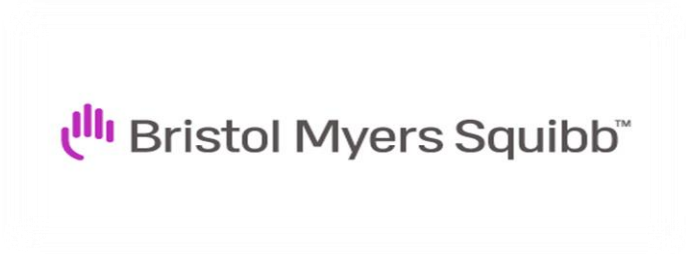


PROTOCOL: CA0731020

A Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Study Comparing the Efficacy and Safety of Golcadomide Plus R-CHOP Chemotherapy vs Placebo Plus R-CHOP Chemotherapy in Participants with Previously Untreated High-risk Large B-cell Lymphoma (GOLSEEK-1)

Compound: Golcadomide (BMS-986369/CC-99282)

Brief Title: A Study to Compare the Efficacy and Safety of Golcadomide Plus R-CHOP vs Placebo Plus R-CHOP in Participants with Previously Untreated High-risk Large B-cell Lymphoma

PHARMACY MANUAL
V-1.0

March 27, 2024

Bristol Myers Squibb
Pharmacy Services
P.O. Box 4000
Princeton, NJ 08543

DOCUMENT HISTORY

Document	Date of Issue	Summary of Change
Manual V 1.0	March 27, 2024	N/A, Version 1

TABLE OF CONTENTS

1 OBJECTIVE

The objective of this Pharmacy Manual is to provide the investigational site with clear and detailed information on the storage, handling, preparation, and administration of clinical product(s) used in the Bristol Myers Squibb CA0731020 protocol.

The information within this Pharmacy Manual is intended to supplement the CA0731020 clinical trial protocol.

2 SPONSOR CONTACTS

If concerns about the quality or appearance of the study drug, or questions regarding product preparation or handling arise, do not dispense the study drug and contact the Sponsor immediately:

General drug supply questions:

Balvinder Dhuck
Trial Supplies Manager
Bristol Myers Squibb
Email: Balvinder.Dhuck@bms.com

Questions regarding drug preparation and pharmacy manual content:

Christiana Thompson, PharmD, RPh
Clinical Research Pharmacist, Pharmacy Services
Bristol Myers Squibb
Email: Christiana.Thompson@bms.com
Alternate Email: pharmacyservices@bms.com

Questions concerning clinical activities and clinical protocol content:

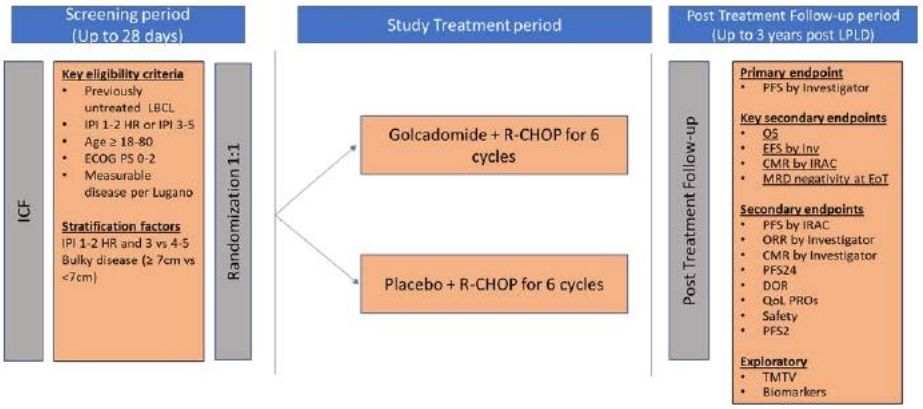
Argyrios Gkasiamis, MD
Clinical Trial Physician – Medical Monitor
Bristol-Myers Squibb Company
Boudry Neuchatel 2017
Switzerland
Phone: +41-32-529-2583
email: Argyrios.Gkasiamis@bms.com

3 STUDY TREATMENT

Study Design:

The study is designed as a randomized, double-blind, placebo-controlled, multicenter, Phase 3 study to compare the efficacy and safety of golcadomide plus R-CHOP vs placebo plus R-CHOP in participants with previously untreated high-risk large B-cell lymphoma. Approximately 850 participants will be randomized at a 1:1 ratio to either golcadomide plus R-CHOP or placebo plus R-CHOP. Randomization will be stratified by IPI score (HR 1-2 and 3 vs 4-5) and bulky disease (≥7 cm vs. < 7 cm).

The study design schema is presented in Clinical Protocol; Figure 5.1-1:



Abbreviations: CMR, complete metabolic response; ECOG, Eastern Cooperative Oncology Group; EOT, end of treatment; DOR, Duration of Response; EFS, Event-free Survival; HR, high risk; ICF, informed consent form; Inv, investigator; IPI, International Prognostic Index; IRAC, Independent Response Adjudication Committee; LBCL, large B-cell lymphoma; MRD, minimal residual disease; ORR, overall response rate; OS, overall survival; PFS, progression free survival; PRO, patient reported outcome; PS. performance status; QoL, quality of life; R-CHOP, rituximab, doxorubicin, vincristine, cyclophosphamide, and prednisone; TMTV, Total Metabolic Tumor Volume.

NOTE: Always refer to the latest version of the CA0731020 Clinical Protocol applicable to your site/region for complete details on treatment and dosing assignments.

3.1 BMS-986369/CC-99282 (GOLCADOMIDE)

3.1.1 *Product Description*

Product Name	BMS-986369/CC-99282 (as the free base) 0.2 mg, 0.3 mg, 0.4 mg capsules *or matching placebo*
Product description and Packaging	Packaging *(all strengths and placebo)*: Each 100 cc round high-density polyethylene (HDPE) bottle with child-resistant closure contains #21 capsules and 1x2g silica gel pouch desiccant Capsule Appearance *(all strengths and placebo)*: Two-piece, white, opaque, size #4 hard capsule filled with white to off-white powder which may contain granules, lumps and plugs
Product Ingredients	Each BMS-986369/CC-99282 capsule contains 0.2 mg, 0.3 mg, or 0.4 mg of BMS-986369 (as the free base), respectively
Storage Conditions	Store 2 to 25°C (36 to 77°F) in tightly closed container (HDPE bottles only), protected from light

3.1.2 *Handling and Dose Preparation*

BMS-986369/CC-99282 and placebo capsules are intended for oral use. All clinical products should be handled in accordance with the product label and as outlined in the Clinical Protocol, investigator's brochure (IB), and the material safety data sheet (MSDS).

BMS-986369/CC-99282 and placebo capsules should be handled according to local institutional guidelines regarding the protective controls (e.g. gloves) required for the preparation, and disposal of investigational products and/or hazardous compounds (if so determined).

Females who are pregnant or are of childbearing potential should not handle or administer BMS-986369/CC-99282 or placebo unless they are wearing gloves. Patients should not extensively handle or open BMS-986369/CC-99282 or placebo capsules and should maintain storage of capsules in the packaging until ingestion.

For further information, please refer to the pregnancy prevention plan for subjects in clinical trials receiving BMS-986369/CC-99282 and placebo capsules, and the MSDS.

Dose Preparation and Administration

Blinding

Study CA0731020 is a double-blind study. BMS-986369/CC-99282 or placebo capsules will be supplied to sites in blinded bottles. No preparation is required for BMS-986369/CC-99282 or placebo capsules.

Capsules of BMS-986369/CC-99282 or placebo will be taken by mouth with or without food. Participants in the Experimental arm will receive 0.4 mg of BMS-986369/CC-99282 once daily for 7 consecutive days for 6 cycles in combination with R-CHOP in 21-day cycles.

A patient diary or instruction card will be provided to the subject for guidance and documentation.

Dose modifications for BMS-986369/CC-99282 and R-CHOP components are permitted in any cycle and should be made stepwise according to Clinical Protocol; Table 7.4-1 unless otherwise agreed to between the investigator and Medical Monitor.

3.1.3 Product Storage and Stability

Store BMS-986369/CC-99282 or placebo capsules 2 to 25°C (36 to 77°F) in tightly closed container (HDPE bottles only), protected from light.

3.2 R-CHOP

3.2.1 Product Description

Product Description/ Class and Dosage Form	**Contents**	**Packaging**
Rituximab Concentrate for Solution for Injection[a b]	500 mg	Each carton contains 1 vial
Rituximab Solution for Injection[a b]	1400 mg	Each carton contains 1 vial
Cyclophosphamide Powder for Solution for Injection[a]	500 mg	Each carton contains 1 vial
Doxorubicin Solution for Injection[a]	50 mg	Each carton contains 1 vial
Vincristine Solution for Injection[a]	1 mg 2 mg	Each carton contains 1 vial
Prednisone tablets[a]	50 mg	Each blister card contains #10 tablets

[a] These products may be obtained by investigational sites as local commercial product in certain countries if allowed by local regulations. In these cases, products may be a different pack size/potency than listed in the table. These products should be prepared/stored/administered in accordance with the package insert or summary of product characteristics (SmPC).
[b] Rituximab biosimilar formulation allowed if permitted by local regulations.

3.2.2 Handling and Dose Preparation

As with all injectable drugs, care should be taken when handling and preparing chemotherapy. Infusions should be prepared using local regulation/guidelines regarding engineering (e.g., a biological safety cabinet, laminar or vertical flow hood) and the administrative controls required for the preparation and administration of hazardous compounds (if so determined), including standard procedures for the safe handling of agents applying aseptic techniques. Gloves are required. If infusion solution comes in contact with the skin or mucosa, immediately wash thoroughly with soap and water. For additional information, please refer to the applicable Safety Data Sheet (SDS), SmPC, or package insert.

Dose Preparation and Administration

Inspect parenteral drug products visually for particulate matter and discoloration prior to administration. Product sourced locally or supplied by BMS (or designee) should be prepared and administered as per the product specific package insert or SmPC. For additional information or with questions on the preparation and handling of products supplied by BMS that are not addressed by the SmPC or package insert please contact Pharmacy Services (pharmacyservices@bms.com).

No preparation is required for prednisone tablets.

3.2.3 Product Storage and Stability

Products should be stored as per the clinical label, package insert or SmPC.

4 SITE TEMPERATURE EXCURSIONS AND TRANSIT

Formulated products (e.g., vials, bottles, kits, etc.) must be stored under the proper conditions as listed on the product label. If any temperature excursions are encountered during on-site storage or during transport, please report these to BMS for assessment. Depending on the type of temperature excursion (on-site or in-transit), use the appropriate form and process for reporting the excursion to BMS, following instructions in the Bristol Myers Squibb, *Job Aid - Investigational Medicinal Product (IMP) Handling at Investigational Sites*.

Proper storage conditions must be maintained during any movements of inventory within an investigational site. Storage conditions must be maintained throughout transport with supporting documentation maintained at the site. Where controlled storage conditions (e.g., temperature, relative humidity, light, etc...) are required during transit, the necessary environmental controls must be in place to ensure that the drug product remains within the acceptable temperature range. Temperature monitoring devices such as min/max device should be implemented during transit.

5 PRODUCT RECEIPT, ACCOUNTABILITY, AND DESTRUCTION

RECEIPT

Shipment Inspection Instructions

1. Open box **immediately** upon receipt.
2. Carefully inspect shipment to ensure all of the supplies were received in good condition, and compare shipment contents to the packing slip, confirm that a correct quantity was delivered, and that all of the listed container ID numbers were received.
3. Sign and date (date of receipt) packing slip and file with study-specific documents.
4. Log all supplies from each shipment in the appropriate Clinical Supplies Inventory Form (provided separately).
5. *The following apply only if an IRT (Interactive Response Technology) system is used*
    a. Log into the IRT system to acknowledge receipt and condition of the supplies.
    b. If receipt of not confirmed in the IRT system, these supplies will *not* be available for dispensing.
    c. For more information, please consult the IRT user manual. For studies which require resupply, the IRT system will automatically coordinate re-supply shipments for all drugs supplied by IRT system to the site.

NOTE: Please maintain the IRT system confirmation emails and other relevant correspondence with your study-specific documents. If you have any issues with not receiving all your IRT system confirmations/emails, then please contact the IRT system helpdesk or your study monitor immediately.

ACCOUNTABILITY

As per the clinical protocol and BMS policy, it is the responsibility of the investigator to ensure that a current disposition record of investigational product accountability and reconciliation is maintained at each investigational site where study drug is inventoried and dispensed.

In addition, records or logs must comply with applicable country/local regulations and guidelines and should include:

- Amount received and placed in storage area
- Amount currently in storage area
- Label ID number or batch number
- Amount dispensed to and returned by subject, including unique subject identifiers
- Amount transferred to another area/site for dispensing or storage
- Non-study disposition (e.g., lost, wasted)
- Amount destroyed at investigational site, if applicable
- Amount returned to the Sponsor, if applicable
- Dates and initials of person responsible for Investigational Product (IP)
- Dispensing/accountability, as per the Site Signature and Delegation Log.

The Sponsor (or designee) can provide forms to facilitate inventory control if the investigational site does not have an established system that meets these requirements.

DESTRUCTION

Study Drug Destruction

Study drugs (those supplied by BMS or sourced by the site/investigator) can be destroyed on site if local policies allow it. It is the Investigator's responsibility to ensure that arrangements have been made for the disposal and that procedures for proper disposal have been established according to applicable regulations, guidelines, and institutional procedures. Appropriate documentation of the disposal must be maintained by the investigational site. **Unused investigational product may be destroyed only following BMS (or designee) inspection, reconciliation, and approval by the responsible Study Monitor (or designee)**.

If required by local country/hospital regulations, drug can be returned to an off-site drug destruction vendor but should only be completed with your Study Monitor (or designee) while they are on site. All drug destruction whether performed on or off site should be documented using the Investigational Product Return Form or local form if approved by Study Monitor (or designee).

Product Quality

Issues that call into question IMP safety, purity, potency, quality and identity (e.g., evidence of suspected tampering of product) must be reported as soon as possible to your study Clinical Trial Monitor and/or Clinical Trial Manager or designee. Report an issue or concern with all BMS supplied IMP and non-IMP suspected to have occurred before the product was transferred to the responsibility of the clinical site (e.g., during manufacturing, packaging and labeling, storage, and/or distribution). For detailed reporting instructions, please refer to the Bristol Myers Squibb, *Job Aid - Investigational Medicinal Product (IMP) Handling at Investigational Sites*.

This includes suspected quality issues for IMP device/drug combination products, and medical devices released for clinical use in Clinical Trials and comparator/marketed product used as an IMP in a clinical study sourced by BMS or vendor.

In the event of a suspected product quality issue, the immediate action to be taken by site is to quarantine the affected product. Do not dispose of the product unless retention presents a risk to personnel (e.g., cytotoxic, risk of injury from broken glass or sharps).

6 IRT AND DATA COLLECTION

For studies utilizing an IRT system, study drug will be assigned to participants via the IRT system. Separate training materials will be sent to each site with regard to IRT usage. All changes, manual drug assignments, and product dispositions must be documented within the IRT system as outlined in the separately provided IRT Site User Manual.

For all studies, site personnel will have the overall responsibility of coordinating the collection of data, completing the electronic Case Report Form (eCRF) and dosing log, and for ensuring

that adequate and accurate participant records are available for all procedures for each participant, as required by the clinical team.

The data reported in the eCRF must be in agreement with the information in the participant's source documents (i.e., medical records).

If required, source documents must provide documentation of all data points in eCRF, to include but not limited to: drug preparation details, date/time of study drug administration, dose of study drug delivered, site of administration, date and location of assessment.