Immunotherapy for neuroblastoma

Daniel Morgenstern
Overview

• The immune system
• Antibody therapy – the current and the future
• Immune checkpoint inhibitors
• Cellular therapies
Neutrophil, Eosinophil, Basophil, Monocyte, T Cell, B Cell, Natural killer, Macrophage
What is cancer immunotherapy?
Antibodies against cancer cells

Antibodies to stimulate the immune system

Cellular therapies

Other drugs to stimulate the immune system

Immunotherapy
Anti-GD2 immunotherapy

Diagram:
- Cancer cell
- Target cancer antigen
- Antibody
- Fc receptor
- NK cell
- Perforin and Granzyme released
Anti-GD2 immunotherapy

Unituxin™
Dinutuximab
Ch14.18
Ch14.18/SP2/0
Anti-GD2

Dinutuximab-beta
Ch14.18/CHO

3F8
Naxitamab
Current uses of anti-GD2 immunotherapy

- At end of upfront treatment to consolidate response

| Induction | Surgery | High dose | Radiotherapy | Immunotherapy |
Current uses of anti-GD2 immunotherapy

- At end of upfront treatment to consolidate response

| Induction | Surgery | High dose | Radiotherapy | Immunotherapy |

- In combination with chemotherapy for relapse/refractory disease

Chemotherapy (temozolomide/irinotecan) | Immunotherapy
Future uses of anti-GD2 immunotherapy

• In combination with induction chemotherapy for upfront treatment

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• Additional combinations in relapse?
Anti-GD2 immunotherapy questions

• How important are cytokines (IL-2 and GM-CSF)?

• How can we reduce the side effects?

• What about alternative immune-stimulating agents (e.g. lenalidomide)?

• How can we use immunotherapy in upfront treatment?
Other targets for antibodies?
Enoblituzumab, anti-B7H3
Immune checkpoint inhibitors

Releasing the brakes on the immune system
T-cell receptor | Antigen

T-cell | PD-1 inhibitor

Tumour cell | PD-1

PD-L1

PD-L1
ICI questions

• Great in some adult cancers, but will they work in children’s cancers?

• How can we predict who will respond?

• What about side effects?
The Mutational Burden of Human Cancer

Mike Lawrence and Gaddy Getz
Cellular therapies
CAR T cells

• Idea:
  • T-cells will kill cancer cells but they need to be directed to recognise these cancer cells
  • Genetically alter T-cells in lab to redirect them to cancer cells

• CAR
  • Chimeric antigen receptor
How to make a CAR

Antibody to recognise cancer cell

Part of T-cell receptor to activate T-cell

T-cell
1. Leukapheresis
2. T-cell activation/transduction
3. Modified T-cell expansion
4. Chemotherapy
5. Modified T-cell infusion

*Cellular reprogramming and ex vivo expansion are conducted at a cell processing facility.*
CAR-T questions

• Work brilliantly in ALL (leukaemia), but what about solid tumours?

• What is the best target?

• Will CAR T-cells get to the tumour, survive, divide and kill cancer cells?

• What about side effects?
Access to trials in Canada

• COG study of antibody and chemotherapy was open at SickKids

• NANT study of lenalidomide and antibody open at SickKids

• Limited access to immune checkpoint inhibitors – more coming

• Member of pediatric CITN trials network