New Trial Starting, Studying Avastin with Adjuvant Chemo

At long last, and after years of planning, a new large phase III randomized clinical trial is getting underway to determine whether adding avastin to chemotherapy as post-operative (adjuvant) treatment for early stage NSCLC provides added benefit compared to chemotherapy alone. This trial, led by the Eastern Cooperative Oncology Group (ECOG) and with the principal investigator Heather Wakelee of Stanford, is designated E1505 and will randomize 1500 patients with stage IB (tumors of 4 cm or larger only) or stage II or IIIA NSCLC to receive four cycles of any one of three chemo regimens alone or with avastin, and the avastin arm will also receive ongoing avastin for up to a year:

Avastin is of great interest in this setting because adding avastin to chemo improved survival for eligible patients with advanced NSCLC by a couple of months (post here), and perhaps a better result in post-op treatment for early stage, surgical disease would translate to a significant increase in the actual cure rate for NSCLC.

A few key points here are that only cisplatin-based chemotherapy regimens are permitted here, because cisplatin-based chemo has been proven to confer a survival benefit as adjuvant treatment, but the same hasn’t yet been seen with carboplatin-based chemotherapy (carbo/taxol was included in earlier versions of the trial, but this regimen was dropped after the results from the CALGB 9633 trial (abstract here) became negative). Interestingly, although cisplatin/gemcitabine and cisplatin/taxotere haven’t been proven in adjuvant chemo trials to improve survival, there have been so many studies showing nearly identical activity of these cisplatin doublets that everyone pretty much agrees that it makes sense to provide several alternatives. The stage IB patients are allowed to be enrolled if they have a tumor of 4 cm or larger, because this subgroup received a benefit from chemo on the CALGB 9633 trial, while those with smaller tumors did not (also described in a prior post here). Finally, the trial will enroll patients who have had squamous cancers resected, because while those with squamous tumors have a higher risk of bleeding in the advanced NSCLC setting, in the adjuvant setting the cancer has been removed, so the risk of bleeding would not be anticipated to be higher in people with a resected squamous tumor compared with other NSCLC subtypes.

This is considered one of the most important questions in the field of early stage lung cancer, so all of the major cooperative groups in North America are joining in this effort to enroll. We can only hope that doctors and patients will be willing to participate. Although Avastin may provide a significant improvement in the cure rate, it’s possible that it will add only increased side effects — the clinical trials with avastin show an increased risk of bleeding, high blood pressure, headaches, and sometimes lower blood counts and increased risk of infection. I
wouldn’t presume I know how it will turn out, but I do think that it may lead to another stepwise improvement in our treatment of lung cancer; if not, it will still have been worth looking carefully for the right answer about the balance of activity and side effect profile.

Importantly, this trial will also collect tissue and blood samples from participants so that we can learn more about the proteins and genes that predict how cancers will behave, and how we might predict who is more likely to benefit from chemo and/or avastin treatment and who is more likely to just experience the adverse effects of treatments.

For those interested in learning more, information on the trial is located here and here. Although it’s just getting started now (July 2007), participating sites should become increasingly available throughout North America in the next several weeks and months.