A randomized phase III study in previously untreated patients with biological high-risk CLL: Fludarabine + cyclophosphamide (FC) versus FC + low-dose alemtuzumab

VERSION OF FORMS

Version date	Changed form	Description
10.03.2005	Original	-
20.10.2005	All forms	Item numbers added
	Registration & Randomization Form (1)	Item 48: question corrected (*and* replaces *or)*
	Treatment Form (4)	Items for G-CSF added (items 18-20)
		Item for corticosteroids added (item 21)
		Items for PCP prophylaxis added (items 22-23)
		Items for CMV prophylaxis added (items 30-31)
		Items for hematology nadirs added (items 53-62)
	Molecular Evaluation Form (8A and 8B)	PB sampling date added (item 4)
		Comment about total vs. gated percentage added
		Item 30: question corrected (*homology* replaces *mutations*)
	CT Scan Form (9)	Item 81: specification other sites added
		Form number corrected on page 2 of 2
	Adverse Event Form (12)	Reference to Treatment Form corrected
		Comment about hematological adverse events added
	Infection Form (13)	Reference to Treatment Form corrected
13.12.2005	Adverse Event Form (12)	Items for SAE and relationship added
	Infection Form (13)	Items for SAE and relationship added
14.04.2008	Registration & Randomization Form (1)	Modification of telephone and fax number
		Addition of item 53, modification of item 40
	Original Pathology form (2A) and	Text ‘Bone marrow biopsy’ replaced by ‘Blood smear’
	Central Pathology form (2B)	Deletion of items 9-12.
	Response Evaluation form (5)	Addition of items 55, 56, 57
		Deletion of items 37, 38
		Item 41,43: addition of text ‘if applicable’ at label 1
		Item 48: label 4= ‘nodular partial remission’ replaced by label 10=‘CR with incomplete BM recovery’
	Molecular Evaluation form (8A) and	Addition of item 48
	Central Molecular Evaluation form (8B)	
	Off Treatment form (10)	Item 6: label 4= ‘nodular partial remission’ replaced by label 10=‘CR with incomplete BM recovery’
		Addition of item 10
	Folow up form (11)	Item 7 and 23: label 4=‘nodular partial remission’ replaced by label 10=‘CR with incomplete BM recovery’

HOVON 68 CLL

REGISTRATION & RANDOMIZATION FORM (1)

Instructions: Please complete this form before randomization to check eligibility. Randomize via Internet through TOP or send this form by fax or report by telephone to HOVON Data Center. Fax +31.10.7041028, Tel +31.10.7041560
Any mistake in patient characteristics or eligibility as given at randomization must be reported immediately by sending the revised form to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: …….. Hospital: …… Patient study number: |___|___|___|

Caller (who registers the patient)		*8*	.....
Responsible physician		*9*	.....
Hospital record number		*10*	.....
Date of birth	[dd/mm/yyyy]	*11*	|____||____||_____|
Sex		*12*	|___| 1=male 2=female
Date of diagnosis CLL	[dd/mm/yyyy]	*16*	|____||____||_____|

ELIGIBILITY (see protocol paragraph 8.1)

Diagnosis of biological high risk CLL	*17*	|___|	0=no	1=yes
≥ 98% homology to germ-line VH gene sequence ("unmutated")	*18*	|___|	0=no	1=yes
Usage of V_H3-12	*53*	|___|	0=no	1=yes
17p deletions confirmed by FISH	*19*	|___|	0=no	1=yes
11q deletions confirmed by FISH	*20*	|___|	0=no	1=yes
Trisomy 12 confirmed by FISH	*21*	|___|	0=no	1=yes
Stage of disease (see protocol appendix B)	*22*	|___|	1=stage A	2=stage B
			3=stage C	
Weight loss ≥ 10% within the previous 6 months	*23*	|___|	0=no	1=yes
Extreme fatigue	*24*	|___|	0=no	1=yes
Fevers ≥ 38.6 °C for ≥ 2 weeks without evidence of infection	*25*	|___|	0=no	1=yes
Night sweats without evidence of infection	*26*	|___|	0=no	1=yes
Evidence of progressive marrow failure as manifested by the development of, or worsening of anemia and/or thrombocytopenia	*27*	|___|	0=no	1=yes
Autoimmune anemia and/or thrombocytopenia poorly responsive to corticosteroid therapy	*28*	|___|	0=no	1=yes
Massive (i.e., > 6 cm below the left costal margin) or progressive splenomegaly	*29*	|___|	0=no	1=yes
Massive nodes or clusters (i.e., > 10 cm in longest diameter) or progressive lymphadenopathy	*30*	|___|	0=no	1=yes
Progressive lymphocytosis with an increase of > 50% over a 2-month period, or an anticipated doubling time of less than 6 months	*31*	|___|	0=no	1=yes
Age 18-75 years inclusive	*32*	|___|	0=no	1=yes
Written informed consent	*33*	|___|	0=no	1=yes
WHO performance status ≥ 3, unless related to CLL	*34*	|___|	0=no	1=yes
Intolerance of exogenous protein administration	*35*	|___|	0=no	1=yes

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

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Patient namecode: …….. Hospital: …… Patient study number: |___|___|___|

Severe cardiac dysfunction (NYHA classification III-IV)	*36*	|___|	0=no	1=yes	
Significant renal dysfunction (serum creatinine ≥ 150 μmol/l (≥ 1.70 mg/dl) or creatinine clearance < 30 ml/min)	*37*	|___|	0=no	1=yes	
Significant hepatic dysfunction (total bilirubin or transaminases > 2 times ULN), unless related to CLL	*38*	|___|	0=no	1=yes	
Suspected or documented CNS involvement by CLL	*39*	|___|	0=no	1=yes	
Known seropositivity of HIV, Hepatitis B and C	*40*	|___|	0=no	1=yes	
Active, uncontrolled infections	*41*	|___|	0=no	1=yes	
Uncontrolled asthma or allergy requiring systemic steroid treatment	*42*	|___|	0=no	1=yes	
Previous treatment with chemotherapy, radiotherapy or immunotherapy for CLL	*43*	|___|	0=no	1=yes	
History of active cancer during the past 5 years, except non-melanoma skin cancer or stage 0 cervical carcinoma	*44*	|___|	0=no	1=yes	
Clinically significant auto-immune hemolytic anemia (AIHA)	*45*	|___|	0=no	1=yes	
Negative pregnancy test if applicable	*46*	|___|	0=no	1=yes	2=not applicable
Nursing if applicable	*47*	|___|	0=no	1=yes	2=not applicable
Willing and able to use adequate contraception during therapy (all men, pre-menopausal women)	*48*	|___|	0=no	1=yes	2=not applicable

DATA FROM HOVON DATA CENTER

Date of randomization	[dd/mm/yyyy]	*14*	|____||____||_____|
Patient study number		*1*	|___|___|___|
Treatment arm allocated		*13*	|___| 1=Arm A: FC <u>without</u> alemtuzumab 2=Arm B: FC <u>with</u> alemtuzumab

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

ORIGINAL PATHOLOGY FORM (2A)

Instructions: This form has to be completed by the local pathologist and sent in together with 5 unstained slides.
Send it to the central pathologist of your respective country as specified in paragraph 4.1 of the protocol.
Please send a copy of this form to:
HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..…….. Hospital: …… Patient study number: |___|___|___|

BLOOD SMEAR

Local PA laboratory / local pathologist ..... *3* .....

Date of smear ..... [dd/mm/yyyy] *4* |____||____||_____|

Original number / section ..... *5* |_____| / |_____|

Localisation of smear ..... *6* .....

Frozen material available ..... *7* |__| 0=no 1=yes

CLL according to the WHO classification ..... *8* |__| 0=no 1=yes

IMMUNOPHENOTYPING*

CD5	*13*	|__|__|__| %	CD79b	*17*	|__|__|__| %
CD19	*14*	|__|__|__| %	kappa	*18*	|__|__|__| %
CD20	*15*	|__|__|__| %	lambda	*19*	|__|__|__| %
CD23	*16*	|__|__|__| %	cyclin D1	*20*	|__|__|__| %

* fill out 111 if positive but percentage unknown

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

CENTRAL PATHOLOGY FORM (2B)

Instructions: This form has to be completed by the central pathologist.
Please send the completed form to:
HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ….....…….. Hospital: …… Patient study number: |___|___|___|

BLOOD SMEAR

Date of smear ..... [dd/mm/yyyy] *4* |___||___||_____|

Original number / section ..... *5* |_____| / |_____|

Localisation of smear ..... *6* .....

CLL according to the WHO classification ..... *8* |__| 0=no 1=yes

IMMUNOPHENOTYPING*

CD5	*13*	|__|__|__| %	CD79b	*17*	|__|__|__| %
CD19	*14*	|__|__|__| %	kappa	*18*	|__|__|__| %
CD20	*15*	|__|__|__| %	lambda	*19*	|__|__|__| %
CD23	*16*	|__|__|__| %	cyclin D1	*20*	|__|__|__| %

* fill out 111 if positive but percentage unknown

Agreement with the local pathologist ..... *21* |__| 0=no 1=yes 2=min. disagreement

Eligible for this trial ..... *22* |__| 0=no 1=yes

Date review ..... [dd/mm/yyyy] *23* |___||___||_____|

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

ON STUDY FORM (3)

Instructions: Please send the completed form within 1 month of randomization.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: …..…….. Hospital: …… Patient study number: |___|___|___|

PATIENT CHARACTERISTICS AT ENTRY

Height	[cm]	*2*	|__|__|__|
WHO performance status	[0-4]	*3*	|__|

MEDICAL HISTORY

History of other hematological or oncological disease		*4*	|__| 0=no 1=yes*
	*Specify	*5*	……
If yes, date diagnosis	[dd/mm/yyyy]	*6*	|____||____||_____|
Concomitant disease		*7*	|__| 0=no 1=yes*
	*Specify	*8*	……

PHYSICAL EXAMINATION

Spleen size below costal margin (by physical examination)	[cm]	*9*	|__|__|.|__|
Largest diameter spleen	[cm]	*10*	|__|__|.|__|
Liver size below costal margin (by physical examination)	[cm]	*11*	|__|__|.|__|
Largest diameter liver	[cm]	*12*	|__|__|.|__|
Palpable lymph nodes		*13*	|__| 0=no 1=yes
Neck right	[cm x cm]	*14*	|__|__|.|__| X *15* |__|__|.|__|
Neck left	[cm x cm]	*16*	|__|__|.|__| X *17* |__|__|.|__|
Axillae right	[cm x cm]	*18*	|__|__|.|__| X *19* |__|__|.|__|
Axillae left	[cm x cm]	*20*	|__|__|.|__| X *21* |__|__|.|__|
Groins right	[cm x cm]	*22*	|__|__|.|__| X *23* |__|__|.|__|
Groins left	[cm x cm]	*24*	|__|__|.|__| X *25* |__|__|.|__|

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

ON STUDY FORM (3)

Instructions: Please send the completed form within 1 month of randomization.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ….....…….. Hospital: …… Patient study number: |___|___|___|

BLOOD CHEMISTRY

Date sample	[dd/mm/yyyy]	26	|___||___||_____|				
Sodium	[mmol/l]	27	|__|__|__|				
Potassium	[mmol/l]	28	|__|__|.|__|				
Creatinine	**[µmol/l]**	29	|__|__|__|	*or*	**[mg/dl]**	|__|.|__|__|	30
Creatinine clearance (on indication)	[ml/min]	31	|__|__|__|				
Uric acid	[mmol/l]	32	|__|.|__|__|				
ASAT	[U/l]	33	|__|__|__|__|				
ASAT Upper Limit of Normal	[U/l]	34	|__|__|__|__|				
ALAT	[U/l]	35	|__|__|__|__|				
ALAT Upper Limit of Normal	[U/l]	36	|__|__|__|__|				
Alkaline phosphatase	[U/l]	37	|__|__|__|				
Bilirubin	**[µmol/l]**	38	|__|__|__|	*or*	**[mg/dl]**	|__|.|__|__|	39
Bilirubin Upper Limit of Normal	**[µmol/l]**	40	|__|__|__|	*or*	**[mg/dl]**	|__|.|__|__|	41
LDH	[U/l]	42	|__|__|__|__|__|				
LDH Upper Limit of Normal	[U/l]	43	|__|__|__|__|__|				
Haptoglobin	[g/l]	44	|__|.|__|__|				
C-reactive protein	[mg/l]	45	|__|__|__|				
Glucose	[mmol/l]	46	|__|__|.|__|				
BUN	[mmol/l]	47	|__|__|.|__|				
Total protein	[g/l]	48	|__|__|__|				
Albumin	[g/l]	49	|__|__|.|__|				
IgG	[g/l]	50	|__|__|.|__|				
IgM	[g/l]	51	|__|__|.|__|				
IgA	[g/l]	52	|__|__|.|__|				
β-2 microglobulin	[mg/l]	53	|__|__|.|__|__|				

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

ON STUDY FORM (3)

Instructions: Please send the completed form within 1 month of randomization.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ….....…….. Hospital: …… Patient study number: |___|___|___|

BONE MARROW AND HEMATOLOGY

Bone marrow aspirate done		54	|___|	0=no	1=yes, fill out Bone Marrow Evaluation Form (6) and Molecular Evaluation Form (8A)
BM sampling date	[dd/mm/yyyy]	55	|____||____||_____|		
Hematology done		56	|___|	0=no	1=yes, fill out Hematological Evaluation Form (7) and Molecular Evaluation Form (8A)
PB sampling date	[dd/mm/yyyy]	57	|____||____||_____|		

ANTI-VIRAL ANTIBODIES

Cytomegalovirus (CMV)	58	|___|	0=negative	1=positive
Epstein-Barr (EBV)	59	|___|	0=negative	1=positive
HIV	60	|___|	0=negative	1=positive
Hepatitis B (HBV)	61	|___|	0=negative	1=positive
Hepatitis C (HCV)	62	|___|	0=negative	1=positive

SPECIFIC INVESTIGATIONS

ECG	63	|___|	0=no abnormalities	1=abnormalities*
*Specify	64	.....		
CT scan done	65	|___|	0=no	1=yes, fill out CT Scan Form (9)
Date CT scan [dd/mm/yyyy]	66	|____||____||_____|		

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

TREATMENT FORM (4)

Instructions: Please send the completed form within 1 month after evaluation of induction treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Cycle ..... [1-6] *2* |__|

PATIENT CHARACTERISTICS

Weight ..... [kg] *3* |__|__|__|.|__|

Surface area ..... [m^2] *4* |__|.|__|__|

WHO performance status ..... [0-4] *5* |__|

ADMINISTRATION OF TREATMENT

Date start of this cycle ..... [dd/mm/yyyy] *6* |____||____||________|

Date last chemotherapy given ..... [dd/mm/yyyy] *7* |____||____||________|

Drug	Theoretical full dose			Total dose actually given		Dosage*		Reason**
Fludarabine	40 mg/m^2 p.o.	d1,2,3	*8*	|__|__|__| [mg]	*9*	|__|	*10*	|__|
Cyclophosphamide	250 mg/m^2 p.o.	d1,2,3	*11*	|__|__|__|__| [mg]	*12*	|__|	*13*	|__|
Alemtuzumab	30 mg s.c.	d–1,0,1 (arm **B** cycle **1**)	*14*	|__|__|__| [mg]	*15*	|__|	*16*	|__|
		d1 (arm **B** cycles **2-6**)						

Specify dose modification and reason ..... (if applicable) *17* .....
.....

*Dosage	**Reason
1 = full dose according to schedule	1 = hematological toxicity
2 = full dose given but delayed	2 = neurotoxicity
3 = dose reduced	3 = both (1 + 2) (specify)
4 = dose reduced and delayed	4 = other toxicity (specify)
5 = not given	5 = combination (specify)
6 = interrupted & resumed	6 = patients condition (specify)
	7 = renal insufficiency
8 = other (specify)	8 = other (specify)
	9 = unknown

G-CSF given ..... *18* |__| 0=no 1=yes

Date start of G-CSF ..... [dd/mm/yyyy] *19* |____||____||________|

Date end of G-CSF ..... [dd/mm/yyyy] *20* |____||____||________|

Corticosteroids given ..... *21* |__| 0=no 1=yes

PCP prophylaxis given ..... *22* |__| 0=no 1=yes

If no, specify why not ..... *23* .....

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

TREATMENT FORM (4)

Instructions: Please send the completed form within 1 month after evaluation of induction treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Cycle ..... [1-6] *2* |__|

EBV AND CMV MONITORING (arm B only)

PCR for EBV done ..... *24* |__| 0=no 1=yes

	Date of sample	Technique[1]	Sensitivity[2]	Result 1[3] Non-quantitative	Result 2 Nr. of copies / ml
	25 |____||____||_____|	*26* |__|	*27* |__|	*28* |__|	*29* |__|__|__|__|__|__|

CMV prophylaxis given ..... *30* |__| 0=no 1=yes 2=not applicable (arm A)

If no, specify why not ..... *31* .....

PCR for CMV done ..... *32* |__| 0=no 1=yes

	Date of sample	Technique[1]	Sensitivity[2]	Result 1[3] Non-quantitative	Result 2 Nr. of copies / ml
week 1	*33* |____||____||_____|	*34* |__|	*35* |__|	*36* |__|	*37* |__|__|__|__|__|__|
week 2	*38* |____||____||_____|	*39* |__|	*40* |__|	*41* |__|	*42* |__|__|__|__|__|__|
week 3	*43* |____||____||_____|	*44* |__|	*45* |__|	*46* |__|	*47* |__|__|__|__|__|__|
week 4	*48* |____||____||_____|	*49* |__|	*50* |__|	*51* |__|	*52* |__|__|__|__|__|__|

[1]Technique
1=non-quant. PCR
2=quant. PCR

[2]Sensitivity
1=1/10[1]
2=1/10[2]
3=1/10[3]
4=1/10[4]
5=1/10[5]
6=1/10[6]
9=not assessable

[3]Result
0=negative
1=positive
2=significant increase
3=significant decrease
9=not assessable

HEMATOLOGY (please report nadir and date when nadir was first reported during this cycle, e.g. between date start of this cycle and start of the next cycle, or in case of the last cycle between date start of this cycle and 30 days after date start of this cycle)

			Nadir		Date nadir first reported
Hemoglobin	**[mmol/l]**	*53*	|__|__|.|__|	[dd/mm/yyyy] *54*	|____||____||_____|
Or hemoglobin	**[g/dl]**	*55*	|__|__|.|__|	[dd/mm/yyyy] *56*	|____||____||_____|
WBC	[x10^9/l]	*57*	|__|__|__|.|__|	[dd/mm/yyyy] *58*	|____||____||_____|
ANC	[x10^9/l]	*59*	|__|__|__|.|__|	[dd/mm/yyyy] *60*	|____||____||_____|
Platelets	[x10^9/l]	*61*	|__|__|__|__|	[dd/mm/yyyy] *62*	|____||____||_____|

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

TREATMENT FORM (4)

Instructions: Please send the completed form within 1 month after evaluation of induction treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Cycle ..... [1-6] *2* |__|

COMPLICATIONS OR EVENTS

Adverse events (CTCAE ≥ 2)..... *63* |__| 0=no 1=yes, please fill out Adverse Event Form (12)

Infections (CTCAE ≥ 2)..... *64* |__| 0=no 1=yes, please fill out Infection Form (13)

Survival status..... *65* |__| 0=alive 1=dead, please fill out Off Treatment Form (10)

Treatment planned..... *66* |__| 0=no further protocol treatment
2=cycle II 3=cycle III
4=cycle IV 5=cycle V
6=cycle VI 8=other*

*Specify *67* .....

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

RESPONSE EVALUATION FORM (5)

Instructions: Please send the completed form within 1 month after evaluation of the relevant treatment cycle, once every 6 months during follow up until progression, at every change in response during follow up and at the request of the HOVON Data Center.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Time of evaluation ..... 2 |___| 3=cycle III 6=cycle VI 7=follow up

Date of evaluation ..... [dd/mm/yyyy] 3 |____||____||_____|

PHYSICAL EXAMINATION

Spleen size below costal margin ..... [cm] 4 |__|__|.|__|
(by physical examination)

Liver size below costal margin ..... [cm] 5 |__|__|.|__|
(by physical examination)

Palpable lymph nodes ..... 6 |__| 0=no 1=yes

Neck right ..... [cm x cm] 7 |__|.|__| X 8 |__|.|__|

Neck left ..... [cm x cm] 9 |__|.|__| X 10 |__|.|__|

Axillae right ..... [cm x cm] 11 |__|.|__| X 12 |__|.|__|

Axillae left ..... [cm x cm] 13 |__|.|__| X 14 |__|.|__|

Groins right ..... [cm x cm] 15 |__|.|__| X 16 |__|.|__|

Groins left ..... [cm x cm] 17 |__|.|__| X 18 |__|.|__|

BLOOD CHEMISTRY

Date sample ..... [dd/mm/yyyy] 19 |____||____||_____|

Sodium ..... [mmol/l] 20 |__|__|__|

Potassium ..... [mmol/l] 21 |__|__|.|__|

Creatinine ..... **[µmol/l]** 22 |__|__|__| *or* **[mg/dl]** |__|.|__|__| 23

Creatinine clearance (on indication) ..... [ml/min] 24 |__|__|__|

Uric acid ..... [mmol/l] 25 |__|.|__|__|

ASAT ..... [U/l] 26 |__|__|__|__|

ALAT ..... [U/l] 27 |__|__|__|__|

Alkaline phosphatase ..... [U/l] 28 |__|__|__|

Bilirubin ..... **[µmol/l]** 29 |__|__|__| *or* **[mg/dl]** |__|.|__|__| 30

LDH ..... [U/l] 31 |__|__|__|__|__|

Haptoglobin ..... [g/l] 32 |__|.|__|__|

C-reactive protein ..... [mg/l] 33 |__|__|__|

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

RESPONSE EVALUATION FORM (5)

Instructions: Please send the completed form within 1 month after evaluation of the relevant treatment cycle, once every 6 months during follow up until progression, at every change in response during follow up and at the request of the HOVON Data Center.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Date of evaluation	[dd/mm/yyyy]	3	|____||____||_____|		

BONE MARROW AND HEMATOLOGY

Biopsy		34	|___|	0=not done	1=done 2=failure
Cellularity		35	|___|	1=low	2=medium 3=high
Fat cells		36	|___|	1= > 15%	2= ≤ 15%
CLL infiltration		55	|___|	0=no	1=yes
Nodular infiltration pattern		56	|___|	0=no	1=yes*
*Are nodules B-lymphoid?		57	|___|	0=no	1=yes
Transformation to Richter's syndrome		39	|___|	0=no	1=yes
Transformation to PLL with > 55% prolymphocytes		40	|___|	0=no	1=yes
Bone marrow aspirate done		41	|___|	0=no	1=yes, fill out Bone Marrow Evaluation Form (6) and Molecular Evaluation Form (8A) if applicable.
BM sampling date	[dd/mm/yyyy]	42	|____||____||_____|		
Hematology done		43	|___|	0=no	1=yes, fill out Hematological Evaluation Form (7) and Molecular Evaluation Form (8A) if applicable.
PB sampling date	[dd/mm/yyyy]	44	|____||____||_____|		

SPECIFIC INVESTIGATIONS

CT scan done		45	|___|	0=no	1=yes, fill out CT Scan Form (9)
Date CT scan	[dd/mm/yyyy]	46	|____||____||_____|		

EVALUATION

WHO performance status	[0-4]	47	|___|	
Response		48	|___|	1=complete molecular remission 2=complete flow cytometric remission 3=complete remission (CR) 10=CR with incomplete BM recovery 5=partial remission 6=stable disease 7=progression after previous response 8=progressive disease

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

BONE MARROW EVALUATION FORM (6)

Instructions: Please fill out this form repeatedly to document diagnosis and evaluation of treatment.
Send this form to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Time of evaluation		*2*	|___|	0=on study 3=cycle III 6=cycle VI 7=follow up
BM sampling date	[dd/mm/yyyy]	*3*	|____||____||_____|	

(date should match item 55 on On Study Form or item 42 on Response Evaluation Form)

BONE MARROW DIFFERENTIAL

Blasts	[%]	*4*	|___|___|___|
Promyelocytes	[%]	*5*	|___|___|___|
Myelocytes	[%]	*6*	|___|___|___|
Metamyelocytes	[%]	*7*	|___|___|___|
Neutrophils (segments & bands)	[%]	*8*	|___|___|___|
Monocytes	[%]	*9*	|___|___|___|
Eosinophils	[%]	*10*	|___|___|___|
Basophils	[%]	*11*	|___|___|___|
Erythroblasts	[%]	*12*	|___|___|___|
Lymphocytes	[%]	*13*	|___|___|___|
Plasma cells	[%]	*14*	|___|___|___|
Ghost cells	[%]	*15*	|___|___|___|
Other*	[%]	*16*	|___|___|___|
	*Specify	*17*	.....

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

HEMATOLOGICAL EVALUATION FORM (7)

Instructions: Please fill out this form repeatedly to document diagnosis and evaluation of treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Time of evaluation ..... *2* |___| 0=on study 3=cycle III 6=cycle VI 7=follow up

Blood sampling date ..... [dd/mm/yyyy] *3* |____||____||_____|

(date should match item 57 on On Study Form or item 44 on Response Evaluation Form)

HEMATOLOGICAL EVALUATION

Hemoglobin	**[mmol/l]**	*4*	|__|__|.|__|	*or*	**[g/dl]**	|__|__|.|__| *5*
Erythrocytes	[x10^{12}/l]	*6*	|__|.|__|			
Reticulocytes	[%]	*7*	|__|__|__|.|__|			
Platelets	[x10^{9}/l]	*8*	|__|__|__|__|			
WBC	[x10^{9}/l]	*9*	|__|__|__|.|__|			
Neutrophils	[%]	*10*	|__|__|__|			
Eosinophils	[%]	*11*	|__|__|__|			
Basophils	[%]	*12*	|__|__|__|			
Lymphocytes	[%]	*13*	|__|__|__|			
Monocytes	[%]	*14*	|__|__|__|			
Ghost cells	[%]	*15*	|__|__|__|			
Other*	[%]	*16*	|__|__|__|			
	*Specify	*17*	.....			

Direct antiglobulin test (Coombs test) ..... *18* |___| 0=negative 1=positive 2=not done

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

MOLECULAR EVALUATION FORM (8A)

Instructions: Please fill out this form repeatedly to document diagnosis and evaluation of treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Time of evaluation ..... 2 |___| 0=on study 3=cycle III 6=cycle VI 7=follow up

BM sampling date ..... [dd/mm/yyyy] 3 |____||____||_____|

PB sampling date ..... [dd/mm/yyyy] 4 |____||____||_____|

(should match items 55 and 57 on On Study Form
or items 42 and 44 on Response Evaluation Form)

Samples sent for central evaluation ..... 5 |___| 0=no 1=yes

Samples sent date ..... [dd/mm/yyyy] 6 |____||____||_____|

FLOW CYTOMETRY

Flow cytometry done ..... 7 |___| 0=no 1=yes

Type of sample used ..... 8 |___| 1=bone marrow 2=peripheral blood 3=BM+PB

Flow cytometry results for BM* (fill out results for PB if flow cytometry is not done on BM)

CD3/CD4 ..... 9 |___|___|___| %

CD3/CD8 ..... 10 |___|___|___| %

CD5/CD19/CD23 ..... 11 |___|___|___| %

CD19/kappa ..... 12 |___|___|___| %

CD19/lambda ..... 13 |___|___|___| %

CD19/CD38 ..... 14 |___|___|___| **gated %**

CD19/ZAP-70 ..... 15 |___|___|___| %

* fill out 111 if positive but percentage unknown, please report total percentages unless stated otherwise (e.g. report gated percentage for CD19/CD38)

FISH ANALYSIS

FISH analysis done ..... 16 |___| 0=not done 1=done 2=failure

Type of sample used ..... 17 |___| 1=bone marrow 2=peripheral blood 3=BM+PB

Method ..... 18 |___| 1=interphase 2=metaphase

Cells analyzed for del(17)(p13) ..... 19 |___|___|___|

Number of cells with del(17)(p13) ..... 20 |___|___|___|

Cells analyzed for del(11)(q22-23) ..... 21 |___|___|___|

Number of cells with del(11)(q22-23) ..... 22 |___|___|___|

Cells analyzed for trisomy 12 ..... 23 |___|___|___|

Number of cells with trisomy 12 ..... 24 |___|___|___|

Cells analyzed for del(13)(q14) ..... 25 |___|___|___|

Number of cells with del(13)(q14) ..... 26 |___|___|___|

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

MOLECULAR EVALUATION FORM (8A)

Instructions: Please fill out this form repeatedly to document diagnosis and evaluation of treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

BM sampling date	[dd/mm/yyyy]	*3*	|____||____||_____|			
PB sampling date	[dd/mm/yyyy]	*4*	|____||____||_____|			

IMMUNOGLOBULIN HEAVY CHAIN SEQUENCING

IgVH sequencing done	*27*	|___|	0=not done	1=done	2=failure
Type of sample used	*28*	|___|	1=bone marrow	2=peripheral blood	
Method	*29*	|___|	1=RNA based	2=DNA based	
Homology [%]	*30*	|___|___|___|			
Mutational status (98% cut-off)	*31*	|___|	1=mutated	2=unmutated	3=inconclusive
Usage of V_H3-21	*48*	|___|	0=no	1=yes	

MINIMAL RESIDUAL DISEASE

MRD by flow cytometry done	*32*	|___|	0=no	1=yes	
Type of sample used	*33*	|___|	1=bone marrow	2=peripheral blood	3=BM+PB
Residual CLL cells PB [%]	*34*	|___|___|___|			
Residual CLL cells BM [%]	*35*	|___|___|___|			
MRD by PCR done	*36*	|___|	0=no	1=yes	
Type of sample used	*37*	|___|	1=bone marrow	2=peripheral blood	3=BM+PB
Residual CLL cells PB [%]	*38*	|___|___|___|			
Residual CLL cells BM [%]	*39*	|___|___|___|			

MATERIAL STORED

Frozen material stored	*40*	|___|	0=no	1=yes	
Type of sample stored	*41*	|___|	1=bone marrow	2=peripheral blood	3=BM+PB

Material suitable for

Viable cells	*42*	|___|	0=no	1=yes	
Protein purification	*43*	|___|	0=no	1=yes	
DNA purification	*44*	|___|	0=no	1=yes	
RNA purification	*45*	|___|	0=no	1=yes	

COMMENTS ……

……

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

CENTRAL MOLECULAR EVALUATION FORM (8B)

Instructions: This form has to be completed by the central molecular biologist.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

BM sampling date ..... [dd/mm/yyyy] *3* |____||____||_____|

PB sampling date ..... [dd/mm/yyyy] *4* |____||____||_____|

FLOW CYTOMETRY

Flow cytometry done ..... *7* |__| 0=no 1=yes

Type of sample used ..... *8* |__| 1=bone marrow 2=peripheral blood 3=BM+PB

Flow cytometry results for BM* (fill out results for PB if flow cytometry is not done on BM)

CD3/CD4 ..... *9* |__|__|__| %

CD3/CD8 ..... *10* |__|__|__| %

CD5/CD19/CD23 ..... *11* |__|__|__| %

CD19/kappa ..... *12* |__|__|__| %

CD19/lambda ..... *13* |__|__|__| %

CD19/CD38 ..... *14* |__|__|__| **gated %**

CD19/ZAP-70 ..... *15* |__|__|__| %

* fill out 111 if positive but percentage unknown, please report total percentages unless stated otherwise (e.g. report gated percentage for CD19/CD38)

FISH ANALYSIS

FISH analysis done ..... *16* |__| 0=not done 1=done 2=failure

Type of sample used ..... *17* |__| 1=bone marrow 2=peripheral blood 3=BM+PB

Method ..... *18* |__| 1=interphase 2=metaphase

Cells analyzed for del(17)(p13) ..... *19* |__|__|__|

Number of cells with del(17)(p13) ..... *20* |__|__|__|

Cells analyzed for del(11)(q22-23) ..... *21* |__|__|__|

Number of cells with del(11)(q22-23) ..... *22* |__|__|__|

Cells analyzed for trisomy 12 ..... *23* |__|__|__|

Number of cells with trisomy 12 ..... *24* |__|__|__|

Cells analyzed for del(13)(q14) ..... *25* |__|__|__|

Number of cells with del(13)(q14) ..... *26* |__|__|__|

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

CENTRAL MOLECULAR EVALUATION FORM (8B)

Instructions: This form has to be completed by the central molecular biologist.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

BM sampling date	[dd/mm/yyyy]	*3*	|____||____||_____|			
PB sampling date	[dd/mm/yyyy]	*4*	|____||____||_____|			

IMMUNOGLOBULIN HEAVY CHAIN SEQUENCING

IgVH sequencing done	*27*	|___|	0=not done	1=done	2=failure
Type of sample used	*28*	|___|	1=bone marrow	2=peripheral blood	
Method	*29*	|___|	1=RNA based	2=DNA based	
Homology [%]	*30*	|___|___|___|			
Mutational status (98% cut-off)	*31*	|___|	1=mutated	2=unmutated	3=inconclusive
Usage of V_H3-21	*48*	|___|	0=no	1=yes	

MINIMAL RESIDUAL DISEASE

MRD by flow cytometry done	*32*	|___|	0=no	1=yes	
Type of sample used	*33*	|___|	1=bone marrow	2=peripheral blood	3=BM+PB
Residual CLL cells PB [%]	*34*	|___|___|___|			
Residual CLL cells BM [%]	*35*	|___|___|___|			
MRD by PCR done	*36*	|___|	0=no	1=yes	
Type of sample used	*37*	|___|	1=bone marrow	2=peripheral blood	3=BM+PB
Residual CLL cells PB [%]	*38*	|___|___|___|			
Residual CLL cells BM [%]	*39*	|___|___|___|			

MATERIAL STORED

Frozen material stored	*40*	|___|	0=no	1=yes	
Type of sample stored	*41*	|___|	1=bone marrow	2=peripheral blood	3=BM+PB

Material suitable for

Viable cells	*42*	|___|	0=no	1=yes	
Protein purification	*43*	|___|	0=no	1=yes	
DNA purification	*44*	|___|	0=no	1=yes	
RNA purification	*45*	|___|	0=no	1=yes	

COMMENTS.....

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

CT SCAN FORM (9)

Instructions: Please fill out this form repeatedly to document diagnosis and evaluation of treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Time of evaluation ..... 2 |___| 0=on study 3=cycle III 6=cycle VI 7=follow up

Date CT scan ..... [dd/mm/yyyy] 3 |____||____||_____|

(date should match item 66 on On Study Form or item 46 on Response Evaluation Form)

Evaluated regions

Cervical ..... 4 |___| 0=no 1=yes

Thorax ..... 5 |___| 0=no 1=yes

Abdomen ..... 6 |___| 0=no 1=yes

Pelvis ..... 7 |___| 0=no 1=yes

Additional investigations ..... 8 |___| 0=no 1=yes*

*Specify 9 .....

.....

SITES OF DISEASE

Involvement: 0=no 1=yes 2=yes, and new lesion 9=unknown

	left			right	
Waldeyers ring	10	|___|			
Cervical	11	|___|	.....	12	|___|
Supraclavicular	13	|___|	.....	14	|___|
Axillary	15	|___|	.....	16	|___|
Mediastinum	17	|___|			
Hilar	18	|___|	.....	19	|___|
Para-aortic	20	|___|	.....	21	|___|
Mesenteric	22	|___|			
Spleen	23	|___|			
Liver	24	|___|			
Iliac	25	|___|	.....	26	|___|
Inguinal	27	|___|	.....	28	|___|
Other*	29	|___|			

*Specify 30 .....

.....

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

CT SCAN FORM (9)

Instructions: Please fill out this form repeatedly to document diagnosis and evaluation of treatment.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Date CT scan..... [dd/mm/yyyy] *3* |____||____||_____|

Indicator lesions

Designated number of indicator lesion must match the number given to this particular lesion on CT Scan Form (9) for on study.

In case of multiple separate lesions from previous single mass:

Design. Nr.	Site*	Measurements [mm x mm]	nr. of lesions	SPD [mm^2]
1	*31* |___|___|	*32* |___|___|___| **X** *33* |___|___|___|	*34* |___|	*35* |___|___|___|___|
2	*36* |___|___|	*37* |___|___|___| **X** *38* |___|___|___|	*39* |___|	*40* |___|___|___|___|
3	*41* |___|___|	*42* |___|___|___| **X** *43* |___|___|___|	*44* |___|	*45* |___|___|___|___|
4	*46* |___|___|	*47* |___|___|___| **X** *48* |___|___|___|	*49* |___|	*50* |___|___|___|___|
5	*51* |___|___|	*52* |___|___|___| **X** *53* |___|___|___|	*54* |___|	*55* |___|___|___|___|
6	*56* |___|___|	*57* |___|___|___| **X** *58* |___|___|___|	*59* |___|	*60* |___|___|___|___|
7	*61* |___|___|	*62* |___|___|___| **X** *63* |___|___|___|	*64* |___|	*65* |___|___|___|___|
8	*66* |___|___|	*67* |___|___|___| **X** *68* |___|___|___|	*69* |___|	*70* |___|___|___|___|
9	*71* |___|___|	*72* |___|___|___| **X** *73* |___|___|___|	*74* |___|	*75* |___|___|___|___|
10	*76* |___|___|	*77* |___|___|___| **X** *78* |___|___|___|	*79* |___|	*80* |___|___|___|___|

**Specify other sites..... (if applicable) *81* .....

.....

***SITE**			
1= Waldeyers ring	6= Axillary left	12= Para-aortic right	16= Iliac left
2= Cervical left	7= Axillary right	13= Mesenteric	17= Iliac right
3= Cervical right	8= Mediastinum	14= Spleen *(total size)*	18= Inguinal left
4= Sup. clavicul. left	9= Hilar left		19= Inguinal right
5= Sup. clavicul. right	10= Hilar right	15= Liver *(total size)*	88= Other**
	11= Para-aortic left		

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

OFF TREATMENT FORM (10)

Instructions: Please send the completed form within 1 month after the patient is taken Off Protocol Treatment:
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..…. Hospital: …… Patient study number: |___|___|___|

Date when taken off protocol treatment	[dd/mm/yyyy]	2	|___||___||_____|	
Number of cycles given	[0-6]	3	|__|	
Alemtuzumab given		4	|__|	0=no 1=yes*
Was serum stored for alemtuzumab (antibodies) assessment?		10	|__|	0=no 1=yes
CMV prophylaxis given		5	|__|	0=no 1=yes
Best response on protocol		6	|__|	1=complete molecular remission 2=complete flow cytometric remission 3=complete remission (CR) 10=CR with incomplete BM recovery 5=partial remission 6=stable disease 8=progressive disease
Reason for going off protocol treatment		7	|__|	0=normal completion 1=no response after 3 cycles 2=progression / relapse after initial response 3=excessive toxicity (including toxic death) 4=no compliance of the patient (especially refusal) 5=intercurrent death 6=major protocol violation 7=withdrawal by investigator for clinical reason not related to protocol treatment 8=other*
	*Specify	8	……	

COMMENTS

……

……

PLEASE RETURN THIS FORM TOGETHER WITH A FOLLOW UP FORM (11)

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

FOLLOW UP FORM (11)

Instructions: Please complete this form for patients taken Off Protocol Treatment. It should at least be filled out at off protocol, at first progression of disease, every 6 months during the first 3 years of follow up and thereafter every year and at the request of the HOVON Data Center.
Send it to: HOVON Data Center, University Hospital Rotterdam - Daniel, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

use a separate form for each change in remission status

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

PATIENT STATUS

Date last known to be alive or date of death ..... [dd/mm/yyyy] *2* |____||____||_____|

Date response evaluation ..... [dd/mm/yyyy] *3* |____||____||_____| (date should match item 3 on Response Evaluation Form (5) for this period)

(most recent evaluation for this period)

Survival status ..... *4* |___| 0=alive 1=dead

Cause of death ..... *5* |___| 1=CLL 2=toxicity* 3=infection* 4=combination* 8=other* 9=unknown

*Specify *6* .....

REMISSION STATUS

Remission status at present ..... *7* |___|
1=complete molecular remission
2=complete flow cytometric remission
3=complete remission
10=CR with imcomplete BM recovery
5=partial remission
6=stable disease
7=progression after previous response
8=progressive disease

Progression / relapse ..... *8* |___| 0=no 1=yes

(not reported previously)

Date of diagnosis progression/relapse ..... [dd/mm/yyyy] *9* |____||____||_____|

Secondary malignancy ..... *10* |___| 0=no 1=yes*

(not reported previously)

*Specify *11* .....

Date of diagnosis sec. malignancy ..... [dd/mm/yyyy] *12* |____||____||_____|

LATE EVENTS (observed since previous Follow Up and > 3 months after completion of protocol treatment)

Late toxicities (CTCAE ≥ 2) ..... *13* |___| 0=no 1=yes*

*Specify *14* .....

Late infections (CTCAE ≥ 2) ..... *15* |___| 0=no 1=yes*

*Specify *16* .....

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

FOLLOW UP FORM (11)

Instructions: Please complete this form for patients taken Off Protocol Treatment. It should at least be filled out at off protocol, at first progression of disease, every 6 months during the first 3 years of follow up and thereafter every year and at the request of the HOVON Data Center.
Send it to: HOVON Data Center, University Hospital Rotterdam - Daniel, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

use a separate form for each change in remission status

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Date last known to be alive or date of death ..... [dd/mm/yyyy] *2* |____||____||_____|

TREATMENT OFF PROTOCOL (after previous Follow Up / Off Treatment and before date last contact present Follow Up)

Treatment given off protocol ..... *17* |__| 0=no 1=chemotherapy* 8=other*

(not reported previously, CLL treatment only)

*Specify *18* .....

Reason for this treatment ..... *19* |__| 1=reinduction 2=consolidation 8=other*

*Specify *20* .....

Date of start of this treatment ..... [dd/mm/yyyy] *21* |____||____||_____|

Date response evaluation ..... [dd/mm/yyyy] *22* |____||____||_____|

Response to this treatment ..... *23* |__|

1=complete molecular remission
2=complete flow cytometric remission
3=complete remission (CR)
10=CR with imcomplete BM recovery
5=partial remission
6=stable disease
7=progression after previous response
8=progressive disease

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

ADVERSE EVENT FORM (12)

Instructions: Please send the completed form, together with the corresponding treatment form, to:
HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Please report all adverse events with CTCAE grade ≥ 2 except hematological adverse events, please use CTCAE version 3.0
Use separate forms for different periods

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Adverse event report related to cycle ..... [1-6] *2* |__|

Date start of this cycle ..... [dd/mm/yyyy] *3* |____||____||_____|

(date should match item 6 on Treatment Form)

Highest CTCAE grade during this period

AE nr		Site*		CTCAE grade		SAE 0=no 1=yes		Relationship to protocol treatment**		Specification
1	*4*	|__|__|	*5*	|__|	*6*	|__|	*7*	|__|	*8*	.....
2	*9*	|__|__|	*10*	|__|	*11*	|__|	*12*	|__|	*13*	.....
3	*14*	|__|__|	*15*	|__|	*16*	|__|	*17*	|__|	*18*	.....
4	*19*	|__|__|	*20*	|__|	*21*	|__|	*22*	|__|	*23*	.....
5	*24*	|__|__|	*25*	|__|	*26*	|__|	*27*	|__|	*28*	.....
6	*29*	|__|__|	*30*	|__|	*31*	|__|	*32*	|__|	*33*	.....
7	*34*	|__|__|	*35*	|__|	*36*	|__|	*37*	|__|	*38*	.....
8	*39*	|__|__|	*40*	|__|	*41*	|__|	*42*	|__|	*43*	.....
9	*44*	|__|__|	*45*	|__|	*46*	|__|	*47*	|__|	*48*	.....
10	*49*	|__|__|	*50*	|__|	*51*	|__|	*52*	|__|	*53*	.....
11	*54*	|__|__|	*55*	|__|	*56*	|__|	*57*	|__|	*58*	.....
12	*59*	|__|__|	*60*	|__|	*61*	|__|	*62*	|__|	*63*	.....

***SITE**

1= allergy/immunology *(incl. drug fever)*	10= hemorrhage/bleeding	19= renal/genitourinary
2= auditory/ear	11= hepatobiliary/pancreas	20= sexual/reproductive function
3= cardiac arrythmia	12= lymphatics	21= syndromes
4= cardiac general	13= metabolic/laboratory	23= blood/bone marrow
5= coagulation	14= musculoskeletal/soft tissue	24= growth and development
6= constitutional symptoms *(incl. non-neutropenic fever)*	15= neurology	25= secondary malignancy
7= dermatology/skin	16= ocular/visual	26= surgery/intra-operative injury
8= endocrine	17= pain	27= vascular
9= GI	18= pulmonary/upper respiratory	88= other

****RELATIONSHIP TO PROTOCOL TREATMENT**

0= unrelated
1= unlikely
2= possible
3= probable
4= definite
5= not assessable

COMMENTS

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PLEASE REPORT INFECTIONS BY FILLING OUT AN INFECTION FORM (13)

Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

INFECTION FORM (13)

Instructions: Please send the completed form, together with the corresponding treatment form, to:
HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Please report all infections with CTCAE grade ≥ 2, please use CTCAE version 3.0
Use separate forms for different periods

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

Infection report related to cycle..... [1-6] *2* |___|

Date start of this cycle..... [dd/mm/yyyy] *3* |____||____||_____|

(date should match item 6 on Treatment Form)

Highest CTCAE grade during this period

Infect. nr.	Site[1]	ANC[2]	CTCAE grade	Agent[3]	SAE 0=no 1=yes	Relationship to protocol treatment[4]	Specification
1	*4* |___|___|	*5* |___|	*6* |___|	*7* |___|	*8* |___|	*9* |___| *10*	.....
2	*11* |___|___|	*12* |___|	*13* |___|	*14* |___|	*15* |___|	*16* |___| *17*	.....
3	*18* |___|___|	*19* |___|	*20* |___|	*21* |___|	*22* |___|	*23* |___| *24*	.....
4	*25* |___|___|	*26* |___|	*27* |___|	*28* |___|	*29* |___|	*30* |___| *31*	.....
5	*32* |___|___|	*33* |___|	*34* |___|	*35* |___|	*36* |___|	*37* |___| *38*	.....
6	*39* |___|___|	*40* |___|	*41* |___|	*42* |___|	*43* |___|	*44* |___| *45*	.....
7	*46* |___|___|	*47* |___|	*48* |___|	*49* |___|	*50* |___|	*51* |___| *52*	.....
8	*53* |___|___|	*54* |___|	*55* |___|	*56* |___|	*57* |___|	*58* |___| *59*	.....
9	*60* |___|___|	*61* |___|	*62* |___|	*63* |___|	*64* |___|	*65* |___| *66*	.....
10	*67* |___|___|	*68* |___|	*69* |___|	*70* |___|	*71* |___|	*72* |___| *73*	.....

[1]SITE

1= Blood culture
2= Catheter
3= Pulmonary
4= Ear/nose/throat
5= GI tract
6= Liver
7= GU tract
8= CNS
9= Skin/sub-cutaneous
10= Fever e.c.i. **
11= Other

[2]ANC

0= <1.0x10^9/l
1= ≥1.0x10^9/l
9= unknown

[3]AGENT

1= Gram-positive bacteria
2= Gram-negative bacteria
3= Fungi
4= Protozoa
5= Virus
6= Mycoplasma
7= Combined agents
8= Other
9= Unknown

[4]RELATIONSHIP TO PROTOCOL TREATMENT

0= unrelated
1= unlikely
2= possible
3= probable
4= definite
5= not assessable

** febrile neutropenia or, when ANC unknown, fever e.c.i. for which antibiotics given

COMMENTS

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Date: |___||___||_____| Name: …… Signature: ……

HOVON 68 CLL

GENERAL COMMENTS FORM (14)

Instructions: Use this form for comments and other relevant information.
Send it to: HOVON Data Center, Erasmus MC – Daniel den Hoed, P.O.Box 5201, 3008 AE ROTTERDAM, The Netherlands.

Patient namecode: ……..... Hospital: …… Patient study number: |___|___|___|

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Date: |___||___||_____| Name: …… Signature: ……