Table S1. Information from sources used for categorization of recommendations

Cancer Type(s)	Test	Purpose(s)	Category[a]	Information from Sources
Acute lymphocytic leukemia	TPMT	PGx	2	"We and others advocate testing for TPMT status prior to initiating thiopurine therapy, so that starting dosages can be adjusted accordingly." (Authors' note: We categorized this as 2 because it does not advocate testing in order to use thiopurine, but only to adjust the dosage once thiopurine is decided to be used.)
Acute myeloid leukemia	CEBPA	Prognostic	2	"These molecular abnormalities are important for prognostication in a subset of patients…" ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.")
	FLT3-ITD	Prognostic	2	"These molecular abnormalities are important for prognostication in a subset of patients…" ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.")
	FLT3-TKD	Prognostic	3	"There is controversy as to whether FLT3-TKD mutations carry an equally poor prognosis." NCCN categorized under "markers with emerging evidence" and that there is "insufficient data" regarding level of evidence
	IDH1	Prognostic	3	"Findings from published reports on the prognostic effects of IDH1 have been inconsistent." NCCN categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results").
	IDH2 R172	Prognostic	3	"Reports on the prognostic effect of IDH2 mutations have also been inconsistent." NCCN categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results").
	IDH2 R140	Prognostic	3	"Reports on the prognostic effect of IDH2 mutations have also been inconsistent." Categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results").
	KIT	Prognostic	2	"These molecular abnormalities are important for prognostication in a subset of patients (category 2A)…" ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.")
	MLL-PTD	Prognostic	3	"MLL-PTD associated with inferior complete remission duration and relapse free survival" but categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results").
	NPM1	Prognostic	2	"These molecular abnormalities are important for prognostication in a subset of patients" ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.")
	RUNX1	Prognostic	3	"RUNX1 mutations associated with poorer outcome" but categorized under "markers with

				emerging evidence" and level of evidence as IIB ("none or inconsistent results").
	WT1	Prognostic	3	"WT1 mutations associated with poorer outcome" but categorized under "markers for emerging evidence" and level of evidence as IIB ("none or inconsistent results").
Breast cancer	H:I ratio	Prognostic	3	"insufficient evidence to make a recommendation for or against the use of tumor gene expression profiles to improve outcomes in defined populations of women with breast cancer."
	CYP2D6	PGx	3	BCBS: "CYP2D6 genotyping does not meet the TEC criteria for directing endocrine therapy regimen selection for women at high risk for primary breast cancer or breast cancer recurrence." NCAB: "CYP2D6 genotyping may be useful as an adjunct to a regimen for prescribing tamoxifen (B-III)". B strength of recommendation indicates that "NACB recommends adoption; there is at least fair evidence that it improves important health outcomes and concludes that benefits outweigh harms", while III indicates that the level of evidence "is insufficient to assess the effects on health outcomes…" AHS: "Adjuvant endocrine therapy should not be selected on the basis of the CYP2D6 genotype." ASCO: "data on CYP2D6 pharmacogenetics are insufficient to recommend testing as a tool to determine an adjuvant endocrine strategy."
	MammaPrint	Prognostic	3	EGAPP: "insufficient evidence to make a recommendation for or against the use of tumor gene expression profiles to improve outcomes in defined populations of women with breast cancer." NCCN: lists purpose as "not clear" and categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results"). NICE: "…not recommended for general use because of uncertainty about overall clinical benefit..."
	Oncotype DX	Prognostic; PGx	1; 2	EGAPP: "insufficient evidence to make a recommendation for or against the use of tumor gene expression profiles to improve outcomes in defined populations of women with breast cancer." NCCN: "panel considers […] assay an option when evaluating patients with primary tumors characterized as 0.6 to 1.0 cm with unfavorable features or >1 cm, and node-negative, hormone receptor-positive, and HER2 negative. ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.") ASCO: "reasonable to use Oncotype DX to identify those patients with a node-negative, ER-positive cancer and low RS who might avoid chemotherapy because of the very small potential benefit." BCBS: "insufficient evidence to determine the clinical validity or utility of Oncotype DX as a predictor of breast cancer recurrence or response to adjuvant chemotherapy in patients with node-*positive* breast cancer. "

				NCAB: "...may be used for predicting recurrence in lymph node–negative, ER-positive patients receiving adjuvant tamoxifen" (level of evidence: I/II, strength of recommendation: A). "may be used to predict benefit from adjuvant chemotherapy […] in node-negative, ER-positive patients" (level of evidence: III; strength of recommendation: B) NICE: "recommended as an option for guiding adjuvant chemotherapy decisions for people with oestrogen receptor positive (ER+), lymph node negative (LN−) and human epidermal growth factor receptor 2 negative (HER2−) early breast cancer…" but "research is recommended on the clinical utility of the test, including robust evidence on the impact of Oncotype DX on clinical decision-making…"
Breast and Ovarian cancer	BRCA	Screening	2	USPSTF: "recommends that women whose family history is associated with an increased risk for deleterious mutations in BRCA1 or BRCA2 genes be referred for genetic counseling and evaluation for BRCA testing" and "this is a Grade B recommendation", which indicates that "there is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial." NICE: "Offer genetic testing in specialist genetic clinics to a relative with a personal history of breast and/or ovarian cancer if that relative has a combined BRCA1 and BRCA2 mutation carrier probability of 10% or more." NACB: "BRCA1 and BRCA2 mutation testing may be used for identifying women who are at high risk of developing breast or ovarian cancer in high-risk families." (level of evidence: expert opinion; strength of recommendation: B-moderate) NCCN: testing recommended for those meeting high risk criteria listed in NCCN guidelines ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate")
Chronic lymphocytic leukemia	TP53	PGx	1	"Patients should be screened for a TP53 deletion pre-treatment (grade A1)" A1 indicates that quality of evidence is "high" and strength of recommendation is "strong"
Colon cancer	BRAF	Screening; Prognostic; PGx	2; 2; 2	NCCN: "mutated BRAF is a marker of resistance to anti-EGFR therapy…" and "mutations in BRAF are a strong prognostic marker" ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate") EGAPP: "level of certainty for BRAF V600E testing to guide antiepidermal growth factor receptor (EGFR) therapy was deemed low" and "Individuals found with the BRAF mutation are unlikely to have Lynch syndrome and, therefore, can avoid the need for expensive MMR gene testing."
	ColoPrint	Prognostic	3	"The test can be considered to have developed clinical validity, with a IIC level of evidence, but does not have proven clinical utility at this time." (IIC indicates that there are 2 or more validation studies available with consistent results).
	Oncotype DX	Prognostic	3	"established clinical validity in its association with recurrence risk in patients with stage II colon cancer in 2 independent randomized validation studies, with a level of evidence of IB,

				but its clinical utility has not yet been established." (IIB indicates that validation studies available show none or inconsistent results)
Colorectal cancer	18q LOH/DCC	Prognostic; PGx	3; 3	ASCO: "Assaying for loss of heterozygosity (LOH) on the long arm of chromosome 18 (18q) or deleted in colon cancer (DCC) protein determination by IHC should not be used to determine the prognosis of operable colorectal cancer, nor to predict response to therapy." NCAB: "The use of […] deleted in colon cancer (DCC for determining prognosis or predicting response to therapy is not recommended"
	KRAS (except c.38G>A (p.G13D))	PGx	1	ASCO: "…all patients with metastatic colorectal carcinoma who are candidates for anti-EGFR antibody therapy should have their tumor tested for KRAS mutations…" NCCN: "recommend, with a category of 2A, the testing of all metastatic disease for the presence of mutations in *KRAS"* ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate") EGAPP: "for patients with metastatic colorectal cancer (mCRC) who are being considered for treatment with cetuximab or panitumumab, there is convincing evidence to recommend clinical use of KRAS mutation analysis"
	Lynch syndrome testing, MMR/MSI	Screening; Diagnostic; Prognostic; PGx	1; 1; 3; 3	EGAPP: "sufficient evidence to recommend offering genetic testing for Lynch syndrome to individuals with newly diagnosed colorectal cancer to reduce morbidity and mortality in relatives." NCCN: "testing for mismatch repair (MMR) proteins should be considered…" and "Stage II MSI-H patients may have a good prognosis and do not benefit from 5-FU adjuvant therapy." ASCO: "Microsatellite instability (MSI) ascertained by polymerase chain reaction (PCR) is not recommended at this time to determine the prognosis of operable colorectal cancer nor to predict the effectiveness of FU adjuvant chemotherapy." NSGC&CGAICC: "Microsatellite instability (MSI) […] should be performed on cancer of the colon and/or rectum (CRC) […] for any patient being evaluated for Lynch syndrome..." ACCC: It is worthwhile for MSI analysis to be requested by the pathologist of newly diagnosed tumours that satisfy one of the following criteria: CRC or endometrial carcinoma under the age of 50, Second CRC under the age of 70 years, CRC under the age of 70 with a simultaneous or previous malignancy associated with Lynch syndrome." ACG: "Patients who meet the Bethesda criteria should undergo microsatellite instability testing of their tumor or a family member's tumor…" (Grade 2B: Weak recommendation, moderate quality evidence). NCAB: "MSI testing […] can be used as a prescreen for hereditary nonpolyposis CRC…" [Level of Evidence: III – Evidence from large prospective studies; IV – Evidence from small retrospective studies. Strength of Recommendation: B - Moderate]**."**
	NRAS	PGx	3	"The EWG found insufficient evidence to recommend for or against testing for mutations in *NRAS…"*
	PIK3CA	PGx	3	The EWG found insufficient evidence to recommend for or against testing for mutations in […]

				PIK3CA…"
	PTEN	PGx	3	The EWG found insufficient evidence to recommend for or against testing for [..] loss of expression of PTEN.
	TP53	Prognostic; PGx	3; 3	ASCO: "Data are insufficient to recommend the routine use of p53 […] in the management of patients with colorectal cancer." NACB: "The use of […] p53 for determining prognosis or predicting response to therapy is not recommended."
	UGT1A1	PGx	2	EGAPP: "evidence is currently insufficient to recommend for or against the routine use of UGT1A1 genotyping in patients with metastatic colorectal cancer who are to be treated with irinotecan…" NACB: "UGT1A1 genotyping is recommended as a useful adjunct for high-intensity irinotecan (Camptosar) dosing regimens (A-II)." ("A" indicates strong recommendation; "II" indicates "evidence is sufficient to determine effects, but the strength of the evidence is limited…")
Glioma	1p/19q	Diagnostic; Prognostic	1; 1	NCCN: "Consider testing for deletions in 1p19q if tumor has components of oligodendroglioma for prognostic purposes."("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate") AHS: "Whenever possible, genetic testing for loss of heterozygosity on chromosomes 1p and 19q should be obtained for all patients with tumours that have oligodendroglial features, in order to improve diagnostic accuracy and prognostic prediction."
	G-CIMP	Prognostic	3	NCCN lists purpose as "positive is favorably prognostic" but categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results").
	IDH (IDH1) c. 395 G>A p.R132H (IDH2)	Diagnostic; Prognostic	2; 2	"favorably prognostic; also a diagnostic marker" (IIB indicates that validation studies available show none or inconsistent results).
Glioma (Glioblastoma)	MGMT	Prognostic; PGx	2; 2	NCCN: "Patients opting for chemotherapy should receive temozolomide if they had MGMT methylation." AHS: "Determination of O^6-methylguanine – DNA methyltransferase (MGMT) promoter methylation status may assist in determination of prognosis."
Glioma (Pilocytic astrocytoma)	BRAF fusion	Diagnostic	3	NCCN listed purpose as "diagnostic" but categorized under "markers with emerging evidence" and level of evidence as IIB ("none or inconsistent results").
Melanoma	BRAF	PGx	1	BCBS: "sufficient validation of the companion diagnostic in the case of vemurafenib and its companion test, the cobas 4800 BRAF V600 Mutation Test" AHS: "Patients with unresectable stage III and stage IV cutaneous melanoma should undergo BRAF biomarker testing […] to determine whether they are candidates for vemurafenib."
Non-small cell lung cancer	ALK	PGx	1	NCCN: "Testing for sensitizing […] ALK gene rearrangements is recommended (category 1) in the NCCN Guidelines for NSCLC […] so that patients with these genetic abnormalities can

			receive effective treatment…" ("Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.") CAP: "*ALK* molecular testing should be used to select patients for ALK-targeted TKI therapy, and patients with lung adenocarcinoma should not be excluded from testing on the basis of clinical characteristics." (Evidence Grade: ALK: B - **"**Body of evidence can be trusted to guide practice in most situations.")
EGFR	PGx	1	ASCO: "…patients with advanced NSCLC […] should have their tumor tested for EGFR mutations to determine whether an EGFR TKI or chemotherapy is the appropriate first-line therapy." NCCN: "Testing for sensitizing EGFR mutations […] is recommended (category 1) in the NCCN Guideliens for NSCLC […] so that patients with these genetic abnormalities can receive effective treatment…" ("Category 1: Based on high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.") BCBS: "…use of tumor-cell EGFR mutation analysis to predict response to erlotinib (Tarceva®) meets the TEC criteria" NICE: "Gefitinib is recommended as an option for the first-line treatment of people with locally advanced or metastatic non-small-cell lung cancer (NSCLC) if they test positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation…" AHS: "Testing for EGFR mutations should take place for all eligible patients with advanced NSCLC and adenocarcinoma (including adenosquamous) histology who are being considered for first-line therapy with gefitinib." CAP: "*EGFR* molecular testing should be used to select patients for EGFR-targeted tyrosine kinase inhibitor (TKI) therapy, and patients with lung adenocarcinoma should not be excluded from testing on the basis of clinical characteristics. ("Evidence Grade: A **-** Body of evidence can be trusted to guide practice.")
ERCC1	Prognostic; PGx	2; 2	NCCN: "High ERCC1 levels are prognostic of better survival for patients with NSCLC when compared to low levels […]. High Levels […] are also predictive of poor response to platinum-based chemotherapy." ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate") ASCO: "The studies suggest that low levels of these markers may be predictive of benefit from chemotherapy; however, there are currently insufficient prospective phase III data to recommend use of these markers."
KRAS	Prognostic; PGx	2	"*KRAS* gene sequencing may be useful for selecting patients as candidates for TKI therapy." ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate")
ROS1	PGx	2	"Consider ROS1 testing; if positive, may treat with crizotinib." ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate")
RRM1	Prognostic;	2;	NCCN: "High RRM1 levels are prognostic of better survival for patients with NSCLC compared

		PGx	2	with low levels of RRM1 expression, independent of therapy. High levels of RRM1 expression are also predictive of poor response to gemcitabine-based chemotherapy." ASCO: "The studies suggest that low levels of these markers may be predictive of benefit from chemotherapy; however, there are currently insufficient prospective phase III data to recommend use of these markers."
Prostate cancer	PCA3 (DD3)	Diagnostic	3	"level IB clinical validity, albeit with a modest improvement in diagnostic accuracy and insufficient evidence to determine the true clinical utility of this assay in routine clinical management."
Thyroid cancer (Medullary)	RET	Screening; Diagnostic	1; 1	ATA: "All patients with a personal medical history of primary C-cell hyperplasia (CCH), MTC, or MEN 2 should be offered germline REarranged during Transfection (*RET)* testing. Grade: A Recommendation" ("A" indicates strongly recommends) NCCN: "testing recommended for all newly diagnosed patients with sporadic MTC and screening in known kindreds with inherited forms…" ("Category 2A: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate")
Various[b]	DPYD	PGx	3	The evidence is insufficient to permit conclusions regarding the effect of DPD […] pharmacogenetic testing on benefits (reduced toxicity) and harms (poorer response to treatment).
	TYMS	PGx	3	"The evidence is insufficient to permit conclusions regarding the effect of […] TS pharmacogenetic testing on benefits (reduced toxicity) and harms (poorer response to treatment)."

Abbreviations: PGx, Pharmacogenomic; ATA, American Thyroid Association; ACCC, Association of Comprehensive Cancer Centres; ACG, American College of Gastroenterology; AHS, Alberta Health Services; ASCO, American Society of Clinical Oncology; BCBS, Blue Cross Blue Shield Technology Evaluation Center; BSH, British Society for Haematology; CAP, College of American Pathologists; CPIC, Clinical Pharmacogenetics Implementation Consortium; EGAPP, Evaluation of Genomic Tests in Practice and Prevention; NACB, National Academy of Clinical Biochemistry; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Care Excellence; NSGC&CGAICC, National Society of Genetic Counselors and Collaborative Group of the Americans on Inherited Colorectal Cancer; USPSTF, United States Preventive Services Task Force

[a] Recommendation category (1 = strongly recommended, 2 = moderately recommended, 3 = not recommended for current clinical use). Multiple recommendation categories are listed for tests with multiple purposes.

[b] Includes colorectal cancer, other gastrointestinal cancer, head and neck, or breast cancer