1947. Influenza Vaccination via Oral Tablet is Protective and Induces a Unique Mucosal Immune Response

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Background. Oral vaccines delivered as tablets offer several advantages over traditional injection-based vaccines including ease of distribution and administration as well as temperature-stable formulation options. Oral vaccination is also advantageous because it directly induces a strong mucosal response, which is thought to be critical for preventing future infections. Here we present results from a phase II clinical challenge study comparing efficacy of an oral recombinant adenovirus-based vaccine expressing hemagluttinin (HA) from A/California 04/09 to that of a commercial injectable quadrivalent (QIV) influenza vaccine.

Methods. In this 2016–2017 clinical trial (NCT02918006), subjects were immunized with either oral vaccine, QIV, or placebo and then challenged 90 days post-immunization with wildtype influenza A H1 virus to measure vaccine efficacy and durability. Protection was assessed by measuring changes in HAI titres, microneutralization, and IgA/IgG ASC assays. Additionally, exploratory flow cytometry evaluated quantitative and qualitative aspects of immunogenicity including markers of activation and mucosal homing on B cells. Analysis was performed on days 0 and 7 post-immunization and 0 and 6 days post-viral challenge. Plasmablasts sorted from PBMCs were then isolated for genomic DNA and sequenced for heavy chain receptor sequencing using NGS analysis.

Results. Of the subjects immunized with Vaxart's oral tablet vaccine, 48% were protected. QIV, by comparison, protected 38% of immunized individuals. Only 37% of Vaxart subjects developed influenza infection compared with 44% of QIV subjects and 71% of placebo subjects. While both vaccines induced a humoral immune response, FACS analysis and NGS revealed that Vaxart subjects had more activated plasmablasts expressing surface mucosal homing markers and a more diverse B cell population than QIV subjects.

Conclusion. Vaxart's oral influenza tablet vaccine protected against influenza infection as well or better than injectable QIV. However, the mechanism of protection appears to be unique to the route of immunization; oral immunization allows for specific homing of influenza specific B cells to sites of infection and produces a more diverse antibody repertoire.

Disclosures. **N. Kolhatkar**, Vaxart, Inc.: Employee, Salary. **K. Gottlieb**, Vaxart, Inc.: Employee, Salary. **K. Kasparek**, Vaxart, Inc.: Employee, Salary. **K. Hodgson**, Vaxart, Inc.: Employee, Salary. **S. Tucker**, Vaxart, Inc: Employee, Salary. **D. Liebowitz**, Vaxart, Inc.: Employee and Investigator, Salary.

1948. A Host-Response Assay Distinguishes Between Simple *Influenza* Patients and *Influenza* Patients With Bacterial Coinfection

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Background. Identifying bacterial coinfection in influenza patients can be difficult as the symptoms of simple influenza vs. mixed infections are often similar, leading to antibiotic overuse. A new host-response assay (ImmunoXpert™) that integrates the levels of three proteins (TRAIL, IP-10, and CRP) was shown to exhibit high performance in distinguishing between bacterial and viral disease in two double-blind validation studies. Here we sought to evaluate its ability to differentiate between simple influenza and influenza with bacterial coinfection.

Methods. The study population included 653 febrile pediatric and adult patients prospectively recruited in the "Curiosity" study. Patient etiology (simple viral vs. mixed infection) was determined by unanimous expert adjudication based on comprehensive clinical, laboratory and radiological assessment. Influenza strains (A or B) were detected using multiplex PCR applied to nasal swabs (Seeplex-RV15). We compared the expert panel diagnosis with the assay that gives three possible outcomes: viral, bacterial (including viral with bacterial coinfection) or equivocal. An equivocal outcome does not provide diagnostic information and is observed in ~10% of cases.

Results. Out of 653 patients, 51 had positive influenza detection and unanimous expert diagnosis: 44 simple viral infections and seven influenza with bacterial coinfections (Figure 1). Antibiotics were prescribed to all seven cases of influenza with bacterial coinfection and to 20/44 cases adjudicated as simple viral infections, indicating an overuse rate of 45%. The assay correctly classified 40 of the 44 simple viral cases (out of the remaining four, two were assigned viral with bacterial coinfection, and two received equivocal outcomes) as well as five of the seven viral with bacterial coinfection cases (the remaining two received equivocal outcomes) supporting the assay's potential to reduce antibiotic overuse 5-fold (from 45% to 4/44 = 9%, $P < 0.001$).

Conclusion. The host–response assay can differentiate between simple influenza and influenza patients with bacterial coinfection, with potential to reduce antibiotic overuse. Utility studies are warranted to demonstrate that the assay can safely assist physicians in correct management of influenza patients.

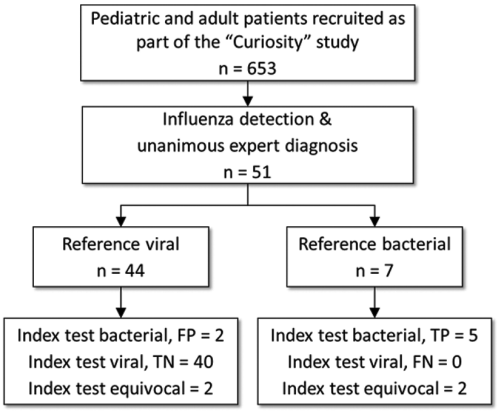

Figure 1. Flow through of febrile patients with positive influenza detection.
FP, false-positive; TN, true-negative; TP, true-positive; FN, false-negative.
The index test is available in Europe as ImmunoXpert™ (CE-IVD), not yet cleared by the FDA.

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1949. Safety and Efficacy of Ambulatory Outpatient Treatment of Febrile Neutropenia in Children With Cancer in Mexico: A Multicenter Randomized Controlled Trial

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Background. Fever and neutropenia (FN) are frequent complications in children with cancer who receive chemotherapy. Although there is evidence of the efficacy of outpatient treatment, inpatient treatment is the standard of care in Mexico City. We aimed to determine whether sequential parenteral-oral outpatient treatment is non-inferior to intravenous inpatient treatment for children with FN in a middle-income setting.

Methods. Randomized controlled clinical trial in subjects 1 to 18 years old with low-risk FN in three hospitals in Mexico City. After 48 to 72 hours of cefepime inpatient treatment, subjects were eligible to participate if they were afebrile for at least 24 hours, had negative cultures and no source of infection. Subjects were randomly assigned to either continue receiving cefepime (inpatient arm) or start receiving cefixime (outpatient arm). Primary end point was treatment failure define as new onset fever, new source of infection or necessity of change antibiotic. Estimated sample size was 68 FN episodes per group. Parametric and nonparametric statistical analyses were performed for comparisons between groups.

Results. Between July 2015 and September 2017, a total of 1,237 episodes of FN were evaluated, of which 469 episodes were eligible. From these, 388 were excluded: 337 due to not meeting the inclusion criteria, eight parents refused to participate, four were evaluated after 72 hours of treatment and three were excluded for other reasons. Of the 117 randomized episodes, 59 were allocated into the outpatient arm and 58 into the inpatient arm. After randomization, demographic and clinical variables did not differ between groups. Treatment failure occurred in 6.9% (4) of patients in the inpatient arm vs. 0% in the outpatient arm ($P = 0.05$). Failures were associated to influenza B infection, catheter related blood stream infection and fever without a source. Mean duration of antibiotics was 4.6 days [SD (standard deviation) 4.5 days, C.I. 95% 3.5–5.8 days] in the outpatient arm and 4.4 days (SD 2.5 days, CI 95%, 3.7–5.0 days) in the inpatient arm ($P = 0.70$).

Conclusion. In our population, outpatient sequential, parenteral-oral treatment with cefixime seems to be as safe and efficacious as parenteral inpatient treatment of low-risk FN episodes.

Disclosures. **All authors:** No reported disclosures.