Early intervention for smoldering multiple myeloma

Early treatment of high-risk asymptomatic smoldering multiple myeloma improves overall survival according to a study from researchers at the University Hospital of Salamanca in Salamanca, Spain.

Commenting on the study, S Vincent Rajkumar (Mayo Clinic, Rochester, MN, USA) said: "This is the first study to show a clear and convincing overall survival benefit in patients with asymptomatic smoldering multiple myeloma. It is the first evidence we have that early intervention in the asymptomatic phase of myeloma can save lives."

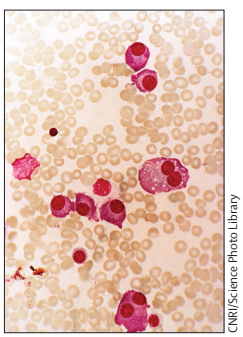
A type of plasma-cell proliferative disease, smoldering multiple myeloma is the very early stage of multiple myeloma without symptoms. Progression to active multiple myeloma occurs in 10% of patients per year in general, although a subgroup of the disease has been identified in which probability of progression is very high. The standard of care for smoldering multiple myeloma is observation.

"Unlike previous studies that failed to show a similar benefit, the authors used risk-stratification models to ensure that patients included in the study were those who were most likely to benefit from therapy", adds Rajkumar.

Researchers randomly allocated 119 patients with high-risk smoldering multiple myeloma to treatment with lenalidomide plus dexamethasone for induction followed by maintenance with lenalidomide (57 patients), or observation (62 patients). With a median follow-up of 40 months (range 27–57), the median time to progression to symptomatic disease was not reached in the treatment group but was 21 months in the observation group (hazard ratio for progression 0·18, 95% CI 0·09–0·32; p<0·001). 47 (76%) patients developed symptomatic disease in observation group compared with 13 (23%) patients in the treatment group. At 3 years, Kaplan–Meier estimates of overall survival showed 94% patients were alive in the treatment group compared with 80% in the observation group (hazard ratio for death 0·31, 95% CI 0·10–0·91; p=0·03).

Sascha Tuchman (Duke University Medical Center, Durham, NC, USA) commented: "Longer term follow-up from this specific study should be of interest but further validation studies are probably low yield, especially when one considers that the vast majority of these patients would progress to symptomatic myeloma requiring therapy in the relatively near future anyhow".

Sharan Prakash Sharma



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Ipilimumab for metastatic uveal melanoma

Uveal melanoma is the most common intraocular cancer in adults, but makes up only 3–5% of all melanomas. Patients with metastatic disease have a poor outcome, with median survival of 12·5 months, and no standard of care exists. One potential treatment, ipilimumab, blocks the activity of an immune checkpoint protein that inhibits activated T cells and restricts the immune response, thereby enhancing antitumour immunity.

A retrospective analysis of 39 patients treated with ipilimumab for metastatic uveal melanoma showed an immune-related response rate of 5·1%—higher than that of any other published treatment for this cancer. Ipilimumab induced stable disease lasting longer than 33 weeks in nine participants (23·1%) and a median overall survival of 9·6 months (95% CI 6·3–13·4, range 1·6–41·6) was reported. Ipilimumab had been administered (3 mg/kg or 10 mg/kg, median of four doses) at four academic centres in the USA and Europe as part of an expanded-access programme or commercial drug; patients had received a median of one previous therapy.

Lead author Richard Carvajal (Memorial Sloan-Kettering Cancer Center, New York, NY, USA) noted: "Uveal melanoma is clinically, genetically, and biologically distinct from cutaneous melanoma. The efficacy of a drug in cutaneous melanoma does not necessarily mean it will be equally effective in uveal melanoma." He added that: "Acknowledging the inherent limitations of small retrospective analyses such as this one, our results suggest that the efficacy of ipilimumab in uveal melanoma may be similar to that in cutaneous melanoma in terms of tumour response; however, definitive conclusions will require larger prospective studies."

Co-author Stephen Hodi (Dana-Farber Cancer Institute, Boston, MA, USA) added, "This study gives some credence to whether ipilimumab can be used in uveal melanoma, and lays the groundwork for that. Ipilimumab is approved for melanoma, and we believe it is a reasonable choice for the subset of patients with uveal melanoma."

Rene Gonzalez (University of Colorado Denver, Denver, CO, USA) said of this study, "This is good news for patients with metastatic uveal melanoma. This should be the new standard of care for this malignancy. And this treatment should be the control arm of any new phase 3 study going forward. A prospective phase 3 to confirm these retrospective results is not necessary considering the poor prognosis of these patients."

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