Immunotherapy

Professor Nicola Stoner
Consultant Cancer Pharmacist
ASPCP Birmingham 15th November 2018
Introduction

- What is immunotherapy?
- Immune system refresher
- Immunotherapy Treatments
  - Monoclonal antibodies
  - Immune checkpoint inhibitors
  - Tumour vaccines
    - Peptide DNA and RNA
    - Dendritic cells
  - Oncolytic viruses
  - Gene therapy
  - Cellular therapy e.g. CAR-T cells
  - Tumour infiltrating lymphocytes (TIL)
- ATMPs and pharmacy
- Future
What is Immunotherapy?

• Treatments that use the immune system to destroy cancer cells.

• Five main groups of immunotherapy Treatments:
  1. Boost the immune system e.g. IFN, IL-2
  2. Antibodies that attach to cancer cell surface proteins e.g. monoclonal antibodies
  3. Encourage white blood cells to destroy cancer
  4. Adoptive cell transfer e.g. CAR-T and TIL
  5. Vaccines
Refresher – The immune system

Cells of the Immune System

- Stem Cell
- Lymphoid Stem Cell
  - Lymphocytes
  - T Cell Progenitor
  - Natural Killer Cell
  - Neutrophil
  - Eosinophil
  - Basophil
- Myeloid Progenitor
  - Granulocytes
  - Monocyte
  - Macrophage
  - Mast Cell

- B Cell Progenitor
- T Cell
  - Th Cell
  - Memory Cell
  - Plasma Cell
  - Dendritic Cell
From: Immuno-oncology: understanding the function and dysfunction of the immune system in cancer
Ann Oncol | © The Author 2012. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.
Cells involved in the Immune System

- **Neutrophils** – Phagocytosis and presenting antigens
- **Macrophages** – phagocytosis, antigen presentation, activating memory cells
- **Dendritic cells** – Main antigen presenting cells, activating T cells and memory cells
- **B cells** – used in humoral immunity. **Plasma cells** (mature B-cells) secrete anti-bodies. **Memory B cells** ‘remember’ foreign antigens to enable quicker antibody response.
- **T cells** – many different subtypes e.g. helper T cells, cytotoxic T cells, regulatory T-cells and memory T cells.
- **Natural killer cells** – Part of innate and adaptive immune systems and destroy pathogens without the need for prior activation. They are important in viral immunity and tumour rejection
T-Cells – the key to cancer immunotherapy

• Immunotherapy relies on activated T-cells
• T-cells mature in the thymus
• T-cell receptor (TCR) on surface of T-cells recognises and responds to antigens
• Dendritic cells activate T-cells: 2-stage process
• Cytotoxic T cells protect from cancer
Immunotherapy Treatments

- BCG vaccines
- Cytokine therapy e.g. interferons & interleukins
- Monoclonal antibodies
- Immune checkpoint inhibitors
- Tumour vaccines
  - Peptide DNA and RNA
  - Dendritic cells
- Oncolytic viruses
- Gene therapy
- Cellular therapy e.g. CAR-T cells
- Tumour infiltrating lymphocytes (TIL)
Monoclonal Antibodies
Monoclonal Antibodies

- Y-shaped immunoglobulin proteins that specifically bind to molecules called antigens, and in so doing elicit an immune response.
Monoclonal antibodies

• Stop, control, or suppress processes that permit cancer growth.
• Make cancer cells more recognisable & susceptible to destruction by immune system.
• Stimulate immune natural killer cell activity.
Types of Anti-cancer Monoclonal Antibodies

**Effector cell**

**Target cell**

- **Activates immune System**
  - Rituximab
  - Alemtuzumab

- **Blocks GF signalling, stimulates apoptosis**
  - Trastuzumab
  - Panitumumab
  - Cetuximab

- **Conjugated Radionuclide**
  - Ibritumomab tiuxetan (Zevalin)

- **Conjugate Cytotoxic Drug**
  - Ado-trastuzumab emtansine (Kadcyla)
  - Gemtuzumab-ozogamicin (Mylotarg)
**MAb hybridisation nomenclature**

**Substems**

- **'o'** (omab) denotes the source is mice or other non-humans – highly immunogenic.

- **'xi'** (ximab) denotes a chimeric antibody, where the constant region of the mouse antibody is replaced with the human form of this section of the protein.

- **'zu'** (zumab) where part of the variable region is replaced by the human form, called humanised.

- **'u'** is pure human protein.

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Each antibody bears on its two short arms identical regions that recognise a specific foreign structure, to which they bind. This principle is exploited in therapeutic antibodies in order to recognise pathogenic and other substances and render them harmless. Whereas early therapeutic antibodies were still partly derived from mouse genes (yellow segments), therapeutic antibodies of the latest generation are indistinguishable from their human counterparts.

Fully human therapeutic antibodies are obtained by infecting a transgenic mouse that carries human genes for the production of immunoglobulins (Ig) with the target for the antibodies that one wishes to produce.
Immune checkpoint inhibitors
Checkpoint proteins

- Cytotoxic T cells display inhibitory checkpoint proteins on their surface.
- Limit activity of T cells
- Activating checkpoint proteins normally down-regulates the immune response.
- A mechanism of cancer survival is to produce these proteins/receptors on the surface of the tumour cell which binds to the ‘checkpoint’ which deactivates the immune cell.
- Current targets
  - PD-1 (programmed cell death protein 1) on the surface of activated T-cells, PD-L1 on the surface of tumour/normal cells,
  - CTLA-4 (cytotoxic T-lymphocyte-associated antigen 4) on the surface of T-cells
Anti T-cell Checkpoint Receptor Therapy

http://www.nzmu.co.nz/anti-pd-1-inhibitors
Checkpoint inhibitors use in practice

• CTLA-4 Inhibitors - Ipilimumab
• PD-1 Inhibitors – Pembrolizumab, Nivolumab
• PD-L1 Inhibitors – Avelumab, Atezolizumab, Durvalumab

• Indications include:
  – Malignant melanoma
  – Urothelial cancer
  – Lung cancer
  – Head and neck cancers
  – Hodgkins Lymphoma
Evolving treatment in metastatic melanoma


Surgical resection

Chemotherapy

IFN

IL-2

HDB

Vemurafenib

Ipilimumab

Dabrafenib

Nivolumab

Pembrolizumab

T-VEC

Cobimetinib + vemurafenib

Dabrafenib + trametinib

Licensed for the treatment of BRAF V600 mutation-positive melanoma

Nivolumab + ipilimumab regimen is approved by NICE for treating advanced (unresectable or metastatic) melanoma in adults

All approvals are marketing authorisations by EMA unless otherwise stated. *2nd line: 11st line.

HDB, high dose bolus; IFN, interferon; IL-2, interleukin-2; NICE, National Institute for Health and Care Excellence.

Immunotherapy - ipilimumab

- Cytotoxic T-lymphocyte antigen-4 (CTLA-4) is a key regulator of T-cell activity.
- Ipilimumab is a CTLA-4 immune checkpoint inhibitor that blocks T-cell inhibitory signals induced by the CTLA-4 pathway, increasing the number of reactive T-effector cells which mobilize to mount a direct T-cell immune attack against tumour cells.
Immunotherapy - pembrolizumab

• Pembrolizumab is a monoclonal antibody which binds to the programmed death-1 (PD-1) receptor and blocks its interaction with ligands PD-L1 and PD-L2.

• Pembrolizumab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2.
Immunotherapy - nivolumab

- Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody (HuMAb)
- Binds to the programmed death-1 (PD-1) receptor and blocks its interaction with PD-L1 and PD-L2.
- Nivolumab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands
Nivolumab indications

- Advanced melanoma as monotherapy/ in combination with ipilimumab
- Locally advanced/ metastatic NSCLC
- Squamous cell cancer of the head and neck
- Advanced renal cell carcinoma after prior therapy
- Locally advanced unresectable or metastatic urothelial carcinoma in adults after failure of prior platinum-containing therapy.
- Treat relapsed/ refractory classical Hodgkins lymphoma after autologous stem cell transplant and treatment with brentuximab
Nivolumab + Iپилиموماب regimen: Complementary inhibition to potentiate T-cell activity and drive anti-tumour responses¹,²

Nivolumab + ipilimumab regimen: PFS vs nivolumab and ipilimumab monotherapies at 3 years

<table>
<thead>
<tr>
<th></th>
<th>NIVO+IPI (n 179/314)</th>
<th>NIVO (n 199/316)</th>
<th>IPI (n 255/315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median PFS, mo (95% CI)</td>
<td>11.5 (8.7–19.3)</td>
<td>6.9 (5.1–9.7)</td>
<td>2.9 (2.8–3.2)</td>
</tr>
<tr>
<td>HR (95% CI) vs. IPI*</td>
<td>0.43 (0.35–0.52)</td>
<td>0.55 (0.45–0.66)</td>
<td>--</td>
</tr>
<tr>
<td>HR (95% CI) vs. NIVO</td>
<td>0.78 (0.64–0.96)</td>
<td>--</td>
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</tr>
</tbody>
</table>

*P<0.001

Nivolumab + ipilimumab regimen:
OS vs nivolumab and ipilimumab monotherapies at 3 years

<table>
<thead>
<tr>
<th></th>
<th>NIVO + IPI (N=314)</th>
<th>NIVO (N=316)</th>
<th>IPI (N=315)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median OS, mo (95% CI)</td>
<td>NR (38.2–NR)</td>
<td>37.6. (29.1–NR)</td>
<td>19.9 (16.9–24.6)</td>
</tr>
<tr>
<td>HR (95% CI) vs. IPI*</td>
<td>0.55 (0.45–0.69)</td>
<td>0.65 (0.53–0.80)</td>
<td>--</td>
</tr>
<tr>
<td>HR (95% CI) vs. NIVO</td>
<td>0.85 (0.68–1.07)</td>
<td>--</td>
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</tr>
</tbody>
</table>

Adapted from Wolchok et al 2017

No. at risk:

| Time (months) | 0  | 3  | 6  | 9  | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 | 48 |
|---------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| NIVO + IPI    | 314| 292| 265| 247| 226| 221| 209| 200| 198| 192| 186| 180| 177| 131| 27 | 3  | 0  |
| NIVO          | 316| 292| 265| 244| 230| 213| 201| 191| 181| 175| 171| 163| 156| 120| 28 | 0  | 0  |
| IPI           | 315| 285| 253| 227| 203| 181| 163| 148| 135| 128| 117| 107| 100| 68 | 20 | 2  | 0  |

*p<0.0001
Immuno-oncology Toxicity

Immune Related Adverse Effects (IrAE)

- Not your typical ‘chemotherapy’ related side effects
- Toxicity is a result of a heightened immune system and there are a number of immune responses which can happen
- ‘Auto-immune’ reactions can occur in potentially any system, but most frequently in skin, GI tract, Liver and Endocrine
- Toxicities, if not treated promptly with corticosteroids/immunosuppression may lead to life threatening complications.
## Signs and Symptoms associated with IrAEs.

<table>
<thead>
<tr>
<th>System</th>
<th>irAE</th>
<th>Signs and/or Symptoms:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal</td>
<td>Immune-mediated colitis</td>
<td>- Diarrhea; Increase in frequency of bowel movements; Abdominal pain</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Blood/mucus in stools or dark, tarry, sticky stools; Bowel perforation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Severe stomach area pain or tenderness; Ileus</td>
</tr>
<tr>
<td>Hepatic</td>
<td>Immune-mediated hepatitis</td>
<td>- Abnormal liver function tests or total bilirubin; Yellowing of skin or whites of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eyes; Dark urine; Easy bruising or bleeding; Severe nausea or vomiting; Right-sided</td>
</tr>
<tr>
<td></td>
<td></td>
<td>abdominal pain; Drowsiness; Decreased appetite</td>
</tr>
<tr>
<td>Skin</td>
<td>Immune-mediated dermatitis</td>
<td>- Pruritus; Rash; Skin changes</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Immune-mediated neuropathies</td>
<td>- Unilateral or bilateral weakness; Sensory alterations; Paresthesia</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Immune-mediated endocrinopathies</td>
<td>- Extreme fatigue; Headaches that will not go away or are unusual; Mental</td>
</tr>
<tr>
<td></td>
<td></td>
<td>status, mood, or behavioral changes; Dizziness or fainting; Hair loss; Feeling</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cold; Constipation; Deepening of voice; Weight gain or loss; Rapid heartbeat;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Increased sweating; Abdominal pain; Unusual bowel habits; Hypotension; Abnormal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>thyroid function tests and/or serum chemistries</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Immune-mediated pneumonitis</td>
<td>- Radiographic changes; New or worsening cough; Chest pain; Shortness of breath</td>
</tr>
<tr>
<td>Renal</td>
<td>Immune-mediated nephritis and</td>
<td>- Increase in serum creatinine; Decrease in urine output; Blood in urine;</td>
</tr>
<tr>
<td></td>
<td>renal dysfunction</td>
<td>Swelling in ankles; Loss of appetite</td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td>- Changes in eyesight or eye inflammation; Severe or persistent muscle or joint pain;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Severe weakness; Changes in laboratory findings indicating involvement of other</td>
</tr>
<tr>
<td></td>
<td></td>
<td>systems, e.g., hematologic, pancreatic</td>
</tr>
</tbody>
</table>
Nivolumab + ipilimumab regimen: Median time to onset of treatment-related irAEs (any Grade)¹

Time to onset of treatment-related irAEs (any Grade) in patients who received nivolumab + ipilimumab regimen across three clinical studies in melanoma (n=448)¹

<table>
<thead>
<tr>
<th>Patients with event n (%)</th>
<th>Median time to onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-related rash*</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>range: 0.0 to 9.7 months</td>
</tr>
<tr>
<td>Immune-related diarrhea or colitis</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>range: 0.0 to 10.4 months</td>
</tr>
<tr>
<td>Immune-related endocrinopathies</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>range: 0.0 to 10.1 months</td>
</tr>
<tr>
<td>Immune-related hepatitis</td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td>range: 0.0 to 11.0 months</td>
</tr>
<tr>
<td>Immune-related pneumonia</td>
<td></td>
</tr>
<tr>
<td>and renal dysfunction</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>range: 0.7 to 6.7 months</td>
</tr>
<tr>
<td>19 (4.2)</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>range: 0.5 to 14.7 months</td>
</tr>
</tbody>
</table>

*Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis, some of them fatal, have been observed.

Please refer to the nivolumab (OPDIVO) Summary of Product Characteristics for the full side-effect profile. Data are pooled data for patients who received nivolumab + ipilimumab regimen in CheckMate 067, 069 and 004 (cohort 8).

¹ Nivolumab (OPDIVO) Summary of Product Characteristics.
Nivolumab + ipilimumab regimen: Median time to resolution of treatment-related irAEs (any Grade)

Time to resolution of treatment-related irAEs (any Grade) in patients who received nivolumab + ipilimumab regimen across three clinical studies in melanoma (n=448)

<table>
<thead>
<tr>
<th>IrAE</th>
<th>Patients with resolution, n (%)</th>
<th>Median time to resolution</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-related rash†</td>
<td>192/284 (67.6)</td>
<td>10.4</td>
<td>range: 0.1 to 74.0+ weeks</td>
</tr>
<tr>
<td>Immune-related diarrhoea or colitis</td>
<td>184/203* (90.6)</td>
<td>3.0</td>
<td>range: 0.1 to 78.7+ weeks</td>
</tr>
<tr>
<td>Immune-related endocrinopathies</td>
<td>59/131* (45.0)</td>
<td></td>
<td>range: 0.4 to 74.4+ weeks</td>
</tr>
<tr>
<td>Immune-related hepatitis</td>
<td>116/125 (92.8)</td>
<td>5.0</td>
<td>range: 0.1 to 53.1 weeks</td>
</tr>
<tr>
<td>Immune-related pneumonitis</td>
<td>29/33 (87.9)</td>
<td>6.1</td>
<td>range: 0.3 to 46.9+ weeks</td>
</tr>
<tr>
<td>Immune-related nephritis and renal dysfunction</td>
<td>17/19 (89.5)</td>
<td>1.9</td>
<td>range: 0.4 to 42.6+ weeks</td>
</tr>
</tbody>
</table>

+Denotes a censored observation (range). *Patients who experienced events without worsening from baseline were excluded from time-to-resolution analysis. †Rare cases of Stevens-Johnson syndrome and toxic epidermal necrolysis, some of them fatal, have been observed.

Please refer to the nivolumab (OPDIVO) Summary of Product Characteristics for the full side effect profile. Data are pooled data for patients who received nivolumab + ipilimumab regimen in CheckMate 067, 069 and 004 (cohort 8).

How does has this changed side-effect management

- MDT relationships with other departments
- Thyroid function monitoring
- Specific side-effect proforma
- Funding for management of side-effects (who pays for infliximab)
- Report side-effect via yellow card
Immuno-oncological agents Immune-related adverse event (IrAE) management guidelines

• Trust guidelines available on the intranet (oncological emergencies)/ TVSCN
Immuno-oncological agents Immune-related adverse event (IrAE) management guidelines

• Depending on the site of auto-immunity, treatment is normally immuno-suppression (1\textsuperscript{st} line corticosteroids, 2\textsuperscript{nd} line dependent on condition e.g. infliximab for colitis) and withholding treatment until resolution e.g. grade 3 toxicity or permanent discontinuation grade 4
Immuno-oncological agents Immune-related adverse event (IrAE) management guidelines

• Endocrinopathies – may require hormone replacement e.g. levothyroxine for hypothyroidism or hydrocortisone for adrenal insufficiency

• All persistent grade 2 or grade 3/4 toxicities should be managed in conjunction with the relevant specialist team.

• All adverse events to be reported to MHRA yellow card
Tumour vaccines
Peptide vaccines

- Cancer cells display peptides which can trigger an immune response
- Immunogenic peptides isolated
- Peptides injected into patient
- Dendritic cells activate T-cells
- Cancer cells destroyed
- Inefficient system
Dendritic cell vaccine

- Patient’s dendritic cells incubated with cancer cell fragments
- Dendritic cells injected into patients
- Dendritic cells activate T-cells in lymph nodes
- Type of cellular treatment

- E.g. Sipileucel-T – dendritic cells exposed to modified protein and gmcsf.
Oncolytic virus vaccines
Oncolytic virus vaccines

- Genetically modified virus with selectivity for cancer cells
- Injected into tumour
- Cancer cell burst open shedding debris
- Dendritic cells collect debris
- Dendritic cells activate T-cells in lymph nodes
- Cancer cells killed
- Example: Talimogene Laherparepvec
Gene Therapy – Talimogene laherparepvec

- First EU licensed gene therapy for metastatic melanoma
- Attenuated herpes simplex virus coding for human granulocyte macrophage colony-stimulating factor (gmcsf)
- Replicates in tumours
- Oncolytic immunotherapy – promotes anti-tumour immune response.
Gene Therapy

A biological medicinal product which contains an active substance which contains or consists of a recombinant nucleic acid used in, or administered to human beings, with a view to regulating, repairing, replacing, adding or deleting a genetic sequence; and its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.
CAR-T cell Therapy
Adoptive cell transfers: CAR-T Cells
Car-T Cell Therapy

• Patient-specific (autologous) cell therapies
• Patient’s own T lymphocytes - genetically modified to express a chimeric antigen receptor (CAR) to confer antigen specificity
• Genetic modification by manufacturer
  – Using viral vector derived from a retrovirus or a lentivirus, which carries the new gene for the chimeric receptor
• Car-T Cell Therapy commissioned sites
Licensed Car-T Cell Therapy (CDF)

- Axicabtagene ciloleucel (Yescarta)
  - Large B Cell lymphoma
- Tisagenlecleucel (Kymriah)
  - B-cell acute lymphoblastic leukaemia (ALL)
  - Childhood leukaemia

- Specifically developed for each individual patient
- Involves reprogramming the patient’s own immune system cells which then target the cancer.
- Trials have shown cure in some patients
Car-T Cell Therapy

CHIMERIC ANTIGEN RECEPTOR T CELLS

A briefing document for Chief Pharmacists

Issued by: The ATMP Working Party – a subgroup of the Pharmaceutical QA Committee

December 2017

Pharmacy Institutional Readiness for Marketed CAR-T Therapy: Guidance for Chief Pharmacists

CAR-T Therapies are newly authorised products within Europe and currently undergoing review via the NICE Technology Appraisals process. They are classed as Advanced Therapy Medicinal Products (ATMPs) and as such, require governance and management by Chief Pharmacists. They present risks which Chief Pharmacists should ensure are minimised. The greatest risks are around tracking and traceability as CAR-T is an individualised therapy with disastrous consequences if not administered to the patient it was intended for. Whilst collaboration with expert cellular product handling colleagues will be key operationally, it may present challenges for Pharmacy to embed this new working relationship. Additionally, CAR-T therapies are associated with toxicities which must be well understood and managed in a timely fashion.

It is advised that the following areas require Pharmacy input prior to an organisation implementing CAR-T Therapy. It is recognised that Pharmacy does not currently have the expertise to handle the products and that, routinely, Pharmacy may not come directly into product contact. However, where Pharmacy is not directly performing the procedures agreed, then roles should be clearly documented in an overarching technical agreement with reference made to approved SOPs.

September 2018
PHARMACY INVOLVEMENT IN MARKETED CAR-T THERAPY
Tumour Infiltrating Lymphocytes (TIL)
Tumour Infiltrating Lymphocytes (TIL)

- Lymphocytes (B & T cell) collected from tumour = TIL
- Cancer attacking TILs isolated and grown in lab
- Patient immune system depleted
- TILs infused into patient
- Relies on pre-existing T cells
- Technical and expensive
- Some success in melanoma and breast cancer
Advanced Therapy Medicinal Products (ATMPs)
ATMP

- Advanced Therapy Medicinal Product
- Biological medicine that is classified as one of the following (or combination of):
  - Gene therapy
  - Somatic cell therapy (SCT)
  - Tissue Engineered Product (TEP)
ATMPs

• Medicines subject to the same requirements as other medicinal products
• Chief Pharmacist is responsible for governance and management of ATMPs
• Most current usage is in clinical trials, but ATMPs are beginning to become available as licensed and unlicensed medicines.
The role of pharmacy in the successful delivery of ATMPs

- Information for Chief Pharmacists

• Issued February 2017 (Ed 1)
• NHS Pharmaceutical Quality Assurance Committee with National Pharmacy Clinical Trials Advisory Group
Role of Pharmacy

• To oversee governance arrangements
• To ensure ATMPs are of appropriate quality for intended use
• Collaborative working with Human Tissue Authority (HTA) designated individual within organisations to develop process and appropriate handling of ATMPs
• Practicalities – Storage, Handling, Delivery, Preparation, Logistics
Does Immunotherapy work for all cancers?

• Works best in:
  – Immunogenic tumours
  – High mutation burden
  – Tumours containing T-cells, PD-L1
  – High levels PD-L1

• Do not work in:
  – Immune excluded tumours
  – No T-cells, no PD-L1
Future

• CAR-T works well in ALL
• Combination of CAR-T and checkpoint inhibitors
• Improvement in toxicity management
• Improvements in biomarkers
Summary

• What is immunotherapy?
• Immune system refresher
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  – Monoclonal antibodies
  – Immune checkpoint inhibitors
  – Tumour vaccines
    • Peptide DNA and RNA
    • Dendritic cells
  – Oncolytic viruses
  – Gene therapy
  – Cellular therapy e.g. CAR-T cells
  – Tumour infiltrating lymphocytes (TIL)
• ATMPs and pharmacy
• Future
Questions?
Immunotherapy

Professor Nicola Stoner
Consultant Cancer Pharmacist
ASPCP Birmingham 15th November 2018