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Lenalidomide as maintenance for every newly diagnosed patient with multiple myeloma

In patients with newly diagnosed multiple myeloma, how to maintain the responses achieved after optimal therapeutic strategies was a challenge, and maintenance therapy emerged as an option aiming to extend the duration of the response through continued treatment and thereby improving progression-free survival and overall survival. Because maintenance treatment is administered as continuous therapy, emphasis is placed on the convenience of administration, tolerability, and toxicity.¹

Lenalidomide is the only approved single agent treatment for patients with newly diagnosed multiple myeloma after transplantation.² In *The Lancet Oncology*, Graham Jackson and colleagues³ confirm the benefit of lenalidomide in terms of progression-free survival. In transplantation-ineligible patients, the findings by Jackson and colleagues also support the results reported with low-dose lenalidomide as maintenance after induction with melphalan, prednisone, and lenalidomide, and are in line with the use of full-dose lenalidomide and dexamethasone as continuous therapy reported in the FIRST trial.^{4,5} Although the debate in this setting has always been whether to use fixed or continuous therapy, the trend now is use of continuous therapy with either lenalidomide or daratumumab after induction with daratumumab in combination with bortezomib plus melphalan and prednisone.⁶

Lenalidomide maintenance seems to be effective, well tolerated, and convenient, despite the lack of overall survival benefit, because of the influence of rescue therapies in the overall survival. Lenalidomide is, therefore, a maintenance therapy option for every

patient with newly diagnosed multiple myeloma, but new therapies or combinations of drugs are needed to improve overall survival in these patients.

Lenalidomide is convenient because it is administered orally, and this study did not report any unexpected toxicity data. Of note, an adequate bone marrow reserve is required for the use of lenalidomide as maintenance treatment and monitoring for second primary cancer is needed. Additional studies assessing health-related quality of life through patient-reported outcomes are necessary to know the patients' perspective.

The approved dose of lenalidomide is 10 mg continuously with the possibility of increasing to 15 mg, but different doses and schedules have been so far used in different trials. In the Myeloma XI trial,³ the initial dose specified by protocol was 25 mg, but this was changed to 10 mg in a protocol modification. Whether different doses and schedules could potentially result in different outcomes is not known, but the results of this study³ regarding the median progression-free survival of 26 months (95% CI 22–31) in transplantation-ineligible patients is similar to that reported in the FIRST trial, in which lenalidomide was given at full dose combined with low-dose dexamethasone. Is it, therefore, possible to switch to low-dose lenalidomide without dexamethasone in transplantation-ineligible patients after induction therapy?

New agents or combinations of these are being investigated as maintenance therapy in this setting and might result in new standards of care. For example, vorinostat was combined with lenalidomide in a subset of patients in this study, and we await the results.



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The results of this study³ support the benefit of lenalidomide maintenance across different subgroups of patients and highlights the progression-free survival benefit in patients with high-risk cytogenetic abnormalities. However, it is important to note that lenalidomide did not overcome the poor prognosis that the presence of high-risk abnormalities confer to patients, and therefore novel treatments to improve the outcomes of these patients are needed.

Whether all patients need continuous maintenance therapy regardless of the quality of the response achieved with previous treatments remains unclear. However, next-generation sequencing and cytometry provide an opportunity to investigate the role of minimal residual disease assessment for tailoring maintenance strategies and would allow physicians to prescribe maintenance therapy and reply to a very common question raised by the patients: how many cycles of treatment does maintenance therapy include? Furthermore, long-term minimal residual disease monitoring could guide pre-emptive treatment preventing clinical relapses and ensuring durable responses.

Maintenance with lenalidomide is the standard of care, but the future has to move towards a personalised medicine approach that aims to improve overall survival

and quality of life, which means giving the right drug to the right patient at the right time for the optimal duration.

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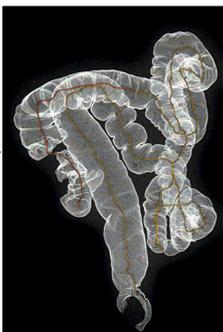
M-VM has received honoraria for lectures from Janssen, Celgene, Takeda, and Amgen, and for participation in advisory boards from Janssen, Celgene, Takeda, Amgen, AbbVie, GlaxoSmithKline, and PharmaMar. VGC declares no competing interests.

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The importance of surgery in colorectal cancer treatment



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In *The Lancet Oncology*, Sara Benitez Majano and colleagues¹ have engaged with a very important topic. Previous data have indicated poorer treatment results for colorectal cancer in both Denmark and England compared with those in similar western countries.² The continuous audit and assessment of outcomes is important to better understand the reality of cancer care each country and thus, this study is of interest to the public.

Majano and colleagues identified that an important difference between the countries studied regarding surgery for colorectal cancer was probably not the technique, but rather the frequency of surgical resection. The proportion of patients treated with resectional surgery ranged from 68.4% in England to 81.3% in Sweden for colon cancer, and from 59.9% in England to 70.8% in Sweden for rectal cancer; this range was wider for patients older than 75 years (colon cancer 59.7% to 80.9%; rectal cancer 45.7% to 61.9%). What

are the implications from these results? Majano and colleagues' paper highlights the importance of surgery in the treatment of colorectal cancer. It is possible that attitudes towards surgery in the older patient population should be altered in England, but the data in this study do not include comorbidity, and the risk for increased perioperative mortality should not be underestimated. It is important to continue to assess results of resectional surgery to avoid doing more harm than good. Preoperative optimisation of patients must be a focus of research, to increase the percentage of patients that are able to undergo resectional surgery in the future.

What other factors could be influencing these results? During the study period, the standardised referral pathway had already been introduced in Denmark in 2010. It has since been introduced in Sweden, Norway, and the UK, but none of these three countries had this process running nationally in 2010. There is scarce

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