 2.45-fold higher (95% CI 1.89 - 3.16) in trastuzumab arms, however that result was associated with heterogeneity. The likelihood of brain metastases was 1.82-fold higher (95% CI 1.16 - 2.85) in patients who received trastuzumab. CONCLUSION: The results from this meta-analysis are sufficiently compelling to consider 1 year of adjuvant trastuzumab treatment for women with HER-2-positive EBC based on the risk: benefit ratio demonstrated in these studies. Adequate assessment of HER-2/neu status is critical, and careful cardiac monitoring is warranted because of cardiac toxicity. Clinical trials should be designed to answer unsolved questions. TI - Adjuvant chemotherapy in patients with HER2-overexpressing breast cancer: a meta-analyses of published randomized trials. AB:To test the hypothesis that the addition of trastuzumab to standard chemotherapy improves disease-free and overall survival in patients with HER2-overexpressing breast cancer. METHODS: A systematic review and meta-analysis of randomized controlled trials in patients with HER2-overexpressing breast cancer was performed. RESULTS: Five randomized trials that compared trastuzumab plus chemotherapy versus chemotherapy alone were identified. The results showed a significant improvement in disease-free survival (hazard ratio 0.71, 95% confidence interval 0.58 to 0.87) and overall survival (hazard ratio 0.69, 95% confidence interval 0.51 to 0.92) with the addition of trastuzumab. CONCLUSION: The addition of trastuzumab to standard chemotherapy appears to improve disease-free and overall survival in patients with HER2-overexpressing breast cancer.
Exemestane after non-steroidal aromatase inhibitor for post-menopausal women with advanced breast cancer
Unified Medical Language System

- Developed by National Library of Medicine
- SPECIALIST Lexicon
  - Linguistic information
- Metathesaurus
  - Biomedical concepts
- Semantic Network
  - Relationships between concepts
Metathesaurus concept

- Concept name
  - Arthroplasty

- Synonyms
  - Reconstruction of joint
  - Repair of joint ...

- Semantic type
  - Therapeutic or Preventive Procedure
Therapeutic or Preventive Procedure USES Medical Device
Pharmacologic Substance TREATS Disease or Syndrome
Body Location or Region LOCATION_OF Biologic Function
Disease or Syndrome OCCURS_IN Population Group
Disease or Syndrome PROCESS_OF Organism
tamoxifen has long been considered the hormonal therapy of choice for patients with estrogen-responsive breast cancer, accumulating clinical data suggest the new generation of aromatase inhibitors and tamoxifen in the treatment of hormone-receptor positive breast cancer. In patients with HER2-overexpressing breast cancer when combined with chemotherapy and has recently been demonstrated to lead to dramatic reductions in breast cancer mortality. Now, we demonstrate that phosphorylation of S305 in ERalpha results in resistance to tamoxifen. We show that phosphorylation of S305 is increased by tamoxifen treatment and that it is correlated with tamoxifen resistance in breast cancer cell lines. These results indicate that phosphorylation of S305 in ERalpha is a potential target for the development of new drugs to overcome tamoxifen resistance in breast cancer.

Our findings suggest that phosphorylation of S305 in ERalpha plays an important role in tamoxifen resistance in breast cancer. Further studies are needed to confirm these findings and to determine the clinical relevance of this finding. However, these results provide a potential target for the development of new drugs to overcome tamoxifen resistance in breast cancer.

Breast Carcinoma

- Tamoxifen
- Exemestane
- Breast Carcinoma

- Tamoxifen

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Domain coverage

- Initially developed for clinical medicine
- Extended to
  - Genetic etiology of disease
  - Substance interactions
  - Pharmacogenomics
- Working on
  - Influenza epidemic preparedness
  - Climate change and health
  - Health promotion
  - Biomedical knowledge processing
Focused on biomedical subdomains, e.g.
- Clinical treatment
- Genetic etiology of disease
- Pharmacogenomics

Overall
- Precision is around 75% (lower for molecular biology)
- Recall is around 60%
Semantic database

- MEDLINE (National Library of Medicine)
  - Bibliographic database of the biomedical research literature
  - More than 21 million citations (1940s to present)
- Semantic relationships extracted
  - 57 million (through 03/31/2012)
- Made available to the research community
  - SQL database
  - RDF triples
Information visualization

Tamoxifen TREATS Breast Carcinoma

CDKN1A gene ASSOCIATED_WITH Aromatase Inhibitors

BARD1 gene STIMULATES Aromatase Inhibitors

Stimulates Breast Carcinoma

Treats CDKN1A gene

Treats BARD1 gene
Tamoxifen TREATS Breast Carcinoma
Tamoxifen TREATS Breast Carcinoma
An alpha-fetoprotein-derived peptide reduces the uterine hyperplasia and increases the antitumour effect of tamoxifen.

Andersen TT, Georgekutty J, Defreest LA, Amaratunga G, Narendran A, Lemanski N, Jacobson HI, Bennett JA.

Center for Cardiovascular Sciences, Albany Medical College, Albany, NY 12208, USA.
anderst@mail.amc.edu

Tamoxifen (Tam) is effective for the treatment and prevention of breast cancer. However, it has toxic drawbacks and has limited-duration utility because, over time, human tumours become refractory to Tam. Recently, a new nontoxic peptide, alpha-fetoprotein-derived peptide (AFPpep) has been proposed for the treatment and prevention of breast cancer. The purpose of this paper is to determine whether combining AFPpep with Tam would increase efficacy and reduce toxicity in experimental models of breast cancer. Low doses of AFPpep and Tam were more effective in combination than either agent alone against breast cancer growth in cell culture, in tumour-xenografted mice, and in carcinogen-exposed rats. alpha-Fetoprotein-derived peptide interfered with Tam-induced uterine hyperplasia in immature mice, and showed no
Exploiting the technology

- Manipulate online information
  - Summarize
  - Visualize
  - Connect text to structured data
- Facilitate literature-based discovery for:
  - Research assistance
  - Observing trends
  - Support for decision making
    - Portfolio analysis
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