

Clinical opinions in general medicine

The first two opinions of 2004 concern themselves with two common, potentially life-threatening, conditions – community-acquired pneumonia (CAP) and colorectal cancer. Legge describes a simplified severity scoring index for CAP, which has the potential to be of great help both general practitioners and hospital physicians. Further prospective evaluation of the index is needed, however, before it can be recommended for widespread use. Second, Dawson describes a hopeful development in the treatment of advanced colorectal cancer. We hope you continue to find these opinions useful and welcome your comments and contributions.

Clinical opinion: refining severity scores in community acquired pneumonia: another new index

TITLE: Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study.
KEY WORDS: Community acquired pneumonia, severity, management, mortality
AUTHORS: Lim WS, Van der Eerden MM, Laing R *et al.*
JOURNAL: *Thorax* 2003; **58**:377–82.

SUMMARY

A new severity score applicable in primary and secondary care may guide the policy for admissions/ward management/HDU care/ITU Transfer and early/late discharge in CAP. This paper presents data from three prospective studies incorporating over 1,000 patients with CAP (from three different countries). The authors were able to develop a five-point score, and the model was then tested against a validation cohort of about 200 patients.

A point was given for each of the following – confusion, urea greater than 7 mmol/litre, respiratory rate equal to or greater than 30 breaths per minute, blood pressure (less than 90 mm systolic or less than 60 mm diastolic) and age equal to or greater than 65 years (CURB). Thus a CURB-65 score was derived at hospital admission. Thirty-day mortality risk for each score was nil 0.7%, one 3%, two 9%, three 17%, four 41.5%, five 57%. Low serum albumin also correlated with serious outcome measures.

OPINION

Severity indices based on American Thoracic Society and British Thoracic Society guidelines already exist as well as a pneumonia severity index (PSI). The CURB-65 scale described in this study is considerably simpler than the 20-point PSI, and correlated well with outcomes such as mortality and need for ITU transfer/ventilation. It is suggested that this simple scoring system can be used to stratify patients with CAP to different management groups, viz scores 0–1: mild pneumonia with very low mortality, suitable for home or out-patient management; score 2: moderate severity suitable for supervised in-patient hospital care; scores 3–5: severe pneumonia; must be treated in hospital with provision of HDU/ITU for highest scores.

Further prospective evaluation of this new index is required but this new severity scale represents an attractive simple scoring system with four easily-obtained clinical points, allowing assessment even in primary care where blood urea measurement is not immediately available.

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Clinical opinion: monoclonal antibody therapy as treatment for advanced cancer – molecular biology becomes clinically relevant

TITLE: The EGFR receptor as a target for anticancer therapy – focus on cetuximab.
KEYWORDS: Cetuximab, epidermal growth factor receptor, antibody therapy, metastatic cancer.
AUTHORS: Baselga J
JOURNAL: *Eur J Cancer* 2001; **37**:S16–22.

SUMMARY

This review paper introduces a new monoclonal antibody therapy for the treatment of advanced cancer. Its development is based on clinical translation of laboratory-based understanding of the molecular processes that promote tumour growth and survival. The epidermal growth factor receptor has a key role in cell signalling and is over-expressed in many cancers. This is associated with aggressive disease and poorer survival. The receptor has therefore been identified as a potential target for therapeutic intervention.

Cetuximab is a chimeric (part-mouse, part-human) monoclonal antibody designed to specifically bind to the epidermal growth factor. Cetuximab inhibits tumour growth and enhances cell death by inhibiting cell proliferation, angiogenesis and metastasis and promoting apoptosis. Early clinical trials have suggested that cetuximab enhances the anticancer effect of radiotherapy and chemotherapy in patients with advanced head and neck and colorectal cancers. Patients who were considered to have failed all standard treatments showed clinical responses in these studies. Cetuximab is well-tolerated, with the commonest side-effects being allergic reactions and an acne-like rash. The rash resolves on stopping treatment. Results of further clinical trials are now being reported.

OPINION

Murine monoclonal antibodies were first described in 1975 and led to the award of a Nobel prize in 1984. Humanised monoclonal antibodies for therapeutic purposes entered clinical practice ten years later. With greater understanding of the molecular biology of cancer has come the opportunity to use monoclonal antibodies as part of anticancer treatment and the prospect of tailoring anticancer therapy to the molecular characteristics of the tumour. It has long been recognised that over-expression of the epidermal growth factor receptor is associated with a poorer prognosis in a variety of solid tumours, including head and neck, colorectal and ovarian cancers.

Rituximab was the first monoclonal antibody to be launched as therapy for B-cell lymphoma in 1998, followed by trastuzumab (Herceptin) in 2001 for the treatment of breast cancer. While rituximab is directed against an antigen on the surface of lymphocytes and enhances the immune response to the tumour, trastuzumab and cetuximab are designed to inhibit growth of tumours bearing growth factor receptors.

Cetuximab therapy is associated with an acne-like rash that does not seem to respond to standard treatments for acne. There is some evidence that the severity of the rash may correlate with tumour response rates.

Results presented at this year's meeting of the American Society of Clinical Oncology suggest that cetuximab increases the response rate to chemotherapy and prolongs the time to disease progression in patients with advanced colorectal cancer. This is an interesting prospect for the management of a disease that is the second commonest cause of cancer death in the UK.

L Dawson, Consultant Medical Oncologist, Edinburgh