Advanced Therapeutics: Is pharmacy prepared for the future?

Joni Donagher[1], Lani Attwood[1], Deshina Naidoo[1], Peter Barclay[1]

[1]*The Children's Hospital at Westmead | Contact: joni.donagher@health.nsw.gov.au*

Background

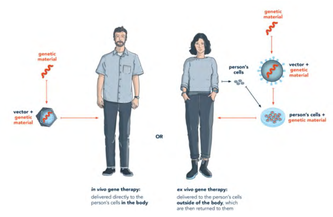
- Advanced therapeutics (AT) are a new class of medicines classified as gene therapies, somatic cell therapies, tissue engineered products or bacteriophage therapies.
- They are currently some of the most expensive treatments in the world however they have the potential to treat rare diseases where there are limited treatment options or cures.
- AT which are classed as genetically modified organisms (GMOs) are regulated by the Office of the Gene Therapy Regulator (OGTR) while their therapeutic use is regulated by the Therapeutic Goods Administration (TGA) in Australia.
- Pharmacy are responsible for custody and preparation of gene therapy products. Some of these are prescription only products and many of these require ultra cold storage in a -80ºC freezer and preparation in a biological safety cabinet.

Types of Advanced Therapeutics

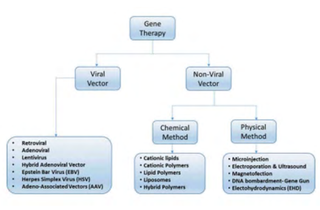
Understanding Gene Therapy

- Ex vivo gene therapy: the transfer of genes to cultured cells outside of the body which are then transferred to the patient.
- In vivo gene therapy: the delivery of a therapeutic gene (DNA) to target cells of a particular tissue using direct administration routes such as intravenous injection.
- Genes can be delivered using viral and non viral vectors.

In vivo and ex-vivo gene therapy



Gene Therapy Delivery Systems



Luxturna® (Voretigene neparvovec)

- Vector: Adeno-associated virus serotype 2
- Used to treat Leber congenital amaurosis (*inherited retinal dystrophy due to mutations in the gene RPE65.*) by delivering a normal copy of the RPE65 gene
- Treatment of both adults and children.

Zolgensma® (Onasemnogene Abeparvovec) – First Use

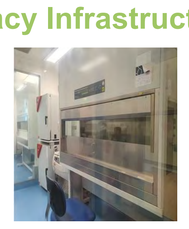
- Vector: Adeno-associated virus serotype 9.
- Used to treat spinal muscular atrophy by providing a copy of the gene that makes human survival motor neuron (SMN) protein.
- Sydney Children's Hospital Network (SCHN) have been involved in the international Zolgensma® clinical trials SPR1NT and SMART.
- SCHN physician instrumental in implementation of new-born screening programme for SMA in NSW and ACT allowing for early intervention in SMA and gene therapy treatment.

History and timeline (SCHN)

Setting up a Pharmacy Service

- Advanced therapeutics such as gene therapy require a dedicated pharmacy service with pharmacists specialising in advanced therapeutics delivery.
- Pharmacists are required for clinical trials, clinical triage, AT preparation, AT procurement, clinician and patient education, development of policies and procedures and risk assessment including institutional biosafety and medicines and therapeutics committee involvement.
- Pharmacists are responsible for the governance and storage of gene therapy and bacteriophage products necessitating specialist infrastructure and regulatory requirements .

Pharmacy Infrastructure



Governance

- All gene therapy products and GMO bacteriophage products have an OGTR licence. The institution and in some cases the pharmaceutical company are responsible for meeting licence requirements.
- The use of GMOs are regulated via the Gene Technology Act 2000.
- Registered Australian products have separate and additional TGA requirements.
- Some products have specific funding via the PBS or with the Ministry of Health.

Advanced Therapeutics Centre at SCHN – Leading the Way

Working with major industry partners, research institutes and the NSW government to develop the infrastructure, organisational frameworks and workforce to deliver these treatments ongoing.

- Clinical trials
  - Regulation, early phase HREC and trials, risk/Indemnity assessments, governance, import permits, ethics input and implementation, evaluating opportunities.
- Workforce training
- Education and Communication
  - Webinars, GCP and Clinical trials training, Health system SOPs and Policies.
- Infrastructure
  - Viral Vector Manufacturing Facility: one of the only viral vector manufacturing facilities in the country and will be managed by SCHN in association with the Office for Health and Medical Research and Health Infrastructure.
  - Pharmacy: Biological containment units.
  - Facilities Management including pharmacy, patient facilities within the hospital and research centres.

Conclusions

- Health system readiness needs to be assessed prior to implementation of any AT service. Advanced therapeutics delivery is expensive with significant capital required for infrastructure and a skilled multidisciplinary workforce is needed to delivery therapy successfully.
- Australia currently has 3 registered AT products and the SCHN has 3 active gene therapy trials. Globally there are >15 AT products registered for use and horizon scanning indicates the number of both registered and clinical trial products are rapidly increasing necessitating the need for comprehensive AT services in Australia.
- This is an exciting time with the introduction of new modalities of disease treatment opening up opportunities for pharmacists with specialised skills to contribute to improved patient outcomes.