

6.1 Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

Signed Written Informed Consent

- 1) Participants must have signed and dated an IRB/IEC-approved written ICF in accordance with regulatory, local, and institutional guidelines. This ICF must be obtained before performing any protocol-related procedures that are not part of normal patient care.

Type of Participant and Target Disease Characteristics

- 2) Participant has histologically confirmed FL (Grade 1, 2, or 3a) as assessed by local pathology. Adequate fresh tumor biopsy tissue or archived tumor biopsy (preferably from the latest relapse if available) with corresponding pathology report for retrospective central pathology confirmation of relapse, is required. Evaluation from fine needle aspirate is not permitted.
 - a) Participant must meet criteria based on investigator's assessment to receive systemic therapy.
 - b) Participant must have relapsed or refractory disease, as assessed by the investigator and defined below:
 - i) Relapsed FL is defined as relapse after an initial response of CR or PR to the most recent prior therapy.
 - ii) Refractory FL is defined as best response of SD or progressive disease to the most recent prior therapy.
- 3) Participant has Eastern Cooperative Oncology Group (ECOG) performance status (PS) of ≤ 2 , ECOG PS 3 is allowed if it is lymphoma-related and not due to comorbidities.
- 4) Participant must have positron emission tomography (PET)-positive disease with at least one PET-positive lesion and measurable disease on cross section imaging by CT, as defined by the Lugano Classification.
- 5) Participant has received at least 1 or more prior lines of systemic therapy with one line consisting of a combination including an anti-CD20 monoclonal antibody (eg, rituximab, obinutuzumab) and an alkylating agent (eg, cyclophosphamide, bendamustine). Prior treatment with radiation therapy does not count as a line of therapy for eligibility.
- 6) Participants with an indication for anti-lymphoma treatment as per investigator assessment based on one of the following criteria (modified GELF criteria), but not limited to:
 - a) Bulky disease defined as a nodal or extra nodal (except spleen) mass > 7 cm in its greater diameter or, involvement of at least 3 nodal or extra nodal sites (each with a diameter greater than > 3 cm)
 - b) Presence of at least one of the following B symptoms:
 - i) Fever ($>38^{\circ}\text{C}$) of unclear etiology
 - ii) Night sweats
 - iii) Weight loss greater than 10% within the prior 6 months
 - c) Splenomegaly with inferior margin below the umbilical line
 - d) Any one of the following cytopenia due to lymphoma:
 - i) Platelets $<100,000$ cells/ mm^3 ($100 \times 10^9/\text{L}$)
 - ii) Absolute neutrophil count (ANC) $< 1,000$ cells/ mm^3 ($1.0 \times 10^9/\text{L}$)

- iii) Hemoglobin < 10g/dL (6.25 mmol/L)
 - e) Pleural or peritoneal serous effusion (irrespective of cell content)
 - f) Any compressive syndrome (for example but not restricted to ureteral, orbital, gastrointestinal)
- 7) Participant must have the following laboratory values:
- a) Absolute neutrophil count $\geq 1,000$ cells/mm³ (1.0×10^9 /L) or $\geq 0.5 \times 10^9$ /L in case of documented bone marrow involvement by lymphoma or hypersplenism secondary from spleen involvement by lymphoma, without growth factor support for 7 days (14 days if pegylated growth factor is used).
 - b) Platelet count $\geq 75,000$ cells/mm³ (75×10^9 /L) unless $\geq 50,000$ cells/mm³ (50×10^9 /L) secondary to documented bone marrow involvement by lymphoma or hypersplenism secondary from spleen involvement by lymphoma, without transfusions for 7 days.
 - c) Hemoglobin ≥ 7.5 g/dL.
- 8) Estimated Glomerular function (eGFR) of ≥ 30 mL/min/1.73m² using the modification of diet in renal disease (MDRD) formula (refer to [APPENDIX 13](#)) or Chronic Kidney Disease - Epidemiology Collaboration formula (CKD-EPI). The same eGFR cutoff applies in case of documented renal involvement by lymphoma.
- d) Serum aspartate transaminase (AST/SGOT) or alanine transaminase (ALT/SGPT) ≤ 2.5 x upper limit of normal (ULN). In case of documented liver involvement by lymphoma, ALT/SGPT and AST/SGOT must be $\leq 5.0 \times$ ULN.
 - e) Serum total bilirubin $\leq 1.5 \times$ ULN (corresponding to mild dysfunction as per National Cancer Institute Organ Dysfunction Working Group [NCI ODWG] criteria). In case of documented liver involvement by lymphoma, serum total bilirubin must be $\leq 3.0 \times$ ULN (corresponding to moderate dysfunction as per NCI ODWG criteria). For cases of Gilberts syndrome, serum total bilirubin $\leq 5.0 \times$ ULN.
- 9) Adequate cardiac function for participants receiving anthracycline based chemotherapy, defined as left ventricular ejection fraction (LVEF) $\geq 45\%$ as assessed by echocardiogram (ECHO) as standard of care or multi-gated acquisition scan (MUGA) if ECHO is not conclusive.
- 10) Participant is willing to receive thromboembolic medications if deemed high risk for thromboembolic events.
- 11) Participant is able to understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
- 12) Participant is willing and able to adhere to the study visit schedule and all other protocol requirements.
- 13) Participant agrees to refrain from donating blood while on study intervention, during dose interruptions, and for at least 28 days following the last dose of study intervention.

Age of Participant

- 14) Participant must be at least 18 years of age, inclusive, at the time of signing the ICF.

Reproductive Status

Note: The investigator or designee shall counsel IOCBP participants (as defined in [APPENDIX 3](#) and [APPENDIX 4](#)) and male (as assigned at birth) participants who are

sexually active with IOCBP on the importance of pregnancy prevention, the implications of an unexpected pregnancy, and the potential of fetal toxicity occurring due to transmission of study intervention present in seminal fluid to a developing fetus, even if the participant has undergone a successful vasectomy or if the partner is pregnant.

Note: The investigator or designee shall evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

Note: Local laws and regulations may require the use of alternative and/or additional contraceptive methods.

Note: The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to potentially decrease the risk for inclusion of an individual with an undetected pregnancy.

15) Female (as assigned at birth) participants must adhere to Pregnancy Prevention Plan requirements (See APPENDIX 3 and APPENDIX 4), including:

- a) Female (as assigned at birth) participants who are not of childbearing potential (as defined in APPENDIX 3 and APPENDIX 4) must have documented proof. Documentation can be obtained from the site personnel's review of the participant's medical records, medical examination, or medical history interview.
 - b) Individuals who are not of childbearing potential are exempt (See APPENDIX 3 and APPENDIX 4) from contraceptive requirements.
 - c) IOCBP must have 2 negative pregnancy tests (minimum sensitivity 25 mIU/mL or equivalent units of human chorionic gonadotropin) as verified by the investigator prior to starting golcadomide:
 - i) A negative serum pregnancy test (sensitivity of at least 25 mIU/mL) at screening (between 10 to 14 days prior to C1D1).
 - ii) A negative serum or urine pregnancy test (Investigator's discretion) within 24 hours prior to Cycle 1 Day 1 of study treatment. Note: the screening serum pregnancy test can be used as the test prior to Day 1 study treatment if it is performed within the prior 24 hours.
 - d) Either commit to true abstinence from heterosexual contact (which must be reviewed on a monthly basis and source documented) or agree to use, and be able to comply with two forms of contraception: one highly effective, and one additional effective (barrier) measure of contraception without interruption 28 days prior to starting IP, during the study treatment (including dose interruptions), and for at least 28 days after the last dose of golcadomide or lenalidomide and for 12 months after the last dose of rituximab, and according to the approved product/prescribing information for components of chemotherapy regimens, as applicable, whichever is longer. Agree to be counseled about pregnancy precautions and risk of fetal exposure.
- 16) IOCBP (assigned females at birth) must agree to abstain from breastfeeding during study participation and for at least 28 days after golcadomide discontinuation and according to the approved product/prescribing information for components of chemotherapy regimens, rituximab and lenalidomide.

- a) Agree to ongoing pregnancy testing during the course of the study, and after the end of study intervention. This applies even if the participant practices true abstinence from heterosexual contact.
- b) IOCBP and male (as assigned at birth) participants who are sexually active with IOCBP must agree to follow instructions for method(s) of contraception as described in Pregnancy Prevention Plan for golcadomide and included in the ICF.
 - i) Avoid conceiving for up to 28 days after the last dose of golcadomide.
 - ii) Agree to refrain from donating ova while on golcadomide for at least 28 days after its discontinuation.
- c) **Male (as assigned at birth) participants must adhere to Pregnancy Prevention Plan requirements (See APPENDIX 3 and APPENDIX 4)**
 - i) Practice true abstinence (which must be reviewed monthly, and source documented) or agree to use a condom during sexual contact with a pregnant female or an FCBP while participating in the study, during dose interruptions and for at least 28 days for golcadomide or lenalidomide, and according to the approved product/prescribing information for components of chemotherapy regimens and rituximab, as applicable, whichever is longer, even if he has undergone a successful vasectomy.
 - ii) Must agree to refrain from donating sperm while on study intervention, during dose interruptions, and for at least 28 days after the last dose of golcadomide or lenalidomide and according to the approved product/prescribing information for components of chemotherapy regimens and rituximab, as applicable, whichever is longer. Agree to be counseled about pregnancy precautions and risk of fetal exposure.
 - iii) IOCBP partners of male participants should be advised to use a highly effective method of contraception during the intervention period and for at least 28 days after the last dose of golcadomide or lenalidomide, or according to the approved product/prescribing information for components of chemotherapy regimens and rituximab, as applicable, for the male participant.
 - iv) Male participants with a pregnant or breastfeeding partner must agree to remain abstinent from sexual activity or use a male condom during any sexual activity (eg, vaginal, anal, oral), even if the participant has undergone a successful vasectomy, during the intervention period and for at least 28 days after the last dose of golcadomide or lenalidomide, or according to the approved product/prescribing information for components of chemotherapy regimens and rituximab, as applicable.
 - v) Breastfeeding partners of male participants should be advised to consult their health care provider about using appropriate highly effective contraception during the time the male participant is required to use condoms.