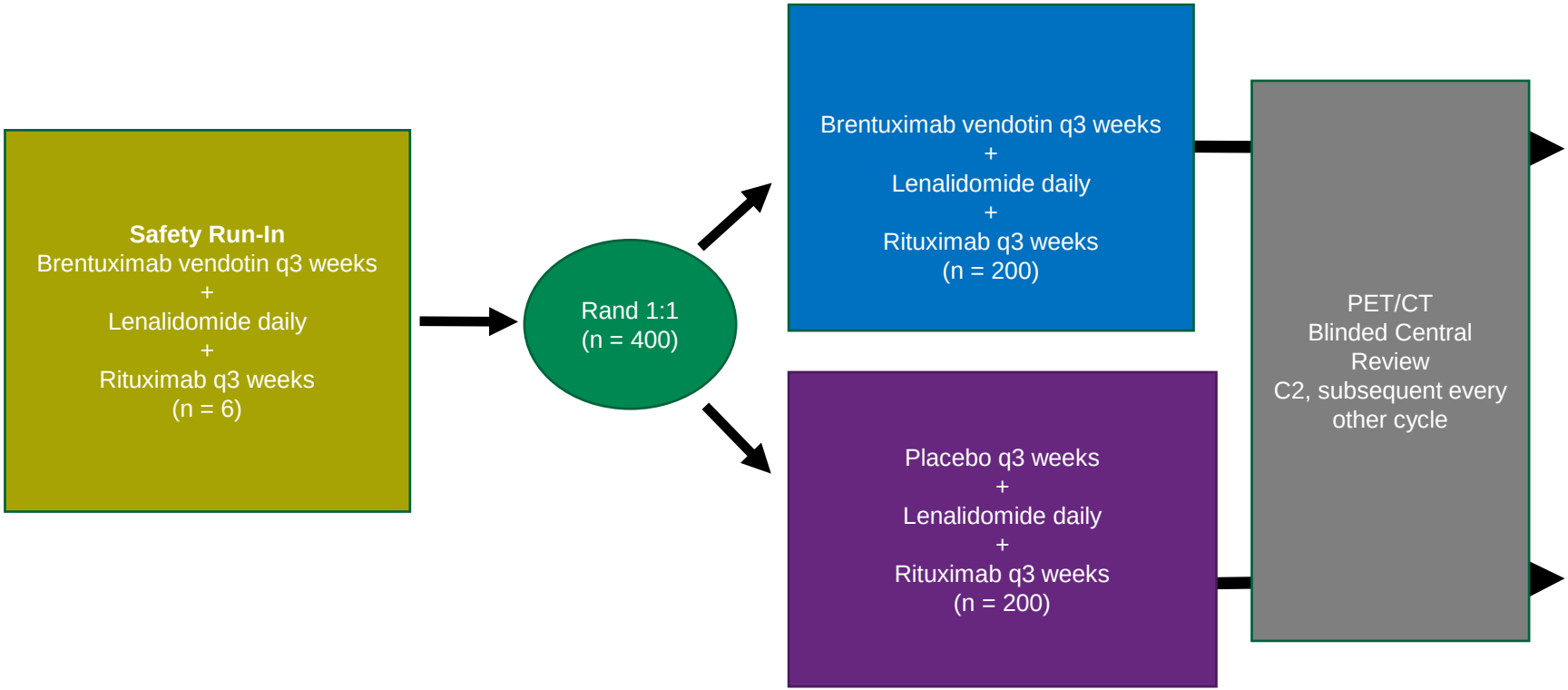
SGN35-031: A randomized, double-blind, placebo-controlled, active-comparator, multicenter, phase 3 study of brentuximab vedotin or placebo in combination with lenalidomide and rituximab in subjects with relapsed or refractory diffuse large B-cell lymphoma (DLBCL)

SeattleGenetics®

Study Design – Schematic



Study Design – Randomized

- 1:1 randomization BV or placebo in combination with lenalidomide and rituximab
  - BV 1.2 mg/kg via intravenous infusion OR placebo every 3 weeks
  - Lenalidomide 20 mg orally
  - Rituximab 375 mg/m2 intravenously on Cycle 1 Day 1
  - Rituximab 1400 mg via subcutaneous injection every 3 weeks from Cycle 2 Day 1
- Stratification factors:
  - CD30 expression: ≥1% CD30 vs. <1% CD30 – *determined by central pathology*
  - Cell of origin (GCB or non-GCB) – determined by local pathology
  - Prior allogenic or autologous SCT (received or not)
  - Prior CAR-T therapy (received or not)
- Treatment may continue as long as there is clinical benefit (SD or better) without progression or unacceptable toxicity

Study Design – Stratification and CD30 expression

- For stratification purposes, subjects will have central pathology lab determination of CD30 expression from a recent biopsy specimen (obtained ≤4 weeks before Day 1)
- If, in the determination of the investigator, it is not medically feasible to undergo central pathology evaluation prior to randomization, and after discussion with the Medical Monitor, the subject may be stratified based on CD30 expression from the local pathology lab.
- Subjects who are stratified based on local pathology lab results must have an archive block sent in for central CD30 evaluation within 2 weeks of enrollment.
- Subjects will be stratified based on a cut-off of ≥1% CD30 tumor expression; ≥1% CD30 tumor expression will be considered CD30 positive while <1% CD30 tumor expression will be considered CD30-undetectable.

Response Assessments

- Disease response per Lugano 2014 will be assessed by both the BICR and the investigator
- Responses will be assessed as follows:
- CT scans of neck, chest, abdomen and pelvis, as well as a PET scan will be assessed at baseline and every 6 weeks thereafter (between Days 15 and 21) .
- Once the PET is negative per the investigator, no further PET scans are required.
- Every 12 weeks beginning at 12 months.
- A diagnostic quality CT-PET scan should also be performed at the time of suspected clinical progression.

Key Inclusion Criteria

- Aged 12 and older with relapsed/refractory (R/R) DLBCL
- Must have ≥2 prior lines of therapy and must be ineligible for stem cell transplant or CAR-T (includes a patient declining CAR-T due to financial, geographic or insurance issues)
- Eastern Cooperative Oncology Group (ECOG) performance status score of 0 to 2
- Must have a fluorodeoxyglucose (FDG)-avid disease by positron emission tomography (PET) and bidimensional measurable disease of at least 1.5 cm by computed tomography (CT), as assessed by the site radiologist.
- Subjects must be registered into the mandatory lenalidomide REMS® program and be willing to comply with its requirements. Per standard lenalidomide REMS® program requirements, all physicians who prescribe lenalidomide for research subjects enrolled into this trial, must be registered in, and must comply with, all requirements of the lenalidomide REMS® program
- For stratification purposes, subjects will have central pathology lab determination of CD30 expression from a recent biopsy specimen (obtained ≤4 weeks before Day 1)

Key Exclusion Criteria

- Previous treatment with brentuximab vedotin or lenalidomide
- History of PML
- Grade 2 or higher peripheral sensory or motor neuropathy at baseline.
- Active cerebral/meningeal disease related to the underlying malignancy.
- Documented history of a cerebral vascular event (stroke or transient ischemic attack), unstable angina, myocardial infarction, or cardiac symptoms consistent with New York Heart Association Class III to IV within 6 months prior to their first dose of brentuximab vedotin
- History of another malignancy within 2 years before the first dose of study drug or any evidence of residual disease from a previously diagnosed malignancy. Exceptions are malignancies with a negligible risk of metastasis or death
- Current treatment with immunosuppressive medications, systemic anti-neoplastic, or investigational agents

Primary & Secondary Objectives

- Primary Objective
  - Progression-free survival (PFS) among subjects between the 2 treatment arms in the ITT population as well as in the CD30(+) subset
- Secondary Objectives
  - Overall Survival (OS) between the 2 treatment arms
  - Objective Response Rate (ORR) between the 2 treatment arms
  - Complete Response (CR) rate between the 2 treatment arms
  - Duration of Objective Response (DOR) rate between the 2 treatment arms
  - Safety and tolerability of the 2 treatment arms

Key Vendors

- Randomization and Trial Supply Management / RTSM (Suvoda)
- Central Laboratories
  - Pathology - Ventana
  - Biomarker testing
  - PK testing
  - IRIS - ICON
- Central Radiology (BioClinica)
- ePro/eDiary – will be an app for a smartphone or a device will be provided; paper back-up will be made available
- GreenPhire – patient reimbursement as applicable
- Unblinded Operations Team (PRA) – IP accountability