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CORRESPONDENCE

Treatment of smoldering multiple myeloma

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We read with interest the News & Views article by Rajkumar and Kyle (Treatment of smoldering multiple myeloma. *Nat. Rev. Clin. Oncol.* **10**, 554–555; 2013)[1] that focused on a recently published study by Mateos and colleagues.[2] We agree with Rajkumar and Kyle that additional studies are needed to determine the patients with SMM who would benefit from early treatment.[1] However, although treatment of a tumour at an early stage is, of course, ideal in attempting to achieve a cure, many questions arise from the underlying study[2] and we would like to raise some further points of discussion not conveyed in the recent editorial.

We mainly argue that the treatment groups were unbalanced in the intensity of treatment received. When comparing the SMM treatment and observation groups, a clear advantage in overall survival must be seen.[1,2] This advantage is related not only to safety and quality-of-life issues for the patient, but is also relevant in terms of understanding the cost effectiveness of treatments. Experimental treatment must be superior in terms of overall survival, either to the gold standard treatment at disease progression (for that population stratified by age), or should be the same treatment for both groups (type and duration). In other words, to demonstrate an advantage for early treatment, the only variable should be the time of treatment initiation (early versus late). In the study by Mateos and colleagues, treatment duration with lenalidomide was almost 3 years (9 months induction + 2 years of maintenance) versus a shorter duration that was not clearly specified in the study for the observation group. It seems, therefore, that patients in the treatment group received consolidation and maintenance with lenalidomide that was not given to the observation group, representing a bias for the study.

Moreover, stratification by age was not the same in the treatment and control groups (63 years of age versus 69 years of age, respectively). Life expectancy can be inferior in an older population of patients, which might explain the high-rate of deaths seen in the observation group. Finally, as underlined by Rajkumar and Kyle, fluorescent *in situ* hybridization (FISH)—an important diagnostic and prognostic tool for SMM—was not mentioned in the study. FISH was recently shown to be able to identify those patients who have a high risk of disease progression (for example, patients with a deletion on chromosome 17p or a translocation between chromosomes 4 and 14). This genetic analysis will help patient stratification in the future. Importantly, due to the peculiarity of beginning a treatment in patients with an asymptomatic disease and the discovery of new and more effective drugs for myeloma, researchers should focus on comparable treatment arms to show advantages in early versus late therapy in SMM.[3,4]

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Competing interests
The authors declare no competing interests.

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