RESULT SUMMARY

Observational Influenza Vaccine Active Surveillance Study: A Phase IV Prospective Multi-Centre Cohort Study to Evaluate the Reactogenicity of bioCSL's Influenza Virus Vaccine

Protocol No:	CSLCT-SAF-14-05
EU PAS/ENCePP register number	ENCEPP/SDPP/7301
Study Product:	2014/2015 Northern Hemisphere Formulation of Enzira (Split Virion, Inactivated Influenza Vaccine)
Sponsor:	bioCSL Pty Ltd.
Contact Details:	63 Poplar Road, Parkville VIC 3052 Australia Tel: +61 3 9389 2000
Indication Studied:	Prophylaxis of Influenza
Development Phase:	Phase IV
Study Initiation Date:	03 October 2014 (first participant enrolled)
Study Completion Date:	15 December 2014 (last participant completed)
Report Type:	Result Summary (based on CSR Final Version 1, dated 11 February 2015)
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Title	Observational Influenza Vaccine Active Surveillance Study: A Phase IV Prospective Multi-Centre Cohort Study to Evaluate the Reactogenicity of bioCSL's Influenza Virus Vaccine
Keywords	Observational, active surveillance, influenza vaccine, multi-centre, cohort study
Rationale and background	The European Medicines Agency (EMA) has provided new interim guidance on enhanced safety surveillance for seasonal influenza vaccines focusing on signal detection for influenza virus vaccines licensed in Europe (EMA/PRAC/222346/2014). This interim guidance focuses on requirements and principles for annual enhanced safety surveillance, to rapidly detect any increased local and systemic reactogenicity that may arise during the influenza vaccine product life-cycle, such as may occur due to significant changes in the manufacturing process or that may potentially arise with updated influenza virus vaccine strains. It is expected that a Post-Authorisation Safety Study (PASS) will be implemented in years when there is at least one influenza virus vaccine strain change, or if there are significant changes in the manufacturing process. If neither of these changes occur in a given year, it is possible that the study may not be implemented in that year, following consultation between bioCSL and regulatory agencies. This PASS is a pilot for the planned full PASS for bioCSL's influenza virus vaccine (IVV), beginning in the second half of 2015 (Study CSLCT-SAF-15-07)
Research question and objectives	This protocol describes an enhanced active surveillance system that will collect and descriptively summarise participant self-reported reactogenicity data, which will be supplemented by primary care or other health provider data on the details of vaccination, and any medically attended Adverse Events (MAEs) in the seven-day period after each bioCSL influenza vaccination in a given year. Descriptive summaries of the reactogenicity and other safety data as defined in the primary and secondary study objectives will allow indirect comparison of data from the study with previous safety data, and data arising from the enhanced safety surveillance system over time, to facilitate safety signal detection for bioCSL's IVV. ***Primary objective*** To characterise the reactogenicity (local, systemic and allergic reactions) within seven days after each influenza vaccination with bioCSL's IVV in participants routinely indicated for influenza vaccination in specified age groups. ***Secondary objective*** To assess the frequency and severity of MAEs with initial symptom onset within seven days after each influenza vaccination with bioCSL's IVV in participants routinely indicated for influenza vaccination in specified age groups.
Study design	People who had been, or were just about to be, routinely vaccinated with bioCSL's IVV were invited to enrol in the study. Study participants were asked to report solicited adverse events (AEs) occurring within seven days after each vaccination and MAEs that had symptom onset within seven days after each vaccination, via an internet-based survey. The rates of AEs after vaccination in the overall cohort and in pre-specified age sub-groups of the cohort were described.
Setting	This observational research study was implemented through the primary care research network of the National Institute for Health Research in the United Kingdom (UK).
Participants and study size	The source population were individuals who presented to general practice for influenza vaccination, either through mass vaccination clinics or opportunistic vaccination during routine consultations for the influenza vaccination season, and who received bioCSL's IVV. This observational post-marketing study was designed to capture the population receiving bioCSL's IVV regardless of age or health status in order to provide a picture of the safety profile in routine practice. Pregnant and immune-compromised participants, and children aged less than five years were not excluded from this study if they were administered bioCSL's IVV as part of routine care, or inadvertently prior to enrolment in the study. In total, 269 participants were enrolled in the study, as compared to the planned

	enrolment of up to 400 participants. Three participants were enrolled in the five to < nine years group; 13 were enrolled in the nine to < 18 years age group; 141 were enrolled in the 18 to < 65 years group; and 112 were enrolled in the ≥ 65 years group. No children under the age of five years were enrolled. The number of participants eligible for analysis was reduced by losses to follow-up; 80 participants did not provide post-enrolment safety data and were therefore not included in the safety analyses.
Variables and data sources	Data collection utilised a mix of investigator site data entry and participant (or parent/guardian) self-reported data entry into a web-accessed electronic database meeting appropriate observational research, regulatory and data protection standards. The types of variables included in the study were: demographics and baseline characteristics; influenza vaccination information; information on other vaccinations received on the same day as or in the 14 days before this year's seasonal influenza vaccine; clinical at-risk indications for complications from influenza; MAEs; and post-vaccination follow-up.
Results	Data for this report were collected between 3 October 2014 and 15 December 2014. During that period, the total number of doses administered was 269 in 269 participants. Three doses were administered in participants ages 5 to < 9 years of age; 13 doses were administered in participants 9 to < 18 years of age; 141 doses were administered in participants 18 to < 65 years of age; and 112 doses were administered in participants ≥ 65 years of age. Of the 269 enrolled participants, 80 did not provide post-enrolment safety data and were therefore not included in the safety analyses. The total number of participants included in the safety analyses was 189. Across all age groups, 45.0% (85/189) of participants reported any solicited local reaction; 11.1% (21/189) of participants reported any solicited systemic symptom; and 7.4% (14/189) of participants reported any solicited allergic reaction. No related MAEs were reported.
Discussion	There were no serious MAEs or related MAEs within seven days following exposure to bioCSL's IVV. The overall reactogenicity profile of bioCSL's IVV obtained for this report is consistent with the established safety profile of the product. No new safety signal or information due to unexpected frequency, intensity or the nature of events was identified from this active surveillance. Similarly, the active surveillance at the time of this report has not identified any new safety information that has not been identified through ongoing routine post-marketing surveillance since the start of the Northern Hemisphere 2014-15 season.
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