PreVent-ACaLL

Pharmacy Manual

Version 4.0

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Contact information – sponsor

Trial email: chip-prevent.rigshospitalet@regionh.dk
Tel: +45 35 45 57 69

Sponsor's pharmacy email: kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk
Tel: +45 44 57 77 85

Study drug description

Acalabrutinib (ACP-196) and Venetoclax (ABT-199).

Study drugs	Quantity per blister card / bottle	Quantity of blister card / bottle needed for full treatment per participant
Venetoclax (Venclyxto) 10 mg in blister card	16 tablets	1
Venetoclax (Venclyxto) 50 mg in blister card	8 tablets	1
Venetoclax (Venclyxto) 100 mg in blister card	8 tablets	3
Venetoclax (Venclyxto) 100 mg in bottle	120 tablets	2
Acalabrutinib 100 mg in bottle	30 capsules	6

Acalabrutinib must be stored between 15°C and 30°C. Venetoclax must be stored between 2°C and 25°C. For detailed description of study drugs incl. dispensation per participant, please see theprotocol.

Study drug Administration

Agent	Dose/day	Route of administration	Cycle	Days
Acalabrutinib	200 mg	Orally	1	1-28
	200 mg	Orally	3	1-28
	200 mg	Orally	3	1-28

Agent	Dose/day	Route of administration	Cycle	Days
Venetoclax	20 mg	Orally	1	1-7
	50 mg	Orally	1	8-14
	100 mg	Orally	1	15-21
	200 mg	Orally	1	22-28
	400 mg	Orally	2	1-28
	400 mg	Orally	3	1-28

Ordering and delivery of study drugs

The study drugs should be ordered when a patient is screened as high risk/high confidence by the CLL-TIM algorithm. All needed study drugs for all three cycles (C1-C3) will be shipped at once, depending on the product's expiration date. The study drugs will be shipped in a temperature-controlled shipper.

The study drugs are delivered to all the sites pre-labeled with study specific labels.

DENMARK

Sites order study drugs by filling out a Drug Order Form (Appendix 1) which must be send to sponsor: chip-prevent.rigshospitalet@regionh.dk and sponsor's pharmacy: kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk. The study drugs must be ordered no later than two weeks before expected delivery and will be delivered directly from sponsor's pharmacy (Region H Pharmacy) to the sites.

HOLLAND

Sites order study drugs by filling out a Drug Order Form (Appendix 2), which must be send to sponsor: chip-prevent.rigshospitalet@regionh.dk and sponsor's pharmacy: kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk. The study drugs must be ordered no later than three weeks before expected delivery and will be delivered directly from sponsor's pharmacy (Region H Pharmacy) to the sites. The site's local pharmacy will distribute the study drugs to the study staff when needed.

SWEDEN

Sites must order study drugs by sending order form to Oriola Sweden AB. For more specific instructions, please contact the national coordinator in Sweden. The study drugs will be delivered by Oriola Sweden AB.

Receipt of study drugs

When the site and/or pharmacy receives the study drugs, following must be done by the recipient immediately upon receipt:

- Check correct number of packages, as notified and stated in the shipment papers are received.
- If a temperature logger is included in the shipment: Check that no temperature deviations have occurred during shipment. Documentation from temperature logger must be sent to sponsor after delivery.
- Check that all seals on the individual packages are un-broken and no other damages are visible.
- Move the trial product to the recommended temperature storage conditions immediately upon receipt.
- Sign for the receipt of the study drugs on the Order and Acknowledgement Form included in the shipment.

  Please document receipt of the shipment by scanning the signed Acknowledgement Form and send it by email to:

For sites in Denmark and Holland

Kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk
and chip-prevent.rigshospitalet@regionh.dk

For sites in Sweden

chip-prevent.rigshospitalet@regionh.dk

In case of any discrepancies in the shipment, following must be done:

Complete the following document:

- ***Delivery Deviation Report Form*** (Appendix 3)

Scan the document and send it by e-mail to:

For sites in Denmark and Holland

Kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk
and chip-prevent.rigshospitalet@regionh.dk

For sites in Sweden

chip-prevent.rigshospitalet@regionh.dk

- Do not dispense any effected study drugs to subjects until further instruction
- Mark the study drugs and store under the specified storage conditions according to label-claim and with temperature monitoring
- Wait for conclusion from sponsor

The study drugs must be stored under secure conditions, i.e. without unauthorized access to the storage facilities.

The study drugs must be handled as described in the protocol.

Study drug accountability

The site and/or pharmacy must maintain accurate drug accountability documentation. This includes:

- Maintaining records of study drug received, dispensed, returned, quarantined and destroyed.
- Ensuring physical inventory agrees with accountability records.

Accountability records may be independently reviewed during on-site monitoring visits.

It is recommended to use the study specific forms "Inventory Logs – Trial medication" (Appendix 4) and "Drug Accountability Form – per subject" (Appendix 5) for any accountability purpose. Please contact your national coordinator or the sponsor to purchase these logs. Remember to save these in the investigator site file.

Storage of study drugs

Acalabrutinib must be stored between 15°C and 30°C. Venetoclax must be stored between 2°C and 25°C.

Any area or storage unit storing study drug must be equipped with an electronic monitoring system that:

- Continuously monitors the temperature.
- Electronically records the temperature at set intervals throughout the day. It is recommended the temperature is electronically monitored at least every 60 minutes.

It is ***strongly recommended*** that the temperature monitoring systems are equipped with automated alerts that immediately notify pharmacy personnel of a temperature excursion.

If a temperature monitoring system does not have an electronic alarm that immediately sends an alert of a temperature excursion, the site must have a written plan in place to:

- Every morning - review the electronic temperature log from the previous night. If this is not possible:
  - The electronic temperature log from the previous night must be reviewed at the start of each day.
  - The goal is to minimize the amount of time study drug is out of temperature if an excursion should occur and for the pharmacy to be resupplied as soon as possible if needed.
  - Delays in identifying a temperature excursion increase the chance of study drug being unusable and increase the length of time site(s) may be required to temporarily close to randomization due to lack of available study drug.
- Follow your institutional procedures for investigational study drug to document date/time temperature logs reviewed, including the person who reviewed the temperature logs and the time period the temperature was reviewed. For this, the PreVent-ACaLL document 'Temperature Log for study drugs' can be used (Appendix 6).

Reporting of temperature deviation to sponsor

If a temperature excursion occurs, immediately quarantine the affected study drug and report the incident to sponsor by writing to chip-prevent.rigshospitalet@regionh.dk with inclusion of the temperature monitoring report. Sponsor will then let you know how to proceed.

Reporting unexpected changes to study drug inventory

All changes to the pharmacy's inventory of Acalabrutinib or Venetoclax*, for reasons other than randomization or resupply*, **must** be reported to sponsor and updated on accountability log as soon as possible.

Destruction of study drugs

Please contact sponsor for green light before any destruction of study drugs takes place. If green light from sponsor has been given, the study drugs should be destructed by following your institutional procedures for study drug destruction. A destruction log can be found in Appendix 7. Remember also to update the accountability log.

Trial documents

All trial documents (including those shown in the Appendix can be retrieved from sponsor by writing to the trial email: chip-prevent.rigshospitalet@regionh.dk.

Appendix

Appendix 1: Drug Order Form – sites in Denmark

Rigshospitalet HOVON

Ordering of study drugs for the PreVent-ACaLL Trial

The study drugs must be ordered no later than 2 weeks before expected delivery

Delivery address:

Contact information on the person placing the order:

Name:
Email:
Tel:

Delivery date: DD-MMM-YYYY

Item	Study drug	Packages/bottles available	Quantity needed per patient (full treatment)	Quantity request	Lot ID *Region H pharmacy*	Exp. date *Region H pharmacy*
1	Venetoclax	10 mg x 16 tabl.	1			
2	Venetoclax	50 mg x 8 tabl.	1			
3	Venetoclax	100 mg x 8 tabl.	3			
4	Venetoclax	100 mg x 120 Tabl.	2			
5	Acalabrutinib	100 mg x 30 Capsules	6			

Name / Signature Date *(DD-MMM-YYYY)*

Please forward the order to: kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk and chip-prevent.rigshospitalet@regionh.dk

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For Pharmacy – acknowledgement of receipt:

Name / Signature Date *(DD-MMM-YYYY)*

Please return order confirmation to: chip-prevent.rigshospitalet@regionh.dk and email on the person placing order (see contact information above).

Apoteket

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Appendix 2: Drug Order Form – sites in Holland

Rigshospitalet HOVON

Ordering of study drugs for the PreVent-ACaLL Trial

The study drugs must be ordered no later than 3 weeks before expected delivery

Delivery address:

Contact information on the person placing the order:

Name:
Email:
Tel:

Delivery date: DD-MMM-YYYY

Item	Study drug	Packages/bottles available	Quantity needed per patient (full treatment)	Quantity request	Lot ID *Region H pharmacy*	Exp. date *Region H pharmacy*
1	Venetoclax	10 mg x 16 tabl.	1			
2	Venetoclax	50 mg x 8 tabl.	1			
3	Venetoclax	100 mg x 8 tabl.	3			
4	Venetoclax	100 mg x 120 Tabl.	2			
5	Acalabrutinib	100 mg x 30 Capsules	6			

Name / Signature Date *(DD-MMM-YYYY)*

Please forward the order to: kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk and chip-prevent.rigshospitalet@regionh.dk

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For Pharmacy – acknowledgement of receipt:

Name / Signature Date *(DD-MMM-YYYY)*

Please return order confirmation to: chip-prevent.rigshospitalet@regionh.dk and email on the person placing order (see contact information above).

REGION Apoteket

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Appendix 3: Delivery Deviation Report Form

REPORT INFORMATION		
Start date of the deviation form:		
Site number:		
Address:		
TRIAL PRODUCT INFORMATION		
Product name:		
Batch number:		
Number of packs:		
Ensure affected IMP are stored separately from other IMP:	**Yes** ☐	**No** ☐
DESCRIPTION OF THE DEVIATION		
Wrong delivery of product:	**Yes** ☐ If yes, please specify below	**No** ☐
Tamper seals intact:	**Yes** ☐	**No** ☐
Visible damages:	**Yes** ☐ If yes, please specify below	**No** ☐
REPORTER		
Name (Capital letters)	Signature	Date

Scan and email to:
kliniskeforsoeg.region-hovedstadens-apotek@regionh.dk and chip-prevent.rigshospitalet@regionh.dk

CONCLUSION OF THE DEVIATION		
New delivery of affected to be sent:	**Yes** ☐	**No** ☐
End date of deviation:		
Expected delivery date:		
Name (Capital letters)	Signature	Date

Return to site email and chip-prevent.rigshospitalet@regionh.dk

CONCLUSION RECEIVED AT SITE		
Name (Capital letters)	Signature	Date

PreVent-ACaLL

Inventory Log - Trial Medication - Delivery same batch number

ISF/TMF section: 10.1

Site number: **Hospital:** **Principal Investigator:**

Trial Medication: *(name/strength/number)*	**Venetoclax 10 mg - 16 tablets in each package**	
Batch number:	***Date of expiry:***	
Date of receipt:	***Total number of packages received:***	***Signature for receipt:***

Dispensed					**Sent for destruction Only packages never dispensed**	
Date	**PID-no.**	**Number of packages dispensed**	**Signature for dispensation**	**Number of packages in storage**	**Date**	**Signature for sent to destruction**

Approval of the content of this document *(Investigator)*	***Date:***	***Name:***	***Signature:***
Comments:			

PreVent-ACaLL

Inventory Log - Trial Medication - Delivery same batch number

ISF/TMF section: 10.1

Site number: **Hospital:** **Principal Investigator:**

Trial Medication: *(name/strength/number)*	Venetoclax 50 mg - 8 tablets in each package	
Batch number:		*Date of expiry:*
Date of receipt:	*Total number of packages received:*	*Signature for receipt:*

Dispensed					Sent for destruction Only packages never dispensed	
Date	PID-no.	Number of packages dispensed	Signature for dispensation	Number of packages in storage	Date	Signature for sent to destruction

Approval of the content of this document *(Investigator)*	*Date:* *Name:* *Signature:*
Comments:	

PreVent-ACaLL

Inventory Log - Trial Medication - Delivery same batch number

ISF/TMF section: 10.1

Site number: **Hospital:** **Principal Investigator:**

Trial Medication: *(name/strength/number)*	**Venetoclax 100 mg - 8 tablets in each package**		
Batch number:		***Date of expiry:***	
Date of receipt:	***Total number of packages received:***	***Signature for receipt:***	

Dispensed					**Sent for destruction Only packages never dispensed**	
Date	**PID-no.**	**Number of packages dispensed**	**Signature for dispensation**	**Number of packages in storage**	**Date**	**Signature for sent to destruction**

Approval of the content of this document *(Investigator)*	***Date:***	***Name:***	***Signature:***
Comments:			

PreVent-ACaLL

Inventory Log - Trial Medication - Delivery same batch number

ISF/TMF section: 10.1

Site number: **Hospital:** **Principal Investigator:**

Trial Medication: *(name/strength/number)*	**Venetoclax 100 mg - 120 tablets in each bottle**		
Batch number:		***Date of expiry:***	
Date of receipt:	***Total number of packages received:***	***Signature for receipt:***	

Dispensed					**Sent for destruction Only bottles never dispensed**	
Date	**PID-no.**	**Number of bottles dispensed**	**Signature for dispensation**	**Number of bottles in storage**	**Date**	**Signature for sent to destruction**

Approval of the content of this document *(Investigator)*	***Date:***	***Name:***	***Signature:***
Comments:			

PreVent-ACaLL

Inventory Log - Trial Medication - Delivery same batch number

ISF/TMF section: 10.1

Site number: **Hospital:** **Principal Investigator:**

Trial Medication: *(name/strength/number)*	**Acalabrutinib 100 mg - 30 capsules in each bottle**		
Batch number:		***Date of expiry:***	
Date of receipt:	***Total number of packages received:***	***Signature for receipt:***	

Dispensed					**Sent for destruction Only bottles never dispensed**	
Date	**PID-no.**	**Number of bottles dispensed**	**Signature for dispensation**	**Number of bottles in storage**	**Date**	**Signature for sent to destruction**

Approval of the content of this document *(Investigator)*	***Date:***	***Name:***	***Signature:***
Comments:			

PreVent-ACaLL

Drug Accountability Form - Per subject

ISF/TMF section: 10.2

Site number: **Hospital:** **Principal Investigator:**

PID - Number:

Trial Drug: ***Venetoclax*** **Dispensed**							**Returned**			**Destruction**	
Date	**Batch number**	**Date of expiry**	**Strength of tablets** Cycle/dose	Need	**Number of tablets dispensed**	**Initials for dispensation**	**Date**	**Number of tablets returned**	**Initials for returned**	**Date**	**Initials for destruction**
			C1D1 dose 20 mg 2 tabl of 10 mg x 1	1 package of 16 tablets							
			C1D8 50 mg 1 tabl of 50 mg x 1	1 package of 8 tablets							
			C1D15 100 mg 1 tabl of 100 mg x 1	1 package of 8 tablets							
			C1D21 200 mg 2 tabl of 100 mg x 1	2 packages of 8 tablets							
			C2D1 400 mg 4 tabl of 100 mg x 1	1 bottle of 120 tablets							
			C3D1 400 mg 4 tabl of 100 mg x 1	1 bottle of 120 tablets							
Trial Drug*:** ***Acalabrutinib **Dispensed**							**Returned**			**Destruction**	
Date	**Batch number**	**Date of expiry**	**Strength of tablets** Cycle/dose	Need	**Number of tablets dispensed**	**Initials for dispensation**	**Date**	**Number of tablets returned**	**Initials for returned**	**Date**	**Initials for destruction**
			C1D1 100 mg 1 tabl of 100 mg x 2	2 bottles of 30 capsules							
			C1D2 100 mg 1 tabl of 100 mg x 2	2 bottles of 30 capsules							
			C1D3 100 mg 1 tabl of 100 mg x 2	2 bottles of 30 capsules							

Approval of the content of this document *(Investigator)*	***Date:***	***Name:***	***Signature:***
Comments:			

Appendix 6: Temperature Log for study drugs

Trial Medication:	**Venetoclax** **Store between 2° and 25° C**	**Acalabrutinib** **Store between 15° and 30° C**
Merged range:	**Store between 15° and 25° C**	
Storage Location:		

Please control the temperature every working day and complete this log

Once a month a printout from the temperature logger covering the last month's storage period must be documented in the investigator site file.

In case the temperature has been below 15°C or above 25°C please do the following:

- Fill in the Temperature Deviation Report Form – send it to chip-prevent.rigshospitalet@regionh.dk
- Store affected Trial Drugs separated from other Trial Drugs under required temperature and with temperature monitoring
- Do not dispense any affected Trial Drugs
- Expect to receive conclusion of the deviation within 5 working days

Month: _____

Day	Temp. range between 15° and 25° C	Reviewed time period	Site Staff Signature	Action taken if temperature outside range	Site Staff Signature
1.					
2.					
3.					
4.					
5.					
6.					
7.					
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9.					
10.					

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PreVent-ACaLL

Drug Destruction Log

ISF/TMF section: 10.10

Site number: **Hospital:** **Principal Investigator:**

Trial Medication	Batch number	Number of packages	Total number of tablets/capsules	Date	Signature for sent to destruction
Venetoclax 10 mg					
Venetoclax 50 mg					
Venetoclax 100 mg blister					
Venetoclax 100 mg bottles					
Acalabrutinib 100 mg					

Destructed after agreement with: (for sponsor)	***Date:***	***Name:***	***Signature:***
Comments:			
Signature for final destruction	***Date:***	***Name:***	***Signature:***