Bladder cancer: advances for high-precision chemotherapy

Richard Béliveau

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A chemotherapy molecule directed specifically at cancer cells using an antibody halves the mortality of patients with metastatic bladder cancer, something never before seen for this type of cancer.

Chemotherapy drugs are cellular poisons used to destroy cancer cells. Despite their great usefulness for the treatment of a very large number of cancers, one of the main problems of these agents remains their toxicity towards several healthy cells in the body, which causes multiple side effects. Let us mention, among other things, the decline in immune cells and platelets, anemia, digestive disorders (nausea, damage to the digestive mucous membranes), hair loss (alopecia), not to mention various cardiac, renal or other complications.

As a result, the dose and duration of treatment are often limited by these side effects, which may prevent complete destruction of cancer cells.

TARGET CANCER CELLS

A promising approach to minimize these side effects is to link chemotherapy drugs to vectors with preferential affinity for proteins present on the surface of cancer cells.

Instead of coming into contact with all the cells of the body via the blood circulation, the chemotherapy agent conjugated to these vectors is instead directed directly towards the cancer cells, which minimizes its interaction with normal cells and therefore the risk of side effects. These are called targeted therapies.

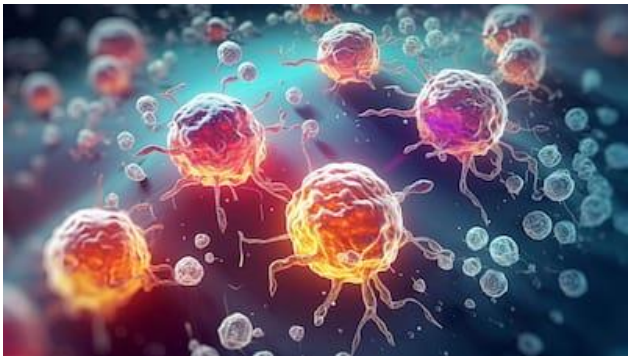
Enfortumab vedotin (PADCEV) represents a good example of the clinical potential of this approach. This medication combines an antibody that specifically recognizes nectin-4 (a protein overexpressed by many cancer cells) conjugated with MMAE (monomethyl auristatin E), a peptide derived from sea slugs that blocks cell division (mitosis).

The antimitotic activity of this peptide is extremely powerful (200 times more than vinblastine, a widely used chemotherapy agent), but it cannot be used as such in the clinic due to its very high toxicity.

However, by combining MMAE with an anti-nectin-4 antibody, the conjugate specifically targets cancer cells and blocks their growth, without interfering with the function of healthy cells.

BLADDER CANCER

A clinical study involving patients with metastatic bladder cancer clearly highlights the potential of this drug (1). In this study, researchers treated 886 patients with advanced bladder cancer with the standard protocol (chemotherapy with gemcitabine and platinum salts) or with the PADCEV conjugate combined with an anticancer immunity stimulator (pembrolizumab).



The results obtained are quite extraordinary, with a 55% reduction in the risk of patient mortality compared to standard chemotherapy.

This effect has very concrete repercussions: instead of a survival of around 16 months on average with the usual treatment, that of patients treated with enfortumab vedotin is doubled and reaches 32 months, with the added bonus of a significant reduction in side effects related to treatment.

Benefits of this order are extremely rare in the field of cancer treatment where the improvement in survival offered by a new treatment is very often just a few months. There is therefore no doubt that these results will pave the way for a reformulation of the standard treatment of bladder cancer and substantially reduce the mortality associated with this disease.

(1) Powles TB et al. EV-302/KEYNOTE-A39 : Open-label, randomized phase III study of enfortumab vedotin in combination with pembrolizumab (EV+P) vs chemotherapy (chemo) in previously untreated locally advanced metastatic urothelial carcinoma (la/mUC). Annals of Oncology. 2023; 34(S2); S1340.

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