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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Marsun, a Phase III, Multicenter, Open Label, Randomized, Controlled Study Investigating Mosunetuzumab-Lenalidomide Versus Investigator Choices in Patients with Relapsed or Refractory Marginal Zone Lymphoma (R/R MZL)

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Background

MZLs are the second most common indolent NHL (iNHL) and comprise three distinct subtypes: (i) extranodal MZL (EMZL), mostly represented by MALT lymphoma; (ii) nodal MZL (NMZL); and (iii) splenic MZL (SMZL). For patients with high tumor burden based on GELF criteria, and patients with symptoms related to disease, first-line treatments rely on immuno-chemotherapy to reach high response rates at the cost of substantial toxicities notably in elderly patients. To date, R/R MZL remain a therapeutic challenge without clear standard of care treatment between immuno-chemotherapy, targeted therapies (i.e. BTK/PI3K inhibitors or the immunomodulatory agent lenalidomide (Len)), mainly because of an underrepresentation of MZL in the "indolent NHL" trials.

Mosunetuzumab is a CD20xCD3 T-cell-engaging bispecific antibody designed to redirect T-cell cytotoxic activity against B-cells with promising efficacy results as monotherapy in various B-cell NHL. Lenalidomide was approved in the USA for R/R MZL based on data from MAGNIFY (MZL=45 patients) and AUGMENT (MZL=63 patients) and previous results of a phase IB study showed that mosunetuzumab in combination with Lenalidomide has a manageable safety profile and encouraging activity in patients with R/R follicular lymphomas (Morschhauser F. et al. ASH 2021)

Here we present details of a trial in progress investigating the efficacy and the safety of mosunetuzumab-lenalidomide, a chemo-free regimen, compared to investigator choice, in patients with R/R MZL in need of systemic treatment and not eligible for local therapy such as radiotherapy or surgery.

Methods

This is an open label, multi-center, international, randomized phase III trial to compare the efficacy of Mosunetuzumab-Lenalidomide with investigator choices exclusively in R/R MZL patients. Patients with a proven diagnosis of EMZL, SMZL or NMZL and previously treated with at least one and no more than three prior systemic treatments are eligible. Previous treatment lines must include at least one systemic line with a drug targeting CD20 (monoclonal antibody at least 2 cycles) with or without chemotherapy (CHOP, bendamustine, CVP, chlorambucil) or targeted treatment such as ibrutinib.

Patients will be stratified according to MZL subtype and time to progression of disease after first-line within 2 years.

Mosunetuzumab will be administered subcutaneously (21 days C1, then 28 days C2-12) and lenalidomide will be given PO 20 mg/day from Day 1 to Day 21 from cycles C2 to C6. For each patient, investigator choice must be decided before randomization between R-Len (12 cycles) and R-chemotherapy (R-Bendamustine or R-CHOP followed by a 6 months maintenance). Both arms will have the same one-year fixed duration.
The primary efficacy endpoint for comparison is progression-free survival (PFS) as determined by investigator (Lugano criteria 2014). Secondary objectives include CR24 (CR at 24 months) as determined by investigator and by central review according to Lugano criteria 2014 based on PET results, overall response rate and CR other than CR24 as determined by investigator, or by central review based on PET result according to Lugano criteria 2014. 260 patients are planned to be enrolled in France, Belgium, Germany, Italy and Portugal with FPI expected in Q3 2023 and approximately 4-year accrual period. The study will comprise a first stage of 10 patients in a safety cohort with mosunetuzumab-lenalidomide followed by a stage 2 with patients randomized 1:1 to receive M-len or investigator choice (125 patients per arm).
The sponsor of the trial is the Lymphoma Academic Research Organisation (LYSARC) in collaboration with GLA and FIL with the support of F.Hoffmann-La Roche Ltd.

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