



UCCH Pathway

UCCH Guideline Chronic Myelogenous Leukemia

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Version Nov/2019

Guideline Chronic Myelogenous Leukemia

Version 03; Nov/2019

According to ELN recommendations 2013

Chronic Myelogenous Leukemia board members

P. Schafhausen, W. Fiedler, S. Janjetovic (Med. Oncology)

F. A. Ayuk (BMT)

A. Mohr (external cooperation partner)

C. Reimer (UCCH)

W. Fehrle, W. Wilczak (Pathology)

U. Göbel (patient representative UCCH)

Responsible author P. Schafhausen (Med. Oncology)

Implemented Nov/2015

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Legend of Colours



= Therapeutic procedure



= Clinical or diagnostic condition



= Diagnostic procedure



= Clinical trial



= Supportive measure



= Referral



= Tumorboard
(including post
tumorboard interaction
with patient that follows
the principles of shared
decision-making)

Work up

- History
- Physical examination
- Lab exam including CBC with differential
- Bone marrow aspirate and biopsy
- Cytogenetics (alternatively interphase FISH if cytogenetics cannot be obtained)
- Multiplex PCR (BCR-ABL)
- Real-time PCR (BCR-ABL^{IS})
- Consider fertility counseling
- Supportive:
 - Offer contact to self help group
 - Offer psychooncological support

- Leukocytosis¹ with granulocyte left shift
- Basophilia
- Facultative: Increased eosinophils, thrombocytosis, splenomegaly

- Philadelphia chromosome positive **and/or**
- BCR-ABL positive



Chronic phase CML (CP)

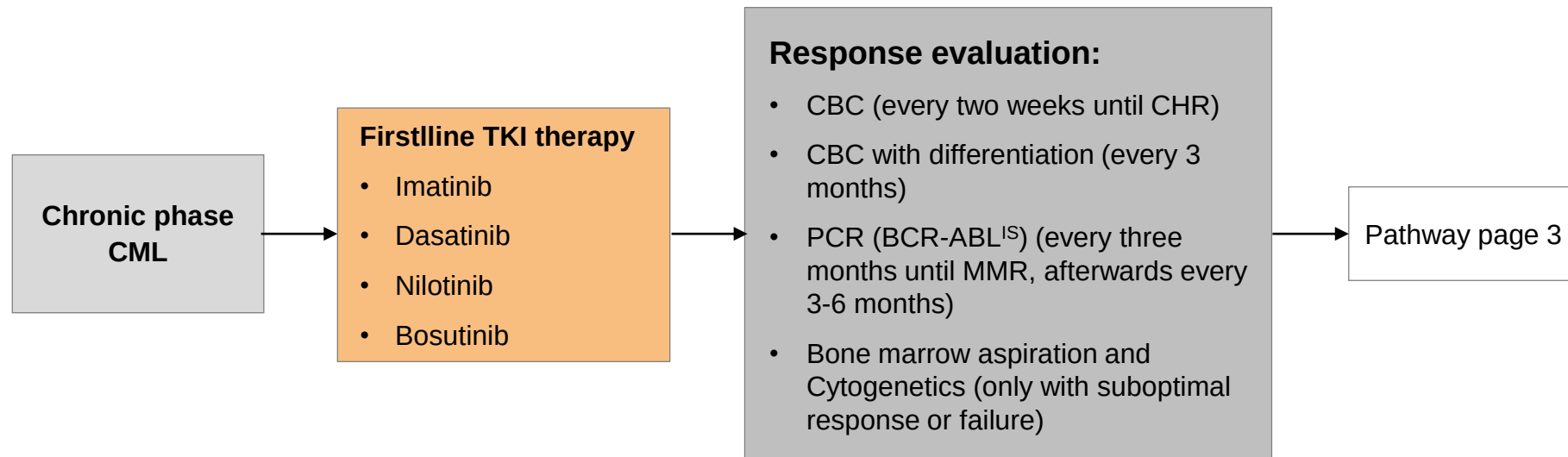
Pathway page 2/3

Accelerated phase (AP)/
Blast phase (BC)

Pathway page 4

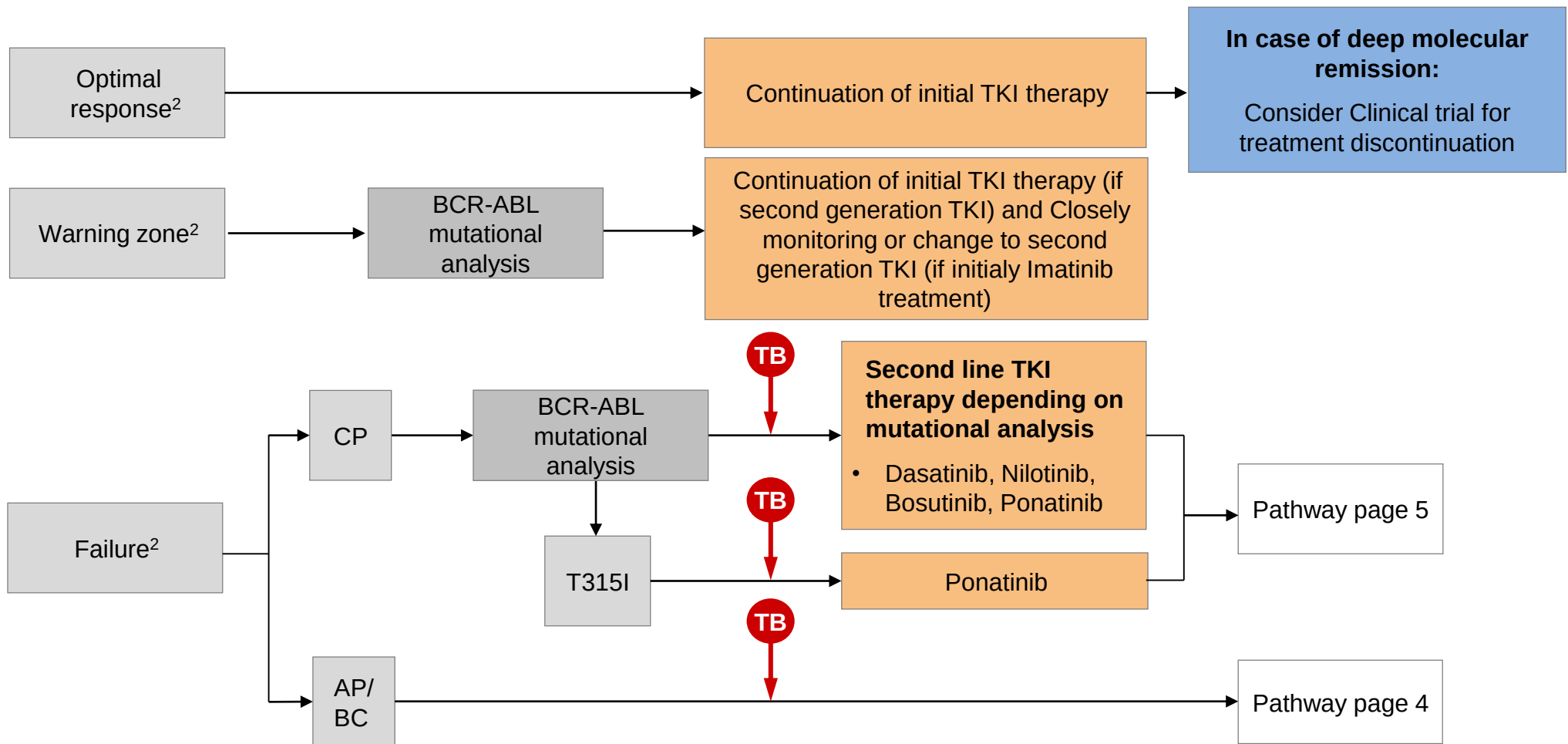
¹ Cyto-reductive therapy with hydroxyurea and/ or fluid replacement therapy if required. Consider furthermore urine alkalinization and leukocytapheresis in case of extreme leucocytosis (>150 nl), symptomatic leukostasis or massive splenomegalie

Pathway page 2: Chronic phase CML (CP)



TKI Tyrosine kinase inhibitors, CBC Complete blood count, CHR Complete hematological response, MMR Major molecular response, CCR Complete cytogenetic response

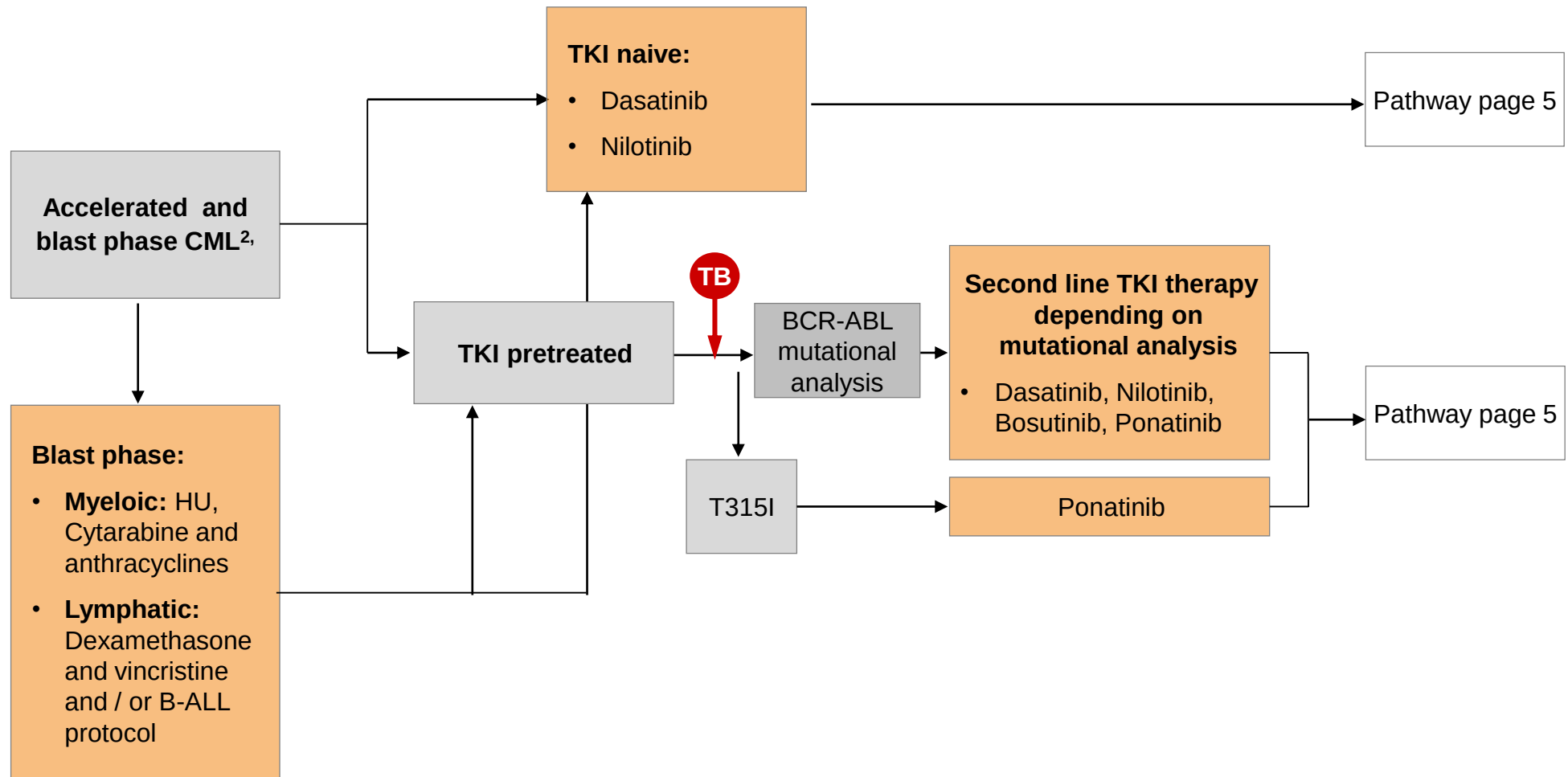
Pathway page 3: Chronic phase CML (CP)



CP Chronic phase, AP Accelerated phase, BC Blast phase, TKI Tyrosine kinase inhibitors

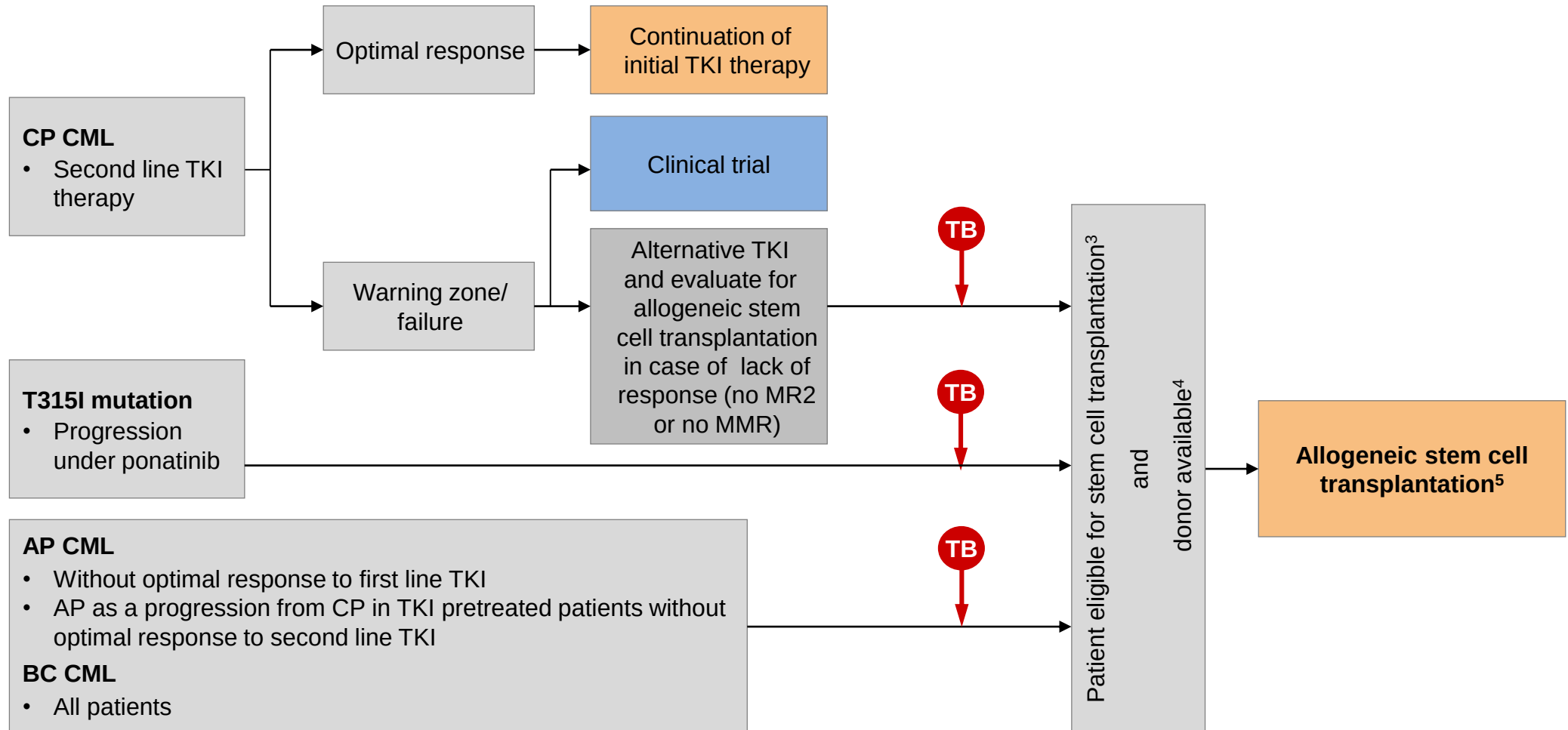
² See definition of response to TKI's as first line treatment on page 6

Pathway page 4: Accelerated phase (AP) and Blast phase (BP) CML



² Transfusion of erythrocytes or thrombocytes in case of symptomatic anemia or thrombocytopenia

Pathway page 5: Allogeneic stem cell transplantation



³ Patient suitable for allogeneic stem cell transplantation concerning age and health situation

⁴ HLA type patient and siblings, search for an unrelated stem cell donor

⁵ Offer contact to self help group in case of stem cell transplantation

Page 6: Definition of the response to TKI's as first line treatment

	Optimal	Warning	Failure
Baseline	NA	High risk or CCA/Ph+, major route	NA
3 mo	BCR-ABL1 $\leq 10\%$ and/or Ph+ $\leq 35\%$	BCR-ABL1 $> 10\%$ and/or Ph+ 36-95%	Non-CHR and/or Ph+ $> 95\%$
6 mo	BCR-ABL1 $< 1\%$ and/or Ph+ 0	BCR-ABL1 1-10% and/or Ph+ 1-35%	BCR-ABL1 $> 10\%$ and/or Ph+ $> 35\%$
12 mo	BCR-ABL1 $\leq 0.1\%$	BCR-ABL1 $> 0.1-1\%$	BCR-ABL1 $> 1\%$ and/or Ph+ > 0
Afterwards	BCR-ABL1 $\leq 0.1\%$	CCA/Ph- (-7, or 7q-)	Loss of CHR Loss of CCR Confirmed loss of MMR Mutations CCA/Ph+

NA Not Applicable, CHR Complete hematological response, MMR Major molecular response, CCR Complete cytogenetic response, CCA Clonal Chromosome Abnormalities

According to Baccarani et al: European LeukemiaNET recommendations for the management of chronic myeloid leukemia: 2013. Blood, August 2013, Volume 122, Number 6

Page 7: Definition of molecular response

Molecular response	BCR-ABL ^{IS}
MR2	$\leq 1\%$
MR 3 / MMR	$\leq 0,1\%$
MR 4	Detectable disease BCR-ABL ^{IS} $\leq 0,01\%$ Undetectable disease cDNA with ≥ 10.000 ABL or ≥ 24.000 GUSB transcripts
MR 4,5	Detectable disease BCR-ABL ^{IS} $\leq 0,0032\%$ Undetectable disease cDNA with ≥ 32.000 ABL or ≥ 77.000 GUSB transcripts
MR 5	Detectable disease BCR-ABL ^{IS} $\leq 0,001\%$ Undetectable disease cDNA with ≥ 100.000 ABL or ≥ 240.000 GUSB transcripts

MMR Major molecular response

DMR = deep molecular remission = $\geq$ MR 4

According to Baccarani et al: European LeukemiaNET recommendations for the management of chronic myeloid leukemia: 2013. Blood, August 2013, Volume 122, Number 6

Cross et al: Standardized definitions of molecular response in chronic myeloid leukemia. Leukemia, Volume 26, pages 2172-2175