Letter to the Editor

Gefitinib versus Docetaxel for Previously Treated NSCLC—Response

Dae Ho Lee and Sang-We Kim

Gefitinib obtained approval in Korea in 2003 based on the result of IDEAL-1, which had shown a higher response rate of 27.5% than that of 7.1% in a docetaxel trial (1, 2). Therefore, at the time of designing our trial, unlike other new agents waiting for approval, gefitinib was already being widely used in daily practice in Korea in second-line setting, but many Korean oncologists still wanted clear evidence for, or against, the use of gefitinib over cytotoxic chemotherapy. Taken altogether, we had chosen "superiority trial" instead of "noninferiority trial" (3, 4) to answer the question of which one was better through head-to-head comparison. With careful consideration, we had chosen one-sided α-error of 5%, instead of usual two-sided α-error of 5% and progression-free survival (PFS) as the primary endpoint, to decrease sample size and accrual time and to obtain meaningful results faster. Alpha error, type I error, or "false positive" is the error of rejecting a null hypothesis even when it is true. Considering better toxicity profile and convenience of administration of gefitinib, we had thought that rather higher α-error could be accepted, even if gefitinib is not superior to docetaxel. Also, we have thought that PFS was better than overall survival (OS) as the primary endpoint because post–discontinuation treatment might complicate interpretation of survival data due to crossover effect on survival. There is still ongoing controversy about the selection of the most appropriate primary endpoint. OS is more important than PFS for patients. However, PFS is a better choice when among many active therapeutic options the effect of each therapy should be measured.

As pointed out, the reason that the PFS curves between the 2 treatments differed only in the final part might be due to maintenance effect of gefitinib treatment, which, however, might be another reason to choose gefitinib over cytotoxic chemotherapy. Of note, a meta-analysis showed that for Asian patients, gefitinib is superior to docetaxel in terms of PFS and objective response rate (5).

Unfortunately, we have not assessed the role of EGFR mutation in this clinical setting, but patient’s mutational status might affect the clinical outcome. Although a sub-group analysis did not show the difference according to the mutation status (3), considering that EGFR mutants might already receive gefitinib or another EGFR tyrosine kinase inhibitor as first-line treatment, further studies are required to evaluate the role of gefitinib as second-line treatment after excluding those patients.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

References

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