Early intervention effective in smouldering multiple myeloma

The development of smouldering multiple myeloma—an asymptomatic precursor of multiple myeloma—might be considerably delayed through early intervention with lenalidomide, according to a recent study.

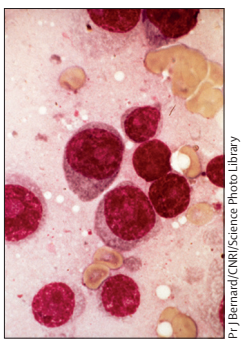
In the randomised, open-label, phase 3 trial, Sagar Lonial (Emory University, Atlanta, GA, USA) and colleagues enrolled 182 patients who had been diagnosed with intermediate-risk or high-risk smouldering multiple myeloma. Patients were randomly assigned 1:1 to receive either oral lenalidomide 25 mg on days 1–21 of every 28-day cycle (n=92) or observation alone (n=90). Treatment was continued until disease progression, toxicity, or patient withdrawal. The primary endpoint was progression-free survival, defined as the time from randomisation to the development of symptomatic multiple myeloma.

At a median follow-up of 35 months (95% CI 30–37), median progression-free survival was significantly longer with lenalidomide than with observation (hazard ratio 0·28, 95% CI 0·12–0·62; p=0·002). 1-year, 2-year, and 3-year progression-free survival was 98%, 93%, and 91% in the lenalidomide group, compared with 89%, 76%, and 66% in the observation group. 44 (50%, 95% CI 39–61) of 88 evaluable patients in the lenalidomide group achieved a partial response or better, with no responses recorded in the observation group. Grade 3 or worse non-haematological adverse events were observed in 25 (28%) of 88 patients in the lenalidomide group versus four (5%) of 86 in the observation group.

"Smouldering multiple myeloma has been an area where there has been significant dichotomy in approach and risk stratification," explained Lonial. "This trial is the largest randomised trial to be performed in smouldering multiple myeloma, and clearly demonstrates benefit for patients at the highest risk of progression, changing standard of care from observation to early intervention."

María Victoria Mateos Manteca (University of Salamanca, Salamanca, Spain) added: "The challenge now is whether we should treat every high-risk asymptomatic myeloma patient with lenalidomide or lenalidomide plus dexamethasone, off-label, or if we should consider these patients as having active multiple myeloma and treat them with the conventional therapeutic approach."

Elizabeth Gourd



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For the **study by Lonial and colleagues** see *J Clin Oncol* 2019; published online Oct 25. DOI:10.1200/JCO.19.01740