

UROTHELIAL CARCINOMA

Vinflunine offers modest but important survival benefit

Long-term follow-up data from a randomized phase III trial has shown that patients with advanced transitional cell carcinoma of the urothelium (TCCU) benefit more from vinflunine plus best supportive care (BSC) than with BSC alone.

Patients with TCCU are typically treated with first-line platinum-based chemotherapy. Although most patients initially respond, with overall survival rates around 14 months, most with advanced TCCU eventually relapse. Few single-agent second-line treatments have demonstrated considerable benefit for these patients. However, vinflunine—a vinca alkaloid that inhibits tubulin polymerization to interrupt cell division and induce apoptosis—was shown in a phase III study reported in 2009 to improve the overall response rate compared with patients receiving only BSC, which included palliative radiotherapy, antibiotic administration and analgesics. In that study, the difference in overall survival did not reach statistical significance (6.9 months versus 4.6 months) in the intention-to-treat population ($P=0.287$). The authors suggested several reasons for this result, including that several patients were in fact ineligible according to the protocol for the trial. Restricting the analysis by excluding these patients revealed that the improvement in overall survival offered by vinflunine was significant ($P=0.040$) after a median follow-up duration of 22.1 months.

In their new report, published in *Annals of Oncology*, the authors extended the follow-up analysis to a median of 45.4 months to assess the durability of the vinflunine effect. They found that 352 patients out of 370 had died at this cut-off time. The median overall survival in the experimental arm was 6.9 months, which compared favourably to the BSC



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alone arm (4.3 months), a difference that reached statistical significance (HR 0.78, 95% CI 0.61–0.96, $P=0.0227$). At 30 months, more patients were considered long-term survivors in the vinflunine plus BSC group than in the BSC alone group, and more patients survived to 40 months.

Although modest, these results do offer some benefit to patients with this difficult to treat cancer. Further insights might be gained by careful stratification of patients according to fine-tuned criteria, as those with TCCU seem to respond differently depending on their ECOG (Eastern Cooperative Oncology Group) performance status, whether metastases of the liver are evident and their haemoglobin levels, amongst other prognostic variables.

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Original article Bellmunt, J. *et al.* Long-term survival results of a randomized phase III trial of vinflunine plus best supportive care versus best supportive care alone in advanced urothelial carcinoma patients after failure of platinum-based chemotherapy. *Ann. Oncol.* doi:10.1093/annonc/mdt007

Further reading Bellmunt, J. *et al.* Phase III trial of vinflunine plus best supportive care compared with best supportive care alone after a platinum-containing regimen in patients with advanced transitional cell carcinoma of the urothelial tract. *J. Clin. Oncol.* 20, 4454–4461 (2009)