• 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

- Initial therapy (n = 446; 44%)
- Salvage therapy (n = 289; 28%)
- Work-up (n = 220; 21%)
- Follow-up (n = 70; 7%)

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
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
• 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
- Immunophenotyping 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
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

NCCN Guidelines Version 1.2013
Melanoma

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)

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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 progression 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 peripheral edema, IL-2 therapy may be considered (category 2B).

6 Administration of multitarget 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.

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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.

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<td>1</td>
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<td>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.</td>
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</table>
| 81    | Multiple Myeloma | Multiple Myeloma | 14q| 1q12       | amplification | ISH | bone marrow | diagnostic | NFE12                | Recommend | not relevant | not relevant | not relevant | not relevant | MTR1-1 | This translation involves the MYC locus and it is considered a high-risk feature. |}
| 82    | Multiple Myeloma | Multiple Myeloma | 16p1       | amplification | not specified | FISH | bone marrow | diagnostic | NFE12 | Recommend | not relevant | not relevant | not relevant | MTR1-1 | Amplifications of 16p1 increases the risk of rapidly progressing and incidence of the myeloma is higher in relapsed chronic myeloid leukemia. |}
| 83    | Multiple Myeloma | Multiple Myeloma | 16p1       | amplification | not specified | FISH | bone marrow | tissue matching for transplant | NFE12 | Recommend | not relevant | not relevant | not relevant | MTR1-1 | May be part of diagnostic workup - this test is not specific or sensitive for diagnosis. |}
| 84    | Multiple Myeloma | Multiple Myeloma | 16p1       | amplification | not specified | FISH | bone marrow | diagnostic | NFE12 | Recommend | not relevant | not relevant | not relevant | MTR1-1 | Tests NOT included: serum free light chain, beta 2 microglobulin, bone marrow image or flow cytometry, serum quantitative immunoglobulins. |}

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