Advances in Immunotherapy for Lymphoma

Ashley Freeman, MD, FRCPC
Immunotherapy Research Fellow
The immune system and cancer

Immunotherapies available for lymphoma

Upcoming immunotherapy clinical trials in BC

The future of lymphoma immunotherapy
The immune system is capable of recognizing and killing cancer cells, but cancer cells are good at hiding.

“Immunotherapy” refers to different types of treatments with a collective aim to restore or enhance the immune system’s ability to kill cancer cells.

Most new lymphoma immunotherapies are currently for relapsed disease or are still in clinical trials.

Immunotherapy is a promising approach to cancer therapy, but we have much to learn.
The immune system and cancer

Adapted from Chen & Mellman Immunity 2013;39:1-10
Abnormal proteins sit on the surface or leak out of cancer cells.

1. Abnormal proteins sit on the surface or leak out of cancer cells.

2. T cells (soldiers of the immune system) are alerted to the presence of abnormal proteins.

3. T cells travel to the site of the tumor.

4. T cells bind to the abnormal proteins on the cancer cell and kill it.

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Immunotherapies for lymphoma: Monoclonal antibodies
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- First line therapy for all B-cell lymphomas
Immunotherapies for lymphoma: Monoclonal antibodies

- Relapsed Hodgkin lymphoma
- Recently FDA-approved for first line therapy of Hodgkin lymphoma in combination with chemotherapy
- NHLs that express CD30

Brentuximab vedotin

Hodgkin lymphoma + CD30+ NHL

Chemotherapy
Immunotherapies for lymphoma: Monoclonal antibodies

- No approved bispecific antibody therapies for lymphoma
- BC Cancer clinical trials open for relapsed B-cell NHL (DLBCL, FL, MCL)
Immunotherapies for lymphoma: Checkpoint inhibitors
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T cell binds to abnormal protein on tumor cell

If PD-1 binds PD-L1, T cell ignores tumor cell

Tumor cell growth
Immunotherapies for lymphoma: Checkpoint inhibitors

T cell binds to abnormal protein on tumor cell

If PD-1 binds PD-L1, T cell ignores tumor cell

Checkpoint inhibitor prevents PD-1-PD-L1 binding

Tumor cell growth

Tumor cell death
Immunotherapies for lymphoma: Checkpoint inhibitors

- Relapsed Hodgkin lymphoma
- BC Cancer clinical trials: indolent NHLs (e.g., FL, CLL), MCL, DLBCL, T cell lymphomas
Immunotherapies for lymphoma: T cell therapies
Immunotherapies for lymphoma: T cell therapy

Identify or genetically engineer tumour reactive T cells

Expand the T cells in the lab and infuse back into patients
Immunotherapies for lymphoma: CAR T cells

- Chimeric Antigen Receptor T cells
Immunotherapies for lymphoma: CAR T cells

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Immunotherapies for lymphoma: CAR T cells

- FDA-approved in 2017 for relapsed, aggressive B cell lymphoma
  - ~50% of patients with complete response
  - Waiting for long term follow up

- Clinical trials in progress:
  - Hodgkin lymphoma
  - Chronic lymphocytic leukemia
  - Follicular lymphoma
Challenges

◦ Unclear why some patients do not respond

◦ Unique and serious toxicities

◦ Available at a limited number of specialized facilities in the US

◦ Cost
Immunotherapies for lymphoma: CAR T cells

- Building Canadian CAR T cell infrastructure
  - Multicenter initiative to produce Canadian CAR T cell products
  - Provide access for Canadian patients to CD19 directed CAR T cells ASAP
  - Create a cost–effective clinical and research platform for future CAR T cell development
Miltenyi CliniMACs Prodigy system for CAR-T cell production

- Fully closed, automated system.
- 10-day T cell engineering and expansion protocol
- Deployable at point-of-use
Immunotherapies for lymphoma: Non-engineered T cell therapy

- Development of a non-engineered T cell trial in Victoria

Driver mutation in DNA → Protein that drives cancer cell growth → T cells recognize proteins
Development of a non-engineered T cell trial in Victoria

- Phase I clinical trial for relapsed follicular and mantle cell lymphoma planned for 2019–2020

- Potential benefits over engineered T cell therapy
  - Safety
  - Personalization
  - Targeting multiple driver mutations simultaneously

Driver mutation specific T cells obtained from blood

T cells expanded in the lab and infused into patient
Future of lymphoma immunotherapy

- Identification of new checkpoints
- Better, safer CAR T cells
- Moving immunotherapies to earlier stages of treatment
- Combination therapies
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