Monitoring Plan Version	2.1	Monitoring Plan Date	20 Oct 2025
Program	Zejula 1L RWE	Investigational Product	Niraparib
Study Number	Niraparib-4002	Protocol Version and Date	Version 2.0 dated 26 Oct 2024
Study Abbreviated Title	An observational study of Niraparib maintenance for 1L ovarian cancer treatment in Taiwan		

Monitoring Plan (ICH-GCP E6 (R2)) – A description of the methods, responsibilities and requirements for monitoring the trial.

This guide serves to provide the basic elements and their expectations of a monitoring plan that should be considered.

The Monitoring Plan should be developed considering that will be tailored to the specific human subject protection and data integrity risks of the trial. The plan should describe the monitoring strategy, the monitoring responsibilities of all parts involved, the various monitoring methods to be used and the rationale for their use. The plan should emphasize the monitoring critical processes. Trial specific elements should also be included if necessary, for plan to be changed, all changes must be documented in a new version.

Particular attention should be given to those aspects that are not routine clinical practice and that require additional training.

The monitoring plan should reference the applicable policies and procedures. The level of monitoring required for the study is risk based and takes into account the risk assessment.

Terminology

Central Monitoring: A remote evaluation carried out by sponsor personnel or representatives (e.g., Data Manager, Statistician, or Monitor).

Off-site Monitoring: Monitoring activities as defined **either within process documents or in the monitoring plan (MP)** that occur away from the study site location (e.g., at a Monitor's home or in a sponsor representative's office). This is also commonly known as **remote monitoring**. It should be done throughout systems available for the study (e.g.: EDC, eTMF, IRT, etc.).

On-site Monitoring: An **in-person evaluation** carried out by sponsor personnel or representative(s) at the site(s) at which the clinical investigation is being conducted.

Source Document Verification (SDV) (Accuracy): Commonly known as **'transcription checking'**, the process by which data within the CRF or other data collection systems are compared to the original source of information (and vice versa) to confirm that the data were transcribed accurately (i.e. data from source matches data in the CRF or other system and vice versa). It should be done on-site.

SDR (Quality): Review of source documentation to check **quality of source**, review **protocol compliance, ensure the Critical Processes and source documentation** (e.g. accurate, legible, contemporaneous, original, attributable) are adequate, to ascertain Investigator involvement and appropriate delegation, and assess compliance to other areas (e.g. SOPs, ICH GCPs). SDR is not a comparison of source data against CRF data. It should be done on-site.

Use the following key to update the template.

Color	Instruction
Black text	Standard language. Do not remove or alter.
Blue text	Portions of the template are instructional and should be removed before finalizing the document.

1. Scope

Objective	**Primary objectives:** To observe effectiveness of Niraparib maintenance therapy in patient with ovarian cancer after frontline chemotherapy **Secondary objectives:** To observe safety of Niraparib maintenance therapy in patient with ovarian cancer after frontline chemotherapy **Exploratory objectives:** To summarize the treatment patterns, including subsequent treatments and their initiating timepoint after Niraparib discontinuation. To explore the factors related to survival benefit of Niraparib maintenance therapy in real-world clinical practice.
Study Title	An Observational Study to Investigate The Effectiveness and Safety of Niraparib Maintenance Therapy after Frontline Chemotherapy for Taiwanese Patients with Advanced Ovarian Cancer
Phase	Observation **Study Number** Niraparib-4002
Applicability	The monitoring plan applies to all Clinny Biotech Limited employees who involve in site management of this study.
SOP Applicability List	

	Sponsor SOP and Form	ClinnyBio SOP and Form
Initiation	FORM-0002201 Site Visit Log	SOP-004 Site Initiation Visit SOP-004-F01 Site Initiation Visit Agenda

			SOP-004-F02 Confirmation Letter for Site Initiation Visit SOP-004-F03 Site Staff Delegation of Activity SOP-004-F04 Site Staff - Project Training Log SOP-004-F05 Site Initiation Visit Report SOP-004-F06 Follow up Letter for Site Initiation Visit
		Monitoring	FORM-0026792 Trial Master File Plan FORM-0033005 Monitoring Plan – Basic Requirements TOOL-0001336 Trial Master File Index	SOP-005 Investigational Site Management SOP-010 IRB/HA Submission SOP-003-F11 Investigator Site File Index SOP-005-F01 Site Visit Report and Issue Guidance SOP-005-F03 Confirmation Letter for Monitoring Visit SOP-005-F04 Site Level Informed Consent Version Tracker SOP-005-F05 Subject Level Informed Consent Review and Tracking Tool SOP-005-F11 Subject Screening and Enrolment Log SOP-005-F13 Subject Identification Log SOP-005-F14 Follow-up Letter for Monitoring Visit SOP-005-F15 Monitoring Visit Report

	Termination	NAP	SOP-007 Termination Visit SOP-007-F01 Site Termination Visit Confirmation Letter SOP-007-F04 Site Termination Report Template SOP-007-F05 Site Termination Visit Follow Up Letter
	General	FORM-0002613 Core ICF Template Takeda Global Base Non-Interventional (Observational) Study Agreement v. 1June2021	POL 001 Anti-Bribery Policy SOP-011 Quality Issue Management
	Data Management	FORM-0002512 Statistical Analysis Plan Template	SOP-013 Clinical Trial Data Management SOP 014 Biostatistics Procedures SOP-013-F01_Data Management Plan Template_08 Jan 2019 SOP-013-F05 User Acceptance Testing Finding Form SOP-013-F06 User Acceptance Testing Approval Form SOP-013-F11 Database Lock Approval Form SOP-013-F12 Database Unlock Approval Form

2. Clinical Operations Representative (COR) Assignment – The monitoring activities may be done by COR or designee. The study team manager should select a COR (CRA) or designee. However, it is essential to evaluate the professional minimum requirements as the following:

Minimum Requirements	**Monitors experience must be commensurate with the level of the study**	The COR (CRA) should be bachelor's degree or above in science/medical field.
	Proficiency in local language	Traditional Chinese
	Knowledge about local regulations	COR (CRA) should have GCP training certificate more than 1 hour within 1 year.
Has a study back up been established?		One project manager and 2 CORs (CRAs) will be assigned from ClinnyBio to this study. CORs (CRAs) can be back up each other and the project manager can also be the deputy if COR (CRA) absent.
Has the Takeda COPM received and reviewed the assigned candidate CV?		Takeda Study's COPM receive and review the CV of the Clinical Operations Representative assigned to the study.

3. Communication Plan - Communication responsibilities, methods, and cadence must be described in the monitoring plan in clear way and considering the different stakeholders. The study contact list must be a stand-alone document which must be up-to-date every change and must be kept in order to guarantee the traceability of personnel involved throughout the study.

3.1 Takeda and Monitoring Vendor Communication:	In this Zejula 1L RWE, ClinnyBio representatives are the primary contact for site staff and vendor about related activities. Takeda representatives could be involved when consultation needs, issue escalation and/or as sponsor representative for external contacts. For the resolution of technical questions, study team member should communicate with the ClinnyBio CRM and Takeda RWE Evidence Scientist in relevant communications. In cases when a Takeda non-core team member needs to communicate with ClinnyBio (e.g. information exchange, request for change in process, request for additional work, etc.) an email to the ClinnyBio representative should be sent.

	ClinnyBio will provide study status update regularly and meet with Takeda when required. The meeting minutes will be taken by ClinnyBio and sent to Takeda for review and comment. The representatives from each party should forward the meeting information and final meeting minutes to responsible study team members. The meeting minutes will also be filed in TMF for documentation.
3.2 Site Communications	Sites will be managed by assigned ClinnyBio study team members who will be ultimately responsible for the site communication and issue escalation. ClinnyBio CORs (CRAs) will contact site staff bi-weekly at least during IRB submission and recruitment period. During the study follow-up period, the contact will be performed monthly at least.
3.3 Other Communications	Generally, in email communication, team members who are responsible for actions should be in the "to" line, team members who receive the email for information should be added to the cc line. All relevant communications (only if the content is not documented in any other manner) is to be filed in Trial Master File. Relevant communications are generally defined as: Communications that are directly related to the study protocol (e.g. subject eligibility, visit procedures, Adverse Events/Serious Adverse Events), important operational issues (e.g. staff changes), and to the overall conduct of the clinical trial to meet local regulatory and ICH requirements. This should exclude communications related to draft documents, financial matters and exchanges of pleasantries. For emails, the most recent version of the email including all discussion threads should be provided. Previous versions are not required. If an email introduces a topic or begins to address an issue, the remainder of the discussion (i.e. considerations, decisions, actions, and outcomes) should be included in the study master file. Preferably issues are addressed in meeting actions/minutes and study FAQ log even if the introduction was via phone or email. Proper meeting minutes help ensure issues are followed to their conclusion. In case that Takeda internal communication is relevant for filing in study master file, the initiator of the correspondence is responsible for filing. Face-to-face or telephone conversations will be summarized and documented. The ClinnyBio study team member involved in the conversation will be responsible for preparing the contact report and filed in trial master file.

		Verbal agreements between Takeda and ClinnyBio will be documented in an e-mail or meeting minutes. Pertinent communications between ClinnyBio and investigative sites will be documented in e-mail, contact report and/or meeting minutes and filed in trial master file accordingly. All personnel involved in a verbal exchange must receive a copy of the e-mail, documenting the conversation.
4. Patient Recruitment and Monitoring Activities: The monitoring plan must establish the foreseen recruitment targets, as described in item 4.1, in order to the COR to be aware.		
4.1 Initial Planned Dates, Recruitment and Site Initiation Objectives	**Number of countries planned to conduct the study**	1
	Enrollment period duration	Jan 2024 to Dec 2024
	First subject screened	Jan 2024
	First subject enrolled	Jan 2024
	Last subject enrolled	Dec 2024 (actual 08 Mar 2025)
	Last subject completed	Jun 2028 (updated to Sep 2028)
	Data base lock	Sep 2028 (updated to Dec 2028)
	Site Activation	Dec 2023
	Site Closure and Site Replace Process	Oct 2028 (updated to Jan 2029)
4.2 Subject Recruitment	Total 35-50 subjects will be enrolled from 5 to 7 study sites. It is estimated to enroll 7 subjects per site.	
4.3 Site Monitoring Procedures		
4.3.1 Site Qualification Visit	NAP	
4.3.2 Site Staff Training	Site staff training will be documented in SOP-004-F04 Site Staff - Project Training Log with training topics and training date. The GCP training certificate and CVs will be collected as qualification documents. Medical license should be obtained if medical license number is not listed in investigator's CV.	

4.3.3 Site Initiation Visit	Site Initiation must be according to SOP-004 Site Initiation Visit. - ClinnyBio will conduct the Site Initiation Visit once the regulatory documents are in place. - COR (CRA) will ensure all applicable ethics approvals and supplies are available at the study sites on or before SIV date. - In addition to the activities described in the applicable SOP and in the project specific 'SVR and Issue Guidance Document' (SOP-005-F01), project specific requirements for the conduct of the initiation visit/calls include (but not limited to): ▪ Study Protocol Training ▪ Specific forms related to EDC (e.g. EDC specific training checklist, User Account forms and access) ▪ Review of eCRF Completion Guideline ▪ ICF collection and SDV process ▪ SAE reporting process ▪ GCP Guidelines ▪ Recruitment plan and potential subject number ▪ Ensure the Site Visit Log is signed and dated by all site staff present during the visit. ▪ Review IRB initial approval and subsequent approval ▪ Ensure the Site Staff Delegation Log completed during the visit. - The COR (CRA) who completes the initiation visit will issue a follow-up letter via e-amil to the site staff within approximately 10 working days after the day of the visit, summarizing items reviewed, issues identified/pending resolution, and addressing any question(s) left outstanding at the visit. A copy of the email should be filed in Trial Master File.	
4.3.4 Defining the Monitoring The plan should describe the monitoring strategy, the monitoring responsibilities	**On-site and off-site Data Monitoring**	On-site Data Monitoring: The signed ICF, medical record and paper worksheet used at study sites will be reviewed during on-site data monitoring. Off-site Data Monitoring: It is not applicable for this study.

	of all the parties involved (e.g.: medical monitoring, data management, clinical supplies, IRT, etc.), the various monitoring methods (central, off-site, and on-site monitoring activities) to be used and their rationale for their use. The rationale for the chosen monitoring strategy should also be described (ICH GCP E6). The plan must also emphasize the monitoring of critical data and processes specific for the study with the intention to reduce risk per ICH GCP E6.	**Blinding and Unblinding Monitoring Process**	NAP
		Critical Data	The critical data of this study include: 1. Informed Consent 2. Key Eligibility Criteria • Diagnosis of ovarian cancer • Response to frontline platinum-based chemotherapy 3. Primary Objective • Effectiveness measured by overall response rate, progression free survival, chemotherapy-free interval, and time to treatment discontinuation. o Niraparib treatment period o Ovarian related treatment other than Niraparib. o Regular tumor assessment o Survival status 4. Secondary Objective • Safety Profile: o All Adver Events (AEs) and Serious Adverse Events (SAEs) o Adverse Drug Reactions (ADRs) o Special Situation reports (SSRs) o AE leading to treatment discontinuation or death. o
		Critical Processes	The critical processes for corresponding data are listed below: 1. Informed Consent:

			• Informed Consent Collection
			  ○ Check date and signature.
			  ○ Ensure patient has been consented under the correct ICF version – compare dates of IRB approved ICF versions against date informed consent signed.
			• Documentation of the date and reason for patient withdrawal of consent to be on the study.
			2. Key Eligibility Criteria
			• Review and verify key inclusion/exclusion criteria including primary diagnose of ovarian cancer and first-line chemotherapy treatment history.
			3. Primary Objective
			• Review and verify ovarian cancer related treatment from index date, during Niraparib treatment, end/discontinuation of treatment and end of study observation period.
			• Review and verify tumor assessment performed from index date to end of study observation period.
			4. Secondary Objective
			• Review and verify Niraparib related safety event from index date to the day prior to enrollment. During the study period, all AEs will be reviewed and verified until the end of safety observation period.
			• Review and verify AEs leading to treatment discontinuation or death
			• Event reporting according to the protocol and local requirements.
			• COR (CRA) and site training – collection, review, assessment and reporting of safety events (i.e. severity, grade, causality) according to the protocol and local requirements.

		Risk Indicators and Thresholds	Risk Indicators and Thresholds which should be considered are (but not limited to): o Potential quality concerns o Number of subjects enrolled o Numerous outstanding action items o Major changes in site staff o Numerous changes to CORs (CRAs) assigned to site o Audit findings not resolved in a timely manner. o Volume of protocol deviations o Backlog of e-Case Report Form
	4.3.4.1 First Monitoring Visit	The first on site monitoring visit will take place within approximately two (2) week after the first subject enrolled in the trial.	
		The following data of the first subject will get 100% SDV during the first monitoring visit. - Informed consent document and consenting process: o current and approved version by the IRB/IEC o obtained for the enrolled subjects in the trial o completed, signed and dated appropriately o documented in source document as obtained prior to enrollment and a copy given to subject - verify that subject meets inclusion/exclusion criteria - confirm the reason and date for patient withdrawal of consent is documented, if applicable. - review and verify safety events occurred from index date.	
	4.3.4.2 Interim Monitoring	The on-site monitoring visits will be performed every 4 to 5 months during recruitment period and every 6 to 8 months during follow-up period. It is estimated to conducted up to 45 visits for this study. The schedule of on-site monitoring visits can be adjusted to actual need and discussed and approved by	

		Takeda. The documentation of visit schedule change is expected in visit report if visit not occurred within above frequency and schedule. The maximum time between on-site visits should not exceed 12 months. **Sites will not be visited if no subjects have been enrolled and/or no new subject visit occurred.**	
		Quality Issues/Safety reporting issues, if applicable	A co-monitoring visit will be performed by ClinnyBio CRM and/or Takeda COPM with each COR (CRA) for the first two site initiation visits at least, and for regular monitoring visits every 3-4 on-site visits. If the visit is for interim analysis database lock, ClinnyBio CRM and/or Takeda COPM will also perform the co-monitoring with COR (CRA) to make sure the data status.
		Clinical Operations Presentative Activities	CORs (CRAs) will perform 50% source document verification (SDV) of all data points for all subjects via on-site monitoring. Where ClinnyBio is contracted to perform on-site monitoring of subject data, 100% SDV of the following points is required for all enrolled subjects: - All informed consent documents for the following: o current and approved versions by the IRB/IEC o obtained for each subject enrolled in the trial o completed, signed and dated appropriately o documented in source document as obtained prior to enrollment and a copy given to subject - verify that subject meets inclusion/exclusion criteria - confirm the reason and date for patient withdrawal of consent is documented. - confirm the reason and date for patient withdrawal of consent is documented.- review and verify all safety events including, ADRs/AEs/SAEs/SSRs through the study according to study requirement.

			The rule for 50% SDV should include 100% SDV for critical data listed above and select other new subject visits occurred since last monitoring visit to achieve total 50% SDV rate. The amount of SDV performed for each subject must be clearly stated on the monitoring visit report. Data queries related to Data Points requiring SDV, are also subject to the same level of SDV. Include information here on the SDV strategy for queries raised after the last scheduled monitoring visit to site. Suggested strategies include: - No SDV of queries raised after the last MV to site - Additional MVs required to perform SDV of queries
		Back-log Issues	The study data will be collected every 3 to 6 months according to protocol defined data collection period. All the data have to be updated within 5 working days of the visit date and the safety events should be entered in eCRF when awareness. If the data entry back-log achieving 30% of the study site, an e-mail will be sent to PI and SC and copy Takeda as reminding. If the data entry back-log achieving 50%, an on-site visit will be triggered under Takeda's approval.
		Study Supplies	NAP
		Biological Sample Management	NAP

		Frequency ISF is checked	The ISF will be reviewed every 2 monitoring visits at least to ensure the completeness and current. Pending activities will be documented in SVR and Follow-Up Letter.
		Reconciliation of ISF and eTMF	All site-specific documents will be forwarded to the Trial Master File. A final review and reconciliation should be performed during the Termination Visit.
		All screened and enrolled subjects will be documented on the Subject Screening & Enrollment Log. The forms will be checked by the COR (CRA) during on-site visits or remotely. The Subject Identification log can only be reviewed and checked during on-site visits to avoid any personal data disclosed.	
	4.3.4.3 Centralized Monitoring (if applicable)	**Document rational in the event centralized monitoring would be adopted for the study. Activities developed must be specific in the monitoring plan to include the following:**	
		How will it be carried out:	NAP
		How will it be reviewed:	NAP
		By whom:	NAP
		How will it be reported:	NAP
		How will it be followed up:	NAP
	4.3.4.4 Off-site Monitoring (Remote Monitoring)	Off-site monitoring is not applicable for this study.	
	4.3.4.5 Close-Out Visit	The site must be closed according to Termination Visit procedure (SOP-007 Termination Visit).	

<table>
<tr><td></td><td>4.3.5 Monitoring Visit Report (MVR) and Communication</td><td colspan="2">COR (CRA) should submit the Draft Monitoring Visit Report (MVR) within 5 working days after last day of the visit. ClinnyBio CRM will approach CRAs to obtain PDF versions of the MVR. All MVRs will be 100% reviewed by CRM and CRM will provide the feedback to COR (CRA) via PDF version. Finalization of MVR should be within 10 working days after last day of visit with electronically signature by both COR (CRA) and CRM and the final signed report will be filed in TMF accordingly.
Send Final MVR to Takeda: MVRs will be provided to Takeda at the completion of all the study activities.

COR (CRA) should send a follow-up letter to the PI/ site staff using the template provided. The follow-up letter will outline any outstanding issues and corresponding actions. The letter can be written in the site's local language and an e-mail or a signed copy should be uploaded into Trial Master Files. The follow-up letter will be sent to the sites no later than 10 working days, as soon as the report of the previous visit is finalized. If significant issues are identified during the visit, the follow up letter should be sent to site within maximum 5 working days. Preferable, the follow-up letter must not have cumulative information in order to avoid misunderstanding of the PI / site staff. The outstanding data, action to be taken and resolutions provided must be highlighted and must be issued to the site staff in a timely manner</td></tr>
<tr><td></td><td></td><td>Results</td><td>Upon review of the eCRF data, the COR (CRA) document the reviewed visit and eCRF pages in monitoring visit reports.</td></tr>
<tr><td></td><td></td><td>Tracking</td><td>All on-site visits will be tracked on the excel sheet with visit date to show the monitoring compliance.</td></tr>
<tr><td></td><td></td><td>Reporting</td><td>Any MVR and communication process deviated from the monitoring plan will be tracked. The compliance rate should achieve 90% of the study. Any major discrepancies occurred will be reported to Takeda for CAPA discussion within 5 working days.</td></tr>
<tr><td colspan="4">5. Issue Management: The requirements for management of clinical study protocol deviations should follow SOP-011 Quality Issue Management.</td></tr>
<tr><td></td><td colspan="3">For all unresolved actions during site visits, significant findings and protocol deviations will be issued and documented in "Issue Tracking Log"</td></tr>
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	Protocol Deviations (PDs) will be identified by CORs (CRAs) during routine monitoring visits during data review. PDs will be tracked in Issue Tracking log using the following Categories: Protocol Deviation: AE/SAE Protocol Deviation: In/Excl Criteria Protocol Deviation: Informed Consent Protocol Deviation: Visit Schedule Protocol Deviation: Others Follow-up Protocol Deviation Apply the following rules when entering Protocol Deviation in Issue Tracking Log: - Break down information for more than one subject by duplicating the entries per subject (if necessary for each subject) - Raise one Issue per Protocol Deviation - Don't use line breaks - Don't use special characters e.g., *, #
6. Adverse Event (AE), Serious Adverse Event (SAE) and Pregnancy Reporting	
Provide details for how COR will review and follow-up regarding SAE and Pregnancy Reporting	Refer to the project specific SAE procedure, the responsible COR (CRA) will ensure that the investigators and site staff understand the requirement to report all AEs/SAEs/SSRs/Pregnancies and report the safety events within timeline. - All fatal or life-threatening SAEs should be reported to Takeda within 1 working day of becoming aware. Other SAEs should be reported to Takeda within 4 calendar days of becoming aware. - All AEs should be reported to Takeda within 7 calendar days of becoming aware. - Requested additional information from Takeda should follow the same reporting timeline as above. CRFs, source documents, and other subject data must be regularly reviewed to check for unreported safety events during scheduled on-site monitoring visits.

		Safety information must be reported on the appropriate form in eCRF and must be consistent with the information available on subject's medical records. Any updated AE reports has to be sent to Takeda within defined timeline, the same as the initial report.
7. Interactive Response Technology IRT) – Provide additional details regarding the following items:		
	System	NAP
	Point of Contact for System Issues	NAP
8. Clinical Trial Material (CTM) - Procedures regarding CTM must be in accordance with the Pharmacy Manual.		
	NAP	
9. Shipment, Ordering, and Inventory of Clinical Supplies at the Site		
	NAP	
10. Investigator Site Files (ISF) – Provide details related to the following items:		
	Investigator Site File Content	The ISF structure will follow SOP-003-F11 Investigator Site File Index.
	Set Up	The ISF with regulatory documents will be provided before or on Site Initiation Visit to site staff by COR (CRA). The wet-ink documents will be filed in ISF or sent to Takeda according to Master TMF plan of this study.
	Maintenance	The ISF should be reviewed regularly according to section 4 of this Monitoring Plan to ensure it is completeness and current. A final review and reconciliation should be performed during the Termination Visit. All site-specific regulatory documents will be forwarded and filed in the trial master file defined in Master TMF Plan.

	Archival	All the study documents will be securely stored and archived after 10 years of study completion. All the wet-ink documents with subject personal information will be filed at study site and/or qualified archiving vendor only and other documents will be filed in both ISF and TMF.

GENERAL COMMENTS

CLINICAL OPERATIONS REPRESENTATIVE APPROVAL

PRINTED NAME	TITLE	SIGNATURE	DATE
LORIS WU	STUDY LEAD		~~Jan 21, 2026~~ Jan 21, 2026
MINNA CHEN	SENIOR REAL WORLD EVIDENCE SCIENTIST	Minna Chen.	Jan 21 2026.