Flaws in the trial design of IFCT-0802

We have deep concerns regarding the design of the IFCT-0802 phase II-III trial of bevacizumab in combination with chemotherapy for small-cell lung cancer (SCLC), extensive disease (ED), published in the May issue of *Annals of Oncology* [1]. ED SCLC is notorious for its dismal prognosis, with overall survival (OS) of only 9–11 months and a 2-year survival rate of <5% [2, 3]. So, OS should be the primary end point of all the clinical trials measuring efficacy in SCLC ED. In cancers like breast where the median survival is long, measuring progression-free survival (PFS) as a surrogate end point has some meaning. First, it takes long time for enough events to occur to measure the impact on OS. Second, PFS becomes very meaningful for patients with significant longevity. But ED SCLC does not belong to this group and enough events occur at a reasonable amount of time to make an assessment.

However, the end point of the study in question is not even PFS but the percentage of disease control at the fourth cycle. In this study, after two chemotherapy induction cycles, the chemotherapy group and chemotherapy plus bevacizumab group receive further four cycles followed by bevacizumab maintenance. So we could not understand the meaning in measuring disease control rate at the end of fourth cycle instead of waiting until the end of six cycles when the chemotherapy is completed? Measuring the disease control rate at the end of six cycles after chemotherapy has been completed would make more sense. However, as mentioned above, we firmly believe that OS should be the primary end point of ED SCLC trials, or at least PFS.

Because of these issues in the study, trials testing bevacizumab in SCLC should not be discouraged. ED SCLC has always been the shame of oncology where we have not been able to make any progress since more than a decade. Better design studies with novel agents are desperately needed in this disease.

B. Gyawali*, T. Shimokata, K. Honda & Y. Ando
Department of Clinical Oncology and Chemotherapy, Nagoya University Hospital, Nagoya, Japan
(∗E-mail: bg.bishalgyawali@gmail.com)

disclosure

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**references**


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Does activity of anticancer drugs in advanced cancer always translates in effectivity in early-stage high-risk disease?

Most anticancer drugs are developed in cancer patients with advanced disease, for whom no standard treatment is available. When active, they are tested in earlier settings and finally in patients with early-stage high-risk disease to obtain an improvement in overall survival.

Many older cytotoxic anticancer drugs, which were first used in cancer patients with advanced disease, have now a place in the adjuvant treatment of patients with early-stage high-risk disease. This is the case for patients with breast cancer with the use of alkylation agents, anthracyclines and taxanes, for patients with nonsmall-cell lung cancer (NSCLC) with platinum-based regimens, colorectal cancer with fluoropyrimidines-based schedules and more recently prostate cancer with taxanes [1] (Table 1).

Also hormonal manipulation, active in advanced metastatic disease proved to be effective in earlier settings as shown in hormone-sensitive breast [e.g. tamoxifen, aromatase inhibitors and prostate cancer (biochemical castration in combination with radiotherapy)].