Nelfinavir with concurrent chemoradiotherapy in NSCLC

Nelfinavir—an orally active HIV protease inhibitor—shows encouraging anti-tumour activity and acceptable safety in patients with locally advanced non-small-cell lung cancer (NSCLC), according to a recent study.

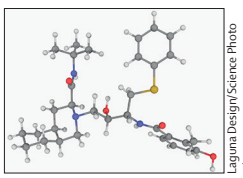
Ramesh Rengan (University of Washington School of Medicine, Seattle, WA, USA) and colleagues did an open-label, single-centre, phase 1–2 trial to assess the safety and anti-tumour activity of nelfinavir combined with concurrent chemoradiotherapy in patients with unresectable stage IIIA–IIIB NSCLC. 35 patients were enrolled between June 29, 2007, and Feb 22, 2012, and received oral nelfinavir—625 mg (n=5) or 1250 mg (n=30) twice daily—before and during concurrent chemoradiotherapy. The phase 1 part of the trial aimed to determine the dose-limiting toxicity, maximally tolerated dose, and recommended phase 2 dose of nelfinavir, whereas the primary efficacy endpoints of the phase 2 part were objective response, local and distant failure, progression-free survival and overall survival.

No dose-limiting toxicity and no grade 4 or worse non-haematological adverse events were recorded. The maximally tolerated dose and recommended phase 2 dose was 1250 mg nelfinavir twice daily.

Median follow-up was 6·8 years. Of patients who had CT scans (n=33) for the evaluation of response, 31 (94%, 95% CI 86–100) achieved an objective response (all partial responses). In all 35 patients, the cumulative incidence of local failure was 39% (95% CI 30·5–47·5) and of distant failure was 60% (51·7–68·3). Median progression-free survival was 11·7 months (95% CI 6·2–17·1) and median overall survival was 41·1 months (95% CI 19·0–63·1).

Rengan said, "We utilised an oral FDA-approved HIV-protease inhibitor nelfinavir that has been shown to inhibit PI3-kinase-dependent DNA repair pathways in tumour cells, thereby acting as a radiosensitiser." According to Raymond Mak (Dana-Farber Cancer Institute, Boston, MA, USA), "While the response rates are interesting, the main outcome of interest in terms of local control is comparable to studies of chemoradiation alone." Eric Ko (Weill Cornell Medicine, New York, NY, USA) commented, "The addition of nelfinavir to chemoradiotherapy appears to improve multiple clinical outcomes with a reasonable toxicity profile, although these conclusions should be validated in the setting of a randomised phase 3 study."

Manjulika Das



Laguna Design/Science Photo Library

Published **Online** August 30, 2019 http://dx.doi.org/10.1016/S1470-2045(19)30567-4

For the **study by Rengan and colleagues** see *JAMA Oncol* 2019; published online Aug 22. DOI:10.1001/jamaoncol.2019.2095