

Authors' reply

We appreciate the comments from Tetsuya Tanimoto and colleagues, and Ian Haines and colleagues. They allow us to clarify a few important points.

Tanimoto and colleagues note that second-line therapies might affect overall survival. We agree with this statement. However, as of June, 2009 (closure of database for analysis), only a minority of patients had received second-line therapy. Therefore, the results were too preliminary to allow reliable conclusions. Moreover, a high proportion of patients with a short progression-free survival had a del(17p) mutation, which predicted a short progression-free survival and overall survival in this trial. Therefore, 3 years after randomisation, genomic aberrations seemed to have a stronger effect on outcome than the type of second-line treatment.

70 patients were assessed as having stable disease after three courses (30 in the fludarabine, cyclophosphamide, and rituximab [FCR] group and 40 in the fludarabine and cyclophosphamide [FC] group); most of them continued with study treatment. So far, more patients in the FC group have received second-line therapies than in the FCR group. A systematic assessment of the response to these therapies would be premature and based on a very small subset of patients.

We do not agree with Haines and colleagues' comments on the study population. The proportion of Binet A patients is very small at only 5%; 31% of patients were Binet C stage. The role of granulocyte colony-stimulating factor (G-CSF) needs to be further investigated. However, results from prospective phase 3 trials have found that first-line treatment for chronic lymphocytic leukaemia (CLL) with FC or fludarabine alone can be applied without the addition of G-CSF or similar growth factors.¹ In this trial, G-CSF was given only in about 2% of courses, again suggesting that FCR or FC could be

safely given in first-line therapy of patients with CLL.

The German CLL Study Group is making every possible attempt to follow up patients from its trials until death to gain insight into the long-term consequences of all treatment modalities. Therefore, this study was not discontinued. Although the results of the first interim analysis were robust, reliable, and significant, we decided to repeat the analysis with 1 additional year of follow-up and a longer median observation time (37.7 months). These results were reported in the published manuscript.

The primary endpoint of this trial was progression-free survival; secondary endpoints were response rates and overall survival. The repeated analysis with a median observation time of 47.4 months has yielded similar results, with FCR causing a longer overall survival. Moreover, progression-free survival is an accepted and recommended endpoint, since progression was clearly defined by the 1996 guidelines and the updated version.^{2,3}

We agree that the study population of this trial is young compared with most CLL patients. As stated in the Article, conclusions of this trial could not be transferred to patients with relevant comorbidity. However, patients older than 65 years tolerated both treatment modalities quite well with no significant differences in toxic effects, since they were selected according to their physical fitness (cumulative illness rating scale and creatinine clearance).

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*M Hallek, A Fink, R Busch, K Fischer
michael.hallek@uk-koeln.de

Department of Internal Medicine I, Center for Integrated Oncology, University of Cologne, 50924 Köln, Germany (MH, AF, KF); and Technical University, Institute for Medical Statistics and Epidemiology, Munich, Germany (RB)

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UK Public Accounts Committee report on health inequalities

Your Nov 13 Editorial (p 1617)¹ on the Public Accounts Committee report into health inequalities in the UK states that the “reasons for this failure [to tackle health inequalities] have now been exposed”. But, inequitable access to primary care and a failure to tackle smoking, cholesterol, and hypertension is not the reason why health inequalities have increased since the Acheson Inquiry of 1997.²

The Acheson Inquiry included 39 recommendations for tackling health inequalities, but only three of these focused solely on action by the National Health Service (NHS). That inquiry and subsequent reports focused on the wider determinants of health.³ Extensive published research supports Donald Acheson's basic premise that “Health inequalities are the outcome of causal chains which run back into and from the basic structure of society”.² These underlying determinants are noticeably absent from the Editorial.

Although we would not dispute that the performance of the NHS on inequalities has been disappointing, it is essential that the lessons of the Marmot Review and Commission on Social Determinants of Health are

not lost.⁴ The current government emphasis on individual responsibility, “nudge”, and fairness⁵ does not address the inequitable structure of society. The decision to scrap the socioeconomic duty of the Equality Act is especially problematic, since this legislation was designed to address the social inequalities that Michael Marmot and others have so convincingly linked to health inequalities.

Successful reduction in health inequalities will necessarily involve the NHS. But significant change will only be achieved with an emphasis on wider determinants and widespread acceptance that “Social injustice is killing people on a grand scale”.³

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Martin Higgins,
***Srinivasa Vittal Katikireddi,**
Philip Conaglen, Colwyn Jones,
Margaret Douglas
vkatikireddi@nhs.net

NHS Lothian, Edinburgh, UK (MH, MD); MRC Social and Public Health Sciences Unit, Glasgow G12 8RZ, UK (SVK); NHS Fife, Windygates, UK (PC); and NHS Health Scotland, Edinburgh, UK (CJ)

- 1 The Lancet. “Claptrap” from the UK’s Department of Health. *Lancet* 2010; **376**: 1617.
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Donald Acheson inspired many of us then at University College London to think creatively about reducing entrenched health inequalities. I personally take responsibility for the “agonising debacle”¹ following his inquiry. Do not blame civil servants or medical advisers, who never recognised the constraint holding back progress in tackling inequalities. Over years I collected evidence of a

systematic failure of leadership in public health,² but failed to persuade any statutory or professional body to take that handicap seriously. It is my fault bureaucrats are reduced to “claptrap” justifying “the worsening situation”.¹

Failing at an institutional level, how about the individual level? I teach trainees about health inequalities and the evidence base for tackling them. The *Evaluation of the Foundation Programme for England*³ just arrived. Across 12 specialties, assessment found public health to be the least interesting to junior doctors (only 41 of 5398 involved). Quality of “educational supervision” for trainees trying public health scored lowest of any specialty. Mea culpa.

The community level? I became honorary consultant to a Pathfinder children’s trust: a key interagency development. The Commissioning Support Programme, which helps children’s trusts achieve their aspirational outcomes, held an illuminating meeting in May, 2009. This meeting claimed that Joint Strategic Needs Assessment (JSNA) would “reduce inequalities”, but asked “is it possible to draw a line from the JSNA to the commissioning decisions?” The answer: a resounding “no”, since inequalities in child health have widened. Sorry.

There are ways to reduce inequalities through commissioning⁴—but don’t tell anyone I told you...

I declare that I have no conflicts of interest.

Woody Caan
a.w.caan@anglia.ac.uk

Anglia Ruskin University, Cambridge CB1 1PT, UK

- 1 The Lancet. “Claptrap” from the UK’s Department of Health. *Lancet* 2010; **376**: 1617.
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Pakistan: the final frontier for a polio-free world

The success of the bivalent polio vaccine trial (Nov 13, p 1682)¹ has re-energised the global polio-eradication campaign. Of the four countries where polio remains endemic, great progress has been made in Nigeria, India, and Afghanistan.² Pakistan, however, accounts for 60% of polio cases among endemic countries, and is the only country with an increase in cases from 2009.² Clearly, therefore, Pakistan is the final frontier for a polio-free world.

There are two major challenges for polio eradication in Pakistan. First, most new cases reported in Pakistan are from flood-affected areas where there has been widespread destruction of infrastructure.² Although vaccinators have been mobilised in great numbers, the displacement of populations, breakdown of cold chains, and poor conditions in refugee camps are some of the reasons why the floods present a staunch challenge to public health officials.²

Second, the tribal areas bordering Afghanistan account for most cases in Pakistan,³ not only resulting in export of the disease to other parts of Pakistan but across the border to Afghanistan as well.⁴ Labelling vaccination a western conspiracy, the Taliban killed the head of the vaccination service and have prevented children there from being vaccinated.⁴ In doing so, they have preserved a critical mass of transmission that poses a major obstacle to eradication.

The bivalent vaccine must replace the current trivalent vaccine, which is known to be ineffective even after multiple doses.⁵ Stakeholders, including the Pakistani government, international agencies, and donors, should focus on implementing measures to vaccinate—and educate—both on the waterfronts and the battlefields.

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