RE: Generalizability of Trial Results to Elderly Medicare Patients With Advanced Solid Tumors

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With interest we have read the analysis of Dr. Lamont and colleagues on three chemotherapy regimens in two different settings, clinical trials vs usual care (1). Using Surveillance, Epidemiology, and End Results—Medicare data, the authors conclude that clinical trials for advanced pancreatic cancer and lung cancers tended to correctly estimate survival for Medicare patients age 65 to 74 years, but to overestimate survival for older Medicare patients. However, the authors did not check the eligibility of patients for the treatments administered. We have analyzed this aspect and found that this may statistically significantly impact the outcome of treatment. We compared the outcome of 394 metastatic colorectal cancer patients treated with standard cytotoxic drugs within a prospective phase III trial using standard safety eligibility criteria (2) vs 309 patients treated outside the scope of this trial but with the same drugs and during the trial accrual period (3). Patients treated outside the trial were divided into two groups: patients who would have qualified for trial participation (n = 224) and patients who failed to meet relevant eligibility criteria (n = 85). We found that the outcome of patients treated outside the trial but who could have qualified was comparable with the outcome of patients treated within the trial, 15.7 months and 17.0 months respectively (two-sided log-rank test, hazard ratio [HR] = 1.03, 95% confidence interval [CI] = 0.87 to 1.23, P = .70). However, the outcome of patients treated outside the trial who did not meet standard eligibility criteria was statistically significantly lower compared with eligible non-trial patients and trial patients, with median overall survival times of 9.3 months (HR = 1.70, 95% CI = 1.11 to 2.84), 15.7 months (HR = 1.03, 95% CI = 1.41 to 17.4), and 17.0 months (95% CI = 15.7 to 18.4), respectively (P < .01, two sided log-rank test) (Figure 1). There was no statistically significant difference in age between these groups, 61 years for the eligible non-trial patients, 61 years for the trial patients, and 63 for the ineligible non-trial patients (P = .28). We concluded that

the external validity of trial results only applies when trial eligibility criteria are respected in general practice. Therefore, the finding of Lamont et al. (1) that trial results are not generalizable in the older patient population may possibly be explained by the fact that these patients are not eligible for trials on criteria other than age. We strongly recommend inclusion of the assessment of standard baseline safety criteria in population-based studies on the outcome of systemic treatments in cancer patients in daily practice.

Funding

This study was supported by the Dutch Colorectal Cancer Group, Netherlands Cancer Organisation, and unrestricted grants from Sanofi-Aventis.

Notes


The study sponsors had no role in the writing of this commentary or the decision to submit for publication.

References

Figure 1. Overall survival for stage IV colorectal cancer patients participating in the CApecitabineIrinotecanOxaliplatin (CAIRO) trial and patients who were treated outside trials and did or did not meet CAIRO eligibility criteria (two-sided log-rank test). CI = confidence interval; OS = overall survival; pts = patients.