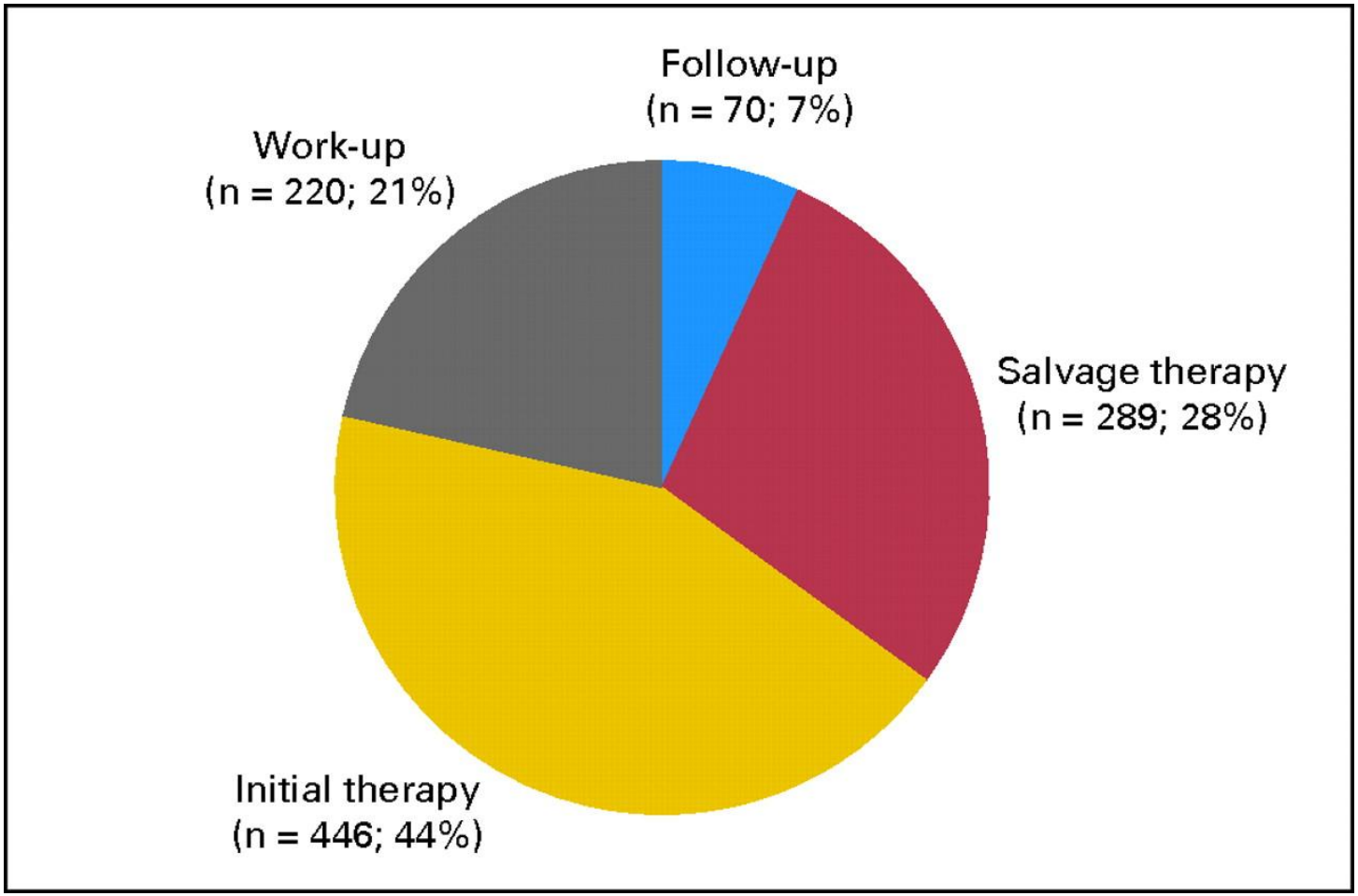
National Comprehensive Cancer Network®

NCCN.org

NCCN Clinical Practice Guidelines™

- **Comprehensive across all stages, modalities and continuum of care**
  - **47 multidisciplinary expert panels with 25-30 experts per panel (Volunteer time and expertise)**
  - **147 separate algorithms**
  - **Cancer screening, diagnosis, treatment and supportive care**
- **Updated at least annually and up to 4 times per year since 1996**
- **Category of evidence and consensus designated for each recommendation**
- **Transparent processes**
- **Centerpiece of suite of tools to support quality oncology care**

Types of Recommendations



Poonacha T K , Go R S JCO 2011;29:186-191

NCCN Categories of Evidence and Consensus

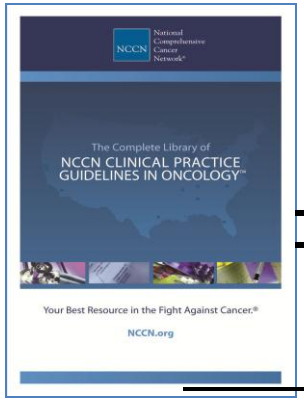
- **Category 1:** Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Category 2A:** Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
- **Category 2B:** Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
- **Category 3:** Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

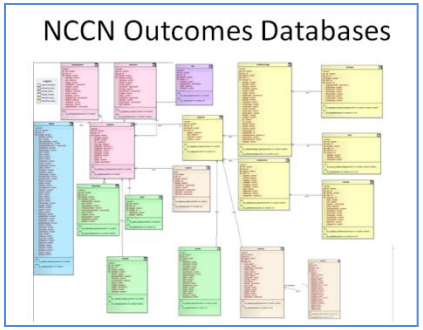
All recommendations are category 2A unless otherwise noted.

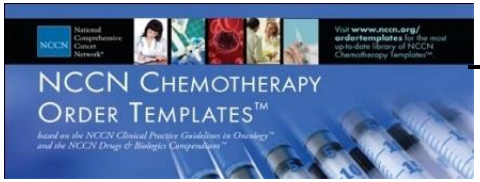
Critical Analysis of Data

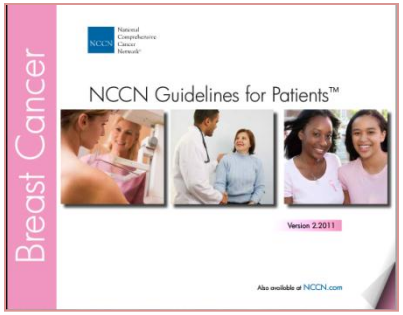
- NCCN Categories of Evidence
  - 1, 2A, 2B, 3
- Quality of evidence
- Extent of evidence
- Consistency of evidence

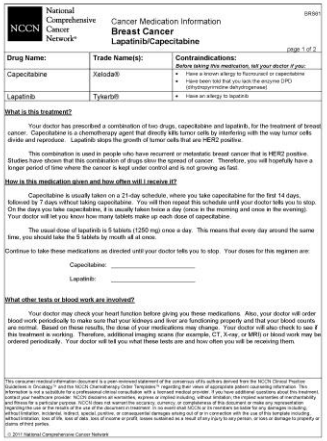
Integrated Suite of NCCN Information Products







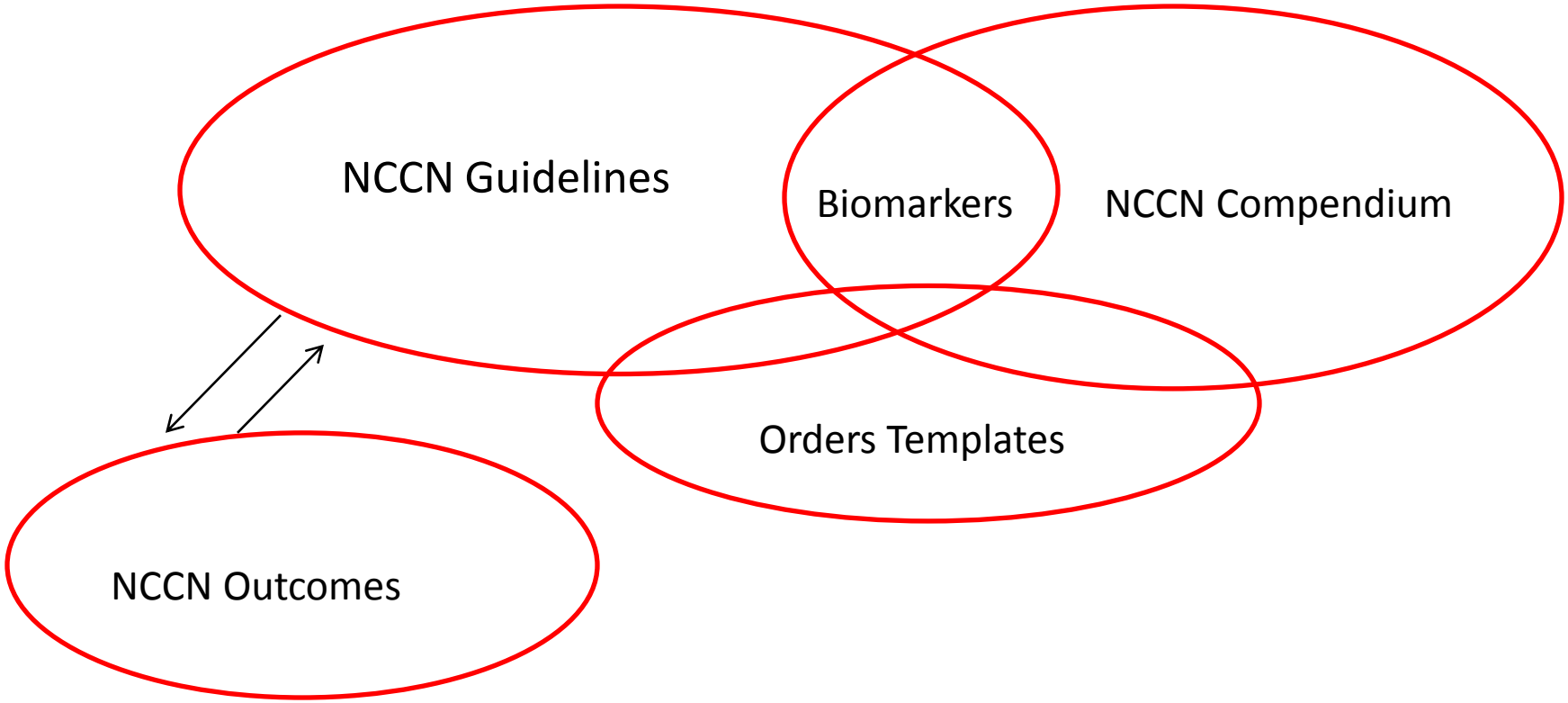




In Development

- To ensure access to appropriate testing as recommended by NCCN Guidelines
- Identify the utility of a biomarker to screen, diagnose, monitor, or provide predictive or prognostic information
- Discriminate between clinically useful biomarkers and those that are not yet clinically indicated

Content Relationships



Choices for NCCN Biomarker Compendium

- Biomarker or Assay?
- Who is the audience?
- Are there good data regarding the analytic and clinical validity of individual tests?
  - How to deal with laboratory developed tests?
  - How to deal with multiplex tests?
  - If there are alternate tests, should we recommend one?
- What to display?

How Does NCCN Define a Biomarker?

- Single mutation, a test done properly that supports a clinical decision
- Gene product, a test done properly that leads to a clinical decision
- Immunophentyping panels and karyotyping to aid in diagnosis
- Tests that incorporate data about a lot of genes or proteins (expression/proteomic profiles)

Evidence of Clinical Utility

NCCN Guidelines Panels require data supporting clinical usefulness for testing

- Data demonstrating that the biomarker affects treatment decisions
- Evidence that the biomarker can divide patients into specific clinically relevant subgroups
- Widespread availability of reliable testing

NCCN Guidelines Panels Existing Recommendations for Testing

Currently more than 800 biomarker recommendations in NCCN Guidelines:

- Determine risk of disease (BRCA-1/BRCA-2)
- Screening (PSA for prostate)
- Diagnostic (BCR/ABL in CML)
- Prognostic (CA 19-9 in pancreas)
- Predictive (ER/PR status in breast)
- Risk of toxicity (UGT1A1*28 allele for irinotecan)
- Response/disease monitoring (AFP; HCG in testicular)

Developing Guidelines for Use of Biomarkers

Considerations

- Tissue availability
- Appropriate test selection
  - LDT
  - Companion Diagnostic
  - Multiplex Test

NCCN Guidelines Recommendation

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2013
Melanoma

NCCN Guidelines Index
Melanoma Table of Contents
Discussion

SYSTEMIC THERAPY OPTIONS FOR ADVANCED OR METASTATIC MELANOMA

Preferred Regimens
- Ipilimumab (category 1)[1,2]
- Vemurafenib (category 1)[3,4]
- Clinical trial
- High-dose Interleukin-2[5,6]

Other Active Regimens
- Dacarbazine
- Temozolomide
- Imatinib for C-KIT mutated tumors
- Dacarbazine- or temozolomide-based combination chemotherapy/biochemotherapy, (including cisplatin and vinblastine with or without IL-2, interferon alfa) (category 2B)[6]
- Paclitaxel (category 2B)
- Paclitaxel/carboplatin (category 2B)

[1] Ipilimumab has the potential for significant immune-mediated complications. Participation in the risk evaluation and mitigation strategy (REMS) program and/or experience in use of the drug as well as resources to follow the patient closely are essential. Ipilimumab should be used with extreme caution, if at all, in patients with serious underlying autoimmune disorders.

[2] Re-induction with ipilimumab may be considered for select patients who experienced no significant systemic toxicity during prior ipilimumab therapy and who relapse after initial clinical response or progress after stable disease > 3 months.

[3] Vemurafenib is recommended for patients with V600 mutation of the BRAF gene documented by an FDA-approved or Clinical Laboratory Improvement Amendments (CLIA)-approved facility.

[4] Vemurafenib has the potential for significant dermatologic complications including cutaneous squamous cell carcinoma and extreme photosensitivity. Regular dermatologic evaluation with referral to a dermatologist is recommended. Patients should also be carefully monitored for the development of other adverse reactions such as joint pain and swelling.

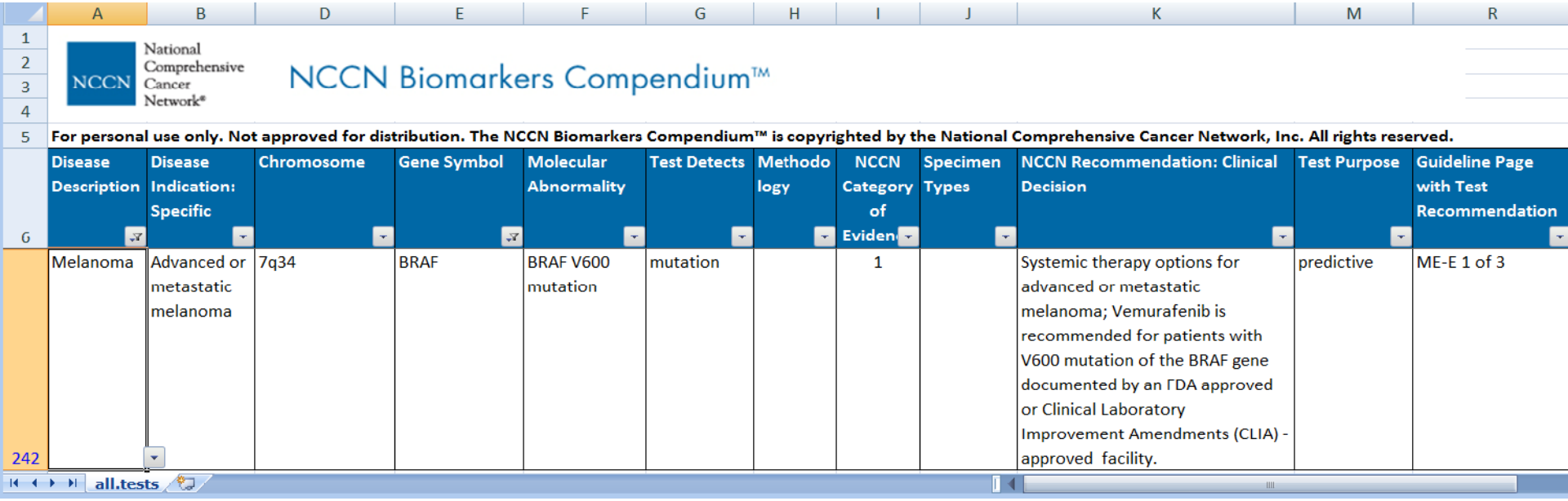
[5] High-dose interleukin-2 should not be used for patients with inadequate organ reserve, poor performance status, or untreated or active brain metastases. For patients with small brain metastases and without significant peritumoral edema, IL-2 therapy may be considered (category 2B).

[6] Administration of multiagent regimens and high-dose interleukin-2 is complex and associated with significant toxicities. Therapy should be restricted to an institution with medical staff experienced in the administration and management of these regimens.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

References on next page

NCCN Biomarkers Compendium™



NCCN Biomarkers Compendium™

For personal use only. Not approved for distribution. The NCCN Biomarkers Compendium™ is copyrighted by the National Comprehensive Cancer Network, Inc. All rights reserved.

Disease Description	Disease Indication: Specific	Chromosome	Gene Symbol	Molecular Abnormality	Test Detects	Methodology	NCCN Category of Evidence	Specimen Types	NCCN Recommendation: Clinical Decision	Test Purpose	Guideline Page with Test Recommendation
Melanoma	Advanced or metastatic melanoma	7q34	BRAF	BRAF V600 mutation	mutation		1		Systemic therapy options for advanced or metastatic melanoma; Vemurafenib is recommended for patients with V600 mutation of the BRAF gene documented by an FDA approved or Clinical Laboratory Improvement Amendments (CLIA) - approved facility.	predictive	ME-E 1 of 3

National Comprehensive Cancer Network®

Raw Data Being Collected

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W
1	DiseaseDesc	disease indication (Guideline: disease)	disease indication: specific	Test	chromosome	gene (HGNC terminology)	Molecular abnormality	Test detects	Methodology	NCCN level of evidence	Specimen types	NCCN recommendation: clinical decision (verbatim from guideline)	NCCN recommendation: clinical decision (assembled from keywords)	Clinical decision component 1: test purpose	Clinical decision component 2: Responsiveness to drug (sens*/resp*) OR , (resis*/nonresp*)	Clinical decision component 3: drug or treatment name	Clinical decision component 4: state (pos*, neg*, high, low, bright, dim)	Clinical decision component: if test purpose is diagnostic or classification, diagnosis goes here and components 2 and 3 are blank	Guideline page with test recommendation	notes	relative cost	LOINC code	Reference
81	Multiple Myeloma	Multiple Myeloma		t(14;16)	14,16		translocation	chromosomal translocation	FISH	2A	bone marrow			diagnostic					MYEL-1	This translocation involves the IGH locus and is considered a high risk feature			
82	Multiple Myeloma	Multiple Myeloma		1q21 amplification	1q21		amplification	chromosomal amplification	FISH	2A	bone marrow			diagnostic					MYEL-1	amplifications of 1q21 increases the risk of MM progression and incidence of the amplification is higher in relapsed than in newly diagnosed patients			
83	Multiple Myeloma	Multiple Myeloma		HLA typing				HLA expression	not specified	2A	not specified			tissue matching for transplant					MYEL-1	may be part of diagnostic workup--is this here to find matches for donors?			
84	Multiple Myeloma	Multiple Myeloma		multiparameter flow cytometry				cell surface and cytoplasmic expression of plasma cell markers	flow	2A	bone marrow			diagnositc?					MYEL-3				
85																				tests NOT included: serum free light chain, beta-2 microglobulin, bone marrow IHC or flow cytometry, serum quantitative immunoglobulins			

National Comprehensive Cancer Network®

NCCN.org