Should pomalidomide or carfilzomib be the initial salvage treatment in myeloma? [Carfilzomib]

Philippe Moreau, Hematology Department, University Hospital, Nantes, France

Carfilzomib is a selective proteasome inhibitor that has demonstrated robust and durable activity and a favorable safety and tolerability profile as a single-agent treatment in heavily pretreated patients with relapsed and/or refractory multiple myeloma (MM) in phase 1 and 2 trials. Grade 3/4 adverse events (AEs) are mostly hematologic and manageable with supportive measures or dose modifications. Importantly, no notable association between carfilzomib and neuropathic events were described. Carfilzomib is now approved in the United States to treat patients with MM who received at least two prior lines of therapy, including bortezomib and an immunomodulatory agent, and who have experienced disease progression during or within 60 days of completing their last therapy. The favourable toxicity profile of carfilzomib, that is less frequently inducing peripheral neuropathy as compared with bortezomib, together with its high efficacy make this drug an attractive candidate for combination in the relapse setting. Promising data have been reported from phase 1 / 2 studies that investigated the use of carfilzomib in combination with immunomodulators, alkylating agents, glucocorticoids, histone deacetylase inhibitors and kinesin spindle protein inhibitors. Carfilzomib is currently evaluated in three phase 3 randomized prospective trials in relapsed and/or refractory MM: Aspire testing lenalidomide-dexamethasone versus carfilzomib plus lenalidomide-dexamethasone, Endeavor studying carfilzomib-dexamethasone versus bortezomib-dexamethasone, and Focus comparing carfilzomib versus best supportive care in end-stage patients. Results of these trials are eagerly awaited.