Protocol Title: A Randomized Phase II Trial in Early Relapsing or Refractory Follicular Lymphoma

Target Population: Adults with Grade 1-3 Follicular Lymphoma, Recurrent or Refractory Follicular Lymphoma

Summary: This randomized phase II trial studies how well obinutuzumab with or without PI3K-delta inhibitor TGR-1202, lenalidomide, or combination chemotherapy work in treating patients with grade I-IIIa follicular lymphoma that has come back or does not respond to treatment.

Key Inclusion Criteria:
- Patients must have follicular lymphoma (grade I, II or IIIa) confirmed at initial diagnosis and at relapse with identifiable fludeoxyglucose F-18 (FDG) avid disease on PET/CT.
- Patients must not have clinical evidence of CNS involvement by lymphoma.
- Patients must have a whole body or limited whole body PET/CT scan performed within 42 days prior to registration AND must have bone marrow biopsy performed within 42 days prior to registration.
- All disease must be assessed and documented on the S1608 FDG-PET/CT assessment form.
- Patients must have either failed to achieve a complete remission, or must have relapsed within 2 years after completing 1st line bendamustine-containing chemoimmunotherapy, as measured from last dose of bendamustine; relapsed patients must not have received any intervening chemotherapy; patients must have received at least 3 cycles of bendamustine as first line therapy; patients who additionally received any maintenance anti-CD-20 antibody based therapy or consolidative radioimmunotherapy within 2 years of the last dose of the bendamustine therapy are eligible; involved field or involved site radiation is not considered a line of therapy; patients who previously received anthracycline based therapy are excluded.
- For all forms of systemic therapy, patients must have completed therapy at least 21 days prior to registration; patients must have completed any radioimmunotherapy at least 84 days prior to registration; patients must have recovered from all treatment related toxicities from these therapies prior to registration.
- Patients must have either failed to achieve a complete remission, or must have relapsed within 2 years after completing 1st line bendamustine-containing chemoimmunotherapy, as measured from last dose of bendamustine; relapsed patients must not have received any intervening chemotherapy; patients must have received at least 3 cycles of bendamustine as first line therapy; patients who additionally received any maintenance anti-CD-20 antibody based therapy or consolidative radioimmunotherapy within 2 years of the last dose of the bendamustine therapy are eligible; involved field or involved site radiation is not considered a line of therapy; patients who previously received anthracycline based therapy are excluded.
- Patients must have blood and tissue specimens collected prior to registration and submitted for translational medicine.
- All patients must have a Zubrod performance status of 0, 1 or 2.
- Patients must be able and willing to receive prophylaxis with daily aspirin, low molecular weight heparin, factor X inhibitors or Warfarin if randomized to lenalidomide; patients must also be willing to receive pneumocystis jirovecii prophylaxis in the event that they are randomized to TGR-1202; patients unable or unwilling to take any listed prophylaxis are NOT eligible.
- No prior malignancy is allowed except for adequately treated basal (or squamous cell) skin cancer, in situ cervical cancer or other cancer for which the patient has been disease free for three years.
- Patients must have the following components of Follicular Lymphoma International Prognostic Index (FLIPI) available from diagnosis, and collected again at time of registration: Age, Lactate dehydrogenase (LDH), Number of nodal groups involved, Serum or plasma hemoglobin, and Ann Arbor stage. Additionally, patients must have beta-2-microglobulin collected at time of registration.

Key Exclusion Criteria:
- Patients must be able to discontinue CYP2C9 substrates with a narrow therapeutic index (e.g. warfarin, phenytoin), if randomized to TGR-1202; patients must discontinue such agents at least 1 week or 5 half-lives prior to beginning protocol therapy (whichever is longer).

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For additional information: https://clinicaltrials.gov/ct2/show/NCT03269669