Palivizumab, a Humanized Respiratory Syncytial Virus Monoclonal Antibody, Reduces Hospitalization From Respiratory Syncytial Virus Infection in High-risk Infants

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ABSTRACT. *Objective.* **To determine the safety and efficacy of prophylaxis with palivizumab in reducing the incidence of hospitalization because of respiratory syncytial virus (RSV) infection in high-risk infants.**

Methods. **A randomized, double-blind, placebo-controlled trial was conducted at 139 centers in the United States, the United Kingdom, and Canada. During the 1996 to 1997 RSV season, 1502 children with prematurity (≤35 weeks) or bronchopulmonary dysplasia (BPD) were randomized to receive 5 injections of either palivizumab (15 mg/kg) or an equivalent volume of placebo by intramuscular injection every 30 days. The primary endpoint was hospitalization with confirmed RSV infection. Children were followed for 150 days (30 days from the last injection). Those with hospitalization as a result of RSV infection were evaluated for total number of days in the hospital, total days with increased supplemental oxygen, total days with moderate or severe lower respiratory tract illness, and incidence and total days of intensive care and mechanical ventilation. The incidence of hospitalization for respiratory illness not caused by RSV and the incidence of otitis media were also evaluated. The placebo and palivizumab groups were balanced at entry for demographics and RSV risk factors. Ninety-nine percent of children in both groups completed the protocol and ~93% received all five scheduled injections.**

Results. **Palivizumab prophylaxis resulted in a 55% reduction in hospitalization as a result of RSV (10.6% placebo vs 4.8% palivizumab). Children with prematurity but without BPD had a 78% reduction in RSV hospitalization (8.1% vs 1.8%); children with BPD had a 39% reduction (12.8% vs 7.9%). When gender, entry age, entry weight, BPD, and gestational age were included in a logistic regression model, the effect of prophylaxis with palivizumab remained statistically significant. The palivizumab group had proportionally fewer total RSV hospital days, fewer RSV hospital days with increased oxygen, fewer RSV hospital days with a moderate/severe lower respiratory tract illness, and a lower incidence of intensive care unit admission. Palivizumab was safe and well tolerated. No significant differences were observed in reported adverse events between the two groups. Few children discontinued injections for related adverse events (0.3%). Reactions at the site of injection were uncommon (1.8% placebo vs 2.7% palivizumab); the most frequent reaction was mild and transient erythema. Mild or moderate elevations of aspartate aminotransferase occurred in 1.6% of placebo recipients and 3.6% of palivizumab recipients; for alanine aminotransferase these percentages were 2.0% and 2.3%, respectively. Hepatic and renal adverse events related to the study drug were similar in the two groups.**

Conclusions. **Monthly intramuscular administration of palivizumab is safe and effective for prevention of serious RSV illness in premature children and those with BPD.** *Pediatrics* **1998;102:531–537;** ***respiratory syncytial virus, monoclonal antibody, prophylaxis, MEDI-493, palivizumab, Synagis, prematurity, bronchopulmonary dysplasia.***

ABBREVIATIONS. RSV, respiratory syncytial virus; IGIV, immune globulin, intravenous; BPD, bronchopulmonary dysplasia; IgG, immunoglobulin G; LRI, lower respiratory tract illness/infection; ICU, intensive care unit.

Respiratory syncytial virus (RSV) is the leading cause of lower respiratory illness in children and is increasingly recognized as an important pathogen in the elderly and immune compromised patients of all ages.[1] In children, the risk of serious RSV illness is highest among those with prematurity, chronic lung disease, congenital heart disease, multiple congenital anomalies, and certain immunodeficiencies. In the United States, RSV infection accounts for more than 90 000 pediatric hospitalizations and 4500 deaths annually.[2]

Monthly infusions of respiratory syncytial virus

*Members of the IMpact-RSV Study Group are listed in the "Appendix."

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Reprint requests to Edward M. Connor, MD, MedImmune, Inc, 35 West Watkins Mill Rd, Gaithersburg, MD 20878.

immune globulin (RSV-IGIV, RespiGam, Massachusetts Public Health Laboratories, Boston, MA) can prevent serious RSV in high-risk infants.[3,4] A randomized, double-blind, placebo-controlled study (PREVENT) of 510 infants with prematurity or bronchopulmonary dysplasia (BPD) showed prophylaxis with RSV-IGIV led to a 41% reduction in hospitalization as a result of RSV infection (RSV hospitalization), significant reduction in a number of other measures of RSV severity, and significant reductions in the incidence of overall respiratory hospitalizations and otitis media.[4] Although safe and effective, RSV-IGIV prophylaxis requires monthly intravenous infusions, each lasting several hours and the administration of a total fluid volume of 15 mL/kg. Although RSV-IGIV is produced using modern viral inactivation methods, because it is a blood product, there is a potential (albeit low) risk of transmission of blood-borne pathogens.

Palivizumab (MEDI-493, Synagis, MedImmune, Inc, Gaithersburg, MD), a humanized immunoglobulin G-1 (IgG-1) monoclonal antibody that binds to the F-protein of RSV, is highly active in vitro against type A and B clinical RSV isolates.[5] The antibody was humanized by recombinant methods by inserting the complementarity determining regions from an F-protein-specific neutralizing murine monoclonal antibody described by Beeler and Coelingh[6] into a human IgG1 framework. In the cotton rat model, this monoclonal antibody has been shown to be 50 to 100 times more potent than an equivalent amount of RSV-IGIV.[5] It has been found to be safe and well tolerated in monthly doses up to 15 mg/kg and, at this highest dose, has been shown to maintain serum concentrations that have been associated with a 99% reduction of RSV in the cotton rat model.[5,7,8] When palivizumab is administered intramuscularly, trough serum concentrations are similar to those after intravenous administration.[8] We conducted a multicenter, multinational phase III trial (IMpact-RSV) to evaluate the safety and effectiveness of monthly administration of palivizumab as prophylaxis for serious RSV illness in high-risk children.

METHODS

IMpact-RSV was a multicenter, randomized (2 treatment to 1 control), double-blind, placebo-controlled trial conducted at 139 centers in the United States (n = 119), Canada (n = 9), and the United Kingdom (n = 11). Children were eligible if they were either: 1) 35 weeks gestation or less and 6 months of age or younger; or 2) 24 months old or younger and had a clinical diagnosis of BPD requiring ongoing medical treatment (ie, supplemental oxygen, steroids, bronchodilators, or diuretics within the past 6 months). Children were excluded if they had any of the following: hospitalization at the time of entry that was anticipated to last more than 30 days; mechanical ventilation at the time of entry; life expectancy less than 6 months; active or recent RSV infection; known hepatic or renal dysfunction, seizure disorder, immunodeficiency, allergy to IgG products; receipt of RSV immune globulin within the past 3 months; or previous receipt of palivizumab, other monoclonal antibodies, RSV vaccines, or other investigational agents. Children with congenital heart disease were excluded, except for those with a patent ductus arteriosus or a septal defect that was uncomplicated and hemodynamically insignificant.

Randomization was performed centrally using an interactive voice randomization system from November 15 through December 13, 1996. Participants were randomized to receive either palivizumab (15 mg/kg) or an equal volume of identically appearing placebo (same formulation, except without antibody and with 0.02% Tween-80 added) by intramuscular injection every 30 days for a total of 5 doses. Palivizumab and placebo were supplied as lyophilized powder in coded vials that were reconstituted by the pharmacist with sterile water for injection (final concentration of palivizumab is 100 mg/mL) and dispensed as a unit dose in a syringe that did not identify the contents.

Patients were followed by the investigator for 150 days from randomization (30 days after the last scheduled injection), regardless of the amount of study drug they received. At each visit and on each hospital day children were evaluated using the Lower Respiratory Tract Illness/Infection (LRI) Score[4] as follows: 0 = no respiratory illness/infection; 1 = upper respiratory tract illness/infection; 2 = mild LRI; 3 = moderate LRI; 4 = severe LRI; 5 = mechanical ventilation. To capture all primary endpoints, all hospitalizations were identified and children with respiratory hospitalizations were tested for RSV antigen in respiratory secretions using commercially available tests. Children were considered to have reached the primary endpoint if: 1) they were hospitalized for a respiratory illness and the RSV antigen test of respiratory secretions was positive; or 2) if children already hospitalized for reasons other than RSV illness had a positive RSV test, and had a minimum LRI score of 3 and at least 1 point higher compared with their last preillness visit.

All hospitalized children were monitored to determine the total days of hospitalization. Children with RSV hospitalization were also monitored for the total days with an increased supplemental oxygen requirement, total days with a moderate or severe respiratory illness (based on the LRI score), and frequency and total days of ICU and mechanical ventilation. The incidence of clinically diagnosed otitis media was recorded for all randomized patients.

Adverse events were reported throughout the study period and each was assessed by the investigators with regard to severity (using a standard toxicity table modified from the Pediatric AIDS Clinical Trials Group) and potential relationship to the study drug. Treatment groups were compared for adverse events by evaluating the number of children in each group with at least one event by body system and the distribution of severity of these events. Serum was collected before the first and last injection for blood urea nitrogen, creatinine, alanine and aspartate aminotransferase, palivizumab concentration, and anti-palivizumab binding. The last two parameters were also measured at one additional interim visit (before the second, third, or fourth injection) based on a randomized schedule. Palivizumab concentrations and anti-palivizumab binding were measured using enzyme-linked immunosorbent assay methods previously described.[7]

All randomized patients were included in the safety and efficacy analyses. Statistical comparison of groups was performed using Fisher's exact test for categorical variables and Wilcoxon rank sum test for continuous variables. The proportion of children with RSV hospitalization at 150 days was estimated by the Kaplan-Meier method as an alternative analysis of the primary endpoint. Logistic regression was also performed on the primary endpoint to evaluate predefined covariates (gender, age, weight, BPD vs premature without BPD). For comparison of hospital days between groups, the data were transformed and reported as days per 100 children.

RESULTS

Characteristics of the Randomized Populations at Entry

A total of 1502 children were randomized—500 to the placebo group and 1002 to the palivizumab group. The United States, the United Kingdom, and Canada randomized 1277 (85%), 123 (8%), and 102 (7%) children, respectively. The mean number of children randomized at a participating institution was 11 (range, 2–25); 8 centers randomized fewer than 5 patients and 27 centers randomized 15 or more. Demographic parameters and RSV risk factors were similar in the two groups (Table 1); slightly more children in the palivizumab group had at least one smoker in the household.

TABLE 1. Summary of Characteristics of the Study Population at Entry

	Placebo (n = 500)	Palivizumab (n = 1002)	P Value
Gender, %			
Male	56.8	56.9	1.000
Female	43.2	43.1	
Race/ethnicity, %			
White	57.4	58.4	.412
Black	25.6	22.8	
Hispanic	10.8	11.0	
Asian	2.4	2.1	
Other	3.8	5.8	
Mean (SE) birth weight, kg	1.3 (0.02)	1.3 (0.02)	.737
Mean (SE) gestational age, wk	29 (0.14)	29 (0.10)	.834
Proportion ≤32 wk, %	83.4	83.8	
Proportion >32 wk, %	16.6	16.2	
Multiple birth, %	27.4	31.7	.095
Mean (SE) weight at entry, kg	4.9 (0.1)	4.8 (0.1)	.335
Mean (SE) age at entry, mo	6.0 (0.21)	5.7 (0.15)	.215
Previous RSV, %	5.6	3.8	.111
RSV neutralizing antibody ≥1:200, %	5.6	5.5	.895
Mean (SE) no. people in house	3.5 (0.07)	3.5 (0.05)	.273
No smoker in household, %	68.6	63.0	.039
Child in day care, %	6.8	6.7	.913
Family history of:, %			
Asthma	35.2	36.1	.732
Hay fever	29.6	28.6	.717
Eczema	16.4	16.5	1.000

Abbreviations: SE, standard error; RSV, respiratory syncytial virus.

Compliance and Serum Palivizumab Concentrations

A total of 1486 (99%) children completed the protocol follow-up (99% placebo, 99% palivizumab). Reasons for noncompletion included death (n = 7), withdrawal of consent (n = 4), or loss to follow-up (n = 5) before day 150 and before any RSV hospitalization. Overall, 94% of the placebo group and 92% of the palivizumab group received all five injections and more than 95% of both groups received at least four injections. The proportion of children who received none, one, two, and three injections was similar in each group. Mean (standard error) trough serum concentrations 30 days after injections one, two, three, and four of 15 mg/kg palivizumab were 37 (1.2) μg/mL, 57 (2.4) μg/mL, 68 (2.9) μg/mL, and 72 (1.7) μg/mL, respectively.

Incidence of RSV Hospitalization

Monthly prophylaxis with palivizumab was associated with a 55% (95% CI = 38%, 72%) reduction in hospitalization as a result of RSV (P = .00004). This result was robust, with similar results obtained in alternative and sensitivity analyses (Table 2). Significant reductions were observed in both children with BPD (39% reduction, P = .038) and premature children without BPD (78% reduction, P < .001).

Significant reduction in RSV hospitalizations were seen in infants >5 kg (51%, P = .014) and ≤5 kg (57%, P = .001) and in infants <32 weeks' gestational age (47%, P = .003) and 32 through 35 weeks' gestational age (80%, P = .002). After adjusting for gender, entry age, entry weight, and BPD in a logistic regression model, treatment with palivizumab remained highly statistically significant (P < .001). When included in the logistic regression analysis, gestational age was not a significant predictor of RSV hospitalization and the palivizumab effect remained statistically significant (P < .001). Trends in reduction of RSV hospitalization similar to that seen in the United States (56% reduction, 44/426 [10.3%] placebo vs 39/851 [4.6%] palivizumab), were seen in the United Kingdom (64% reduction, 4/40 [10.0%]) vs 3/83 [3.6%]) and Canada (40% reduction, 5/34 [14.7%] vs 6/68 [8.8%]).

Secondary Efficacy Endpoints

Children randomized to palivizumab had significantly fewer total days (per 100 children) of RSV hospitalization (62.6 placebo days vs 36.4 palivizumab days, P < .001), days with increased oxygen (50.6 days vs 30.3 days, P < .001), and days with an LRI score of 3 or greater (47.4 days vs 29.6 days, P < .001). Overall, the incidence of intensive care unit (ICU) admissions and mechanical ventilation for RSV was low. A few children with complex underlying disease and consequently prolonged hospitalization greatly influenced the distribution of days of

TABLE 2. Summary of Analysis of RSV Hospitalization

	Placebo	Palivizumab	% Reduction (95% CI)	P Value
Primary analysis (incidence of RSV hospitalizations)*	53/500 (10.6%)	48/1002 (4.8%)	55% (38, 72)	<.001
Alternative analysis (Kaplan-Meier†)	53/500 (10.6%)	48/1002 (4.8%)	55% (38, 72)	<.001
Sensitivity analyses				
Dropout before 150 days and no endpoint‡	53/500 (10.6%)	49/1002 (4.9%)	55% (38, 72)	<.001
Respiratory hospitalization but no RSV test done§	56/500 (11.2%)	54/1002 (5.4%)	52% (35, 69)	<.001
Primary inclusion populations				
Premature (no BPD)	19/234 (8.1%)	9/506 (1.8%)	78% (66, 90)	<.001
BPD	34/266 (12.8%)	39/496 (7.9%)	39% (20, 58)	.038

Abbreviations: RSV, respiratory syncytial virus; CI, confidence interval; BPD, bronchopulmonary dysplasia.
* Fisher's exact test.
† Kaplan-Meier estimate of the proportion at 150 days. Deaths before RSV hospitalization, withdrawals, and lost events were treated as censored.
‡ The number of children who stopped follow-up before day 150 and had no endpoint through the last follow-up visit and would have been hospitalized if the proportion hospitalized was equal to that of the other treatment group added to observed incidence of RSV hospitalization. For placebo 5 children × 0.048 (RSV hospitalization rate in palivizumab group) = 0.24 (0 added events); for palivizumab 11 children × 0.106 (RSV hospitalization in placebo) = 1.17 (1 added event).
§ Number of children with respiratory hospitalizations and evidence of infection (coryza, fever) who had no alternative etiology added to observed incidence of RSV hospitalization. Three no antigen respiratory hospitalizations (0.6%) in the placebo group and 6 (0.6%) in the palizivumab group.

these parameters. Three percent of placebo patients and 1.3% of palivizumab recipients had RSV ICU admissions ($P = .026$); total days were 12.7 and 13.3, respectively ($P = .023$). The placebo and treated groups did not show significant differences in incidence of mechanical ventilation (0.2% vs 0.7%, $P = .280$) or total days of mechanical ventilation (1.7 days vs 8.4 days, $P = .210$).

Palivizumab recipients had significant reductions in the incidence (31% vs 24%, $P = .011$) and total days per 100 children (242 days vs 191 days, $P = .005$) of all hospitalizations and the incidence (22% vs 16% $P = .008$) and total days per 100 children (180 days vs 124 days, $P = .004$) of respiratory hospitalizations. These differences were attributable to the observed reduction of RSV hospitalizations, because no significant differences were observed in the incidence (14% vs 13%, $P = .470$) or total days per 100 children (118 days vs 88 days, $P = .369$) of respiratory hospitalizations unrelated to RSV. The proportion of children with at least one episode of otitis media was similar in both placebo and palivizumab recipients (40% vs 42%, $P = .505$).

Safety and Immunogenicity

The number of children reporting adverse events judged by the blinded investigator to be related to the study drug was similar in the placebo (10%) and the palivizumab (11%) groups. No statistically significant differences were found in related events by body system (Table 3). Discontinuation of injections for adverse events related to palivizumab was rare (0.3%).

Overall, 1.8% of the placebo group and 2.7% of the palivizumab group reported adverse events related to the injection site. These included erythema (1.2% vs 1.4%), pain (0.0% vs 0.6%), induration/swelling (0.2% vs 0.6%), and bruising (0.4% vs 0.3%). These events were generally mild and of short duration; none was serious. The proportion of children who reported fever (3.0% vs 2.8%) or rash (0.2% vs 0.9%) judged related to the study drug was similar in the placebo and palivizumab groups (Table 3). Hepatic transaminases were measured at baseline and before the fourth injection in all patients. Compared with the placebo group (1.6%), mild or moderate elevations of aspartate aminotransferase occurred in a slightly higher percentage (3.6%) of palivizumab recipients, however, a corresponding pattern in alanine aminotransferase elevation was not seen (2.0% and 2.3%, respectively). Hepatic adverse events that were judged by the blinded investigator and reported as related to the study drug were comparable in the two groups (Table 3). Measured elevations of creatinine or blood urea nitrogen and renal adverse events were infrequent and occurred at a similar rate in both groups.

Five (1.0%) children in the placebo group and 4 (0.4%) in the palivizumab group died during the trial; no death was judged related to palivizumab. Two children in the palivizumab group and none in the placebo group died during hospitalization for RSV; 1 following surgery for tympanostomy tubes after recovery from RSV, another child with BPD had complications including liquid ventilation and bronchopneumonia. Three placebo (0.6%) and 7 palivizumab (0.7%) had RSV hospitalizations of 14 days or greater. Evaluation of their medical history and course of RSV did not reveal evidence of unanticipated severity of disease or risk factors other than severe BPD.

Anti-palivizumab binding was measured at intervals throughout the study. Titers greater than 1:40 were found in 2.8% of the placebo group and 1.2% of the palivizumab group. These were generally single elevations and were not associated with a pattern of adverse events or low palivizumab concentrations.

TABLE 3. Most Frequently Reported Adverse Events That Were Judged by the Blinded Investigator as Potentially Related to Study Drug*

	Placebo	Palivizumab	*P* Value
Fever	3.0%	2.8%	.870
Nervousness	2.6%	2.5%	.865
Injection site reaction	1.6%	2.3%	.444
Diarrhea	0.4%	1.0%	.357
Rash	0.2%	0.9%	.179
AST increased	0.6%	0.5%	.726
URI	0.4%	0.5%	1.000
Liver function abnormal†	0.2%	0.3%	1.000
ALT increased	0.4%	0.3%	.670
Vomiting	0.4%	0.3%	.670
Cough	0.2%	0.3%	1.000
Rhinitis	0.6%	0.3%	.406

Abbreviations: AST, aspartate aminotransferase; URI, upper respiratory tract illness; ALT, alanine aminotransferase.
* Reported events in at least 3 children in the palivizumab group are provided along with the corresponding incidence in the placebo group. These represent adverse events reported by the investigator and include those identified by protocol mandated testing and other clinically indicated evaluations.
† Refers primarily to elevations of both AST and ALT.

DISCUSSION

This study provides the first demonstration of the effectiveness of a monoclonal antibody in an infectious disease in humans. Monthly intramuscular injections of 15 mg/kg of palivizumab reduced the incidence of hospitalization because of a RSV infection compared with placebo by 55% (95% CI = 38%, 72%), which compares favorably to a 41% (95% CI = 10%, 72%) reduction previously reported with RSV-IGIV.[4]

Although the PREVENT trial[4] established the effectiveness of antibody (RSV-IGIV), the study was not large enough to assess significant differences in subsets of the population studied. For example, efficacy was not statistically significant in premature infants without BPD nor in children <5 kg at entry (although the trends in these subsets were the same as for the entire study population). The sample size in the IMpact-RSV study was large enough to allow exploration of these issues. Significant reductions in RSV hospitalizations were seen in both premature infants without BPD and those with BPD who received palivizumab and in children by weight and gestational age. The study has established that palivizumab protects against serious RSV disease regardless of BPD status, gestational age, or weight of a high-risk child receiving prophylaxis.

Analysis of total days of RSV hospitalization parameters was consistent with the effect seen in the primary endpoint. Children receiving palivizumab prophylaxis had fewer RSV hospital days, fewer days with increased supplemental oxygen, and fewer days with a moderate or severe lower respiratory tract illness (all $P < .001$). Analysis of total days of ICU and mechanical ventilation were influenced by the low incidence of these events overall. Palivizumab reduced the incidence of ICU admission for RSV disease ($P = .026$). A slightly higher percentage of children in the palivizumab group were mechanically ventilated (0.2% vs 0.7%); however, this difference was not statistically significant and medical review of these patients' medical records did not identify any unexpected finding in these children with regard to the course of RSV. Of interest, this RSV-specific monoclonal antibody was not found to have a significant effect on respiratory hospitalizations not attributable to RSV infection or on otitis media.

This trial was designed to show the efficacy of palivizumab in prevention of serious RSV illness. In this controlled setting, the overall incidence of RSV hospitalizations in the placebo group seemed to be lower than clinical experience would suggest. This may be consistent with observations in other placebo-controlled trials[9,10] and is particularly relevant in the setting of RSV, where education by study investigators and other personnel regarding prevention of exposure, among other factors, is likely to influence the RSV infection and hospitalization rate.

Monthly intramuscular administration of palivizumab (15 mg/kg) resulted in mean trough serum concentrations of 37 μg/mL after the initial injection and then maintenance of concentrations >40 μg/mL after subsequent injections. This latter concentration was chosen as the target in this study because preclinical data in cotton rats demonstrated that animals who had levels greater than this threshold had a two log (99%) reduction in pulmonary RSV.[5] In a study in children mechanically ventilated with RSV,[11] this dose was not associated with a clinical effect but was shown to produce an antiviral effect in tracheal secretions, consistent with the protection against serious RSV lower respiratory tract disease seen in this trial.

Palivizumab injections were well tolerated. Monthly prophylaxis was not associated with significant toxicities. This is consistent with the safety profile observed in earlier trials.[7,8] Reactions at the site of injection were uncommon; when they occurred, they were generally mild and of short duration. A few children had palivizumab discontinued for systemic events, including vomiting, diarrhea, or fever. The proportion of children reporting adverse events by body system that were judged to be related to the study drug was similar in the placebo and palivizumab groups. There was no evidence of enhanced RSV disease among children receiving prophylaxis.

Although murine components of this humanized monoclonal antibody were almost exclusively limited to the antibody combining sites,[5] it was important to determine whether children developed antipalivizumab antibodies. Such antibodies could bind to the monoclonal antibody and result in decreased serum levels or could result in immune complex formation or direct immunotoxicity. Palivizumab immunogenicity has been studied carefully throughout its clinical development. Studies in healthy adults have identified only antiidiotypic antibody of the type found naturally in the immune response (Investigational New Drug File, MEDI-493, MedImmune, Inc, Gaithersburg, MD). In pediatric studies, transient low-level anti-palivizumab binding has been observed by enzyme-linked immunosorbent assay in a small percentage of children.[7,8] This reactivity was not protein A bindable (thus not consistent with IgG) and occurred in both the placebo and palivizumab recipients, suggesting that it represents nonspecific binding. In the IMpact-RSV trial, the incidence of anti-palivizumab reactivity in children receiving palivizumab was low (and lower than the control group) throughout the study. Alteration in palivizumab levels, specific adverse events, or changes in clinical laboratory parameters have not been observed in children with detectable binding. When children have been followed for up to 1 year after palivizumab prophylaxis (when they are both older and have no palivizumab detectable in serum), this binding has not been observed (Investigational New Drug File, MEDI-493, MedImmune, Inc, Gaithersburg, MD). Studies are underway to evaluate immunogenicity and safety when palivizumab is reintroduced during a second RSV season.

Recommendations for RSV prophylaxis with RSV-IGIV have been published previously.[12] Yet the currently available prophylaxis with RSV-IGIV requires several hours of administration time, repeated intravenous access, and 15 mL/kg of fluid load. These issues have been important factors in decision-making regarding the patient population in which RSV-IVIG has been used. Palivizumab represents an important advance in RSV prophylaxis. The observed 55% reduction in RSV hospitalization and better safety profile make palivizumab a logical alternative for RSV prophylaxis. Its ease of administration will allow prophylaxis to be feasible for a broader range of premature infants at risk for serious RSV illness. Because it is given by intramuscular injection, palivizumab will facilitate administration of RSV prophylaxis in settings such as the practitioner's office and by the visiting nurse in the home setting.

In summary, palivizumab is safe and effective for prevention of serious RSV illness in premature infants (≤35 weeks gestation), including those with BPD. Monthly intramuscular administration is well tolerated. Prophylaxis with this monoclonal antibody results in a significant (55%) reduction in RSV hospitalization in children at high risk for severe RSV infection.

APPENDIX

Members of the IMpact-RSV Study Group († indicates advisory/writing committee and ‡ indicates lead statistician): Donald Null, Jr, MD†, Colleen Bimle, RN, CCRC, Allegheny University Hospitals, Allegheny General, Pittsburgh, PA; Leonard Weisman, MD†, Karen Johnson, MD, Baylor College of Medicine, Texas Children's Hospital, Houston, TX; Jean Steichen, MD†, Tari Grat-

ton, University of Cincinnati College of Medicine, Cincinnati, OH; Sudeep Singh, MD, SARC Research Center, Fresno, CA; Elaine Wang, MD, CM, FRCP(C), Elizabeth Asztalos, MD, FRCP(C), The Hospital for Sick Children, Toronto, Ontario, Canada; Ann M. Loeffler, MD, Parvin H. Azimi, MD, Children's Hospital Oakland, Oakland, CA; Jay M. Lieberman, MD, Nancy E. O'Donnell, MS, RN, Memorial Miller Children's Hospital, Long Beach, CA; R. J. Cooke, FRCP, FAAP, K. McCormick, MB, MRLP, University of Newcastle upon Tyne, UK; Winston Koo, MD†, MBBS, FRACP, Mouhanad Hammami, MD, Hutzel Hospital, Wayne State University, Detroit, MI; Professor A. D. Milner, Paul Gaon, MB, BS, MRCP, St Thomas' Hospital, London, UK; Sharon Nachman, MD, Kathryn P. Tarpey, CPNP, SUNY Stonybrook Health Science Center, Stony Brook, NY; Pablo J. Sánchez, MD, R. Sue Broyles, MD, University of Texas Southwestern Medical Center, Dallas, TX; Denise Bratcher, DO, Mary V. Ball, RN, CCRC, University of Louisville School of Medicine, Louisville, KY; Francis J. Duda, MD, Peté M. DeCuir, RN, BSN, Baystate Medical Center Children's Hospital, Springfield, MA; Bernard Pollara, MD, PhD, Linda S. Nelson, ARNP, MSN, University of South Florida, Tampa, FL; Michael Balbus, MD, Michelle J. Schultz, RNC, NNP, Research Medical Center, Kansas City, MO; Bradley E. Chipps, MD, Sutter Memorial Hospital, Sacramento, CA; Laurence B. Givner, MD, Michael O'Shea, MD, Wake Forest University School of Medicine, Winston-Salem, NC; Mark Everard, MBChB, MD, FRCPCH, Sheffield Children's Hospital, Sheffield, UK; Kathleen Pfeffer, MD, Allison J. Page, APRN, University of Utah Health Sciences Center, Salt Lake City, UT; Penelope H. Dennehy, MD, Rhode Island Hospital, Providence, RI; John Modlin, MD†, Torunn Rhodes, MD, Dartmouth Medical School, Lebanon, NH; John DeVincenzo, MD†, University of Tennessee, Memphis and LeBonheur Children's Hospital, Memphis, TN; Bruce Nickerson, MD, Antonio Arrieta, MD, Children's Hospital of Orange County, Orange, CA; François D. Boucher, MD, FRCPC, Centre Hospitalier Universitaire de Québec, Pavillon CHUL, Ste-Foy, Québec, Canada; Ronald E. Keeney, MD†, Thomas E. Young, MD, Clinical Research Institute, Wake Medical Center, Raleigh, NC; John C. Stevens, MD, Indiana University, Indianapolis, IN; Ronald Ariagno, MD†, Marian Adams, MD, Stanford University at Packard Children's Hospital, Palo Alto, CA; Mark J. Polak, MD, Susan K. Lynch, MD, West Virginia University School of Medicine, Morgantown, WV; Jeffrey S. Gerdes, MD, Marrisa Kuba, CRNP, Pennsylvania Hospital, Philadelphia, PA; Moustafa Aouthmany, MD, Kim LaMar, CNNP, St Vincent Medical Center, Toledo, OH; Gordon Y. W. Chang, MD, Grace Stuart, Cooper Hospital University Medical Center, Camden, NJ; Mark M. Shelton, MD, Sami K. W. Hadeed, MD, Cook Children's Medical Center, Fort Worth, TX; Ushanalini Vasan, MD, Amy Hennessy, RN, Rush-Presbyterian St Luke's Medical Center College, Chicago, IL; Ram Yogev, MD†, Children's Memorial Hospital, Chicago, IL; Robert C. Welliver, MD, Debra Tristram, MD, State University of New York at Buffalo, Buffalo, NY; Catherine Albin, MD, Santa Clara Valley Medical Center, San Jose, CA; Thomas T. Jefferson, MD, Little Rock Children's Clinic, Little Rock, AR; Gerald D. Purdy, MD, Carolynne M. Buckner, RN, BSN, The Children's Hospital at Bronson Methodist Hospital, Kalamazoo, MI; Jerrold Schlessel, MD, Concepcion Sia, MD, North Shore University Hospital, Manhasset, NY; Ben Tan, MD, Koravangattu Sankaran, MD, Royal University Hospital, Saskatoon, Canada; Colin J. Morley, MD, FRCPCH, Deborah K. White, RGN, RSCN, University of Cambridge, UK; H. Cody Meissner, MD, Ivan Frantz, MD, Floating Hospital for Children at New England Medical Center, Boston, MA; Shobhana A. Desai, MD, Christian W. Stanley, MSN, Thomas Jefferson University, Philadelphia, PA; Richard Inwood, MD, Lorraine E. Solecki, RNC, Newark Beth Israel Medical Center, Newark, NJ; Ellen Wald, MD†, Karen Smail, CRNP, Children's Hospital of Pittsburgh, Pittsburgh, PA; Renee Ellen Fox, MD, Vicki Taciak, CRTT, University of Maryland School of Medicine, Baltimore, MD; C. Lucy Park, MD, Dharmapuri Vidyasagar, MD, University of Illinois at Chicago Hospital, Chicago, IL; Gregory Redding, MD†, Dennis E. Mayock, MD, University of Washington School of Medicine, Seattle, WA; Peter D. Reuman, MD, Shands Hospital at the University of Florida, Gainesville, FL; Ellen M. Bifano, MD, SUNY Health Science Center at Syracuse, Crouse Irving Memorial Hospital, Syracuse, NY; Benjamin Estrada, MD, Mary Y. Mancao, MD, University of South Alabama Hospitals, Mobile, AL; Brenda Hook, MD, Georgia McDavid, RN, University of Texas-Houston Medical School, Houston, TX; Judith L. Rowen, MD, Janak A. Patel, MD, University of Texas Medical Branch, Galveston, TX; Joan Robinson, MD, Bonita Lee, MD, University of Alberta, Edmonton, Alberta, Canada; William Rodriguez, MD, Julita Arrobio, MD, Children's National Medical Center, Washington, DC; James R. Hocker, MD, Connie McConnell, RN, Children's Hospital of Illinois, Peoria, IL; Giovanni Piedimonte, MD, Ilene Sosenko, MD, University of Miami School of Medicine, Miami, FL; Bakulesh Patel, MD, Suzanne Shervinski, CRNP, Geisinger Medical Center, Danville, PA; Paul E. Stobie, MD, Kathy Perea, RN, Presbyterian Hospital, Albuquerque, NM; Stephen A. Chartrand, MD, Mark C. Wilson, MD, Creighton University, Omaha, NE; Robert de Lemos, MD, Rangasamy Ramanathan, MD, Women's and Children's Hospital, Los Angeles County-University of Southern California, Los Angeles, CA; Bruce A. Barnett, MD, Children's Medical Center of Northwest Ohio, Toledo, OH; Stephen R. Luber, MD, FAAP, Rockwood Clinic, Spokane, WA; William V. Raszka, Jr, MD, University of Vermont School of Medicine, Burlington, VT; Douglas S. Holsclaw, Jr, MD, Debra L. Klein, RN, BSN, Allegheny University-Hahnemann, Philadelphia, PA; Barbara J. Law, MD, University of Manitoba, Winnipeg, Manitoba, Canada; Michael J. Balsan, MD, Brenda H. Douglass, MD, Tod Children's Hospital, Youngstown, OH; Brian P. O'Sullivan, MD, Rhoda Spaulding, FNP, University of Massachusetts Medical Center, Worcester, MA; Russell B. Van Dyke, MD, Ayesha Merza, MD, Tulane University School of Medicine, New Orleans, LA; J. Owen Hendley, MD, Robert J. Boyle, MD, University of Virginia Health Sciences Center, Charlottesville, VA; Patricia A. Hughes, DO, Michael J. Horgan, MD, Albany Medical Center, Albany, NY; Roy C. Maynard, MD, M. Kathryn Teufert, RNC, NNP/PNP, Children's Hospital and Clinics, Minneapolis, MN; Marc Majure, MD, Duke University Medical Center, Durham, NC; Jeffrey A. George, DO, Dawn R. Kuerschner, RNC, MS, NNP, Lutheran General Children's Hospital, Park Ridge, IL; Vivek Ghai, MD, Dolly Thomas, MD, Illinois Masonic Medical Center, Chicago, IL; Noni MacDonald, MD, FRCP(C)†, Tom Kovesi, MD, Marc Blayney, MD, FRCP(C), Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada; Chitra S. Mani, MD, FAAP, Marshall University School of Medicine, Huntington, WV; Venusto H. San Joaquin, MD, Linda Roberts, ARNP, University of Oklahoma Health Sciences Center and Children's Hospital of Oklahoma, Oklahoma City, OK; Andrew Wiznia, MD, Michael Rosenberg, MD, PhD, Bronx Lebanon Hospital Center, Bronx, NY; Padmani Karna, MD, Dennis L. Murray, MD, Sparrow Hospital, Lansing, MI; Warren Lenney, MD†, Sadie Clayton, RN, North Staffordshire Hospital, Staffordshire, UK; David G. Oelberg, MD, Marilyn M. Reininger, RN, Eastern Virginia Medical School, Norfolk, VA; Stephen C. Eppes, MD, Judith A. Childs, PhD, CCRC, Alfred I. duPont Hospital for Children, Wilmington, DE; William C. Gruber, MD, Thomas R. Hazinski, MD, Vanderbilt University, Nashville, TN; Evan A. Steinberg, MD, Laurence C. Lopez, MD, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA; Greg R. Elliott, MD, Medical College of Virginia/Virginia Commonwealth University, Richmond, VA; Jessie R. Groothuis, MD, Ross Products Division, Abbott Laboratories, Columbus, OH; Eric E. A. F. Simoes, MD, University of Colorado School of Medicine and The Children's Hospital, Denver, CO; Amin Hakim, MD, Francis Mimouni, MD, Maimonides Medical Center, Brooklyn, NY; Lorry Rubin, MD, Sunil K. Sood, MD, Schneider Children's Hospital of Long Island Jewish Medical Center, New Hyde Park, NY; H. Farouk Sadiq, MD, Cardinal Glennon Children's Hospital, St Louis, MO; T. G. Marshall, FRCP, Mrs. D. Miller, Royal Hospital for Sick Children, Edinburgh, UK; M. R. Drayton, MD, FRCPCH, S. O'Neill, RN, University Hospital of Wales, Cardiff, UK; Philip Chetcuti, DM, FRCP, Leeds General Infirmary, Leeds, UK; Diana L. Trupp, MD, Joya Heart, MD, Loma Linda University Children's Hospital, Loma Linda, CA; Ellen R. Cooper, MD, Elizabeth R. Brown, MD, Boston Medical Center/Boston University School of Medicine, Boston, MA; Anbukili Chetty, MD, Thomas B. Rice, MD, Children's Hospital of Wisconsin/Medical College of Wisconsin, Milwaukee, WI; David Rupar, MD, Carolinas Medical Center, Charlotte, NC; Cheng T. Cho, MD, PhD, Richard D. Leff, PharmD, University of Kansas Medical Center, Kansas City, KS; Stephen D. Levine, MD, Jay K. Kolls, MD, Children's Hospital, New Orleans, LA; Michael Hall, MB, FRCPCH, Susan L. Smith, Princess Anne Hospital, Southampton, UK; Lawrence Schwartz, MD, Infections Limited, PS, Tacoma, WA; Richard J. Lemen, MD, University of Arizona Health Science Center, Tucson, AZ; Caroline Breese Hall, MD, Christine E. Long, MPH, University of Rochester Medical Center, Rochester, NY; Howard Panitch, MD,

Susan M. Kolb, CRNP, MSN, Allegheny University of the Health Sciences, St Christopher's Hospital for Children, Philadelphia, PA; John L. Colombo, MD, C. Gerald Judy, MD, University of Nebraska Medical Center, Omaha, NE; Barry L. Golembe, MD, Jack D. Anderson, MD, The Nalle Clinic, Charlotte, NC; Jane McDonald, MD, Deidre McCormack, RN, Montreal Children's Hospital, Montreal, Quebec, Canada; Dennis P. Ruggerie, DO, Catherine Triplett, RNC, Great Falls Clinic, Great Falls, MT; Michael W. Odom, MD, Graciela Lopez-Cox, RN, MSN, University of Texas Health Science Center, San Antonio, TX; Mark H. Sawyer, MD, James D. Connor, MD, University of California, San Diego, La Jolla, CA; Jaime E. Fergie, MD, Kevin Purcell, PharmD, MD, Driscoll Children's Hospital, Corpus Christi, TX; Anand D. Kantak, MD, Dianne M. Fihe, RNC, Children's Hospital of Akron, Akron, OH; H. Dele Davies, MD, MSC, FRCPC, Ian Mitchell, MD, FRCPC, Alberta Children's Hospital, Calgary, Alberta, Canada; K. N. Siva Subramanian, MD, Yolande Smith, MD, Georgetown University Medical Center, Washington, DC; Elaine Barefield St John, MD, University of Alabama at Birmingham, Birmingham, AL; Jeffrey W. Stolz, MD, Catherine Sheils, MD, Children's Hospital of Boston, Boston, MA; Frederick Cox, MD, William Foshee, MD, Medical College of Georgia, Augusta, GA; Ruben Diaz, MD, Shannon Coonce, PharmD, MD, University Medical Center, Las Vegas, NV; Harry L. Keyserling, MD, Caminade Bosley Padrick, RN, MN, MPH, Emory University School of Medicine, Atlanta, GA; Catherine Lamprecht, MD, Floyd R. Livingston, MD, Nemours Children's Clinic, Orlando, FL; Joanne M. Langley, MD, MSc, Dalhousie University, IWK-Grace Health Centre, Halifax, Nova Scotia, Canada; Peter Weller, MA, MB, FRCPCH, Birmingham Children's Hospital, Birmingham, UK; Gerd J. Cropp, MD, Augusto Sola, MD, University of California at San Francisco, San Francisco, CA; Mary L. Kumar, MD, MetroHealth Medical Center, Cleveland, OH; Craig D. Lapin, MD, Penelope Carlisle, RN, MS, Connecticut Children's Medical Center, Hartford, CT; Robert Martz, MD, Michael Radetsky, MD, Lovelace Health Systems, Albuquerque, NM; Samir Midani, MD, The Nemours Children's Clinic, Jacksonville, FL, Mobeen H. Rathore, MD, University of Florida Health Science Center, Jacksonville, FL; Eduardo J. Riff, MD, Nemours Children's Clinic, Ft Myers, FL; Gregory F. Shay, MD, Elisabeth Hogvall, RN, MSN, Kaiser Permanente Medical Care Program, Oakland, CA; Donald W. Russell, MD, Partners Clinical Research, Inc, Asheville, NC; Anne H. Thomson, MD, FRCP, Sarah M. Lawrey, RSCN, John Radcliffe Hospital, Oxford, UK; Karen Hardy, MD, Kayla Harvey, PNP, California Pacific Medical Center, San Francisco, CA; Ronald Turner, MD, Medical University of South Carolina, Charleston, SC; Edward O. Cox, MD, Adrian Dana, MD, DeVos Children's Hospital, Grand Rapids, MI; Ashima Madan, MD, El Camino Medical Group, Sunnyvale, CA; James Wallace, MD, Dennis C. Stevens, MD, MS, University of South Dakota School of Medicine, Sioux Falls, SD; Basim Asmar, MD, Noreen A. Selewski, RN, BSN, Wayne State University, Children's Hospital of Michigan, Detroit, MI; Julia Kelly, MD, Maricopa Medical Center, Phoenix, AZ; Tamra Klerr, Susan Spruill, MS, PPD Pharmaco International, Inc, Wilmington, NC; and Edward M. Connor, MD†, David Carlin, PhD‡, Franklin H. Top, Jr, MD†, MedImmune, Inc, Gaithersburg, MD.

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