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| I. WHAT IS BEING STUDIED? | 2009 H1N1 VACCINE |
| 1. Study Objective | Immunogenicity and safety of H1N1 vaccine 21 days after 1 st of 2 proposed doses |
| 2. Study Design | Randomized observer-blind, parallel-group trial, single site, 240 pts divided into two groups of 120 and then each group further divided into 18-49yrs and 50-64yrs |
| 3. Inclusion Criteria | Healthy adults between 18-64 years of age |
| 4. Exclusion Criteria | Confirmed or suspected H1N1 infection, already received an experimental H1N1 vaccine, pregnant |
| 5. Interventions Compared | 15 µg dose and 30µg dose IM injection |
| 6. Outcomes Evaluated | Rise in antibody titer 21 days after vaccination, proportion of subjects with rise in titer or seroconversion, factor increase in the geometric mean titer Secondary – adverse effects |
| II. Are the results of the study valid? | |
| 1. Was the assignment of patients randomized? | Yes, computer driven randomization |
| 2. Were all patients who entered the trial properly accounted for and attributed at its conclusions? | Yes, no one unaccounted for. |

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| 3. Was follow-up complete? | Yes, all subjects accounted for at the end of the initial f/u period which was 7 days for adverse events. Long term f/u data is being collected but is unavailable |
| 4. Were patients, health workers and study personnel “blind” to treatment? | Administrators of vaccine were not but they had no further involvement in study, patients were blinded. |
| 5. Were study groups similar at the start of the trial? | Yes, all groups similar in having more whites and females, ages basically equal in the 15 and 30 µg groups |
| 6. Aside from the experimental intervention, were the groups treated equally | Yes, followed same protocols and kept 7 day diary to document any adverse events |
| III. What were the results? | |
| 1. How large was the treatment effect? | By day 21 antibody titers of 1:40 or greater 116/120 (96.7) in 15µg and 112/120 (93.3) in 30µg dose, also geometric mean titer increased by factor of 10.7 and 18.6 in the 15µg and 30µg doses respectively, seroconversion (increase in titer) in 74.2 of all subjects |
| 2. What was the estimated treatment effect at a 95% confidence interval? | 15µg – antibody titer 1:40 or greater (91.1-98.7) 96.7 30µg – antibody titer 1:40 or greater (87.4-96.6) 93.3 |
| IV. Will the results help me in caring for my patients? (applicable ?) | Possibly, This is a preliminary report N=240 in otherwise healthy patients. The impact and seroconversion rates on the most vulnerable subgroups likely to have the vaccine is yet to be determined. The study also occurred during a pandemic in the same geographic region and its impact on seroconversion can confound the |

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| | <p>results. It appears that a single dose of 15µg may provide sufficient seroconversion in otherwise healthy patients</p> |
| <p>1. Were all clinically important outcomes considered?</p> | <p>The authors demonstrated primary outcome efficacy in terms of seroconversion after vaccination. Vaccine efficacy with disease severity, prevention or complication rates were not included as outcome measures. In the short term, there appeared to be no deaths or serious adverse effects such as Guillian-Barre Syndrome though subjects continue to be monitored. Local discomfort/redness/etc from injection was 46.3% for all subjects. Systemic events in 45% with most common being headache, myalgia, and malaise</p> |
| <p>2. Are treatment outcomes worth the potential harms?</p> | <p>Possibly, there is no long-term data on potential mal effects. One dose of vaccine seems to provide an adequate rise in antibody titers. Impact on infection rate with sero-conversion was not determined. The study suggests that smaller single dose vaccine may be sufficient and appears to have minimal harms in the short term.</p> |

Additional Comments: Preliminary data on a relatively small number of subjects when considering the vastness of recommended immunization programs. In the context of a being a timely report on dosing requirements, short term mal effects and seroconversion rates, preliminary data suggests the monovalent H1N1 may be sufficient. A single dose of vaccine could increase compliance as there would be patients who would inevitably not get the second dose. Additionally, the smaller dose being adequate means that four times as many people can be vaccinated as 15 micrograms can be used instead of 60 micrograms (dose for two 30 microgram vaccines).

There needs to be longer follow up and inclusion of more patients to see if any serious adverse effects such as GBS develop. The elderly, pediatrics, and those with immune-compromise need to be evaluated as these are groups who would benefit most from vaccination.