Are we representing the true population in oncology trials?

We thank Kang et al. [1] for their trial ML17032 published in the recent issue of *Annals of Oncology*. This confirmed the noninferiority of capecitabine to infusional 5-fluorouracil as part of palliative combination chemotherapy for advanced gastric cancer. In the accompanying editorial, Wong and Cunningham [2] make the important point that current evidence indicates doublet chemotherapy regimens are inferior to triplet regimens in this setting.

We would like to raise awareness to the mismatch that exists between the physician selected trial populations upon which this evidence relies and the real-world populations that comprise advanced gastric and oesophageal cancer. The degree of selection is illustrated by the median age in the ML17032 study which was 56 years (range 22–74 years). This compares with the typical gastric cancer population where, for example, in the UK, the median age at death is 77 years with 82% of patients being over the age of 70. This problem underlies the entire evidence base for palliative chemotherapy in this tumour type. The REAL-2 trial, the largest trial to date has a median patient age of 63 [3]. In spite of attempts to address this problem with pooled analyses [4], level 1 evidence is lacking for a large cohort of these patients.

This issue is not unique to upper gastrointestinal cancer and the ageing population in the Western world can be expected to lead to a marked increase in the number of elderly patients seeking treatment over the coming decades.

One might argue that the focus of evidence on the younger minority accurately reflects sensible use of chemotherapy by limiting it to those in whom the risk–benefit trade-off is likely to be favourable. However, evidence indicates that age is not a negative predictive factor for response or a negative prognostic factor for survival outcomes in gastric or oesophageal cancer [5]. It may be that the toxicity of triplet or even doublet regimens may indeed outweigh any anticancer benefit in the elderly. Only by assessing single-agent, doublet and triplet therapy at appropriate doses in the elderly population, will we secure a comprehensive evidence base and determine a standard treatment in this important group of patients.

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references


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