addition anticholinergic therapy to standard β₂-agonist ther-
apy in patients presenting with more severe acute asthma.

Mary Beth Bollinger, DO
Baltimore, MD

OMALIZUMAB PROVIDES LONG-TERM CONTROL IN PATIENTS WITH MODERATE-TO-SEVERE ALLERGIC ASTHMA


Purpose of the Study. To examine the ability of omali-
zumab, an anti-immunoglobulin E (anti-IgE) agent, to
maintain long-term disease control in patients with mod-
erate-to-severe allergic asthma.

Study Population. Four hundred eighty-three patients
with moderate-to-severe allergic asthma maintained on
beclomethasone dipropionate.

Methods. Four hundred eighty-three patients with phys-
ician-diagnosed moderate-to-severe allergic asthma were
investigated in a 24-week double-blind extension trial.
These patients were a subset of 546 patients that were
maintained on randomized treatment of omalizumab dur-
ing a 28-week double blind steroid reduction phase of the
core trial. During the 28-week steroid reduction phase of
the core trial, the lowest sustainable dose of beclometha-
sone dipropionate was established. Patients in this trial
had positive prick skin tests to common inhalant allergens
and IgE levels of >30 to <700 IU/mL. The extension part
of the trial was a 24-week double blind extension with
placebo control. Standard doses of omalizumab were used
throughout the 24-week extension period and given every
2 to 4 weeks based on body weight and IgE level. The use
of concomitant asthma medication was permitted and in-
vestigators were allowed to adjust the beclomethasone
dipropionate dose or switch patients from beclometha-
sone dipropionate to other asthma medications if deemed
necessary. Patients were followed clinically for asthma
symptoms and exacerbations. Mean doses of inhaled cor-
ticosteroids and other asthma medications were recorded,
and forced expiratory volume in 1 second (FEV₁) by spi-
rometry was recorded.

Results. More omalizumab-treated patients (33.5%) than
placebo-treated patients (13.5%) were able to com-
plete the extension period without requiring inhaled cor-
ticosteroid treatment. The mean beclomethasone dipropi-
ionate equivalent dose throughout the extension period
was lower in the omalizumab group (25 μg/day) than the
placebo group (43 μg/day). Disease control was sustained
in 76% of omalizumab patients compared with 59.4% of
placebo patients free from an asthma exacerbation during
the extension period. Compared with placebo, fewer pa-
tients in the omalizumab group used other concomitant
asthma medications during the extension. Treatment with
omalizumab was well-tolerated and the incidence of ad-
verse events was similar between groups.

Conclusions. These results suggest that omalizumab is
a promising new agent for the long-term control of allergic
asthma.

Comments. The role of anti-IgE therapy in
asthma and other allergic diseases is a topic of increasing
interest as these drugs may soon come to market. This
study nicely shows that omalizumab provides long-term
benefit and hints of a possible steroid-sparing effect, which
is always of increasing interest with the widespread use of
inhaled corticosteroids. However, additional long-term
studies are needed to better assess the overall cost benefit
analysis of these products. They are likely to be very ex-
pensive and if only a minimal steroid-sparing effect is
found, their role may be very limited.

Wanda Phipatanakul, MD
Boston, MA

SELECTIVE INTRACELLULAR DELIVERY OF DEXAMETHASONE INTO ACTIVATED ENDOTHELIAL CELLS USING AN E-SELECTIN-DIRECTED IMMUNOCONJUGATE

2002;168:883–889

Purpose of the Study. To determine if a dexamethasone-
anti-E-selectin conjugate can be specifically delivered to
activated endothelial cells and exert its biological effects in
a cell-specific manner.

Study Population. Experiments were performed using
human and mouse endothelial cell cultures.

Methods. Dexamethasone was conjugated to anti-hu-
mans E-selectin and the resulting immunoconjugate was
characterized in terms of its ability to bind to E-selectin and
endothelial cells, to be internalized, and to exert biological
activity on the endothelial cells. Binding of the dexametha-
sone-anti-E-selectin conjugate to endothelial cells was an-
alyzed by immunohistochemistry and flow cytometry. In-
ternalization and localization of the dexamethasone
conjugate was studied with confocal laser scanning micros-
copy (CLSM) and immunotransmission electron micros-
copy (Immu-TEM). Activity of the drug was analyzed
using a mouse endothelial cell line transfected with a glu-
corticoid-responsive reporter gene construct and the
drug’s effect on interleukin (IL)-8 expression was assayed
using Northern blotting.

Results. The dexamethasone conjugate bound to acti-
vated, but not resting, human endothelial cells when the
drug-treated cell cultures were stained with antibodies
directed against anti-human E-selectin or dexamethasone.
Flow cytometry confirmed these results. CLSM and Im-
mu-TEM demonstrated binding of the dexamethasone
conjugate to activated, but not resting, cell surfaces 10 and
20 minutes after incubation and after 1 hour, cell surface
staining began to decrease and intracellular staining in-
creased. The dexamethasone conjugate was able to activate
a glucocorticoid-responsive reporter gene to a similar de-
gerent to that seen with free dexamethasone. Northern blot-
ting demonstrated downregulation of IL-8 expression in
activated human endothelial cells treated with the dexam-
ethasone conjugate. Again, this effect was similar to that
seen with free dexamethasone.

Conclusions. Conjugated dexamethasone-anti-E-select-
in is specifically targeted to active endothelial cells and
internalized by these cells. The results also suggest that
the conjugate drug retains the ability to regulate transcrip-
tion.

Reviewers’ Comments. Although targeted drug therapy
is not a novel concept, these experiments suggest that a
nontoxic drug can be targeted to a specific cell type and
retain biological activity. Unlike a drug targeted to kill
cancer cells, this approach utilizes an antiinflammatory
drug to downregulate proinflammatory cytokines and cell
surface receptors with the idea that the toxicity associated
with immune suppression would be minimized.

Elizabeth C. Matsui, MD
Robert A. Wood, MD
Baltimore, MD
SELECTIVE INTRACELLULAR DELIVERY OF DEXAMETHASONE INTO ACTIVATED ENDOTHELIAL CELLS USING AN E-SELECTIN-DIRECTED IMMUNOCONJUGATE

Elizabeth C. Matsui and Robert A. Wood

Pediatrics 2003;112;486
SELECTIVE INTRACELLULAR DELIVERY OF DEXAMETHASONE INTO ACTIVATED ENDOTHELIAL CELLS USING AN E-SELECTIN-DIRECTED IMMUNOCONJUGATE

Elizabeth C. Matsui and Robert A. Wood

*Pediatrics* 2003;112;486

The online version of this article, along with updated information and services, is located on the World Wide Web at:

/content/112/Supplement_2/486.2.full.html