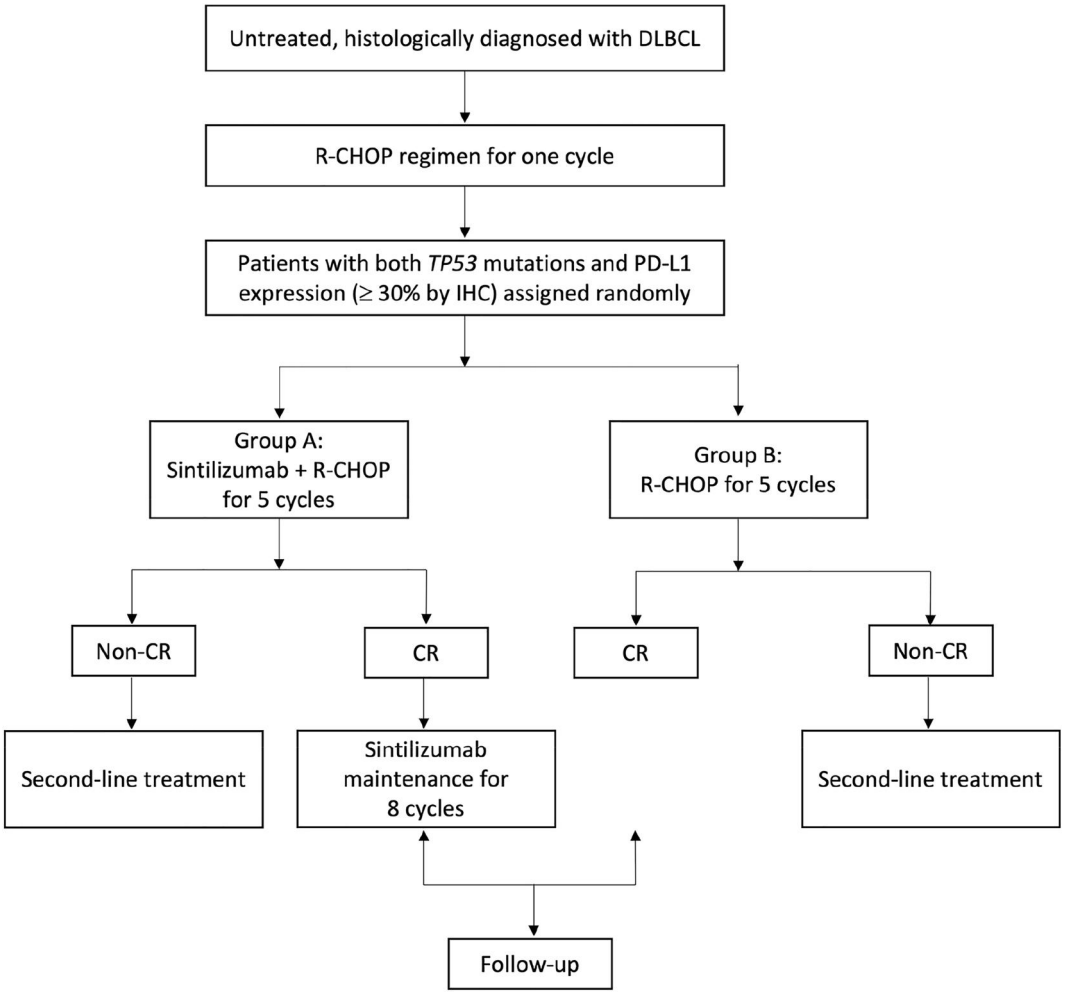

OT27 | PHASE II/III STUDY OF R-MINICHOP ± ORAL AZACITIDINE IN PARTICIPANTS AGE 75 YEARS OR OLDER WITH DIFFUSE LARGE B CELL AND RELATED LYMPHOMAS

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Introduction: Diffuse large B cell lymphoma (DLBCL) is an aggressive but potentially curable malignancy. Nearly one-third of patients are >75 y, and advanced age is an adverse prognostic variable. R-miniCHOP, a dose attenuated version of standard R-CHOP, offers a 2-year progression-free survival (PFS) of 47% based on phase II data (Peyrade F et al, 2011). For comparison, patients age 60-80 have about a 75% 2-year overall survival (OS) with R-CHOP chemotherapy (Coiffier B et al., 2002).

A key dilemma is identifying which older patients with DLBCL should be considered for curative intent chemoimmunotherapy. The FIL (Fondazione Italiana Linfomi; Italian Lymphoma Foundation) has developed a tool accounting for age, comorbidities, and ability to perform daily and instrumental activities to classify patients as fit, unfit, or frail (Tucci A et al, 2015), with a key observation being improved survival when curative intent chemoimmunotherapy was delivered to fit and unfit patients. (Merli F et al., 2021). However, there is no prospective validation of frailty assessment and treatment outcomes.

Epigenetic deregulation is a feature of DLBCL in older patients. Preclinical models show that pre-treatment with hypomethylating agents improves the anti-tumor effect of the agents contained in R-

CHOP (Clozel T et al., 2013). Early studies of azacitidine with R-CHOP showed promising efficacy and acceptable toxicity (Martin P et al., 2022). The availability of oral azacitidine is appealing, reduces the infusion burden of treatment, and is agnostic to cell-of-origin.

Methods: S1918 is a randomized trial of R-miniCHOP ± oral azacitidine in patients >75 y with newly diagnosed aggressive B-cell non Hodgkin lymphomas (NCT04799275). This is the first randomized study in this population conducted in North America by the National Clinical Trials Network (NCTN) and will enroll 384 patients. Patients receive prephase therapy with prednisone 60–100 mg × 4–7 days to improve performance status and decrease early treatment-related mortality (Owens CN et al., 2015; Pfreundschuh M et al., 2008). A safety run-in has been completed.

The phase II objective is to determine if oral azacitidine + R-miniCHOP should be tested further against R-miniCHOP based on estimates of 1-year PFS. The phase III objective is to compare OS at 2 years between arms.

S1918 incorporates the FIL Tool for baseline frailty assessment and a serial comprehensive geriatric assessment to evaluate effects of therapy on quality of life and functional status. Key correlative tests include circulating tumor DNA (ctDNA) assays to explore if ctDNA quantity and methylation patterns correlate with response.

S1918 has potential to impact future trial design and change the standard of care for patients > 75 y with aggressive lymphoma with its randomized design, incorporation of baseline frailty and geriatric assessments, and utilization of ctDNA correlatives.

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Keywords: aggressive B-cell non-Hodgkin lymphoma, combination therapies, ongoing trials

Conflicts of interests pertinent to the abstract.

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OT28 | PHASE 3 TRIAL OF SUBCUTANEOUS EPCORITAMAB + R-CHOP VERSUS R-CHOP IN PATIENTS (PTS) WITH NEWLY DIAGNOSED DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL): EPCORE DLBCL-2

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Introduction: In pts with newly diagnosed DLBCL, standard treatment with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) has a 5-year progression-free survival (PFS) rate of 67.0%, 58.4%, and 45.8% for International Prognostic Index (IPI) 2, 3, and 4–5, respectively (Ruppert et al., *Blood* 2020). Epcoritamab is a subcutaneously administered, bispecific antibody that binds CD3 on T cells and CD20 on B cells, inducing potent and selective T-cell–mediated killing of malignant CD20+ B cells (Hutchings et al., *Lancet* 2021). Epcoritamab monotherapy demonstrated deep and durable responses (overall response rate [ORR], 63%; complete response rate, 39%; median duration of response, 12 months) and was generally well tolerated in pts with relapsed/refractory (*R/R*) aggressive, large B-cell lymphoma (LBCL) (Thieblemont et al., *J Clin Oncol* 2022). Results from an ongoing phase 1/2 study in high-risk pts with newly diagnosed DLBCL (EPCORE NHL-2 arm 1; NCT04663347) show that epcoritamab + R-CHOP has promising efficacy and a manageable safety profile in high-risk pts with IPI 3–5. Among efficacy-evaluable pts ($n = 31$), ORR was 100% and complete metabolic response (CMR) was 77%; cytokine release syndrome (CRS) events ($n = 17/33$; 52%) were mostly low-grade, had predictable timing, and did not lead to treatment discontinuation (Falchi et al., ASCO 2022, abstract 7523). These encouraging data support further evaluation of epcoritamab + R-CHOP for the treatment of newly diagnosed DLBCL.

Methods: This phase 3, global, multicenter, open-label study (NCT05578976) evaluates the efficacy and safety of epcoritamab + R-CHOP in adults newly diagnosed with one of the following CD20