CLINICAL CAPSULES

Oseltamivir in Pneumonia

CONTRAINDICATIONS

Oseltamivir's (Tamiflu) benefits aren't limited to treating and preventing influenza, Beth L. Nordstrom, Ph.D., reported in a poster presentation at the 44th Interscience Conference on Antimicrobial Agents and Chemotherapy.

In a retrospective cohort study of a U.S. insurer's claim data, sponsored by Hoffmann-La Roche Ltd, patients of all ages who had received oseltamivir were at significantly lower risk for pneumonia, particularly the oldest and youngest age groups.

Among children aged 1-12, the proportion with a diagnosis of pneumonia was 0.7% among the 586 for whom oseltamivir was dispensed on the day of influenza diagnosis, compared with 2.5% of the 17,886 who did not receive oseltamivir, a 66% risk reduction

In patients aged 13-59, pneumonia was diagnosed in 1.3% of the 10,649 who received the drug, compared with 2.1% of the 41,007 who did not-a reduction of 19%. In adults aged 60 and above, the difference was 1.7% of 463 with oseltamivir versus 8.8% of 3,298 without, a 59% drop.

The impact of oseltamivir on antibiotic dispensing and hospitalization was also greater in the youngest and oldest age groups. Antibiotic use dropped with oseltamivir by 30% in the 1-12 year olds, by 9% in the 13-59 year olds, and 14% in the 60-plus group. Hospitalizations were reduced by 71% with oseltamivir in the 1-12 year olds, by 25% in the 13-59 age group and 45% in the 60-plus patients, Dr. Nordstrom reported.

Teen With Rabies Recovers

A teenaged girl who contracted rabies from a bat and received an experimental treatment has been upgraded to fair con-

fluM:st Event Influenza Virus Vaccine Any event Cough Runny Nose/Nasal Congestion Sore Throat Initiability Headache Chillis Vomiting 65.4 26.8 48.1 12.6 19.5 17.8 6.1 47 Live, Intranasal 2004-2005 Formula FOR NASAL ADMINISTRATION ONLY Vomiting Muscle Aches Decreased Activity Rx only Brief summary of Prescribing Information INDICATIONS AND USAGE 6.1 14.0 ever*: Temp 1 Temp 2 Temp 3 ote: Ther 9.5 2.2 uMist is indicated for active immunization for the prevention of disease caused by influenza A and B viruses in healthy hildren and adolescents, 5-17 years of age, and healthy adults, 18-49 years of age. FluMist is not indicated for immunization of individuals less than 5 years of age, or 50 years of age and older, or for therapy of influenza, nor will it protect against infections and illness caused by infectious agents other than influenza A or B viruses. Under no circumstances should FluMist® be administered parenterally. Number of evenuences process processing and the second sec Individuals with a history of hypersensitivity, especially anaphylactic reactions, to any component of FluMist, including eggs or eoo products, should not receive FluMist. egg products, should not reside Hulkst." Fulkit is contrainated in children and adolescents (5-17 years of age) receiving aspinin therapy or aspirin-containing Hulkst should not be administered to individual with have a traitory of Guilla-Barra fragments. Fulkits should not be administered to individual with have a traitory of Guilla-Barra fragments and entrained to the like view and the should not be administered to individual with haven or suspected immune definering deseases with a controller munomodelisment, gammangdoullement, and thread admonstrate and constituent such as human immunodelisment, such a maling and y leaves and thread admonstrate and constituent patients who may be immunosuppressive of have attered to componied immune status as a consequence of traitment with systemic controcsteriots, akylating drugs, antimetabolites, radiation, or other immunosuppressive therapies. For the cohort of 128 children who received FluMist[®] (influenza Virus Vaccine Live, Intranasal) across three consecutive years, rates of solicited adverse events were not significantly increased when compared to placebo recipients.

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ral: CARE IS TO BE TAKEN BY THE HEALTH CARE PROVIDER FOR THE SAFE AND EFFECTIVE USE OF THIS PRODUCT. Administration of FuMist should be postponed until after the acute phase (at least 72 hours) of febrile and/or respiratory illnesses.

respiratory messes. Information for Vaccine Recipients or Parents/Guardians: Vaccine recipients or their parents/guardians should be informed by the tended care proves of the potential benefits and tend workfull, and the need for two dhes for the list use should be advised to and does contained (e.g., within the same household within the meconoransmice) and should be advised to and does contained (e.g., within the same household within the meconoransmice) and 21 days. The vaccine recipient of the parent/guardian accompanying the vaccine recipient should be told in report any supported beatweets to the thysican or clinic where the vaccine was administed see ADVERSE FUNT REFORMENT. supported adverse events to the physician or drinic viewe the viscoir was administered (see AVVERSE EVENT REPORTING, Drug Interactions: Children or addisectures who are receiving asprin threapy are apprint containing therapy should not necele Fluidbit see CONTRANDICATIONS, Fluidbit compounds that are adveragatient thread and area threapy threapy threapy fluidbit see CONTRANDICATIONS, Fluidbit compounds that are adveragatient thread and area threapy threapy threapy administer Fluidbit until 48 hours after the research or provide the adversarial fluidbit until 48 hours after the essention of arbitrat party and that antiviral agents not be administered or thready administer Fluidbit until 48 hours after the research or provide the adversarial fluidbit until 48 hours after the constant of a thready thready and that antiviral agents not be administered or concurrent, used of Fluidbit until 48 hours after the vectores thready indicated. There are no data regarding or administration of Fluidbit viewel and immuno provides administered concurrently with other vaccines have not been determined. Therefore, Fluidbit subjects two research are administered concurrently with other vaccines have not been determined. Therefore, Fluidbit subjects two research are accounce within one month of adhere to these infervals when administering Fluidbit.

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up to three veeks. Carcinogenesis, Mutagenesis, Imgainment of Pertility: FluMist has not been evaluated for its carcinogenic or mutagenic potential or its potential to imgain fertility. Pergenary Calcegory C3-Animal reproduction studies have not been conducted with FluMist. It is also not known whether FluMist can cause Heal harm when administered to a pregnant woman or affect reproduction capacity. Therefore, FluMist studin of the administered to pregnant woman. Narsing Mothers: It is not known whether FluMist can cause Heal harm when administered to a pregnant woman or affect reproduction capacity. Therefore, FluMist international models and the studies of the studies of the studies of the studies of the studies are exceeded in International Mothers: It is not known whether FluMist calculated the studies of the studies of the studies of the studies of the studies are exceeded in International administered to pregnant woman. Pediatric Use: The safety of FluMist in infents and children -c00 months of age has not been established. If they respond differently from younger individuals. The safe use of FluMist in persons 65 years and older has not been established.

ADVERSE REACTIONS

EXPLOSE INCOMING Serious Adverse Events: Across all clinical trials, serious adverse events (SAEs) were monitored after vaccination for 42 days in children and for 28 days in adults. SAEs occurred at a similar rate (<1%) in FluMist and placebo recipients for both healthy children and healthy adults. user rearry universitation treamy adults. Derait, across the placebo-controlled trais in adults and children, the incidence of selected adverse reactions that may be complications of influenza (such as pneumonia, bronchilis, bronchiotiis, or central nervous system events) was similar in FMMst and placebo orouns.

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Manufactured and Marketed by: MedImmune Vaccines, Inc. Gaithersburg, MD 20878	Medimmune Vaccines, Inc.	U.S. Govt. License No. 1652 Issue Date: September 2004
FLU04-229		© 2004, MedImmune Vaccines, Inc



years, traise or source averes events were not significantly increased when compared to placebo necipients. Medically Attended Events (n. Dilitions and Addressents: A large randomised double-fund) placebo-controlled tria in healthy officient of through 11 years of age was conducted al 31 clinics in the Morthen California Kaiser-Permanette Health Maintenance Organization (HMO) to assess the raise of mericially attended events (MME) within 42 days of vaccination. Participants were randomized 2:1 laracine placebo, that of 65C realizable children 5-17 years of age were enrolled, incluing 3244 byos and 3413 gifts. Dittes 65657 children 2:066 were 5-8 years of age and 4051 i were 9-17 years of age. Dose two for children less than nine years of age was to be administered 28 to 42 days after Dose One.

werd 9-17 years or age. Lose woll or children ess than time years or age was to be administered 2-to 4-c days atter Date presenting MAS were obtained from the Kalaer-Perenente comparison the hardin case utilized in distances for meshaped and upped diagnosts: a current trait children essential traiter and the second second and within four encipeeding to queet diagnosts: a current respiratory traiter essential traiter and traiter essential and traiter and traiter and were second to queet diagnosts: a current second traiter and tra

syndrome, or myocardits (influenza-associated rare disorders) were reported in this study, including 5-7 years of age, four individual MEs were significantly increased and 11 were significantly decreased and 11 were significantly decreased and 11 were significantly increased rates of the significant increased of the four individual MEs associated with increased risk, a holiogical association with Hulkits is plausible association with a significantly increased rate of the significant increased rates of the significant increase of the significant increase in the significant increase in the subsect of healthy adults 15 were significant in the significant increase of the significant increase in the subsect of healthy adults 18-40 were significant increase in the subsect of healthy adults 18-40 were significant increase in the subsect of healthy adults 18-40 were significant were were not in the significant increase in the subsect of healthy adults 18-40 were significant increase in La as defined by the COC in the Table - Significant increase in La as defined by the COC in the Table - Significant process for the significant increase in the subsect of healthy adults 18-40 wears of age are shown in Table 2. Statistically significant increase in La as defined by the COC in the Table - Significant the compared the time of the coch in the coch in the coch in the significant increase in La as defined by the COC in the Table - Significant the compared the compared to the time for the coch in the significant increase in the subsect of healthy adults 18-40 wears of age are shown in Table - Significant the coch in the table - Significant the coch in the coch in the coch in the coch in the table of the tork of thealthy adults 18-40 wears of age are shown in

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vaccine and Placedo Recipients; Healthy Adults 18-49 Years of Age				
	FluMist N=2548*	Placebo N=1290°		
Event	(%)	(%)		
Any event	71.9*	62.6		
Cough	13.9*	10.8		
Runny Nose	44.5*	27.1		
Sore Throat	27.8*	17.1		
Headache	40.4	38.4		
Chills	8.6*	6.0		
Muscle Aches	16.7	14.6		
Tiredness/Weakness	25.7*	21.6		
Fever:				
Oral Temp >100°F	1.5	1.3		
Oral Temp >101°F	0.5	0.7		
Oral Temp >102°F	0.1	0.2		
Oral Temp >103°F	0.0	0.0		

Denotes statistically significant p-value " 0.05; no adjustments for multiple comparisons; Fisher's exact method Number of evaluable subjects (those who returned diary cards). [97.9% of FluMist recipients and 97.9% of placebo recipients.]

97.9% of placebo recipients.] Other Adverse Events in Childrean and Adults: In addition to the solicited events, parents of subjects in the Pediatric Efficacy trial also reported other adverse events that occurred during the course of the trial. Annong healthy children age 60-71 monts, the events that occurred in a lass 1% of FMARK tercipients and at higher refle compared to placebo were: advormed panel 37.9% FMARK to 0% placebol, othis media (1.4% FMARK to 0% placebol, accohertal intry (2.1% FMARK to 1.4% placebol (bitworp) pose two. None on these differences subject and events that course in addition to the solicited events, adults who perfoquent on these differences of age in the Adult Effectiveness Study age reported other adverse events that occurrent of the rinks and 0.2% FMARK to 2.5% FMARK to 3.1% placebol, and smalls 41.% FMARK to haven a subjective to 1.4% placebol (bitworp) bate two. None or adults 18.4 gives of age in the Adult Effectiveness Study age reported other adverse events that occurrent of the rinks that 2.2% placebol, intrins 6.2% FMARK to 3.1% placebol, and smalls 41.% FMARK to Adverse aerbit reported north effectiveness internations and the result effectiveness study age reported other adverse events that occurrent of the rinks that is the internation taken is constrained by the results of the related to the results the results that adverse events that occurrent the occurrent of the rinks that by the performance internation taken the result the results that adverse events that occurrent the results that adverse events the occurrent of the rinks that the results that adverse events the results that the results the results the results that the results the results that the results the results that the results that the results that the results that the results the results that the results the results that the resu rse events reported post-licensure have included nausea, rash, hypersensitivity reactions (including hylaxis, facial edema, and urticaria). These events occurred at similar rates in FluMist versus placebo recipient

Annually, 20-40 cases of Gullain-Barré syndrome (GBS) that occur within 42 days of administration of inactivated influenza vancine are reported to VAERS. In 2003-2004, one case of GBS with temporal association with HuMist was reported. Evidence of a causal relationship between influenza vancines, including HuMist, has not been estable ADVERSE EVENT REPORTING

ADVERSE EVENT REPORTING Reporting by vocable recipients or the parents/puardians of vaccinees and health care providers of all adverse events occurring after vaccine administration is encouraged. The U.S. Department of Health and Human Services QHH4R) has established a Vaccine Adverse Event Reporting System (MARER) to account all proofs of suspected adverse events after the administration of any vaccine. The WERS full-free number is 1-800-822-7967. Reporting forms may also be obtained at the FUW bits bet http://www.sers.org.

DOSAGE AND ADMINISTRATION FOR NASAL USE ONLY. DO NOT ADMINISTER PARENTERALLY.

milat should be administered according to the following schedule.				
Age Group	Vaccination Status	Dosage Schedule		
Children age 5 years	Not previously vaccinated	2 doses (0.5 mL each, 60 days apart		
through 8 years	with FluMist	± 14 days) for initial season		
Children age 5 years	Previously vaccinated	1 dose (0.5 mL)		
through 8 years	with FluMist	per season		
Children and Adults age 9	Not applicable	1 dose (0.5 mL)		
through 49 years		per season		

r healthy children age 5 years through 8 years who have not previously received FluMist vaccine, the recommended sage schedule for riasal administration is one 0.5 mL dose followed by a second 0.5 mL dose given at least 6 weeks c. Dhy limited data are available on the degree of protection in children who receive one dose. xater... voing miniteru utatia artie availautie un une degrete or protection in crititaren Who receive one dose. For all other healthy individuals, including children age 5-8 years who have previously received at least one dose of FluMist, the recommended schedule is one dose.

rumes, ei recummenzes sundicute 5 one 008. Hildelf schuld beschnisteret plor to exposure to influenza, The peak of influenza activity is variable from year to year, sur generally occurs in the U.S. between late Describer and early March. Because the duration of protection induced by Filkelfs in di Norton and yearly antiplicitic variation in the influenza strains is possible, annual revacutation may increase the likelihood of protection. Saed on Fulkelfs reschulting influenzia indicated September 2004.

dition at the Children's Hospital of Wisconsin (Wauwatosa), a hospital spokesperson said in an interview at press time.

The girl is the first known person to survive rabies without receiving a vaccine. The bat bit the girl last September. She reportedly thought that the bite was just a scratch, and she and those with her assumed, incorrectly, that only healthy bats could fly, so she did not see a doctor for a vaccine. She presented to Children's Hospital on October 18 with symptoms of rabies, including slurred speech and fluctuating consciousness.

The doctors induced a temporary coma and treated her with antiviral drugs to boost her immune system and allow her natural immunity to fight the virus. The details of the treatment and the specifics of the drugs have been withheld pending publication.

A rabies vaccine will prevent the disease only if given within days of exposure; it is useless in saving the patient's life in advanced cases.

Neonatal Infections Limit Growth

Extremely low-birth-weight infants (401-1000 g) who developed neonatal infections were significantly more likely to have neurodevelopmental problems in early childhood, compared with noninfected infants in a cohort study of 6,093 children, said Barbara J. Stoll, M.D., of Emory University, Atlanta, and her colleagues.

The infants were assessed at 18-22 months' corrected gestational age and classified as uninfected (2,161 infants), clinical infection only (1,538 infants), sepsis (1,922 infants), sepsis and necrotizing enterocolitis (279 infants), or meningitis, either with or without sepsis (193 infants). At follow-up, 41% of the children had at least one neurodevelopmental problem (JAMA 2004;292:2357-65).

Scores of less than 70 on the Mental Development Index and the Psychomotor Development Index were significantly more common among children with any of the previously mentioned infections, compared with uninfected children. In addition, children in any of the infection groups were significantly more likely to have cerebral palsy, vision impairment, and neurodevelopmental impairment, and to have a head circumference in less than the 10th percentile, compared with uninfected children.

11-Valent Vaccine Shows Promise

A new 11-valent pneumococcal conjugate vaccine (Pn-PD) was safe and effective in a randomized, single-blind study of 154 infants who received the vaccine at ages 2, 4, 6, and 12-15 months, reported Anu Nurkka of the National Public Health Institute in Helsinki, Finland, and colleagues.

The vaccine used Haemophilus influenzae protein D as a carrier and contained pneumococcal capsular polysaccharides of serotypes 1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F. Overall, three doses of Pn-PD provoked a strong antibody response, compared with a control vaccine, with a significant booster response after the fourth dose (Pediatr. Infect. Dis. I. 2004;23:1008-14). Mild local skin reactions were common.