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Tel: 02-2875-7449

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Sample Information

Patient Name: 董來恩 Gender: Male ID No.: A128114320 History No.: 47911626

Age: 39

Ordering Doctor: DOC4205A 柯博伸

Ordering REQ.: 0CAGEPM Signing in Date: 2022/09/27

Path No.: S111-97909 **MP No.:** MY22028

Assay: Oncomine Myeloid Assay

Sample Type: Blood

Date of blood drawing: 2022/09/21

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Blast Phase Chronic Myeloid Leukemia

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Relevant Blast Phase Chronic Myeloid Leukemia Variants

Gene	Finding
ABL1	ABL1 p.(T315I) c.944C>T, BCR-ABL1 fusion, ABL1 p.(Q252H) c.756G>C

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	ABL1 p.(T315I) c.944C>T ABL proto-oncogene 1, non-receptor tyrosine kinase Allele Frequency: 63.16% Prognostic significance: NCCN: Poo	ponatinib ^{1, 2}	asciminib ¹ ponatinib ^{1, 2} allogeneic stem cells omacetaxine	0
IA	BCR-ABL1 fusion BCR activator of RhoGEF and GTPase - ABL proto-oncogene 1, non-receptor tyrosine kinase		asciminib 1 dasatinib + chemotherapy 1, 2 imatinib*2 imatinib* + chemotherapy 2 ponatinib 1, 2 allogeneic stem cells azacitidine blinatumomab bosutinib + chemotherapy bosutinib + inotuzumab ozogamicin brexucabtagene autoleucel cytarabine cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin cytarabine + mitoxantrone dasatinib dasatinib + inotuzumab ozogamicin decitabine gemtuzumab ozogamicin + chemotherapy imatinib + inotuzumab ozogamicin inotuzumab ozogamicin + nilotinib inotuzumab ozogamicin + nilotinib nilotinib nilotinib + chemotherapy ponatinib + chemotherapy tisagenlecleucel-t venetoclax + chemotherapy	0
	Diagnostic significance: Chronic My		None	0
IA	ABL1 p.(Q252H) c.756G>C ABL proto-oncogene 1, non-receptor tyrosine kinase Allele Frequency: 28.16% Prognostic significance: NCCN: Poo	None	None	0
Public * Inclu	data sources included in relevant therapies: FDA1, N data sources included in prognostic and diagnostic des biosimilars	significance: NCCN, ESMO		
•	werrs informed by bublic data sources: 🗸	Contrainidicated, V Resistance		

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Prevalent cancer biomarkers without relevant evidence based on included data sources $KRAS\ p.(G12A)\ c.35G>C$

Variant Details

DNA	A Sequence vari	ants						
Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ABL1	p.(Q252H)	c.756G>C	COSM12609	chr9:133738356	28.16%	NM_005157.6	missense	1999
ABL1	p.(T315I)	c.944C>T	COSM12560	chr9:133748283	63.16%	NM_005157.6	missense	1998
KRAS	p.(G12A)	c.35G>C	COSM522	chr12:25398284	3.41%	NM_033360.4	missense	1996
IDH1	p.(G105=)	c.315C>T		chr2:209113192	45.62%	NM_005896.3	synonymous	1999
CALR	p.(K368del)	c.1102_1104delAAG		chr19:13054574	3.41%	NM_004343.4	nonframeshift Deletion	1995

Gene Fusions (R	NA)		
Genes	Variant ID	Locus	Read Count
BCR-ABL1	BCR-ABL1.B14A2.1	chr22:23632600 - chr9:133729451	14193

Biomarker Descriptions

ABL1 (ABL proto-oncogene 1, non-receptor tyrosine kinase)

Background: The ABL1 proto-oncogene encodes the ABL1 non-receptor tyrosine kinase, a member of the ABL family which also includes ABL2¹. Based on its cellular localization (cytoplasmic or nuclear), ABL1 regulates various cellular functions, including cell growth, adhesion, survival, invasion, or migration²³. ABL1 is most extensively studied in hematological malignancies, where constitutive activation of the ABL1 gene is associated with Philadelphia chromosome (Ph+) leukemias. Ph+ (also denoted as t(9;22) (q34;q11)) is a translocation event involving rearrangement of the kinase domain of ABL1 on chromosome 9 with the promoter region of the partner gene BCR on chromosome 22².

Alterations and prevalence: BCR-ABL1 fusions are reported in more than 90% of chronic myeloid leukemia (CML) cases, 25-35% of adult acute lymphoblastic leukemia (ALL) cases, and 3-5% of childhood ALL cases^{4,5,6,7}. Other known fusion partners in hematological cancers include NUP214, ETV6, and EML1^{2,5}. Somatic missense mutations such as E255K/V, F317C/I/L/V, F359C/I/V, G250E, T315A/I, V299L, and Y253H are observed in the kinase domain of the BCR-ABL1 fusion, and are associated with resistance to first-generation tyrosine kinase inhibitors (TKI). In comparison to hematological cancer, ABL1 alterations (including somatic mutations and amplification) occur rarely in solid tumors².

Potential relevance: The BCR-ABL1 fusion is a diagnostic marker for Ph+/BCR-ABL1 CML8. Secondary mutations in the kinase domain (KD) of the BCR-ABL1 fusion are associated with poor prognosis, as they confer resistance to various first- or second-line TKls8. Several targeted TKls are approved by the FDA for activated BCR-ABL1, primarily in hematological cancers. These include imatinib9 (2001), dasatinib¹0 (2006), and ponatinib¹¹ (2012) in CML and ALL, as well as nilotinib¹² (2007) and bosutinib¹³ (2012) in CML. While imatinib is recommended as a first-line TKI for BCR-ABL1 fusion, variant-specific TKIs for KD mutations include nilotinib for T315I, Y253H, E255K/V, or F359V/C/I; dasatinib for F317C/I/L/V, T315I/A, or V299L; and bosutinib for T315I, V299L, G250E, or F317L CML8. Ponatinib is approved for T315I CML and ALL, as the mutation confers resistance to imatinib, dasatinib, nilotinib, and bosutinib8. The ABL myristoyl pocket (STAMP) inhibitor, asciminib, has also been approved (2021) for adults with BCR-ABL1 T315I mutated Philadelphia-chromosome positive (Ph+) chronic myeloid leukemia (CML) in chronic phase¹4.

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Biomarker Descriptions (continued)

KRAS (KRAS proto-oncogene, GTPase)

<u>Background:</u> The KRAS proto-oncogene encodes a GTPase that functions in signal transduction and is a member of the RAS superfamily which also includes NRAS and HRAS. RAS proteins mediate the transmission of growth signals from the cell surface to the nucleus via the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways, which regulate cell division, differentiation, and survival^{15,16,17}.

Alterations and prevalence: Recurrent mutations in RAS oncogenes cause constitutive activation and are found in 20-30% of cancers. KRAS mutations are observed in up to 10-20% of uterine cancer, 30-35% of lung adenocarcinoma and colorectal cancer, and about 60% of pancreatic cancer¹⁸. The majority of KRAS mutations consist of point mutations occurring at G12, G13, and Q61^{18,19,20}. Mutations at A59, K117, and A146 have also been observed but are less frequent^{21,22}.

Potential relevance: The KRAS inhibitor, sotorasib²³, is approved (2021) for the treatment of adult patients with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC). The FDA has granted breakthrough therapy designation (2021) to the small molecule inhibitor, adagrasib, for KRAS G12C positive in non-small cell lung cancer following prior systemic therapy²⁴. The small molecular inhibitor, RO-5126766, was also granted breakthrough designation (2021) alone for KRAS G12V mutant non-small cell lung cancer or in combination with defactinib, for KRAS mutant endometrial carcinoma and KRAS G12V mutant non-small cell lung cancer²⁵. Additionally, onvansertib²⁶ was granted fast track designation (2020) for second-line treatment of patients with KRAS-mutated metastatic colorectal cancer (mCRC). The EGFR antagonists, cetuximab²⁷ and panitumumab²⁸, are contraindicated for treatment of colorectal cancer patients with KRAS mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146)²². Additionally, KRAS mutations are associated with poor prognosis in NSCLC²⁹.

Relevant Therapy Summary

■ In this cancer type	In this cancer	type and other can	cer types	X No evidend	ce
ABL1 p.(T315I) c.944C>T					
Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
ponatinib	•	0	•	0	×
asciminib	0	0	×	×	×
omacetaxine	×	0	×	×	×
allogeneic stem cells	×	×	×	0	×
BCR-ABL1 fusion					
Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
Relevant Therapy dasatinib + chemotherapy	FDA O	NCCN	ЕМА	ESMO	Clinical Trials*
dasatinib + chemotherapy	0	0	0	×	×
dasatinib + chemotherapy ponatinib	0	0	0	×	×
dasatinib + chemotherapy ponatinib asciminib	0 0	0 0 x	O O X	×	×
dasatinib + chemotherapy ponatinib asciminib imatinib + chemotherapy	0 0 0 *	0 0 x 0	0 0 × 0	× × ×	X X X
dasatinib + chemotherapy ponatinib asciminib imatinib + chemotherapy Allogeneic hematopoietic stem cell transplantation	0 0 0 × ×	0 0 x 0	O O X	× × × ×	X X X X

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Relevant Therapy Summary (continued)

■ In this cancer type
O In other cancer type
In this cancer type and other cancer types
X No evidence

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
bosutinib + blinatumomab	×	0	×	×	×
bosutinib + chemotherapy	×	0	×	×	×
bosutinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone	×	0	×	×	×
bosutinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone	×	0	×	×	×
bosutinib + cytarabine + HyperCVAD	×	0	×	×	×
bosutinib + cytarabine + HyperCVAD + methotrexate	×	0	×	×	×
bosutinib + inotuzumab ozogamicin	×	0	×	×	×
bosutinib + steroid	×	0	×	×	×
bosutinib + vincristine + dexamethasone	×	0	×	×	×
brexucabtagene autoleucel	×	0	×	×	×
cytarabine	×	0	×	×	×
cytarabine + daunorubicin	×	0	×	×	×
cytarabine + daunorubicin + etoposide	×	0	×	×	×
cytarabine + etoposide + idarubicin	×	0	×	×	×
cytarabine + fludarabine + idarubicin + filgrastim	×	0	×	×	×
cytarabine + idarubicin	×	0	×	×	×
cytarabine + mitoxantrone	×	0	×	×	×
dasatinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone	×	0	×	×	×
dasatinib + blinatumomab	×	0	×	×	×
dasatinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone	×	0	×	×	×
dasatinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone	×	0	×	×	×
dasatinib + cytarabine + HyperCVAD	×	0	×	×	×
dasatinib + cytarabine + HyperCVAD + methotrexate	×	0	×	×	×
dasatinib + inotuzumab ozogamicin	×	0	×	×	×
dasatinib + steroid	×	0	×	×	×

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Relevant Therapy Summary (continued)

■ In this cancer type
O In other cancer type
O In this cancer type and other cancer types
X No evidence

0 0 0 0 0	* * * * * * * * * * * * * * * * *	× × × × × × × ×	*
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Relevant Therapy Summary (continued)

■ In this cancer type
O In other cancer type
O In this cancer type and other cancer types
X No evidence

BCR-ABL1 fusion (continued)					
Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials
ponatinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone	×	0	×	×	×
ponatinib + blinatumomab	×	0	×	×	×
ponatinib + chemotherapy	×	0	×	×	×
ponatinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone	×	0	×	×	×
ponatinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone	×	0	×	×	×
ponatinib + cytarabine + HyperCVAD	×	0	×	×	×
ponatinib + cytarabine + HyperCVAD + methotrexate	×	0	×	×	×
ponatinib + steroid	×	0	×	×	×
ponatinib + vincristine + dexamethasone	×	0	×	×	×
tisagenlecleucel-t	×	0	×	×	×
venetoclax + azacitidine	×	0	×	×	×
venetoclax + cytarabine	×	0	×	×	×
venetoclax + decitabine	×	0	×	×	×
imatinib (Accord)	×	×	•	×	×
imatinib (Accord) + chemotherapy	×	×	•	×	×
imatinib (Koanaa)	×	×	•	×	×
imatinib (Koanaa) + chemotherapy	×	×	•	×	×
interferon alpha-2b	×	×	•	×	×

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Relevant Therapy Details

Current FDA Information

In this cancer type

O In other cancer type

In this cancer type and other cancer types

FDA information is current as of 2022-08-17. For the most up-to-date information, search www.fda.gov.

ABL1 p.(T315I) c.944C>T

ponatinib

Cancer type: Accelerated Phase Chronic Myeloid Leukemia, Acute Lymphoblastic Leukemia, Blast Phase Chronic Myeloid Leukemia, Chronic Phase Chronic Myeloid Leukemia Label as of: 2022-02-15 Variant class: BCR-ABL1 T315I mutation

Indications and usage:

ICLUSIG® is a kinase inhibitor indicated for the treatment of adult patients with:

- Chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors.
- Accelerated phase (AP) or blast phase (BP) CML or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other kinase inhibitors are indicated.
- T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL.

Limitations of Use: ICLUSIG® is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CML.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/203469s035lbl.pdf

asciminib

Cancer type: Chronic Phase Chronic Myeloid Label as of: 2021-10-29 Leukemia

Variant class: BCR-ABL1 T315I mutation

Indications and usage:

SCEMBLIX® is a kinase inhibitor indicated for the treatment of adult patients with:

- Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs). This indication is approved under accelerated approval based on major molecular response (MMR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Ph+ CML in CP with the T315I mutation.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215358s0000rig2lbl.pdf

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BCR-ABL1 fusion

O asciminib

Cancer type: Chronic Phase Chronic Myeloid Label as of: 2021-10-29 Leukemia

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Indications and usage:

SCEMBLIX® is a kinase inhibitor indicated for the treatment of adult patients with:

- Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP), previously treated with two or more tyrosine kinase inhibitors (TKIs). This indication is approved under accelerated approval based on major molecular response (MMR). Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Ph+ CML in CP with the T315I mutation.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/215358s0000rig2lbl.pdf

O dasatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2021-06-29

Variant class: BCR-ABL1 fusion [t(9;22) (g34;q11)]

Indications and usage:

SPRYCEL® is a kinase inhibitor indicated for the treatment of

- newly diagnosed adults with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) in chronic phase.
- adults with chronic, accelerated, or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib.
- adults with Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) with resistance or intolerance to prior therapy.
- pediatric patients 1 year of age and older with Ph+ CML in chronic phase.
- pediatric patients 1 year of age and older with newly diagnosed Ph+ ALL in combination with chemotherapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/021986s025lbl.pdf

O ponatinib

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2022-02-15

Variant class: BCR-ABL1 fusion [t(9;22) (q34;q11)]

Indications and usage:

ICLUSIG® is a kinase inhibitor indicated for the treatment of adult patients with:

- Chronic phase (CP) chronic myeloid leukemia (CML) with resistance or intolerance to at least two prior kinase inhibitors.
- Accelerated phase (AP) or blast phase (BP) CML or Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) for whom no other kinase inhibitors are indicated.
- T315I-positive CML (chronic phase, accelerated phase, or blast phase) or T315I-positive Ph+ ALL.

Limitations of Use: ICLUSIG® is not indicated and is not recommended for the treatment of patients with newly diagnosed CP-CMI

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/203469s035lbl.pdf

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Current NCCN Information

In this cancer type

O In other cancer type

In this cancer type and other cancer types

Variant class: BCR-ABL1 T315I mutation

Variant class: BCR-ABL1 T315I mutation

NCCN information is current as of 2022-08-01. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ABL1 p.(T315I) c.944C>T

ponatinib

Cancer type: Chronic Myeloid Leukemia, Chronic Variant class: BCR-ABL1 T315I mutation

Phase Chronic Myeloid Leukemia

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Resistant (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

O asciminib

Cancer type: Chronic Phase Chronic Myeloid

Leukemia

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Resistant (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

O omacetaxine

Cancer type: Chronic Phase Chronic Myeloid

Leukemia

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Resistant (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

O ponatinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 T315I mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion

O cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 1

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 1

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 1

Population segment (Line of therapy):

■ (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 1

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

Allogeneic hematopoietic stem cell transplantation

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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BCR-ABL1 fusion (continued)

O blinatumomab

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

bosutinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + blinatumomab

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

 bosutinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Refractory, Relapsed (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + cytarabine + HyperCVAD

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + cytarabine + HyperCVAD + methotrexate

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O bosutinib + inotuzumab ozogamicin

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + steroid

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O bosutinib + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O brexucabtagene autoleucel

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O cytarabine

Cancer type: Acute Myeloid Leukemia Variant cla

Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

cytarabine + mitoxantrone

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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BCR-ABL1 fusion (continued)

O dasatinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + blinatumomab

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Refractory, Relapsed (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O dasatinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + cytarabine + HyperCVAD

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + cytarabine + HyperCVAD + methotrexate

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + inotuzumab ozogamicin

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O dasatinib + steroid

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O dasatinib + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O decitabine

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O gemtuzumab ozogamicin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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BCR-ABL1 fusion (continued)

O imatinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O imatinib + blinatumomab

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

imatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

imatinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Refractory, Relapsed (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O imatinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O imatinib + cytarabine + HyperCVAD

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

imatinib + cytarabine + HyperCVAD + methotrexate

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O imatinib + inotuzumab ozogamicin

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O imatinib + steroid

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell (Induction therapy); Other recommended intervention

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O imatinib + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell (Induction therapy); Other recommended intervention

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O inotuzumab ozogamicin

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O inotuzumab ozogamicin + nilotinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O inotuzumab ozogamicin + ponatinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O nilotinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O nilotinib + blinatumomab

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell (Induction therapy); Other recommended intervention

■ B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O nilotinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

 nilotinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Refractory, Relapsed (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O nilotinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O nilotinib + cytarabine + HyperCVAD

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

nilotinib + cytarabine + HyperCVAD + methotrexate

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O nilotinib + steroid

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell (Induction therapy); Other recommended intervention

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O nilotinib + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib

Cancer type: Accelerated Phase Chronic Myeloid Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

Leukemia

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

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BCR-ABL1 fusion (continued)

O ponatinib + asparaginase + cytarabine + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib + blinatumomab

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

ponatinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Refractory, Relapsed (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O ponatinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib + cytarabine + HyperCVAD

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib + cytarabine + HyperCVAD + methotrexate

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O ponatinib + steroid

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- B-cell (Induction therapy); Other recommended intervention
- B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

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BCR-ABL1 fusion (continued)

O ponatinib + vincristine + dexamethasone

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

B-cell (Induction therapy); Other recommended intervention

B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O tisagenlecleucel-t

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

■ B-cell; Relapsed, Refractory (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

O venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Population segment (Line of therapy):

(Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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BCR-ABL1 fusion (continued)

O azacitidine

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2B

Population segment (Line of therapy):

(Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2B

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2B

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2B

Population segment (Line of therapy):

(Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

O ponatinib

Cancer type: Myeloid/Lymphoid Neoplasms with Variant class: ABL1 fusion

Eosinophilia

NCCN Recommendation category: 2A

Population segment (Line of therapy):

Chronic Phase, Blast Phase (Line of therapy not specified); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Fusion Genes [Version 1.2022]

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Current EMA Information

In this cancer type

O In other cancer type

In this cancer type and other cancer types

EMA information is current as of 2022-08-17. For the most up-to-date information, search www.ema.europa.eu/ema.

ABL1 p.(T315I) c.944C>T

ponatinib

Cancer type: Accelerated Phase Chronic Myeloid Leukemia, Acute Lymphoblastic Leukemia, Blast Phase Chronic Myeloid Leukemia, Chronic Phase Chronic Myeloid Leukemia Label as of: 2022-05-11

Variant class: BCR-ABL1 T315I mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/iclusig-epar-product-information_en.pdf

BCR-ABL1 fusion

imatinib (Accord), imatinib (Accord) + chemotherapy

Cancer type: Accelerated Phase Chronic Myeloid Leukemia, Acute Lymphoblastic Leukemia, Blast Phase Chronic Myeloid Leukemia, Chronic Myeloid Leukemia, Chronic Phase Chronic Myeloid Leukemia Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

https://www.ema.europa.eu/en/documents/product-information/imatinib-accord-epar-product-information_en.pdf

Label as of: 2022-06-23

imatinib (Koanaa), imatinib (Koanaa) + chemotherapy

Cancer type: Accelerated Phase Chronic Myeloid Leukemia, Acute Lymphoblastic Leukemia, Blast Phase Chronic Myeloid Leukemia, Chronic Myeloid Leukemia, Chronic

Label as of: 2021-10-01

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Phase Chronic Myeloid Leukemia

Reference:

https://www.ema.europa.eu/en/documents/product-information/imatinib-koanaa-epar-product-information_en.pdf

interferon alpha-2b

Cancer type: Chronic Myeloid Leukemia Label as of: 2021-07-06 Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

https://www.ema.europa.eu/en/documents/product-information/introna-epar-product-information_en.pdf

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BCR-ABL1 fusion (continued)

O dasatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2022-06-10

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

https://www.ema.europa.eu/en/documents/product-information/dasatinib-accord-epar-product-information_en.pdf

O dasatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2022-06-17

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

 $https://www.ema.europa.eu/en/documents/product-information/sprycel-epar-product-information_en.pdf \\$

O imatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2022-06-09

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

https://www.ema.europa.eu/en/documents/product-information/imatinib-teva-epar-product-information_en.pdf

imatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2022-04-05

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

https://www.ema.europa.eu/en/documents/product-information/glivec-epar-product-information_en.pdf

O ponatinib

Cancer type: Acute Lymphoblastic Leukemia Label as of: 2022-05-11

Variant class: BCR-ABL1 fusion [t(9;22)

(q34;q11)]

Reference:

 $https://www.ema.europa.eu/en/documents/product-information/iclusig-epar-product-information_en.pdf$

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Current ESMO Information

In this cancer type In other cancer type

In this cancer type and other cancer types

ESMO information is current as of 2022-08-01. For the most up-to-date information, search www.esmo.org.

ABL1 p.(T315I) c.944C>T

O ponatinib

Cancer type: Chronic Phase Chronic Myeloid

Variant class: BCR-ABL1 T315I mutation

Leukemia

ESMO Level of Evidence/Grade of Recommendation: V / A

Population segment (Line of therapy):

Resistant, Refractory (First-line therapy, Second-line therapy, Third-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51. (Corrigendum: 03 October 2018)]

O allogeneic stem cells

Cancer type: Chronic Phase Chronic Myeloid Variant class: BCR-ABL1 T315I mutation

Leukemia

ESMO Level of Evidence/Grade of Recommendation: V / B

Population segment (Line of therapy):

Resistant, Refractory (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51. (Corrigendum: 03 October 2018)]

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Prognostic Details

Current NCCN Information

NCCN information is current as of 2022-08-01. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ABL1 p.(T315I) c.944C>T

Prognostic significance: NCCN: Poor

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 KD mutation

NCCN Recommendation category: 2A

Summary:

Point mutations in the BCR-ABL1 kinase domain are a frequent mechanism of secondary resistance to TKI therapy and are associated with poor prognosis and higher risk of disease progression.

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

ABL1 p.(Q252H) c.756G>C

Prognostic significance: NCCN: Poor

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 KD mutation

NCCN Recommendation category: 2A

Summary:

 Point mutations in the BCR-ABL1 kinase domain are a frequent mechanism of secondary resistance to TKI therapy and are associated with poor prognosis and higher risk of disease progression.

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

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Diagnostic Details

Current NCCN Information

NCCN information is current as of 2022-08-01. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

BCR-ABL1 fusion

Diagnostic significance: Chronic Myeloid Leukemia

Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

NCCN Recommendation category: 2A

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

Current ESMO Information

ESMO information is current as of 2022-08-01. For the most up-to-date information, search www.esmo.org.

BCR-ABL1 fusion

Diagnostic significance: Chronic Myeloid Leukemia

Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)]

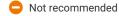
Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51.

(Corrigendum: 03 October 2018)]

Alerts Informed By Public Data Sources

Current NCCN Information











NCCN information is current as of 2022-08-01. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

ABL1 p.(T315I) c.944C>T

bosutinib

Cancer type: Accelerated Phase Chronic Myeloid
Leukemia, Blast Phase Chronic Myeloid Leukemia,
Chronic Phase Chronic Myeloid Leukemia

Variant class: BCR-ABL1 T315I mutation
Leukemia, Blast Phase Chronic Myeloid Leukemia

Summary:

NCCN Guidelines® include the following supporting statement(s):

"BCR-ABL1 mutations that should NOT be treated with bosutinib, dasatinib or nilotinib in the second-line setting."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

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ABL1 p.(T315I) c.944C>T (continued)

dasatinib

Cancer type: Accelerated Phase Chronic Myeloid
Leukemia, Blast Phase Chronic Myeloid Leukemia,
Chronic Phase Chronic Myeloid Leukemia

Variant class: BCR-ABL1 T315I mutation
Leukemia,
Chronic Phase Chronic Myeloid Leukemia

Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "BCR-ABL1 mutations that should NOT be treated with bosutinib, dasatinib or nilotinib in the second-line setting."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

nilotinib

Cancer type: Accelerated Phase Chronic Myeloid
Leukemia, Blast Phase Chronic Myeloid Leukemia,
Chronic Phase Chronic Myeloid Leukemia

Variant class: BCR-ABL1 T315I mutation
Leukemia,
Chronic Phase Chronic Myeloid Leukemia

Summary:

NCCN Guidelines® include the following supporting statement(s):

"BCR-ABL1 mutations that should NOT be treated with bosutinib, dasatinib or nilotinib in the second-line setting."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

bosutinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Treatment options based on BCR-ABL1 mutation profile."

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

dasatinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "Treatment options based on BCR-ABL1 mutation profile."

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2022]

nilotinib

Cancer type: Acute Lymphoblastic Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

■ "Treatment options based on BCR-ABL1 mutation profile."

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ABL1 p.(T315I) c.944C>T (continued)

bosutinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Among the BCR-ABL1 kinase domain mutations, T315I confers the complete resistance to imatinib, dasatinib, nilotinib, and bosutinib."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

dasatinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Among the BCR-ABL1 kinase domain mutations, T315I confers the complete resistance to imatinib, dasatinib, nilotinib, and bosutinib."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

imatinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Among the BCR-ABL1 kinase domain mutations, T315I confers the complete resistance to imatinib, dasatinib, nilotinib, and bosutinib."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

nilotinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Among the BCR-ABL1 kinase domain mutations, T315I confers the complete resistance to imatinib, dasatinib, nilotinib, and bosutinib."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

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BCR-ABL1 fusion

imatinib

Cancer type: Accelerated Phase Chronic Myeloid Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)] Leukemia

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Imatinib is not recommended for patients with disease progression on prior TKI therapy."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

omacetaxine

Cancer type: Accelerated Phase Chronic Myeloid Variant class: BCR-ABL1 fusion [t(9;22)(q34;q11)] Leukemia

Summary:

NCCN Guidelines® include the following supporting statement(s):

"Omacetaxine is not a treatment option for patients who present with accelerated phase CML."

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 3.2022]

Current ESMO Information

Contraindicated









ESMO information is current as of 2022-08-01. For the most up-to-date information, search www.esmo.org.

ABL1 p.(T315I) c.944C>T

bosutinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

■ "T315I is resistant to all TKIs except ponatinib."

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51. (Corrigendum: 03 October 2018)]

dasatinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

■ "T315I is resistant to all TKIs except ponatinib."

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51. (Corrigendum: 03 October 2018)]

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ABL1 p.(T315I) c.944C>T (continued)

imatinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

■ "T315I is resistant to all TKIs except ponatinib."

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51.

(Corrigendum: 03 October 2018)]

nilotinib

Cancer type: Chronic Myeloid Leukemia Variant class: BCR-ABL1 T315I mutation

Summary:

ESMO Clinical Practice Guidelines include the following supporting statement:

■ "T315I is resistant to all TKIs except ponatinib."

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Myeloid Leukemia [Ann Oncol (2017) 28 (suppl 4): iv41-iv51.

(Corrigendum: 03 October 2018)]

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Signature	S
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Testing Personnel:

Laboratory Supervisor:

Pathologist:

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