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# HONG KONG BREAST CANCER FOUNDATION
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## Summary of Session 4
## Immunotherapy in breast cancer

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### A brief overview of immunotherapy

The immune system is central to tumour formation because malignant cells can only develop into a tumour by evading immunosurveillance that normally destroys defective cells.[1] Immunotherapy targets the mechanisms used by malignant cells to evade the immune system, stimulating T cells to recognize and attack tumour cells.[2] Currently approved immunotherapies block the receptors and ligands that malignant cells use to mask themselves from the immune system, thereby exposing them to attack.[2] However, this approach is associated with an increased risk of an autoimmune response.[2]

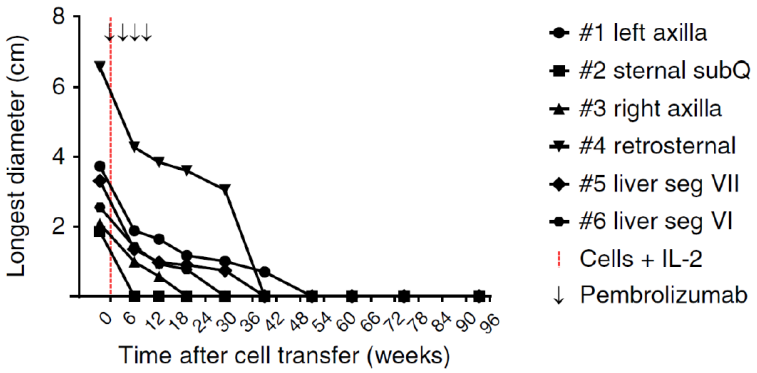
Other cytotoxic therapies, such as radiation or chemotherapy, may be used to destroy tumour cells, allowing antigen-presenting cells to phagocytose tumour cell fragments, which are then used to "educate" killer T cells on which cells to destroy.[2]

### Sophisticated immunotherapy in a patient with chemo-refractory oestrogen receptor (ER)-positive human epidermal growth factor receptor-2 (HER2)-negative metastatic breast cancer

The development of immunotherapy for breast cancer has predominantly focused on patients with triple-negative (ER-negative, progesterone receptor-negative and HER2-negative) breast cancer, as these patients are more likely to develop mutations that can be recognized by T cells. However, hormone receptor-positive breast cancer tends to be less mutagenic and, therefore, more difficult to target using immunotherapy.[3]

In a recent study, tumour-infiltrating lymphocytes (TILs) derived from a patient's tumour biopsies were screened for their reactivity against mutated peptides identified through a genetic screening process.[3] The mutant-peptide–reactive T cells were cultured and prepared as an autologous infusion for the patient.[3] The patient also received chemotherapy and immunotherapy with interleukin-2 and pembrolizumab to support an effective immune response against her tumour cells (Figure 1). Notably, the rate of tumour shrinkage was different across six target lesions, which may be indicative of the level of T cell infiltration in each lesion.[3] After 22 months, all lesions were completely eradicated and the patient was declared cancer free.[3]

**Figure 1.** Size of target lesions in a patient administered mutant-peptide–reactive TILs at Week 0[3]




*IL, interleukin; subQ, subcutaneous; TILs, tumour-infiltrating lymphocytes*

Of note was the variation in density, location and reactivity of T cells within individual biopsies from the patient's tumour. However, T cells that recognize tumour cells circulate in the blood, which may increase the probability of collecting a sample that includes a T cell clone that reacts to relevant mutations identified in individual tumour biopsies. Therefore, identifying T cells with tumour-specific reactivity may offer a future method of highly specific, individualized immunotherapy.

**Summary**

Targeting tumours with a low mutational burden may be difficult using immunotherapy alone. Genomic analysis may be used to identify potential antigens, which can then be screened against T cell samples from the patient. Antigen-reactive T cells may then be cultured and re-introduced to the patient alongside immunotherapy to provide an effective, individualized therapy.

## Case study from Dr Wing Hong Kwan

A patient presented to Dr Kwan with a large mass in her right breast and multiple positive axillary lymph nodes from level I–III. A biopsy revealed that the patient had triple-negative breast cancer and a computed tomography scan revealed an absence of metastases.

Neoadjuvant chemotherapy was recommended, and so the patient was administered a single dose of carboplatin and paclitaxel. However, she experienced severe adverse events and discontinued treatment shortly thereafter.

For 6 months following the attempted neoadjuvant therapy, the patient relied on Chinese herbal medicine before returning to the clinic with further tumour growth and ulceration of her right breast. The patients' entire right upper limb was swollen, which extended into the supraclavicular fossa and lower part of her neck. In an attempt to reduce discharge and clear the ulcerated area, radiation therapy was administered to her right breast. To encourage the patient to adhere to her treatment plan, a chemotherapy regimen that was expected to have low toxicity was recommended (eribulin [1.23 mg/m$^2$] on Day 1 and Day 15 of a 28-day cycle).

While the patient's disease did not progress further, her response to the first two cycles of chemotherapy was suboptimal. After learning of a study in which a programmed death ligand-1 inhibitor administered in combination with eribulin doubled response rates in patients with triple-negative breast cancer, Dr Kwan incorporated pembrolizumab into the patient's treatment regimen (200 mg on Day 15 of her third cycle of therapy).

The patient responded to the first cycle of pembrolizumab therapy and swelling in her upper limb decreased. However, the greatest response was observed in the area of the breast treated with radiation therapy. She continued to respond to therapy through six cycles of treatment, but

experienced treatment-related febrile neutropenia, so treatment was suspended until she recovered. During her seventh cycle of therapy, the patient experienced pneumonitis and immunotherapy was stopped, while she was treated with steroids, before initiating a new treatment regimen.

## References


1. Umar A. *Cancer Prev Res* 2014;7:1067–1071.
2. Chen DS, Mellman I. *Immunity* 2013;39:1–10.
3. Zacharakis N, et al. *Nat Med* 2018;24:724–730.