



Sample Information

Patient Name: 李玠霖
Gender: Male
ID No.: M122142615
History No.: 44097952
Age: 37

Ordering Doctor: DOC1751J 蕭樑材
Ordering REQ.: 0CQENXB
Signing in Date: 2023/08/31

Path No.: M112-00242
MP No.: MY23066
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/08/25

Reporting Doctor: DOC5444B 楊靜芬 (Phone: 8#5444)

Note:

Sample Cancer Type: Acute Myeloid Leukemia

Table of Contents	Page	Report Highlights
Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)	2	2 Relevant Biomarkers
Biomarker Descriptions	2	37 Therapies Available
Relevant Therapy Summary	4	0 Clinical Trials
Relevant Therapy Details	8	
Alert Details	43	

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	BCR::ABL1 fusion BCR activator of RhoGEF and GTPase - ABL proto-oncogene 1, non-receptor tyrosine kinase	allogeneic stem cells azacitidine cytarabine cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim cytarabine + idarubicin cytarabine + mitoxantrone dasatinib decitabine imatinib	asciminib ^{1,2} bosutinib ^{1,2} dasatinib ^{1,2} dasatinib + chemotherapy ² imatinib* ^{1,2} imatinib* + chemotherapy ² nilotinib ^{1,2} ponatinib ^{1,2} asciminib + chemotherapy blinatumomab bosutinib + chemotherapy bosutinib + inotuzumab ozogamicin brexucabtagene autoleucel dasatinib + inotuzumab ozogamicin	0

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO
* Includes biosimilars/generics

Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
		liposomal cytarabine-daunorubicin CPX-351 nilotinib venetoclax + chemotherapy	imatinib + inotuzumab ozogamicin inotuzumab ozogamicin inotuzumab ozogamicin + nilotinib inotuzumab ozogamicin + ponatinib nilotinib + chemotherapy ponatinib + chemotherapy tisagenlecleucel-t	
IA	RUNX1 p.(R166Q) c.497G>A RUNX family transcription factor 1 Allele Frequency: 44.10%	allogeneic stem cells azacitidine cytarabine cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim cytarabine + idarubicin cytarabine + mitoxantrone decitabine liposomal cytarabine-daunorubicin CPX-351 venetoclax + chemotherapy	None	0

Public data sources included in relevant therapies: FDA¹, NCCN, EMA², ESMO

* Includes biosimilars/generics

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
RUNX1	p.(R166Q)	c.497G>A	COSM36055	chr21:36252865	44.10%	NM_001754.4	missense	2000

Gene Fusions (RNA)

Genes	Variant ID	Locus	Read Count
BCR-ABL1	BCR-ABL1.B14A2.1	chr22:23632600 - chr9:133729451	16298

Biomarker Descriptions

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

Background: The ABL1 proto-oncogene encodes the ABL1 non-receptor tyrosine kinase¹. ABL1 is a member of the Abelson (ABL) family of non-receptor tyrosine kinases that shares 90% homology with its paralog ABL2². Based on its cellular localization (cytoplasmic or nuclear), ABL1 regulates various cellular functions, including cell growth, adhesion, survival, invasion, or migration^{3,4}. 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 resulting in the fusion of the BCR promoter region on chromosome 22 with the ABL1 kinase domain on chromosome 9, which leads to unregulated tyrosine kinase activity of ABL1 and contributes to the immortality of leukemic cells^{2,3,5,6}.

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^{7,8,9,10}. Other known fusion partners in hematological cancers include NUP214, ETV6, and EML1^{3,8}. Somatic missense mutations such as E255K/V, F317C/I/L/V, F359C/I/V, G250E, T315A/I, V299L, A337T, P465S and Y253H are observed in the kinase domain of the BCR-ABL1 fusion, and are associated with resistance

Biomarker Descriptions (continued)

to first-generation and second generation tyrosine kinase inhibitors (TKI). In comparison to hematological cancer, ABL1 alterations (including somatic mutations and amplification) occur rarely in solid tumors³.

Potential relevance: The BCR-ABL1 fusion is a diagnostic marker for Ph+/BCR-ABL1 CML^{11,12}. BCR-ABL1 fusion is also associated with poor/adverse risk in acute myeloid leukemia (AML) and ALL^{13,14,15}. Several targeted TKIs are approved by the FDA for activated BCR-ABL1, primarily in hematological cancers. These include imatinib¹⁶ (2001), dasatinib¹⁷ (2006), and ponatinib¹⁸ (2012) in CML and ALL, as well as nilotinib¹⁹ (2007) and bosutinib²⁰ (2012) in CML. 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 TKIs¹¹. Imatinib is recommended as a first-line TKI for BCR-ABL1 fusion, while variant-specific TKIs for KD mutations include asciminib for T315I in chronic phase (CP)-CML and ponatinib for T315I in CP-CML and ALL, as the mutation confers resistance to imatinib, dasatinib, nilotinib, and bosutinib¹¹. 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 the chronic phase²¹.

BCR (BCR activator of RhoGEF and GTPase)

Background: The BCR gene encodes the BCR activator of RhoGEF and GTPase, a large oligomeric multidomain protein with serine/threonine protein kinase, guanine nucleotide exchange factor (GEF) and GTPase-activating domains^{2,22}. The Philadelphia chromosome, a reciprocal translocation between chromosomes 22 and 9, t(9;22)(q34.1;q11.2), is frequently found in patients with chronic myelogenous leukemia (CML)⁵. This translocation results in the fusion of the BCR promoter region on chromosome 22 with the ABL1 kinase domain on chromosome 9, which leads to unregulated tyrosine kinase activity of ABL1 and contributes to the immortality of leukemic cells^{2,3,5,6}.

Alterations and prevalence: BCR-ABL1 fusions are reported in more than 90% of CML cases, 25-35% of adult acute lymphoblastic leukemia (ALL) cases, and 3-5% of childhood ALL cases^{7,8,9,10}. Other known fusion partners of BCR in hematological cancers include JAK2, FGFR1 and PDGFRA^{23,24,25}. Somatic mutations in BCR are predominantly missense and observed in about 8% of skin cutaneous melanoma, 6% of uterine corpus endometrial carcinoma, 5% of diffuse large B-cell lymphoma, 3% of stomach adenocarcinoma and colorectal adenocarcinoma, and 2% of lung adenocarcinoma, cervical squamous cell carcinoma, lung squamous cell carcinoma, and kidney renal papillary cell carcinoma^{26,27}. Amplification is observed in about 4% of sarcoma and uterine carcinosarcoma, 3% of bladder urothelial carcinoma, and 2% of adrenocortical carcinoma, ovarian serous cyst adenocarcinoma, lung squamous cell carcinoma, thymoma, head and neck squamous cell carcinoma, skin cutaneous melanoma, and lung adenocarcinoma^{26,27}.

Potential relevance: The BCR-ABL1 fusion is a diagnostic marker for Ph+/BCR-ABL1 CML¹¹. The BCR-JAK2 fusion t(9;22)(p24.1;q11.2) is a diagnostic marker for myeloid/lymphoid neoplasms with eosinophilia²⁸. BCR-ABL1 fusion defines a distinct molecular subtype of AML according to the World Health Organization (WHO) and is associated with poor/adverse risk in both AML and ALL^{12,13,14,15}. Several targeted tyrosine kinase inhibitors (TKIs) are approved by the FDA for activated BCR-ABL1, primarily in hematological cancers. These include imatinib¹⁶ (2001) and dasatinib¹⁷ (2006) in CML and ALL, nilotinib¹⁹ (2007), bosutinib²⁰ (2012), and asciminib²¹ (2021) in CML, and ponatinib¹⁸ (2012) in ALL. 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 TKIs¹¹.

RUNX1 (RUNX family transcription factor 1)

Background: The RUNX1 gene encodes the runt-related transcription factor (RUNX) 1, part of the RUNX family of transcription factors which also includes RUNX2 and RUNX3²⁹. All RUNX proteins share several conserved regions with similar functionality including a highly conserved N-terminal 'runt' domain responsible for binding DNA, a C-terminal region composed of an activation domain, inhibitory domain, protein interacting motifs, and a nuclear matrix targeting signal³⁰. Each of these proteins are capable of interacting with core binding factor beta (CBFβ) to form the core binding factor (CBF) complex. Consequently, RUNX1, RUNX2, and RUNX3 are collectively known as core binding factor alpha (CBFα) since they can each function as the alpha subunit of CBF. Specifically, CBFβ binds to the 'runt' domain of RUNX1 leading to RUNX1 stabilization and increased affinity of the CBF complex for promoters involved in hematopoietic differentiation and cell cycle regulation^{31,32}. RUNX1 is frequently mutated in various hematological malignancies³². Germline mutations in RUNX1 result in a rare autosomal dominant condition known as familial platelet disorder, with predisposition to acute myeloid leukemia (FPD/AML)^{33,34}. Somatic mutations and chromosomal translocations in RUNX1 are often observed in myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and chronic myelomonocytic leukemia (CMML)³².

Alterations and prevalence: RUNX1 is frequently rearranged in hematological malignancies with over 50 different observed translocations³⁵. The most recurrent translocation, t(12;21)(q34;q11), results in ETV6-RUNX1 fusion and is observed in 20-25% of childhood ALL^{36,37,38}. This translocation is also observed in adult ALL at a lower frequency (2%)^{37,38}. Another recurrent translocation, t(8;21)(q22;q22), results in RUNX1-RUNX1T1 fusion and is observed in 5-10% of AML³⁹. The RUNX1-RUNX1T1 fusion, consists of the RHD domain of RUNX1 and the majority of RUNX1T1, which promotes oncogenesis by altering transcriptional regulation of RUNX1 target genes^{32,39}. Somatic mutations in RUNX1 include missense, nonsense, and frameshift mutations resulting in loss of function or dominant negative effects³². RUNX1 mutations are reported in approximately 10% of de novo AML as well as 10-15% of MDS^{13,26,32,40}.

Biomarker Descriptions (continued)

Potential relevance: AML with RUNX1-RUNX1T1 fusions is considered a distinct molecular subtype by the World Health Organization (WHO)^{12,13}. Translocations involving RUNX1, specifically t(8;21)(q22;q22)/RUNX1-RUNX1T1 in AML and t(12;21)(q34;q11)/ETV6-RUNX1 in ALL, are associated with favorable risk^{13,14,15}. On the other hand, mutations in RUNX1 confer poor prognosis in AML, MDS, and systemic mastocytosis (SM)^{13,40,41}

Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ✕ No evidence

BCR::ABL1 fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
dasatinib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	✕
imatinib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	✕
nilotinib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input checked="" type="radio"/>	✕
bosutinib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	✕
asciminib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	✕	✕
ponatinib	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	✕	✕
Allogeneic hematopoietic stem cell transplantation	✕	<input checked="" type="radio"/>	✕	✕	✕
azacitidine	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine + daunorubicin	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine + daunorubicin + etoposide	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine + etoposide + idarubicin	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine + fludarabine + idarubicin + filgrastim	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine + idarubicin	✕	<input checked="" type="radio"/>	✕	✕	✕
cytarabine + mitoxantrone	✕	<input checked="" type="radio"/>	✕	✕	✕
decitabine	✕	<input checked="" type="radio"/>	✕	✕	✕
liposomal cytarabine-daunorubicin CPX-351	✕	<input checked="" type="radio"/>	✕	✕	✕
venetoclax + azacitidine	✕	<input checked="" type="radio"/>	✕	✕	✕
venetoclax + cytarabine	✕	<input checked="" type="radio"/>	✕	✕	✕
venetoclax + cytarabine + fludarabine + idarubicin + filgrastim	✕	<input checked="" type="radio"/>	✕	✕	✕
venetoclax + decitabine	✕	<input checked="" type="radio"/>	✕	✕	✕
dasatinib + chemotherapy	✕	<input type="radio"/>	<input type="radio"/>	✕	✕
imatinib + chemotherapy	✕	<input type="radio"/>	<input type="radio"/>	✕	✕
asciminib + chemotherapy	✕	<input type="radio"/>	✕	✕	✕

Relevant Therapy Summary (continued)

 In this cancer type
  In other cancer type
  In this cancer type and other cancer types
  No evidence

BCR::ABL1 fusion (continued)

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

Relevant Therapy Summary (continued)

 In this cancer type
  In other cancer type
  In this cancer type and other cancer types
  No evidence

BCR::ABL1 fusion (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
imatinib + steroid	×	○	×	×	×
imatinib + vincristine + dexamethasone	×	○	×	×	×
inotuzumab ozogamicin	×	○	×	×	×
inotuzumab ozogamicin + nilotinib	×	○	×	×	×
inotuzumab ozogamicin + ponatinib	×	○	×	×	×
nilotinib + blinatumomab	×	○	×	×	×
nilotinib + chemotherapy	×	○	×	×	×
nilotinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone	×	○	×	×	×
nilotinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone	×	○	×	×	×
nilotinib + cytarabine + HyperCVAD	×	○	×	×	×
nilotinib + cytarabine + HyperCVAD + methotrexate	×	○	×	×	×
nilotinib + steroid	×	○	×	×	×
nilotinib + vincristine + dexamethasone	×	○	×	×	×
ponatinib + blinatumomab	×	○	×	×	×
ponatinib + chemotherapy	×	○	×	×	×
ponatinib + cyclophosphamide + cytarabine + daunorubicin + methotrexate + PEG-L-asparaginase + vincristine + dexamethasone + prednisone	×	○	×	×	×
ponatinib + cytarabine + daunorubicin + etoposide + methotrexate + vincristine + dexamethasone	×	○	×	×	×
ponatinib + cytarabine + HyperCVAD	×	○	×	×	×
ponatinib + cytarabine + HyperCVAD + methotrexate	×	○	×	×	×
ponatinib + steroid	×	○	×	×	×
ponatinib + vincristine + dexamethasone	×	○	×	×	×
tisagenlecleucel-t	×	○	×	×	×
imatinib (Accord)	×	×	○	×	×
imatinib (Accord) + chemotherapy	×	×	○	×	×
imatinib (Koanaa)	×	×	○	×	×
imatinib (Koanaa) + chemotherapy	×	×	○	×	×

Relevant Therapy Summary (continued)

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ✕ No evidence

RUNX1 p.(R166Q) c.497G>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
Allogeneic hematopoietic stem cell transplantation	✕	●	✕	✕	✕
azacitidine	✕	●	✕	✕	✕
cytarabine	✕	●	✕	✕	✕
cytarabine + daunorubicin	✕	●	✕	✕	✕
cytarabine + daunorubicin + etoposide	✕	●	✕	✕	✕
cytarabine + etoposide + idarubicin	✕	●	✕	✕	✕
cytarabine + fludarabine + idarubicin + filgrastim	✕	●	✕	✕	✕
cytarabine + idarubicin	✕	●	✕	✕	✕
cytarabine + mitoxantrone	✕	●	✕	✕	✕
decitabine	✕	●	✕	✕	✕
liposomal cytarabine-daunorubicin CPX-351	✕	●	✕	✕	✕
venetoclax + azacitidine	✕	●	✕	✕	✕
venetoclax + cytarabine	✕	●	✕	✕	✕
venetoclax + cytarabine + fludarabine + idarubicin + filgrastim	✕	●	✕	✕	✕
venetoclax + decitabine	✕	●	✕	✕	✕

Relevant Therapy Details

Current FDA Information

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

FDA information is current as of 2023-07-19. For the most up-to-date information, search www.fda.gov.

BCR::ABL1 fusion

☐ asciminib

Cancer type: Chronic Phase Chronic Myeloid Leukemia **Label as of:** 2023-06-26

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).
- Ph+ CML in CP with the T315I mutation.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215358s003lbl.pdf

☐ bosutinib

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

Label as of: 2023-04-20

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

Indications and usage:

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

- Newly-diagnosed chronic phase Ph+ chronic myelogenous leukemia (CML).
- Chronic, accelerated, or blast phase Ph+ CML with resistance or intolerance to prior therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/203341s024lbl.pdf

BCR::ABL1 fusion (continued)

○ dasatinib

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

Label as of: 2023-02-08

Variant class: BCR-ABL1 fusion [t(9;22)(q34;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/2023/021986s027lbl.pdf

○ imatinib

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

Label as of: 2022-08-19

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

Indications and usage:

GLEEVEC® is a kinase inhibitor indicated for the treatment of:

- Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- Patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in blast crisis (BC), accelerated phase (AP), or in chronic phase (CP) after failure of interferon-alpha therapy.
- Adult patients with relapsed or refractory Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL).
- Pediatric patients with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) in combination with chemotherapy.
- Adult patients with myelodysplastic/myeloproliferative diseases (MDS/MPD) associated with platelet-derived growth factor receptor (PDGFR) gene re-arrangements.
- Adult patients with aggressive systemic mastocytosis (ASM) without the D816V c-Kit mutation or with c-Kit mutational status unknown.
- Adult patients with hypereosinophilic syndrome (HES) and/or chronic eosinophilic leukemia (CEL) who have the FIP1L1-PDGFRα fusion kinase (mutational analysis or fluorescence in situ hybridization [FISH] demonstration of CHIC2 allele deletion) and for patients with HES and/or CEL who are FIP1L1-PDGFRα fusion kinase negative or unknown.
- Adult patients with unresectable, recurrent and/or metastatic dermatofibrosarcoma protuberans (DFSP).
- Patients with Kit (CD117) positive unresectable and/or metastatic malignant gastrointestinal stromal tumors (GIST).
- Adjuvant treatment of adult patients following resection of Kit (CD117) positive GIST.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/021588s062lbl.pdf

BCR::ABL1 fusion (continued)

○ nilotinib

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

Label as of: 2021-09-23

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

Indications and usage:

TASIGNA® is a kinase inhibitor indicated for the treatment of:

- Adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase.
- Adult patients with chronic phase (CP) and accelerated phase (AP) Ph+ CML resistant to or intolerant to prior therapy that included imatinib.
- Pediatric patients greater than or equal to 1 year of age with Ph+ CML-CP and CML-AP resistant or intolerant to prior tyrosine-kinase inhibitor (TKI) therapy.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022068s035s036lbl.pdf

○ 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-CML.

Reference:

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

Current NCCN Information

☒ In this cancer type ☐ In other cancer type ☒ In this cancer type and other cancer types

NCCN information is current as of 2023-07-03. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

BCR::ABL1 fusion

● azacitidine

Cancer type: Acute Myeloid Leukemia

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

BCR::ABL1 fusion (continued)

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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 3.2023]

● 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):

- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

BCR::ABL1 fusion (continued)

● 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 3.2023]

● liposomal cytarabine-daunorubicin CPX-351

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 3.2023]

● 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):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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 3.2023]

● 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 3.2023]

BCR::ABL1 fusion (continued)

● 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):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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 3.2023]

● 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 3.2023]

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

BCR::ABL1 fusion (continued)**● 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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● decitabine

Cancer type: Acute Myeloid Leukemia

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia

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

NCCN Recommendation category: 3

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

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

NCCN Recommendation category: 3

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

○ bosutinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

BCR::ABL1 fusion (continued)

○ dasatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ imatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ nilotinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ bosutinib**

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 1.2023]

○ bosutinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ 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 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)

○ 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 1.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ dasatinib

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 1.2023]

BCR::ABL1 fusion (continued)**○ dasatinib**

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]

○ imatinib

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 1.2023]

○ imatinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (First-line therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ imatinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (First-line therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]**○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]**○ 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 1.2023]**○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ nilotinib

Cancer type: Accelerated Phase Chronic Myeloid Leukemia

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]**○ 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 1.2023]**○ 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 1.2023]**○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

○ 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 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ ponatinib**

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (First-line therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)**○ 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 1.2023]

○ 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 1.2023]

○ 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

Reference: NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]

○ 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 1.2023]

BCR::ABL1 fusion (continued)

○ 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 1.2023]

○ asciminib

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

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 Gene Fusions [Version 1.2023]

○ asciminib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ bosutinib

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

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 Gene Fusions [Version 1.2023]

BCR::ABL1 fusion (continued)

○ bosutinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ dasatinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ dasatinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ imatinib

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

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 Gene Fusions [Version 1.2023]

BCR::ABL1 fusion (continued)

○ imatinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ nilotinib

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ nilotinib + chemotherapy

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

○ ponatinib

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

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 Gene Fusions [Version 1.2023]

BCR::ABL1 fusion (continued)**○ ponatinib + chemotherapy**

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

NCCN Recommendation category: 2A

Population segment (Line of therapy):

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

Reference: NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]

RUNX1 p.(R166Q) c.497G>A**● azacitidine**

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

RUNX1 p.(R166Q) c.497G>A (continued)

● cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● Allogeneic hematopoietic stem cell transplantation

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● cytarabine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

RUNX1 p.(R166Q) c.497G>A (continued)**● cytarabine + mitoxantrone**

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● liposomal cytarabine-daunorubicin CPX-351

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

RUNX1 p.(R166Q) c.497G>A (continued)**● venetoclax + cytarabine**

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

RUNX1 p.(R166Q) c.497G>A (continued)**● cytarabine + etoposide + idarubicin**

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 3

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

● venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 3

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

Current EMA Information

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types

EMA information is current as of 2023-07-19. For the most up-to-date information, search www.ema.europa.eu/ema.

BCR::ABL1 fusion

☐ asciminib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

Label as of: 2023-03-02

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

Reference:

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

☐ bosutinib

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

Label as of: 2023-05-17

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

Reference:

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

☐ dasatinib, dasatinib + chemotherapy

Cancer type: Acute Lymphoblastic Leukemia, Chronic Phase Chronic Myeloid 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

☐ 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

Label as of: 2022-12-14

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

☐ imatinib (Koanaa), imatinib (Koanaa) + chemotherapy

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

Label as of: 2021-10-01

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

Reference:

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

BCR::ABL1 fusion (continued)**○ imatinib, imatinib + chemotherapy**

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

Label as of: 2023-03-29

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

○ imatinib, imatinib + chemotherapy

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

○ nilotinib

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

Label as of: 2022-06-13

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

Reference:

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

○ ponatinib

Cancer type: Acute Lymphoblastic Leukemia

Label as of: 2022-10-21

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

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 2023-07-03. For the most up-to-date information, search www.esmo.org.

BCR::ABL1 fusion

● dasatinib

Cancer type: Acute Myeloid Leukemia

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

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

Population segment (Line of therapy):

- (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

● imatinib

Cancer type: Acute Myeloid Leukemia

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

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

Population segment (Line of therapy):

- (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

● nilotinib

Cancer type: Acute Myeloid Leukemia

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

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

Population segment (Line of therapy):

- (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

○ dasatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- (First-line therapy)

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

BCR::ABL1 fusion (continued)

○ imatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- (First-line therapy)

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 Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- (First-line therapy)

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

○ bosutinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- Resistant, Refractory (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)]

○ dasatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- Resistant, Refractory (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)]

BCR::ABL1 fusion (continued)

○ imatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- Resistant, Refractory (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)]

○ nilotinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

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

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

Population segment (Line of therapy):

- Resistant, Refractory (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)]

○ dasatinib

Cancer type: Chronic Phase Chronic Myeloid Leukemia

Variant class: t(9;22)(q34;q11.2)

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

Population segment (Line of therapy):

- Resistant, Refractory (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)]

Alerts Informed By Public Data Sources

Current NCCN Information

 Contraindicated  Not recommended  Resistance  Breakthrough  Fast Track

NCCN information is current as of 2023-07-03. For the most up-to-date information, search www.nccn.org. For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

BCR::ABL1 fusion

imatinib

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

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 2.2023]

omacetaxine

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

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 2.2023]

References

1. Pendergast. The Abl family kinases: mechanisms of regulation and signaling. *Adv. Cancer Res.* 2002;85:51-100. PMID: 12374288
2. O'Leary et al. Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. *Nucleic Acids Res.* 2016 Jan 4;44(D1):D733-45. PMID: 26553804
3. Greuber et al. Role of ABL family kinases in cancer: from leukaemia to solid tumours. *Nat. Rev. Cancer.* 2013 Aug;13(8):559-71. PMID: 23842646
4. Colicelli. ABL tyrosine kinases: evolution of function, regulation, and specificity. *Sci Signal.* 2010 Sep 14;3(139):re6. PMID: 20841568
5. Miyazaki et al. Amplification of BCR protein associated with oncogenesis in human hepatocellular carcinoma. *Dig Dis Sci.* 1997 May;42(5):927-37. PMID: 9149044
6. Chuang et al. Abr and Bcr are multifunctional regulators of the Rho GTP-binding protein family. *Proc Natl Acad Sci U S A.* 1995 Oct 24;92(22):10282-6. PMID: 7479768
7. Achkar et al. A rare chronic myeloid leukemia case with Philadelphia chromosome, BCR-ABL e13a3 transcript and complex translocation involving four different chromosomes. *Oncol Lett.* 2010 Sep;1(5):797-800. PMID: 22966382
8. De et al. ABL1 fusion genes in hematological malignancies: a review. *Eur. J. Haematol.* 2011 May;86(5):361-71. PMID: 21435002
9. De et al. Cytogenetics in pre-B and B-cell acute lymphoblastic leukemia: a study of 208 patients diagnosed between 1981 and 2008. *Cancer Genet. Cytogenet.* 2010 Jul 1;200(1):8-15. PMID: 20513528
10. Leoni et al. Tyrosine kinase inhibitors in BCR-ABL positive acute lymphoblastic leukemia. *Haematologica.* 2015 Mar;100(3):295-9. PMID: 25740105
11. NCCN Guidelines® - NCCN-Chronic Myeloid Leukemia [Version 2.2023]
12. Khoury et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. *Leukemia.* 2022 Jul;36(7):1703-1719. PMID: 35732831
13. NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]
14. NCCN Guidelines® - NCCN-Acute Lymphoblastic Leukemia [Version 1.2023]
15. Döhner et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood.* 2022 Sep 22;140(12):1345-1377. PMID: 35797463
16. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/021588s062lbl.pdf
17. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021986s027lbl.pdf
18. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/203469s035lbl.pdf
19. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022068s035s036lbl.pdf
20. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/203341s024lbl.pdf
21. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215358s003lbl.pdf
22. Malmberg et al. Bcr (breakpoint cluster region) protein binds to PDZ-domains of scaffold protein PDZK1 and vesicle coat protein Mint3. *J Cell Sci.* 2004 Nov 1;117(Pt 23):5535-41. PMID: 15494376
23. Bellesso et al. Atypical chronic myeloid leukemia with t(9;22)(p24,11.2), a BCR-JAK2 fusion gene. *Rev Bras Hematol Hemoter.* 2013;35(3):218-9. PMID: 23904814
24. Barnes et al. Functional characterization of two rare BCR-FGFR1+ leukemias. *Cold Spring Harb Mol Case Stud.* 2020 Apr;6(2). PMID: 31980503
25. Baxter et al. The t(4;22)(q12;q11) in atypical chronic myeloid leukaemia fuses BCR to PDGFRA. *Hum Mol Genet.* 2002 Jun 1;11(12):1391-7. PMID: 12023981
26. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat. Genet.* 2013 Oct;45(10):1113-20. PMID: 24071849
27. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov.* 2012 May;2(5):401-4. PMID: 22588877
28. NCCN Guidelines® - NCCN-Myeloid/Lymphoid Neoplasms with Eosinophilia and Tyrosine Kinase Gene Fusions [Version 1.2023]
29. de et al. Runx transcription factors in the development and function of the definitive hematopoietic system. *Blood.* 2017 Apr 13;129(15):2061-2069. PMID: 28179276
30. Chuang et al. RUNX family: Regulation and diversification of roles through interacting proteins. *Int. J. Cancer.* 2013 Mar 15;132(6):1260-71. PMID: 23180629
31. Jung et al. Prognostic factor analysis in core-binding factor-positive acute myeloid leukemia. *Anticancer Res.* 2014 Feb;34(2):1037-45. PMID: 24511052
32. Sood et al. Role of RUNX1 in hematological malignancies. *Blood.* 2017 Apr 13;129(15):2070-2082. PMID: 28179279

References (continued)

33. Béri-Dexheimer et al. Clinical phenotype of germline RUNX1 haploinsufficiency: from point mutations to large genomic deletions. *Eur. J. Hum. Genet.* 2008 Aug;16(8):1014-8. PMID: 18478040
34. Hayashi et al. Myeloid neoplasms with germ line RUNX1 mutation. *Int. J. Hematol.* 2017 Aug;106(2):183-188. PMID: 28534116
35. De et al. RUNX1 translocations and fusion genes in malignant hemopathies. *Future Oncol.* 2011 Jan;7(1):77-91. PMID: 21174539
36. De et al. ETV6 fusion genes in hematological malignancies: a review. *Leuk. Res.* 2012 Aug;36(8):945-61. PMID: 22578774
37. Pui et al. Acute lymphoblastic leukemia. *N. Engl. J. Med.* 2004 Apr 8;350(15):1535-48. PMID: 15071128
38. NCCN Guidelines® - Acute Lymphoblastic Leukemia [Version 2.2019]. 2019 May 15
39. Huret et al. Atlas of genetics and cytogenetics in oncology and haematology in 2013. *Nucleic Acids Res.* 2013 Jan;41(Database issue):D920-4. PMID: 23161685
40. NCCN Guidelines® - NCCN-Myelodysplastic Syndromes [Version 1.2023]
41. NCCN Guidelines® - NCCN-Systemic Mastocytosis [Version 1.2020]