Press release October 10, 2024

LYSA and GLA launch MorningLyte, an international randomized phase III clinical study comparing a treatment combining a CD20xCD3 T-cell engaging bispecific antibody and Lenalidomide to standard immunochemotherapy in patients with previously untreated follicular lymphoma.

LYSA and GLA launch MorningLyte, a clinical trial comparing an innovative treatment combining a bispecific antibody (mosunetuzumab) with an immunomodulator (lenalidomide) to standard immunochemotherapy in patients with follicular lymphoma. Led by LYSA/LYSARC in collaboration with the GLA in 7 countries with support from other academic cooperative groups and in partnership with Roche, this study will enroll 790 patients, with the goal to establish a new standard in first line treatment of FL.

Follicular lymphoma is the 2nd most common B-cell lymphoma and the archetype of indolent lymphoma. For patients requiring treatment due to a high tumor mass at diagnosis, the usual treatment initially combines chemotherapy with an anti-CD20 monoclonal antibody specifically directed against lymphoma cells followed by maintenance treatment with the anti-CD20 antibody alone.

Despite improved outcomes with this initial immunochemotherapy approach, most patients will still relapse underlining the need for novel therapies to increase the antitumor activity and to prolong remission. Also, these chemotherapy-containing regimens come with substantial short and long-term toxicities, prompting for new treatment schemes with a potentially improved safety profile.

In recent years, innovative immunomodulatory drug combinations have emerged, such as the combination of lenalidomide and the anti-CD20 antibody rituximab, optimizing antitumor activity through the synergy of these two molecules. The RELEVANCE trial by LYSA showed this new regimen provided similar efficacy to standard immunochemotherapy in patients with advanced-stage, previously untreated follicular lymphoma, encouraging the further development of new "chemo-free" strategies (without chemotherapy).

Combining a novel bispecific antibody with an immunomodulatory agent

A new class of immunotherapy has appeared more recently: bispecific antibodies with two simultaneous actions, B-lymphoma cell targeting and immune T-cell recruiting. This CD20-targeting therapeutic class has shown remarkable efficacy in patients with relapsed or refractory follicular lymphoma. Moreover, preliminary results of pilot studies testing these bispecific antibodies in first line treatment, alone or in combination with lenalidomide are very promising, fueling the hope that these new immunotherapies are superior to classical immunochemotherapy in first line FL.

The MorningLyte study [NCT06284122] is a Phase III, international, multicenter, interventional trial designed to compare the efficacy and safety of mosunetuzumab plus lenalidomide to standard of care immunochemotherapy in patients with previously untreated high-tumor burden follicular lymphoma.

We hope to be able to prove that an innovative chemotherapy-free regimen provides greater efficacy than the standard immunochemotherapy in treating patients with follicular lymphoma. This treatment should not only provide a better response, and a longer remission over time, but could also possibly improve patients' quality of life.

An academic worldwide expertise:

This vast international study, designed by LYSA/LYSARC (an academic cooperative group active in France, Belgium and Portugal) and GLA (an academic cooperative group active in Germany) in partnership with Roche, relies on close collaboration with other academic cooperative groups such as GELTAMO (Spain) and SAKK (Switzerland).

A companion study will also be carried out in Japan, in partnership with Chugai (sponsor for Japan).

Patients:

More than 790 patients will participate in 8 different countries. This study will be carried out in a defined population of patients aged 18 years or more, with no age restriction, with untreated follicular lymphoma requiring treatment for the first time.

It should be noted that patients with HIV, with a controlled disease and an undetectable viral load, will be able to participate in this study.

Study schedule:

The patient recruiting period will last almost 3 years. All randomized patients will be treated for 30 months. From the end of treatment, patients will be followed every 3 months for the first two years, then every 6 months for the next 3 years, and then annually until the end of the study. The primary objective is improvement of progression-free survival.

The end of the study will occur when all randomized patients have been followed for at least 7 years after the last randomized patient (or have stopped the study prematurely). The overall total duration of the study will be 10 years.

The study has been initiated on May 17, 2024. Enrollment is ongoing since June 18, 2024, date of the first randomized patient. To date, 50 patients have been included in the study in France and Belgium.

> **Prof. Franck MORSCHHAUSER, president of LYSA/LYSARC:** " *LYSA group has ensured and maintained a very successful continuity in follicular lymphoma research over the past 40 years. After the PRIMA and RELEVANCE studies carried out by LYSA, the implementation of bispecific antibodies in first line treatment to replace anti-CD20 monoclonal antibodies is the most logical and conceptually most attractive step in the current state of knowledge. MorningLyte is the first academic study co-designed with GLA in follicular lymphoma and LYSA is very pleased to also benefit from the expertise of GELTAMO, AGMT, SAKK and our Japanese colleagues to bring this effort to fruition."*
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> **Prof. Dr. Christian Buske (chair of the working group "Indolent Lymphoma" and former president of the GLA): "***MorningLyte will be one of the most important studies for follicular lymphoma of the recent years as it has the realistic chance to change our standard treatment in first line follicular lymphoma around 20 years after the introduction of immunochemotherapy. Such a large academic study needs joint efforts on a European and international level and we as GLA are proud to partner with LYSA/LYSARC to bring this pivotal study to success, together with our Austrian, Spanish, Swiss and Japanese colleagues."*

Focus on lenalidomide and Mosunetuzumab

Lenalidomide is a known molecule, modulating the immune system and taken orally. Its efficacy in combination with an anti-CD20 antibody, in a chemotherapy-free regimen, has already been demonstrated. The RELEVANCE study, also sponsored by LYSA/LYSARC, conducted on 1030 patients with previously untreated advanced follicular lymphoma, was the first study to show that treatment without chemotherapy might be sufficient as a first-line treatment.

Mosunetuzumab is a first-in-class CD20xCD3 T-cell engaging bispecific antibody designed to target CD3 on the surface of T-cells and CD20 on the surface of B-cells. A robust clinical development program for mosunetuzumab is ongoing, investigating the molecule as a monotherapy and in combination with other medicines, for the treatment of people with B-cell non-Hodgkin lymphomas, including follicular lymphoma and diffuse large B-cell lymphoma, and other blood cancers.

About the LYSA (The Lymphoma Study Association) / LYSARC (The Lymphoma Academic Research Organization) collaborative group:

LYSA, The Lymphoma Study Association, is an academic, nonprofit, internationally leading cooperative group bringing together multidisciplinary expertise in the field of lymphoma. Its operational structure located in Pierre-Bénite (69), France, the LYSARC (The Lymphoma Academic Research Organization) has all the functions and integrated platforms dedicated to anatomical pathology, biology and imaging to conduct clinical studies. LYSA has more than 500 members, researchers and medical experts, with a network of about 90 clinical research centers in France, Belgium and Portugal. LYSA's missions are to promote clinical research, improve disease prevention, management, and treatment of patients with lymphoma and broadcast knowledge on all types of lymphoma.
LYSARC - Lymphoma Research Experts (experts-recherche-lymphome.org)

About GLA (German Lymphoma Alliance):
The German Lymphoma Alliance is an academic non-profit internationally leading cooperative group, focusing to foster clinical and translational research in patients with non-Hodgkin lymphoma. It has over 400 members and involves active participating study centers all over Germany. https://www.german-lymphoma-alliance.de/home.html

About GELTAMO (Grupo Español de Linfomas/Trasplante Autólogo de Médula Ósea):
The purpose of the Foundation is the study and treatment of lymphomas and other lymphoproliferative syndromes. The Foundation ensures the promotion, development and dissemination of all kinds of scientific work, educational, health, preventive, technical and economic. https://www.geltamo.com/

About AGMT ((Arbeitsgemeinschaft medikamentöse Tumortherapie):
The registered association AGMT is a non-profit association of scientifically active clinicians and researchers in the fields of hematology and oncology, among others.

About SAKK (Schweizerische Arbeitsgemeinschaft für Klinische Krebsforschung):
The Swiss Group for Clinical Cancer Research (SAKK) is a nonprofit organization that has been conducting clinical studies in the field of oncology since 1965. https://www.sakk.ch/fr

About Chugai (Chugai Pharmaceutical Co., Ltd.):
Chugai, headquartered in Tokyo, Japan, is a research-based pharmaceutical company with world-class drug discovery capabilities, including proprietary antibody engineering technologies. Chugai is an important member of the Roche Group. https://www.chugai-pharm.co.jp/english/

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