Novel Regenerative Medicine Product, CLBS12 (HONEDRA®), for the Treatment of Critical Limb Ischemia due to Arteriosclerosis Obliterans and Buerger's Disease

Atsuhiko Kawamoto, Yasuyuki Fujita, Yutaka Furukawa, Hiroyoshi Yokoi, Nobuyoshi Azuma, Shuzo Kobayashi, Takeyasu Ohtake, Kazuki Tobita, Ikuro Kitano, Junichi Yamaguchi, Wataru Shimizu, Naotaka Murata, Amane Kozuki, Hideaki Obara, Masahide Furukawa, Masato Nakamura, William K. Sietsema, Sapna Ghuman, Ronnda L. Bartel, Douglas W. Losordo, Kristen K. Buck

CLBS12 is a regenerative medicine product consisting of GCSF-mobilized, autologous CD34+ cells presenting pro-angiogenic properties.
In November 2017, we commenced CLBS12-P01, an open label, controlled, randomized, multicenter study to estimate the efficacy and confirm the safety of CLBS12 in patients with critical limb ischemia (CLI) due to arteriosclerosis obliterans (ASO) with a single-arm sub-study in patients with CLI due to Buerger's disease (BD). The study was designed in conjunction with PMDA and powering for statistical significance of efficacy was not required. The CLBS12 program was awarded SAKIGAKE designation by the MHLW in March 2018.
Enrollment in CLBS12-P01 originally proceeded satisfactorily but was severely impeded by the multiple states of emergency declared in Japan during 2020 and 2021 as a result of the COVID-19 pandemic. Study enrollment was suspended in January 2022 following treatment of 26 subjects in the ASO group (14 receiving standard of care, 12 receiving CLBS12) and 7 subjects in the BD sub-group.
The safety analysis demonstrated an acceptable benefit-risk profile of CLBS12 for treating CLI. Treatment emergent adverse events (TEAEs) were mostly mild to moderate in intensity and were balanced across the treatment groups.
The study data analysis also demonstrated probable efficacy of CLBS12 for the treatment of CLI. Specifically, CLBS12-treated subjects (ASO and BD) reached continuous CLI-free status, the primary endpoint, faster than the ASO control arm receiving standard-of-care. The differences were not statistically significant but there was a definite trend demonstrating probable efficacy.
The study sponsor has already started discussion with the PMDA for conditional approval of this cellular product.