subgroups (6.3 vs 7.2 months chemosensitive; 3.4 vs 5.7 months chemorefractory).

Treatment-emergent adverse events (TEAEs) were more frequent with topotecan. Any TEAE of any grade occurred in 94.3% of the topotecan and 88.8% of the cabazitaxel groups, and ≥grade 3 TEAE occurred in 71.6% and 58.4%, respectively. Overall, 29 deaths resulted from TEAEs. TEAEs that led to death and were considered possibly related to treatment were neutropenic infection in 3 patients, febrile neutropenia in 2 patients, neutropenic sepsis in 1 patient, and cardiopulmonary failure in 1 patient.

Randomized, Prospective Trial of Customized Neoadjuvant Versus Standard Chemotherapy Gets Underway

Written by Rita Buckley

The first prospective, multicenter, randomized Phase 2 study to test the use of customized chemotherapy (CT) in locally advanced stage IIIA (N2) non–small cell lung cancer (NSCLC) is currently recruiting patients. The rationale and design of the Customized Neoadjuvant Versus Standard Chemotherapy in NSCLC Patients With Resectable Stage IIIA (N2) Disease trial [CONTEST; NCT01784549] were presented in a poster session.

The most powerful prognostic factor in stage IIIA NSCLC is clearance of mediastinal lymph nodes and pathologic complete response (pCR). A pCR is obtained in 5% to 15% of patients with a significantly prolonged survival. The discovery of predictive molecular tumor biomarkers, such as mutations in the epidermal growth factor receptor (EGFR), has sparked interest in their use for delivery of individualized treatment strategies to increase response rate and survival of patients with NSCLC.

The hypothesis of this study is that NSCLC patients who receive therapy determined by their baseline histology and tumor marker levels will attain higher response rates than patients in the control arm who receive standard CT. At 18 sites, a total of 168 subjects (112 in the investigational arm, and 56 in the standard care arm) with resectable stage IIIA (N2) NSCLC will be centrally randomized in a 2:1 ratio to receive before resection either standard CT with cisplatin (CDDP) plus docetaxel (Doc) or 1 of 6 customized CT arms using predetermined values for excision repair cross-complementation group 1 (ERCC1), ribonucleotide reductase M1 (RRM1), thymidylate synthase (TS), and EGFR mutations. These arms, by biomarker, are

- EGFR+: gefitinib
- EGFR–/nonsquamous (NS)/TS–/ERCC1–: CDDP + pemetrexed
- EGFR–/squamous (S) or NS/TS+/ERCC1–/RRM1+: CDDP + Doc
- EGFR–/S or NS TS+/ERCC1–/RRM1–: CDDP + gemcitabine (Gem)
- EGFR–/S or NS TS+/ERCC1+/RRM1+: Doc + vinorelbine
- EGFR–/S or NS TS+/ERCC1+/RRM1–: Doc + Gem

The primary endpoint is pCR at 30 days, on independent pathology review, using an intention-to-treat analysis. Secondary outcomes are overall survival (OS), disease-free survival (DFS), and overall survival at 1, 2, and 5 years; overall response; and safety. Biological and tissue samples will be collected for exploratory molecular-profiling analyses and biomarker studies.

Specimens will be sent to Response Genetics (Los Angeles, CA, USA) for the evaluation of ERCC1, RRM1, and TS using reverse transcription polymerase chain reaction (RT-PCR). EGFR mutations will be assessed with Sanger sequencing.

Every 4 months for 3 years, and then every 6 months for 2 years following surgery, patients will be assessed for adverse events related to the study drugs, and their therapies received after the study, DFS, and survival will be documented. Periodic evaluation of the trial data will be conducted by an independent data-monitoring committee to ensure patient safety and the validity and scientific merit of the study. The final analysis will be conducted after the targeted number of events (pCR) is reached, or in 24 months, after study initiation.

The study is designed to determine the feasibility of the customized treatment approach and the logistical problems associated with a biomarker-driven strategy in NSCLC.