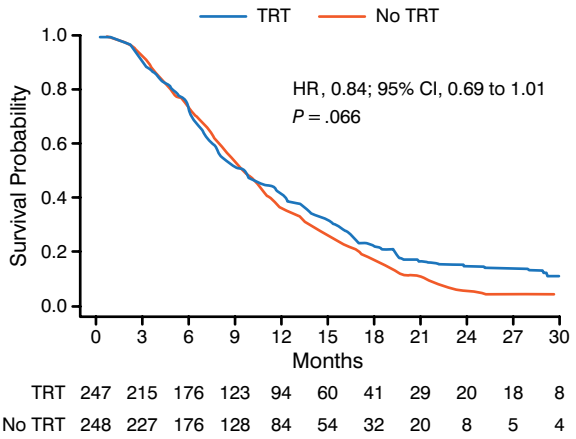
Eligibility requirements for CREST were patients aged ≥ 18 years with ES-SCLS disease, who had a World Health Organization (WHO) performance status score of 0 to 2 and had shown either a complete response (CR), a partial response (PR), or a "good response" to 4 to 6 platinum-based chemotherapy treatments. Exclusions included any brain, leptomeningeal, or pleural metastases, and any previous brain radiotherapy or TRT. Patients were randomized and stratified by institute and presence or absence of intrathoracic disease, and then received PCI 2 to 7 weeks after chemotherapy and either TRT (10 fractions of 3 Gy) or no TRT. The primary end point of the study was OS, with secondary end points of progression-free survival (PFS), local control, failure pattern, and toxicity. The study was designed at 80% power to detect a hazard ratio of 0.76 for OS at 1 year (2-sided, with 5% significance). Accounting for a 5% dropout rate between randomization and start of treatment, 483 patients needed to be randomized. Accrual was successful, with 498 patients enrolled in 42 centers primarily in The Netherlands and the United Kingdom. The median patient age was 63 years, and 55% of participants were men and 45% were women. Over one-half of patients had a WHO performance status score of 1, whereas another one-third had WHO 0 and 10% had WHO 2 scores. In terms of their response to chemotherapy, just over 70% of patients had PR, one-fourth showed "good" response, and just 5% had a CR. As seen in other studies, nearly 90% of such patients with ES-SCLC treated with chemotherapy had persistent intrathoracic disease.

The primary end point was not met for OS because the hazard ratio did not meet criteria for statistical significance (HR, 0.84; 95% CI, 0.69 to 1.01; $P = .066$). However, in reviewing the OS curves, Dr Slotman said that the curves did begin to diverge in a statistically significant way at about 9 to 12 months in favor of TRT, and that the survival at 24 months was "highly statistically significant" ($P = .004$). Intrathoracic progression data showed strong statistical significance, with 43.7% of patients progressing who had received TRT compared with 79.8% for the control group ($P < .001$). Treatment was well tolerated, with all toxicities (cough, dysphagia, dyspnea, esophagitis, fatigue, insomnia, nausea/vomiting, and headache) with no difference between the arms and restricted to grade 3 on the Common Terminology Criteria for Adverse Events v3 scale. Dr Slotman concluded that TRT administered in addition to PCI for patients with ES-SCLC improved OS and PFS, and that TRT should be offered in addition to PCI to patients with a response to initial chemotherapy.

Figure 1. Overall Survival in CREST



CREST, Chest Radiotherapy Extensive Stage Trial; TRT, thoracic radiotherapy.
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Capecitabine Compared With Capecitabine Plus Oxaliplatin Chemoradiotherapy

Written by Emma Hitt Nichols, PhD

Preliminary findings demonstrate that patients with rectal cancer receiving radiotherapy with a combination of capecitabine and oxaliplatin have better local regional control compared with those receiving capecitabine plus radiotherapy. Hua Ren, MD, Cancer Hospital Chinese Academy of Medical Sciences, Beijing, China, presented interim data from the ongoing phase 3 open-label Adjuvant Treatment of Concurrent R and CAPOX or Capecitabine Alone for Stage II and III Rectal Cancer trial [NCT00714077].

The current postoperative therapy regimen for patients with advanced rectal cancer usually consists of radiotherapy and the chemotherapeutic agent capecitabine. It is unknown whether combination capecitabine and platinum-based chemotherapy has superior effects on clinical outcomes. This multicenter study assessed the efficacy and safety of these 2 chemoradiotherapy treatment regimens.

A total of 414 patients with rectal cancer were stratified by their pathologic stage (II or III) and randomized 1:1 to either the capecitabine (Cap) group (190 patients) or the capecitabine/oxaliplatin (CapOx) group (224 patients). Capecitabine was administered at 825 mg/m^2 alone (Cap) or at 825 mg/m^2 twice daily with 50 mg/m^2 oxaliplatin at the beginning of each week (CapOx). All patients underwent radiotherapy at 50 Gy in 25 fractions

with 2 dose cycles of concurrent chemotherapy. After 5 weeks of treatment, each group received 4 to 6 dose cycles of CapOx and fluorouracil.

By 3-year follow-up, there were no differences in disease-free survival rate in the Cap group compared with the CapOx group (71.79% vs 71.6%; $P = .799$). Overall survival rates were also similar (89.0% vs 85.1%, $P = .916$). Although there was no difference in cumulative metastatic rate (19.9% vs 20.7%, $P = .834$), patients in the Cap group had a higher local recurrence rate than those in the CapOx group (8.1% vs 3.2%, $P = .034$).

There were no newly identified toxicities in either group. However, the Cap group had significantly fewer cases of thrombocytopenia (6.7% vs 14.2%, $P = .012$) and fatigue (60.3% vs 71.8%, $P = .014$).

The authors concluded that although there were significant differences in local recurrences, further patient recruitment is needed to obtain planned sample size calculations.

Concomitant TMZ Does Not Improve Effectiveness of WBRT for Brain Metastases From Breast Cancer

Written by Emma Hitt Nichols, PhD

The addition of temozolomide (TMZ) does not improve the efficacy of whole-brain radiation therapy (WBRT) for the treatment of brain metastases from breast cancer. Kim I. Cao, Institut Curie, Paris, France, and colleagues presented data from a phase 2 prospective randomized multicenter study.

TMZ, an oral alkylating agent, has radiosensitizing properties and has demonstrated promise in previous phase 2 studies involving WBRT. However, these studies did not include sufficient samples of patients with brain metastases from breast cancer, despite the need for improved treatments for such patients. The present phase 2 trial was intended to determine whether concomitant TMZ with WBRT could improve outcomes for these patients.

Patients were eligible for this study if they had intraparenchymal metastases from breast cancer that were newly diagnosed, inoperable, and not suitable for radiosurgery. A total of 100 patients were randomly assigned to 2 treatment groups, one of which received WBRT (3 Gy × 10 to 30 Gy) alone, while the other received WBRT concomitantly with 75 mg/m^2/d of TMZ.

Radiologic objective response was the primary end point, determined by brain magnetic resonance imaging 6 weeks after the end of treatment. This end point was defined as a partial or complete response based upon World Health Organization–modified criteria. There were multiple secondary end points, including overall survival (OS) and local progression-free survival (PFS). Neurologic symptoms and safety data were also collected.

The primary end point was similar between the 2 study arms; the objective response rates were 30% and 36% for concomitant (WBRT + TMZ) therapy and for WBRT alone, respectively, which was not a significant difference. No patients showed complete response. Neither the median OS nor PFS was statistically significant. The median OS was 11.1 months in the WBRT arm compared with 9.4 months in the concomitant therapy arm. The median PFS was 7.4 months in the WBRT arm compared with 6.9 months in the concomitant therapy arm. The concomitant therapy arm did not show more neurologic improvement than the WBRT arm. Additionally, the concomitant therapy was well tolerated (reversible lymphopenia was the most serious acute toxicity).

The authors concluded that adding TMZ to WBRT did not significantly improve outcomes in patients with brain metastases from breast cancer on the basis of the outcomes studied.

Radiotherapy With and Without T for GBM

Written by Emma Hitt Nichols, PhD

Hypofractionated radiotherapy (HRT) is more effective with temozolomide (T) than without it and as effective as standard (Stupp regimen) radiotherapy (SRT) with T in improving the overall survival of elderly patients with glioblastoma (GBM). Shyam Tanguturi, MD, Brigham and Women's Hospital, Boston, Massachusetts, USA, and colleagues presented data from a retrospective study.

The Stupp regimen of HRT (SRT) is commonly used with T for the treatment of elderly patients with GBM. However, there has been insufficient study, and no randomized trials, comparing SRT with and without T to HRT. This retrospective study was designed to compare SRT and HRT alone and with T (SRT + T and HRT + T, respectively).

One hundred thirty-five patients who had been treated with SRT (59.4–60 Gy in 30–33 fractions) or HRT (40 Gy in 15 fractions) alone or with T (SRT + T and HRT + T) and who had been diagnosed with GBM between 1994 and 2013 were included in this study. Prognostic factors and overall survival were calculated.

The primary end point was overall survival. The data were also analyzed to determine if other factors, such as prognostic factors, differed between the groups or were associated with increased mortality.