

HOVON 68 CLL – CASE REPORT FORMS

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 Registration & Randomization Form (1) Treatment Form (4) Molecular Evaluation Form (8A and 8B) CT Scan Form (9) Adverse Event Form (12) Infection Form (13) | Item numbers added Item 48: question corrected (<i>and</i> replaces <i>or</i>) 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) PB sampling date added (item 4) Comment about total vs. gated percentage added Item 30: question corrected (<i>homology</i> replaces <i>mutations</i>) Item 81: specification other sites added Form number corrected on page 2 of 2 Reference to Treatment Form corrected Comment about hematological adverse events added Reference to Treatment Form corrected |
| 13.12.2005 | Adverse Event Form (12) Infection Form (13) | Items for SAE and relationship added Items for SAE and relationship added |
| 14.04.2008 | Registration & Randomization Form (1) Original Pathology form (2A) and Central Pathology form (2B) Response Evaluation form (5) Molecular Evaluation form (8A) and Central Molecular Evaluation form (8B) Off Treatment form (10) Follow up form (11) | Modification of telephone and fax number Addition of item 53, modification of item 40 Text 'Bone marrow biopsy' replaced by 'Blood smear' Deletion of items 9-12. 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' Addition of item 48 Item 6: label 4= 'nodular partial remission' replaced by label 10='CR with incomplete BM recovery' Addition of item 10 Item 7 and 23: label 4='nodular partial remission' replaced by label 10='CR with incomplete BM recovery' |

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: |__|__|__|

- 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 without alemtuzumab
2=Arm B: FC with alemtuzumab

Date: |__||__||____| Name: Signature:

HOVON 68 CLL

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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

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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:

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 [cm] 9 |__|__|. |__|
(by physical examination)
Largest diameter spleen..... [cm] 10 |__|__|. |__|
Liver size below costal margin..... [cm] 11 |__|__|. |__|
(by physical examination)
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:

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 | __ _ _ _ | <i>or</i> | [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 | __ _ _ _ | <i>or</i> | [mg/dl] | __ _ _ _ _ | 39 |
| Bilirubin Upper Limit of Normal | [μmol/l] | 40 | __ _ _ _ | <i>or</i> | [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:

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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.....
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Date: |__||__||__| Name: Signature:

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 [m²] 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) d1 (arm B cycles 2-6) | 14 __ __ __ [mg] | 15 __ | 16 __ |
| 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:

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 __ __ __ __ __ |

| | | |
|--|---|--|
| <p>(1)Technique 1=non-quant. PCR 2=quant. PCR</p> | <p>(2)Sensitivity 1=1/10¹ 2=1/10² 3=1/10³ 4=1/10⁴ 5=1/10⁵ 6=1/10⁶ 9=not assessable</p> | <p>(3)Result 0=negative 1=positive 2=significant increase 3=significant decrease 9=not assessable</p> |
|--|---|--|

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 __ __ _____ | | |
| <u>Or</u> 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:

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:

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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 [$\mu\text{mol/l}$] 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 [$\mu\text{mol/l}$] 29 |__|__| or [mg/dl] |__|. |__| 30

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

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

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

Date: |__||__||__| Name: Signature:

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:

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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:

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 [x10¹²/l] 6 |__|.|__|

Reticulocytes [%] 7 |__|_|_|.|__|

Platelets [x10⁹/l] 8 |__|_|_|_|

WBC [x10⁹/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

.....
.....
.....

Date: |__||__||____| Name: Signature:

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 __ __ __ % | CD19/lambda 13 __ __ __ % |
| CD3/CD8 10 __ __ __ % | CD19/CD38 14 __ __ __ gated % |
| CD5/CD19/CD23 11 __ __ __ % | CD19/ZAP-70 15 __ __ __ % |
| CD19/kappa 12 __ __ __ % | |

* 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:

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

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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 __ __ __ % | CD19/lambda 13 __ __ __ % |
| CD3/CD8 10 __ __ __ % | CD19/CD38 14 __ __ __ gated % |
| CD5/CD19/CD23 11 __ __ __ % | CD19/ZAP-70 15 __ __ __ % |
| CD19/kappa 12 __ __ __ % | |

* 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:

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.....
.....

Date: |__||__||____| Name: Signature:

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:

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

COMMENTS

.....

Date: |__||__||_____ Name: Signature:

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

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.....

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

Date: |__||__||____| Name: Signature:

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
 (most recent evaluation for this period) Evaluation Form (5) 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 incomplete 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:

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

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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 | | Relationship to protocol treatment** | | Specification | | | |
|-------|-------|-------------|------|-------|--------------------------------------|----|---------------|----|----|-------|
| | | | 0=no | 1=yes | | | | | | |
| 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 arrhythmia | 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

.....

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

Date: |__||__||____| Name: Signature:

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 | | Relationship to protocol treatment ⁽⁴⁾ | | Specification |
|-------------|---------------------|--------------------|-------------|--------|----------------------|--------|-------|---|--|---------------|
| | | | | | | 0=no | 1=yes | | | |
| 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 | 10= Fever e.c.i. ** |
| 2= Catheter | 11= Other |
| 3= Pulmonary | |
| 4= Ear/nose/throat | |
| 5= GI tract | |
| 6= Liver | |
| 7= GU tract | |
| 8= CNS | |
| 9= Skin/sub-cutaneous | |

(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

.....
.....

Date: |__||__||____| Name: Signature:

HOVON 68 CLL

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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: |_|_|_|_|_|

Area with horizontal dotted lines for writing general comments.

Date: |_|_|_|_|_| Name: Signature: