Trial Watch

**Phase I trial of Clostridium difficile vaccine commences**

Acambis (Cambridge, U.K. and Cambridge, MA, USA) has announced that it has commenced clinical trials of its investigational vaccine against Clostridium difficile.

C. difficile is a commonly acquired infection in hospital settings, causing diarrhoea and colitis. A newly emerged, highly virulent strain of the bacterium has been attributed to the sharp increase in the number of infections and associated deaths across the world.

In 2004, 43,000 cases of C. difficile infection were reported in the UK, a 23% higher rate of incidence compared with the previous year. In Quebec, Canada, the number of infections doubled and the number of fatal cases increased by 60% between March 2000 and April 2004. The Centers for Disease Control and the Anaerobe Reference Laboratory (UK) have conducted tests which confirm that the emerging virulent strain is the cause of the recent and current outbreaks witnessed in the UK, Canada, USA and The Netherlands.

Acambis’ Chief Executive Officer, Gordon Cameron, highlighted the impact of the infection in hospitals: “It is estimated that C. difficile infection costs the UK National Health Service alone more than £200 million a year because of extended hospital stays, which can be up to 3 weeks for elderly patients. C. difficile is a burden to hospitals and long-term care facilities and a cause of increasing anxiety for patients entering hospitals. There is clearly a substantial need for an effective way to prevent C. difficile infection.”

The Phase I trial aims to determine the safety, tolerability and immunogenicity of the vaccine developed by Acambis, as well as the optimal dosage. If effective, this toxoid vaccine will provide immunity against toxins A and B, which are the toxins responsible for causing diarrhoea.

“C. difficile has long been a problem for hospitals, but with the emergence of the new virulent strain, the number of outbreaks in hospitals is rapidly increasing, resulting in higher numbers of infection and death. There is currently no effective means of preventing future outbreaks of C. difficile. Acambis is the only known company developing a vaccine to protect against C. difficile infection and we are pleased to have entered the important clinical testing development stage”, said Thomas Monath, Acambis’ Chief Scientific Officer.

**Avant reports positive results from Phase II trial of CholeraGarde®**

Avant Immunotherapeutics (MA, USA) have announced positive preliminary results with their vaccine candidate against cholera (CholeraGarde®), based on an attenuated form of the bacterium Vibrio cholerae.

The double-blind, randomized, placebo-controlled study, which entered Phase II testing in 2002, was conducted by the Centre for Health and Population Research of the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) in collaboration with the International Vaccine Institute (IVI), Korea.

In children aged 9 months to 5 years, the single-dose oral vaccine was found to be well tolerated and highly immunogenic, with protective immune responses observed in 77% of vaccinees. There are, at present, no licensed cholera vaccines for use in pediatric patients under 2 years of age.

To date, more than 400 people have received CholeraGarde in the USA and Bangladesh. The vaccine has been well tolerated and highly immunogenic in both inpatient and clinical field settings, with 75% of adults generating protective immune responses by 7 days post-vaccination.

Avant intend to incorporate CholeraGarde into its VitriLife technology project, which involves developing thermostable live bacterial vaccines that are able to be stored without refrigeration. “Thermostability of Avant’s CholeraGarde is an important milestone to the development of an effective cholera vaccine for biodefense and global health purposes, settings where its use would be of the greatest urgency,” said John Mekalanos of Harvard Medical School (MA, USA), which developed the vaccine together with Avant.

The Phase II trials in Bangladesh aim to assess the safety and immunogenicity of the vaccine first in adults, followed by younger pediatric populations, and is expected to be completed in the latter part of 2005.
