

Phase III Study of Denileukin Diftitox for Patients With Cutaneous T-Cell Lymphoma

This multicenter, randomized study examined the efficacy, clinical benefit, and safety of 2 doses of denileukin diftitox (DD) compared to placebo. Findings were reported by Dr. H. Miles Prince and colleagues in the March 8 issue of the *Journal of Clinical Oncology*. A total of 144 patients with stage IA–III CD25-positive cutaneous T-cell lymphoma (CTCL) were enrolled in the study. Patients were categorized by disease stage and randomized to receive DD at 9 µg/kg per day (n=45) or 18 µg/kg per day (n=55), or placebo (n=44). Treatment was administered on days 1–5 of each 21-day cycle for up to 8 cycles. The study's primary endpoint was overall response rate (ORR), and secondary endpoints included progression-free survival (PFS), duration of response (DR), time to response (TTR), and time to treatment failure (TTF). Patients received a median of 6 cycles. Previous therapy, which was received by 90% of patients, had no effect on response to DD. The study findings showed a significantly higher ORR in patients receiving the 2 doses of DD compared to placebo (37.8% in 9 µg/kg and 49.1% in the 18 µg/kg vs 15.9% in placebo group). Disease progression was seen in 21% of patients receiving DD compared to 52.3% of patients receiving placebo. PFS was also longer in patients in the DD groups: 971 days in patients receiving 9 µg/kg, 794 days in patients receiving 18 µg/kg, and 124 days in patients receiving placebo. Furthermore, DR and TTR were also longer in those receiving both doses of DD. The multivariate analysis found no variable significantly associated with response. The safety analysis revealed that sepsis occurred more frequently in placebo patients (6.8% vs 0%; $P=.05$). Toxicity related to capillary leak/vascular leak syndrome was reported in 10% of DD-treated patients, and adverse events were more common during the first 2–3 courses of treatment.

NCCN Amends Guidelines on Colorectal Cancer

According to the National Comprehensive Cancer Network's (NCCN) most recent guidelines on colorectal cancer (CRC), bevacizumab, cetuximab, panitumumab, and irinotecan should not be used for adjuvant treatment of stage II or III colon cancer outside of a clinical trial. Although adjuvant therapy is frequently administered in clinical practice to stage III CRC patients, no randomized trials have shown a benefit from bevacizumab, cetuximab, panitumumab, or irinotecan in stage II or III cancers. Dr. Paul Engstrom, the chair of the NCCN panel, who spoke at the NCCN 15th Annual Conference on March 11, 2010, recommended oxaliplatin, 5-fluorouracil, and leucovorin (FOLFOX) as adjuvant therapy, without the addition of these other agents. Previous trials, including

the phase III National Surgical Adjuvant Breast and Bowel Project (NSABP) protocol C-008, the MOSAIC (Multi-center International Study of Oxaliplatin/5-fluorouracil/Leucovorin in the Adjuvant Treatment of Colon Cancer) trial, and a recently unpublished pooled analysis, demonstrated limited or no benefit from adjuvant therapy. The amended guidelines recommend that testing for mismatch repair proteins be considered for all patients younger than 50 years. The NCCN panel also included v-raf murine sarcoma viral oncogene homolog B1 (BRAF) testing as an optional part of the work-up in metastatic disease if *KRAS* is not mutated. For rectal cancers, BRAF testing was also added to the guidelines. Also amended in the guidelines were the criteria for transanal excision. The procedure should now only be performed in T1 patients with negative margins and no lymphovascular or perineal invasion, and it should also be tailored to the patient. Preoperative radiotherapy is the preferred treatment for all rectal cancer patients, and capecitabine can be used to substitute for 5-FU radiotherapy. FOLFOX is recommended after resection to complete 6 months of adjuvant chemotherapy.

CD44 Polymorphisms Aid in Determining Risk of Recurrence in Gastric Cancer

According to researchers who analyzed blood and tissue samples from 137 patients, polymorphisms of the CD44 gene could help detect gastric cancer patients who have an increased risk of tumor relapse. Dr. Thomas Winder, who presented the findings at the American Society of Clinical Oncology Gastrointestinal Cancers Symposium, analyzed blood or formalin-fixed, paraffin-embedded tissue samples from patients with local stage II and III gastric cancer. Over a median of 3.3 years, tumor recurrence was observed in 45% of patients; the 3-year probability of recurrence was 0.52. In a univariate analysis, median time to recurrence for patients with the G allele (GG; AG) at the CD44 +4883G>A gene locus was 2.1 years and 7 years for patients without the G allele ($P=.022$). OS for patients with and without the G allele was 4.1 years and 7 years, respectively ($P=.079$). For patients with the A allele (AA; AG) at the CD44 +779G>A gene locus, median time to recurrence was 2.2 years compared to 7 years in those without the A allele; OS in patients with and without the A allele was 3.8 and 7.3 years, respectively ($P=.018$). In patients with at least one favorable allele, the median time to recurrence was 7 years compared with 1.7 years in those with no favorable alleles. Median OS was 7.3 years for patients with at least 1 favorable allele, and 3.6 years for those with no favorable alleles. The findings demonstrated that patients with either of the 2 alleles relapsed almost 5 years earlier than patients without these alleles.