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## Lung alert

### A potential role for inhibitors of XIAP in the treatment of NSCLC

Non-small cell lung cancer (NSCLC) remains the leading cause of cancer mortality worldwide. The pathogenesis of NSCLC involves the evasion of apoptosis. One way this is achieved is via the overexpression of inhibitor of apoptosis proteins (IAPs). Eight human IAPs have been identified, the best characterised and most potent being X-linked IAP (XIAP).

The study investigated the use of XAC 1396-11, a phenylurea-based small molecule inhibitor of XIAP, in combination with cytotoxic agents. It aimed to see if the use of XAC 1396-11, to reduce the cellular threshold for apoptosis, would sensitise NSCLC to cytotoxic agents.

XAC 1396-11 induced apoptotic cell death in a time- and concentration-dependent manner in NSCLC cell lines. It showed synergy in combination with the cytotoxic agents vinorelbine, cisplatin and gemcitabine, but not taxotere. Treatment with XAC 1396-11 followed by vinorelbine was the most synergistic.

A current standard chemotherapy regime for the treatment of NSCLC of a platin (cisplatin) and vinorelbine was investigated with XAC 1396-11. This showed greatest synergy at low concentrations, potentially allowing dose reduction of the cytotoxic agents, thereby potentially reducing chemotherapy-induced toxicity whilst maintaining the therapeutic effect.

This study highlights a potential therapeutic role for XAC 1396-11 in combination with chemotherapy in the treatment of NSCLC.

► **Dean EJ**, Ward T, Pinilla C, *et al*. A small molecule inhibitor of XIAP induces apoptosis and synergises with vinorelbine and cisplatin in NSCLC. *Br J Cancer* 2010;**102**:97–103.

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