Investigational Antibody Effective Against RSV

BY PATRICE WENDING
Chicago Bureau

TORONTO — The investiga-
tional drug motavizumab may offer high-risk infants additional protection against respiratory syncytial virus disease, Dr. Xavier Carbonell-Estrany, MD, PhD, reported at a poster presentation at the annual meeting of the Pediatric Aca-
demic Societies.

Motavizumab demonstrated noninferiority to palivizumab with a 26% relative reduction in the primary end point of respi-
ranatory syncytial virus (RSV) hos-
pitalizations in a phase III mul-
ticenter study with 6,635 preterm infants, the investiga-
tors wrote.

The overall incidence of hos-
pitalization was low in both groups: 1.4% for patients treated with motavizumab and 1.9% for those treated with palivizumab.

Additionally, in a subset of pa-
tients, motavizumab significant-
lly reduced the secondary end point of outpatient medically at-
tended lower respiratory tract in-
fants treated by a crossover groups with palivizumab: 2.5% of 1,227 patients vs. 4.1%, 1,183 patients.

Motavizumab (Numax) is an enhanced potency, RSV-specific, humanized monoclonal antibody that has shown a similar safety and pharmacokinetic profile in phase I and II trials to palivizumab (Synagis), an RSV-specific monoclonal antibody that is the standard of care for infants at high risk for RSV, they said.

Motavizumab, which mar-
kets palivizumab and is develop-
ing motavizumab, sponsored the trial. Dr. Carbonell-Estrany is a member of the steering commit-
tee of the Motavizumab Study Group and was acting as consultan on this occasion for MedImmune.

“I am very pleased with the study results for motavizumab,” said lead author Dr. Carbonell-Estrany, chair of neonatology at the University of Barcelona’s Hospital Clinic and vice presi-
dent of the Spanish Neonatal Soci-
ety, said in a statement. “As a practicing neonatologist, I look forward to the potential to use this next-generation antibody to help reduce RSV-related hos-
pitalizations and LRIs in the out-
patient setting.”

Motavizumab is manufactured in 347 centers in 24 countries.

It included both infants who were 6 months of age or younger at the time of randomization with a gestational age of 35 weeks or fewer at birth, and chil-
dren who were 24 months of age or younger with a diagnosis of chronic lung disease of prematu-
tury requiring treatment within 6 months before the time of ran-
domization.

Over two consecutive RSV sea-
sons, 6,635 patients were ran-
domized to receive motavizumab or palivizumab 15 mg/kg intra-
muscularly monthly, with 150 days of follow-up. Each child par-
ticipated in the study for a single RSV season.

A total of 3,329 children were randomized to motavizumab and 3,306 to palivizumab. Overall, 59 motavizumab pa-
tients and 60 palivizumab pa-
tients were lost to follow-up, had consent withdrawn, or died.

No death was considered to be related to the study drugs and there were no RSV-related deaths.

The most frequently reported cardiac death in both groups was SIDS, with four in the mo-
tavizumab and two in the palivizumab group.

Drug-related adverse events were comparable between the motavizumab group and the palivizumab group (258 vs. 298), as were drug discontinuations (10 vs. 11).

Injection site reactions were more common in the mo-
tavizumab group than the palivizumab group (110 vs. 89), the authors reported.

Higher Respiratory Syncytial
Virus Load Could Be Protective

BY PATRICE WENDING
Chicago Bureau

We hypothesize that an adequate viral load is needed to induce an optimal inflammatory response.

We studied the correlation between RSV nasal wash viral load and lower respiratory tract events in a prospective cohort study while at Baylor College of Medicine, Houston.

We analyzed nasal wash specimens from 101 infants less than 2 years of age who presented to an ED with clinical signs of infection.

Children with an ele-
vated respiratory syn-
cytial viral load were more likely to be dis-
charged home, to re-
quar without more than 24 hours of intravenous fluids, and to not require intu-
bation, Dr. Berkeley L. Bennett and associates reported in a poster presentation at the annual meeting of the Pediatric Academic Societies.

These trends did not reach statistical significance, there was a highly significant as-
sociation between higher RSV load and the need for more than 24 hours of oxygen ther-
apy.

RSV load had an independent and protec-
tive effect on duration of oxygen therapy in a stepwise multivariable regression analysis that included RSV load. age, duration of illness, in-
terleukin-8 (IL-8), and interleukin-10 (IL-10).

A 10-fold increase in RSV load decreased the need for more than 24 hours of oxygen ther-
apy by 43%.

“We hypothesize that an adequate viral load is necessary to induce an optimal in-
flammatory response that is capable of con-
trolling the disease,” Dr. Bennett of Cincin-
nati Children’s Hospital Medical Center, in a article.

“Alternatively, with a small amount of viral load, you get a weak in-
flammatory response, and the disease will

FDA Warns on Antibiotic,
Calcium Solution Interaction

BY ELIZABETH MECHCATIE
Senior Writer

Fatal cases of calcium-ceftriaxone precipitates in the lungs and kid-
neys of both term and premature newborns have prompted a warning and a new contraindication regarding concomitant use of the intravenous antibiotic ceftriaxone with calcium or calcium-containing solutions or products.

Last month, the Food and Drug Administration posted an alert on its MedWatch Web site informing health care professionals that cef-
triaxone sodium for injection (Ro-
cephin) “must not be mixed or ad-
ministered simultaneously with calcium-containing solutions or products, even via different infusion lines.”

In addition, calcium-containing solu-
tions or products should not be ad-
mixed within 48 hours of the last ad-
mixture of ceftriaxone, ac-
cording to the FDA. This informa-
tion is included in a “Dear healthcare professional” letter issued by the manufacturer, Roche.

The FDA alert and Roche letter also emphasized that IV ceftriaxone should not be used to treat hyper-
bilirubinemic neonates, especially those with newborn sepsis.

Letters to editors in vitro studies that have shown that ceftriaxone “can displace biliru-
bin from its binding to serum albu-
mun,” which can result in biliru-
binic acid nephropathy and calcium nephropathy.

Related information had been in-
cluded in the pediatric use section of the prescribing information, but is now included in the contra-
indications section to “more prominently reinforce” this information, accord-
ing to the letter.

The contraindications section also includes the statement that ceftria-
one “should not be administered concurrently with calcium-contain-
ing solutions or products in new-
borns because of the risk of precip-
ite calcium-ceftriaxone sodium.”

The Roche letter describes post-
marketing reports of “isolated neonatal deaths” that were associat-
ed with calcium-ceftriaxone precipi-
tates in the lungs and kidneys.

Some of the cases, ceftriaxone and the calcium-containing solutions or medications had been administered by different routes and at different times.

Particulates also can form when diluents that contain calcium, such as Ringer’s solution or Hartmann’s so-
lution, are used to reconstitute cef-
triaxone for injection, according to the letter.

The contraindications, warnings, precautions, adverse reactions, and dosage and administration sections of the Rocephin label have been up-
dated to reflect these revised recom-

dendations. For more information, Roche can be contacted at 800-526-
6367.

The approved indications for cef-
triaxone include treatment of lower respiratory tract infections, skin and skin structure infections, urinary tract infections, intra-abdominal in-
fecions, acute bacterial otitis media when caused by susceptible organ-
isms, and surgical prophylaxis.

For more information, go to www.fda. gov/medwatch/safety/2007/safety07.html#Rocephin. Adverse reactions should be reported to Roche at 800-526-
6367, or to the FDAs MedWatch program at 800-332-1088 or www.fda.gov/medwatch.