

Ten Best Readings Relating to Melanoma

Adil Daud, MD

From the Cutaneous Oncology Division at the
H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida.

Balch CM, Buzaid AC, Soong SJ, et al. Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma. *J Clin Oncol.* 2001;19:3635-3648.

The AJCC revised staging system for cutaneous melanoma became official in 2002. The authors discuss the major changes in the system, which allows more precise classification and improves the accuracy of predicting prognosis and outcomes.

Davies H, Bignell GR, Cox C, et al. Mutations of the BRAF gene in human cancer. *Nature.* 2002;417:949-954.

As BRAF is a serine/threonine kinase that is commonly activated by somatic point mutation in human cancer, it may provide new therapeutic opportunities in malignant melanoma.

Carr KM, Bittner M, Trent JM. Gene-expression profiling in human cutaneous melanoma. *Oncogene.* 2003;22:3076-3080.

The authors review the use of complementary DNA microarray technology to study gene expression patterns in cutaneous melanoma and highlight recent advances concerning the identification of novel melanoma disease-related genes. The fundamentals of microarray technology and analysis are also discussed.

Kirkwood JM, Manola J, Ibrahim J, et al. A pooled analysis of eastern cooperative oncology group and intergroup trials of adjuvant high-dose interferon for melanoma. *Clin Cancer Res.* 2004;10:1670-1677.

In patients with high-risk resected melanoma, high-dose interferon for melanoma is effective adjuvant therapy with evidence for improved relapse-free survival and moderate improvement in overall survival based on two prospective randomized studies but not in the pooled analysis. Analyses of predictors of relapse and response are needed to improve the specificity of this treatment.

Wheatley K, Ives N, Hancock B, et al. Does adjuvant interferon-alpha for high-risk melanoma provide a worthwhile benefit? A meta-analysis of the randomised trials. *Cancer Treat Rev.* 2003;29:241-252.

This meta-analysis provides the most reliable synthesis of the data currently available. Adjuvant interferon-alpha produces clear reductions in recurrence of high-risk

melanoma, with some evidence of an effect of dose of interferon-alpha, but it is unclear whether this translates into a worthwhile survival benefit. Additional data are needed to resolve these issues.

Berwick M, Armstrong BK, Ben-Porat L, et al. Sun exposure and mortality from melanoma. *J Natl Cancer Inst.* 2005;97:195-199.

To evaluate the association between measures of skin screening and death from cutaneous melanoma, data were collected from patients with cutaneous melanoma regarding measures of intermittent sun exposure, perceived awareness of the skin, skin self-screening, and physician screening. The authors reported that sunburn, high intermittent sun exposure, skin awareness histories, and solar elastosis were statistically significantly inversely associated with death from melanoma. Melanoma thickness, mitoses, ulceration, and anatomic location on the head and neck were statistically significantly positively associated with melanoma death.

Tsao H, Atkins MB, Sober AJ. Management of cutaneous melanoma. *N Engl J Med.* 2004;351:998-1012.

This review article on cutaneous melanoma focuses on melanoma screening, high-risk populations, staging, and treatment, adjuvant therapy, and treatment of distant disease. More precisely targeted treatment approaches and rational treatment selection are needed; currently advanced disease is best managed by participation in clinical trials.

Gallagher RP. Sunscreens in melanoma and skin cancer prevention. *CMAJ.* 2005;173:244-245.

Good evidence shows that sunscreens, when assiduously applied, can reduce risk of actinic keratoses and squamous cell skin cancer. However, there is no convincing evidence that sunscreen use will reduce risk of basal cell carcinoma or melanoma.

Rosenberg SA, Dudley ME. Cancer regression in patients with metastatic melanoma after the transfer of autologous antitumor lymphocytes. *Proc Natl Acad Sci U S A.* 2004;101(suppl 2):14639-14645.

Recent clinical trials show that autologous cell transfer after lympho-depleting chemotherapy can cause the regression of large, vascularized tumors in patients with refractory metastatic melanoma. These studies are clarifying the

requirements for successful immunotherapy of patients with advanced metastatic disease and are leading to additional clinical trials with gene-modified lymphocytes.

Cormier JN, Xing Y, Ding M, et al. Population-based assessment of surgical treatment trends for patients with melanoma in the era of sentinel lymph node biopsy. *J Clin Oncol.* 2005;23:6054-6062.

Although treatment trends are improving, SLN biopsy continues to be underused, particularly in the elderly and minority populations, in patients with truncal and head/neck melanomas, and in some geographic regions of the United States.

Additional recommended readings:

Davies H, Bignell GR, Cox C, et al. Mutations of the BRAF gene in human cancer. *Nature.* 2002;417:949-954.

Brose MS, Volpe P, Feldman M, et al. BRAF and RAS mutations in human lung cancer and melanoma. *Cancer Res.* 2002;62:6997-7000.

Pollock PM, Harper UL, Hansen KS, et al. High frequency of BRAF mutations in nevi. *Nat Genet.* 2003;33:19-20.

Kirkwood JM, Ibrahim JG, Sosman JA, et al. High-dose interferon alfa-2b significantly prolongs relapse-free and overall survival compared with the GM2-KLH/QS-21 vaccine in patients with resected stage IIB-III melanoma: results of intergroup trial E1694/S9512/C509801. *J Clin Oncol.* 2001;19:2370-2380.

Chudnovsky Y, Khavari PA, Adams AE. Melanoma genetics and the development of rational therapies. *J Clin Invest.* 2005;115:813-824.

Demierre MF, Nathanson L. Chemoprevention of melanoma: an unexplored strategy. *J Clin Oncol.* 2003;21:158-165.