S07.5

First in human data on BSG005, a genetically engineered polyene macrolide evaluated in a double-blinded placebo-controlled Phase 1 trial

Philip Ryan[1], Annsofi Nihlén[2], Peder Andersen[3], David W. Denning[4], Tine Kold Olesen[3]
[1]Nucleus Network, Melbourne, Victoria, Australia, [2]PKxpert, Norra Vallg. 20, SE-21125 Malmö, Sweden, [3]Biosergen, Vestre Rosten 81,7075 Tiller, Trondheim , Norway, [4]Manchester Fungal Infection Group, Core Technology Facility, University of Manchester, Manchester Academic Health Science Centre, Manchester, UK

Objectives: BSG005, is a novel genetically engineered polyene macrolide demonstrating enhanced preclinical safety and efficacy profiles in vitro and in vivo compared to the currently marketed similar class of drugs for treatment of invasive fungal infection. We performed a first-in-human, Phase 1, randomized, double-blind, placebo-controlled dose-escalation trial to investigate safety, tolerability, and pharmacokinetics (PK) of BSG005 after single - (SAD) and multiple dosing (MAD) in healthy subjects.

Materials and Methods: We enrolled 38 males and females aged 18 to 55 years, with body mass index 18.0 -32.0 kg/m^2 (inclusive) and body weight of more than 50 kg, and no significant prior medical history or clinically relevant abnormality in clinical laboratory tests in our Phase 1 trial. Each cohort of 6 subjects was randomized 2:1 to receive BSG005 or placebo with sequential dose escalation contingent on safety and PK data review by a safety review committe. In SAD, 24 subjects were enrolled in 4 cohorts receiving a single IV infusion at BSG005 doses of 0.015, 0.035, and 0.1 mg/kg or placebo. In MAD, we enrolled 14 subjects in 2 cohorts to receive multiple IV infusions once daily for 7 days at a dose levels 0.035 mg/kg and 0.05 mg/kg or placebo with 12 subjects completing the MAD part while 2 subjects withdrew consent.

Safety analysis data included enrolled subjects who were administered at least one dose of study treatment with subjects being analyzed according to treatment received.

Results: Demographic and baseline characteristics were similar of subjects receiving BSG005 versus Placebo with mean age of 27.5 years, and mean BMI of 24.51 kg/m^2 (33 Males; 5 Females). Single and multiple IV infusion(s) of BSG005 were safe with no clinically relevant changes in post-baseline analysis of clinical laboratory parameters – including kidney and liver data, vital signs, or clinically relevant abnormalities in electrocardiograms. Infusion-related AEs (IRR) (Grade 1-2) including fever, rigors, chills, headaches were reported for some subjects in SAD cohorts. IRRs were reported to disappear or become miniscule after repeated infusions in MAD cohorts. Injection site reactions (ISR) such as pain, swelling, erythema and phlebitis were present in a dose-dependent manner among all subjects receiving active treatment in the MAD cohorts. PK data showed that systemic exposure increased approximately proportional to dose. The observed systemic clearance was low and the mean half-life after single dose was approximately 7-10 hours. Upon once daily dosing steady state was reached within 4-5 days and minor accumulation was observed after 7 days.

Conclusion: Single and multiple dose intravenous infusions of BSG005 were safe in the healthy subjects. Adverse events were mild to moderate in severity, the majority of AEs being infusion-related in the SAD and phlebitis in the MAD, and no SAEs were seen in the study. Basic PK parameters were established. Our Phase 1 results provide robust evidence of systemic safety enabling the initiation of subsequent studies in patients with invasive fungal infection.