Monoclonal Antibodies in Tumor Therapy

Contributions to Oncology
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Monoclonal Antibodies in Tumor Therapy

Present Stage, Chances and Limitations

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Drug Dosage

The authors and the publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication.
However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package
for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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Foreword

This volume is dedicated to Professor Dr. phil. Hans Gerhard Schwick on the occasion of his sixtieth birthday. Its theme, 'Monoclonal Antibodies in Tumor Therapy', is an attempt to review some of the most important achievements which have emerged during the rapid progress of a science to which H. G. Schwick has devoted his life's work.

That the company, founded by Emil von Behring at the turn of the century, should be under his leadership is without doubt a result, not only of his creative flair for science, but also of his talent for enthusing his colleagues with the spirit of cooperation and for demonstrating the vital importance of his science.

'His science' - the sphere of immunology and the related fields of biochemistry, hemostaseology and clinical chemistry. This is the home of his investigations on pepsin cleavage of human immunoglobulins, discoveries which made possible wide-ranging anti-infectious intravenous plasma therapy. This is also the field that has nurtured developments in plasma fractionation and enabled the production of highly purified factor concentrates, inhibitors and trace proteins, a field to whose advances his work has contributed so much.

The path of his career led from the laboratory bench, under the guidance of his teacher and mentor H. E. Schultze, to cooperation with a whole range of research institutes and universities. His active membership and participation in committees of numerous scientific organizations, and the various distinctions awarded him, attest to the high degree of international recognition he has received. This, coupled with his successes in the field of pharmaceutical research, was not without consequence: H. G. Schwick joined the Board of Directors at Behringwerke in 1968, and has now been Chairman since 1980.
In the tradition founded by Emil von Behring, H. G. Schwick possesses the ability to demonstrate the practical value behind this science of the immunological processes in the human body. And in medicine today, the trend is clearly towards establishing the immunological determinants of every disease so that knowledge can be gained of the conditions underlying their pathogenesis.

H. G. Schwick has always viewed immunology as a practical science, and his many experiments have provided clear and concise illustrations of complex regulatory processes. Perhaps it is precisely this eye for the essential which has helped pave his way to success.

Together with all his friends and co-workers, we wish him continued success along this path, and all the best for his sixtieth birthday.

Marburg, April 1988

W. Bernhardt
E.-G. Afting

Preface

Monoclonal antibodies are under discussion as representing a new chance in tumor immunotherapy. Indeed, the localization of tumors in patients with the use of radiolabelled monoclonal antibodies is already possible. Provided all the conditions for standardizing this technique are fulfilled and all possibilities now available to optimize immunoscintigraphy are taken advantage of, immunoscintigraphy of tumors is now ready for clinical routine use. This may provide hope in tumor immunotherapy.

However, the dosimetric studies clearly revealed that the amount of antibody localizing at the tumor site compared to normal tissue is too low to reach tumor-specific cytotoxicity without intolerable side effects by radionuclides, toxins or cytostatics linked to the antibody.

Future research has thus to concentrate on this problem, e. to look for new antibody specificities with enhanced tumor localization and to develop new antibody preparations with reduced binding to normal tissue.

Tumor immunotherapy with conjugated and unconjugated monoclonal antibodies suffers from the xenogeneity of the murine immunoglobulin. Consequently, the chance should be taken to humanize these antibodies and to evaluate the potency of these preparations in tumor therapy. In case the anti-idiotypic response of the patient against the applied murine immunoglobulin
proves to be essential for the effect in tumor therapy, a new way of treating tumor patients by immunization would be opened up. All in all, we are just beginning to evaluate the potency of monoclonal antibodies in tumor therapy. There are a number of reasons to be optimistic, but they should not tempt us to overlook the problems which have to be solved.

Marburg, April 1988 H. H. Sedlacek

Abbreviations

ADCC antibody-dependent cytotoxicity
AML acute myeloid leukemia
AILL acute non-lymphocytic leukemia
C constant region of IgG
CDR complementary determining region
CLL chronic lymphatic leukemia
CTCL chronic cell leukemia
CMC complement-mediated cytolysis
DTPA dethylene-triamine-penta-acetic acid
EBV Epstein Barr virus
ECT emission computer tomography
EGF epithelial growth factor
ELISA enzyme-linked immunosorbent assay
Fab Fab fragment of IgG
F(ab')2 F(ab')2 fragment of IgG
Fc fragment crystalline of IgG
G-CSF granulocyte-macrophage colony-stimulating factor
human antibodies against murine antibodies
HIFG high molecular milk fat globulin
IL-2 Interleukin 2
LCL lymphatic cell leukemia
MAb monoclonal antibody
MAP mouse antibody production test
MW molecular weight
NCA non-specific cross-reacting antigen
NK cells natural killer cells
PDGF platelet-derived growth factor
RES reticuloendothelial system
SCLC small cell lung carcinoma
TAA tumor-associated antigen
TAE tumor-associated epitopes
TRF transferrin
TuMAb tumor monoclonal antibodies
V variable region of IgG