Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	T-ALL
Molecular Abnormality:	Comprehensive flow cytometric immunophenotyping to include B, T and myeloid lineage markers
Test:	Comprehensive flow cytometric immunophenotyping to include B, T and myeloid lineage markers
Chromosome:	
Gene Symbol:	
Test Detects:	Protein expression
Methodology:	Flow cytometry
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	The initial immunophenotyping panel should be sufficiently comprehensive to establish a leukemia associated phenotype (LAP) that may include expression of non-lineage antigens. These LAP are useful in classification, particularly mixed lineage leukemias, and as a signature for minimal residual disease (MRD) detection.
Test Purpose:	Classification, Diagnostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5, ALL-A Page:12
Notes:	Typical Immunophenotype, T-ALL: TdT+. variable for all of the following: CD1a, CD2, CD3, CD4, CD5, CD7, CD8, CD34. •Pro-T-ALL: cCD3+, CD7+, CD1a-, CD2-, CD4-, CD8-, CD34+/-. Pre-T-ALL: cCD3+, CD7+, CD1a-, CD2+, CD4-, CD8-, CD34+/-. •Cortical T-ALL: cCD3+, CD7+, CD1a+, CD2+, CD4+, CD8+, CD34-. •Medullary T-ALL: cCD3+, sCD3+, CD7+, CD1a-, CD2+, CD4+ or CD8+, CD34- •ETP T-ALL: Lack of CD1a and CD8 expression, weak CD5 expression with less than 75% positive blasts, and expression of one or more of the following myeloid or stem cell markers on at least 25% of lymphoblasts: CD117, CD34, HLA-DR, CD13, CD33, CD11b, and/or CD65.

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 1 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL
Molecular Abnormality:	Comprehensive flow cytometric immunophenotyping to include B, T and myeloid lineage markers
Test:	Comprehensive flow cytometric immunophenotyping to include B, T and myeloid lineage markers
Chromosome:	
Gene Symbol:	
Test Detects:	Protein expression
Methodology:	Flow cytometry
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	The initial immunophenotyping panel should be sufficiently comprehensive to establish a leukemia associated phenotype (LAP) that may include expression of non-lineage antigens. These LAP are useful in classification, particularly mixed lineage leukemias, and as a signature for minimal residual disease (MRD) detection.
Test Purpose:	Classification, Diagnostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5, ALL-A Page:12
Notes:	Typical Immunophenotype B-ALL, not otherwise specified: CD10+, CD19+, CD79a+, cCD22+, sCD22+, CD24+, PAX5+, TdT+, variable CD20, variable CD34. • Early precursor B-ALL (pro-B-ALL): CD10-, CD19+, cCD79a+, cCD22+, TdT+. • Common B-ALL: CD10+. pre-B-ALL: cytoplasmic mu+, sIg-, CD10+/-. • Precursor B-ALL (pre-B-ALL): cytoplasmic mu+, sIg-, CD10+/-.

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 2 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	Comprehensive flow cytometric immunophenotyping to include B, T and myeloid lineage markers
Test:	Comprehensive flow cytometric immunophenotyping to include B, T and myeloid lineage markers
Chromosome:	
Gene Symbol:	
Test Detects:	Protein expression
Methodology:	Flow cytometry
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	The initial immunophenotyping panel should be sufficiently comprehensive to establish a leukemia associated phenotype (LAP) that may include expression of non-lineage antigens. These LAP are useful in classification, particularly mixed lineage leukemias, and as a signature for minimal residual disease (MRD) detection.
Test Purpose:	Classification, Diagnostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5, ALL-A Page:12
Notes:	Typical Immunophenotype, B-ALL with recurrent genetic abnormalities: • Hyperdiploidy (DNA index >1.16; 51065 chromosome without structural abnormalities): CD10+, CD19+, CD34+, CD45- • Hypodiploidy (• t(9;22)(q34;q11.2); BCR-ABL1: CD10+, CD19+, TdT+, CD13+, CD33+, CD117-. • t(v;11q23); MLL rearranged: CD10-, CD19+, CD24-, CD15+ • t(12;21)(p13;q22); TEL-AML1: CD10+, CD19+, TdT+, CD13+, CD34+ • t(1;19)(q23;p13.3); E2A-PBX1: CD10+, CD19+, CD20 variable, CD34+/-, cytoplasmic mu+ • t(5;14)(q31;q32); IL-3-IGH: CD10+, CD19+

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 5 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	(1;19)(q23;p13.3) translocation
Test:	(1;19)(q23;p13.3) E2A-PBX1 translocation
Chromosome:	t(1;19)(q23;p13.3)
Gene Symbol:	TCF3-PBX1
Test Detects:	Translocation
Methodology:	Cytogenetics, FISH, RT-PCR
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 10 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	(12;21)(p13;q22) translocation
Test:	(12;21)(p13;q22) TEL-AML1 translocation
Chromosome:	t(12;21)(p13;q22)
Gene Symbol:	ETV6-RUNX1
Test Detects:	Translocation
Methodology:	Cytogenetics, FISH, RT-PCR
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 11 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	(5;14)(q31;q32) translocation
Test:	(5;14)(q31;q32) IL3-IGH translocation
Chromosome:	t(5;14)(q31;q32)
Gene Symbol:	IL3-IGH
Test Detects:	Translocation
Methodology:	Cytogenetics, FISH, RT-PCR
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 12 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	(9;22)(q34;q11.2) translocation
Test:	(9;22)(q34;q11.2) BCR-ABL1 translocation
Chromosome:	t(9;22)(q34;q11.2)
Gene Symbol:	BCR-ABL1
Test Detects:	Translocation
Methodology:	Cytogenetics, FISH, RT-PCR
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 13 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	(v;11q23) translocation
Test:	(v;11q23) MLL rearranged
Chromosome:	t(v;11q23)
Gene Symbol:	MLL
Test Detects:	Translocation
Methodology:	Cytogenetics, FISH, RT-PCR
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 14 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	Flow cytometric DNA cell cycle analysis
Test:	Flow cytometric DNA cell cycle analysis
Chromosome:	
Gene Symbol:	
Test Detects:	Hyperdiploidy, Hypodiploidy
Methodology:	Flow cytometry
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 17 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	Hyperdiploidy
Test:	Hyperdiploidy
Chromosome:	
Gene Symbol:	
Test Detects:	Hyperdiploidy
Methodology:	Cytogenetics, FISH
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 19 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	B-ALL with recurrent genetic abnormalities
Molecular Abnormality:	Hyperdiploidy
Test:	Hyperdiploidy
Chromosome:	
Gene Symbol:	
Test Detects:	Hypodiploidy
Methodology:	Cytogenetics, FISH
NCCN Category of Evidence:	2A
Specimen Types:	Bone marrow lymphoblasts, Peripheral blood lymphoblasts
NCCN Recommendation - Clinical Decision:	Diagnosis. Genetic Characterization. Optimal risk stratification and treatment planning requires testing marrow or peripheral blood lymphoblasts for specific recurrent genetic abnormalities using: • Karyotyping of G-banded metaphase chromosomes (cytogenetics); • Interphase fluorescence in situ hybridization (FISH) testing including probes capable of detecting the major recurrent genetic abnormalities; • Reverse transcriptase polymerase chain reaction (RT-PCR) testing for fusion genes (eg, BCR-ABL). Additional optional tests include: • Flow cytometric DNA index/ploidy testing (additional assessment for hyperdiploidy and hypodiploidy). Classification: Together these studies allow determination of the World Health Organization (WHO) ALL subtype and cytogenetic risk group.
Test Purpose:	Classification, Diagnostic, Prognostic
When to Test:	
Guideline Page with Test Recommendation:	ALL-1 Page:5
Notes:	Subtypes: B-cell lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities include hyperdiploidy, hypodiploidy, and commonly occurring translocations: t(9;22)(q34;q11.2)[BCR-ABL1];t(v;11q23)[MLL rearranged]; t(12;21)(p13;q22)[TEL-AML1]; t(1;19)(q23;p13.3)[E2A-PBX1]; t(5;14)(q31;q32)[IL3-IGH; relatively rare]. Cytogenetic risk groups are defined as follows: Good risk: Hyperdiploidy (51-65 chromosomes and/or DNA index > 1.16; cases with trisomy of chromosomes 4,10, and 17 appear to have the most favorable outcome); t(12;21)(p13;q22):TEL-AML1. Poor risk: Hypodiploidy (<44 chromosomes and/or DNA index <0.81); t(v;11q23: MLL rearranged; t(9;22)(q34;q11.2): BCR-ABL1 (defined as high risk in the pre-TKI era); Complex karyotype (5 or more chromosomal abnormalities).

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 21 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	ABL1 kinase domain mutation analysis
Test:	ABL kinase domain mutation analysis
Chromosome:	9q34.1
Gene Symbol:	ABL1
Test Detects:	Mutation
Methodology:	
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	Consider *ABL* gene mutation testing for Ph+ ALL (AYA), Ph+ ALL (Adult) for relapse/refractory disease.
Test Purpose:	Treatment decision
When to Test:	
Guideline Page with Test Recommendation:	ALL-7 Page:11, ALL-D 3 of 4 Page:20
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 27 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	Abnormal immunophenotypes
Test:	Flow cytometry
Chromosome:	
Gene Symbol:	
Test Detects:	Protein expression
Methodology:	
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	Year 1 (every 1-2 months), bone marrow aspirate as indicated. If bone marrow aspirate is done: comprehensive cytogenetics, FISH, flow cytometry and consideration of molecular tests.
Test Purpose:	Surveillance
When to Test:	
Guideline Page with Test Recommendation:	ALL-7 Page:11
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 28 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	Abnormal immunophenotypes
Test:	Multicolor flow cytometry
Chromosome:	
Gene Symbol:	
Test Detects:	Abnormal immunophenotypes
Methodology:	Flow cytometry
NCCN Category of Evidence:	2A
Specimen Types:	Sampling of bone marrow mononuclear cells is preferred
NCCN Recommendation - Clinical Decision:	Minimal Residual Disease assessment. Timing of MRD assessment: Upon completion of intial induction; Additional timepoints may be useful depending on the regimen used
Test Purpose:	Monitoring
When to Test:	
Guideline Page with Test Recommendation:	ALL-3 Page:7, ALL-4 Page:8, ALL-5 Page:9, ALL-6 Page:10, ALL-F Page:23
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 29 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	Chromosomal abnormalities
Test:	Comprehensive cytogenetics
Chromosome:	
Gene Symbol:	
Test Detects:	Chromosomal abnormalities
Methodology:	
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	Year 1 (every 1-2 months), bone marrow aspirate as indicated. If bone marrow aspirate is done: comprehensive cytogenetics, FISH, flow cytometry and consideration of molecular tests.
Test Purpose:	Surveillance
When to Test:	
Guideline Page with Test Recommendation:	ALL-7 Page:11
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 30 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	Chromosomal abnormalities
Test:	FISH
Chromosome:	
Gene Symbol:	
Test Detects:	
Methodology:	
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	Year 1 (every 1-2 months), bone marrow aspirate as indicated. If bone marrow aspirate is done: comprehensive cytogenetics, FISH, flow cytometry and consideration of molecular tests.
Test Purpose:	Surveillance
When to Test:	
Guideline Page with Test Recommendation:	ALL-7 Page:11
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 31 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	Fusion genes and clonal rearrangements
Test:	Real time quantitative PCR
Chromosome:	
Gene Symbol:	
Test Detects:	Fusion genes and clonal rearrangements
Methodology:	RQ-PCR
NCCN Category of Evidence:	2A
Specimen Types:	Sampling of bone marrow mononuclear cells is preferred
NCCN Recommendation - Clinical Decision:	Minimal Residual Disease assessment. Timing of MRD assessment: Upon completion of intial induction; Additional timepoints may be useful depending on the regimen used
Test Purpose:	Monitoring
When to Test:	
Guideline Page with Test Recommendation:	ALL-3 Page:7, ALL-4 Page:8, ALL-5 Page:9, ALL-6 Page:10, ALL-F Page:23
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 32 | Under Review

Disease Description:	Acute Lymphoblastic Leukemia
Specific Indication:	
Molecular Abnormality:	TPMT gene polymorphisms
Test:	TPMT gene polymorphisms
Chromosome:	6p22.3
Gene Symbol:	TPMT
Test Detects:	Polymorphisms
Methodology:	
NCCN Category of Evidence:	2A
Specimen Types:	
NCCN Recommendation - Clinical Decision:	For patients receiving 6-MP, consider testing for TPMT gene polymorphisms, particularly in patients that develop severe neutropenia after starting 6-MP.
Test Purpose:	Treatment decision
When to Test:	
Guideline Page with Test Recommendation:	ALL-D 1 of 4 Page: 18, ALL-D 2 of 4 Page: 19
Notes:	

Guideline: Acute Lymphoblastic Leukemia v.1.2014, as of 12/4/2014 10:22:20 AM NCCN Reference ID: 33 | Under Review