ATMPs on the horizon

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CATAPULT Cell and Gene Therapy

Who are LAT and the ATTCs?

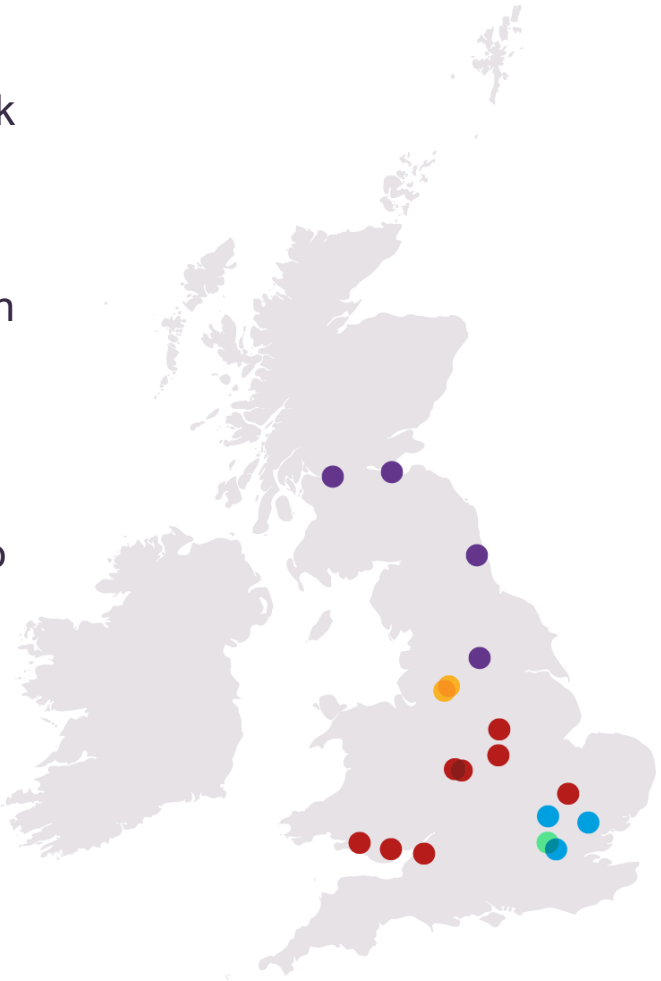
The ATTC (Advanced Therapy Treatment Centre) network is funded by Innovate UK and the Industrial Strategy Challenge Fund

London Advanced Therapies (LAT) is funded by Research England

The centres are working together, along with the Cell and Gene Therapy Catapult to specifically look at the training requirements for the current workforce and what needs to be put in place for them to be ready to deliver the treatments that are currently being developed.

This series of webinars is designed to help increase the awareness of advanced therapies and their impact in the clinic

Find out more at https://www.theattcnetwork.co.uk/



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ATMPs on the horizon

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The first stop for professional medicines advice

WHAT WILL BE COVERED

Focus on 4 ATMPs due to arrive in 2021, subject to NICE approval

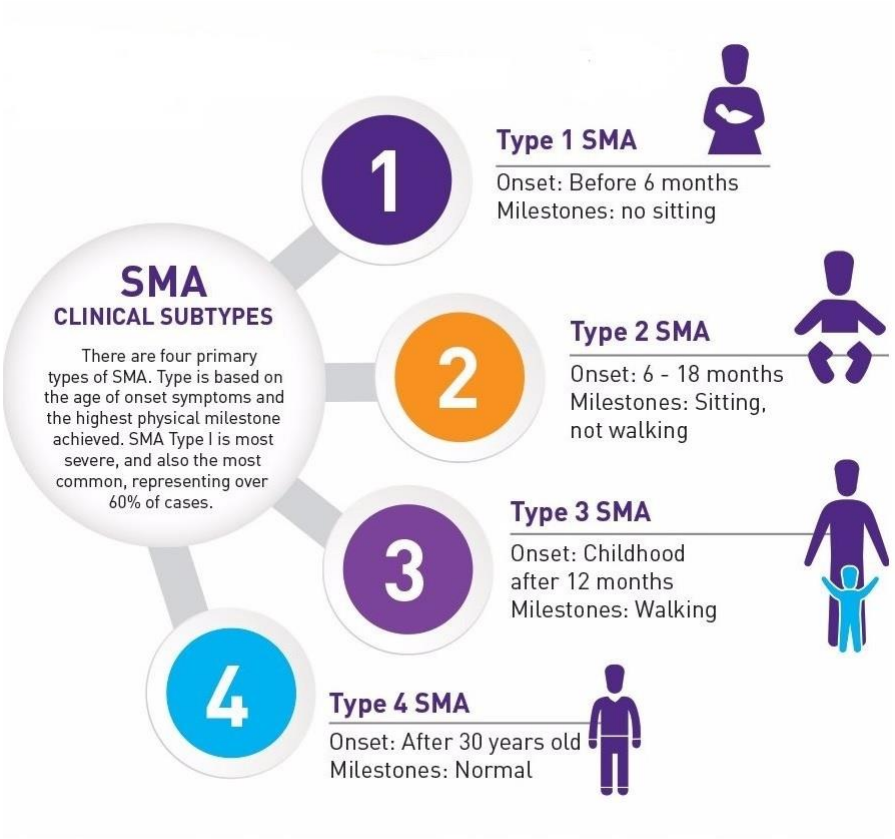
- Onasemnogene abeparvovec (*Zolgensma*)
- Lisocabtagene maraleucel (*Breyanzi*)
- Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)
- Lenadogene nolparvovec (*Lumevoq*)

Where to find more information on ATMPs in development

Onasemnogene abeparvovec (*Zolgensma*)

5q spinal muscular atrophy (SMA)

- Rare genetic neuromuscular disorder
- Degeneration of motor neurones in the spinal cord causes progressive muscle weakness and loss of movement
- Lack sufficient functional survival motor neurone protein (SMN)
- Decreases in severity from type 0 to 4
- Between 670 and 1,350 people living with SMA in the UK
- About 70 babies born each year

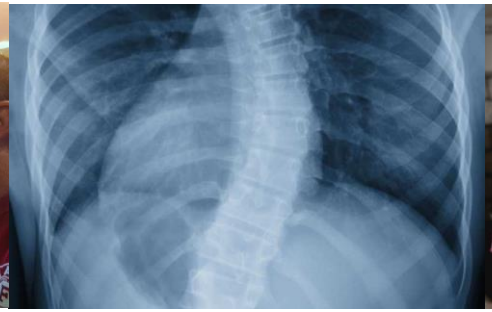


Clinical presentation

Differs according to age of onset and severity

- **SMA-1 (<6 months)** 'non-sitters', respiratory and swallowing problems, spinal curvature, reduced life expectancy
- **SMA-2 (7 – 18 months)** 'sitters', some have swallowing and breathing problems
- **SMA-3 (18 months – 18 years)** problems standing and walking
- **SMA-4 (adults)** muscle weakness






Onasemnogene abeparvovec (*Zolgensma*)

Treatment pathway

- Multidisciplinary supportive care aims to minimise the impact of disability, address complications and improve quality of life – respiratory, gastroenterology and orthopaedic care, plus nutritional support, physiotherapy, assistive technologies, occupational therapy and social care

- July 2019, intrathecal nusinersen recommended by NICE for treating 5q SMA in people with pre-symptomatic SMA, or SMA types 1, 2 or 3

- Risdiplam, a SMN2 gene pre-mRNA splicing modifier that increases SMN protein levels due 2021

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Onasemnogene abeparvovec (*Zolgensma*)

- **Onasemogene abeparvovec** is an *in vivo* gene therapy that uses an adeno-associated virus vector (AAV9) to carry the gene for SMN protein into nerve cells, enabling them to produce SMN
- Made by Novartis Gene Therapies
- Licensed in the UK May 2020 for treating patients with 5q SMA with a bi-allelic mutation in the SMN1 gene and a clinical diagnosis of SMA-1, or with 5q SMA with a bi-allelic mutation in the SMN1 gene and up to 3 copies of the SMN2 gene
- Limited experience in patients aged ≥2 years with body weight >13.5kg

Onasemnogene abeparvovec (*Zolgensma*)

Delivery mode Intravenous infusion over 1 hour via peripheral vein, within 8 hours of drawing into syringe (and within 14 days of receiving vials)	**Dose and duration of therapy** Single dose of 1.1×10^{14} vector genomes (vg)/kg of body weight
Presentation Vials containing solution for infusion (nominal conc. 2×10^{13} vector genomes/mL) 10mL vials contain 5.5 or 8.3mL *Zolgensma*	**Pre- treatment** Systemic corticosteroids started one day before *Zolgensma* for a total of 30 days Testing for presence of AAV9 antibodies prior to infusion

Onasemnogene abeparvovec (*Zolgensma*)

Handling and storage Personal protective equipment needed Supplied frozen, requires thawing Must use within 14 days of receipt *Genetically modified microorganism (GMM) class = Biosafety level 1*	**Infrastructure requirements** Pharmacy aseptic facilities and for storage, thawing and temperature monitoring
Patient monitoring and follow up Tapering corticosteroid dose, monitor liver function, platelet count and troponin-I level, temporary containment and GMO waste management	**Service implications** *Zolgensma* should be administered in suitable clinical centre, supervised by a physician experienced in managing patients with SMA

Onasemnogene abeparvovec (*Zolgensma*)

Efficacy

Open-label PIII STR1VE US study (n=22)

- 91% of patients aged <6 months (with 1 or 2 copies of SMN2) experienced event-free survival (no need for permanent ventilatory support) at 14 months (p<0.0001 vs. a natural history cohort)
- 59% were able to sit for 30 seconds and 27% achieved head control at 18 months of age

Published data compared outcomes of 12 SMA-1 infants who received *Zolgensma* in a PI study vs. a cohort of 16 natural history SMA patients and 27 healthy infants enrolled in another study

- All treated with *Zolgensma* survived (and achieved major motor milestones) at 24 months vs. 38% in control group

Open-label PIII STRIVE-EU study (n=33, aged <6 months with 1 or 2 copies of SMN2) – interim data

- 97% patients survived event-free, including 93.8% who could have reached 10.5 months of age and 56.3% who could have reached 13.6 months of age (vs. 50% and 25%, respectively, in an untreated natural history cohort)

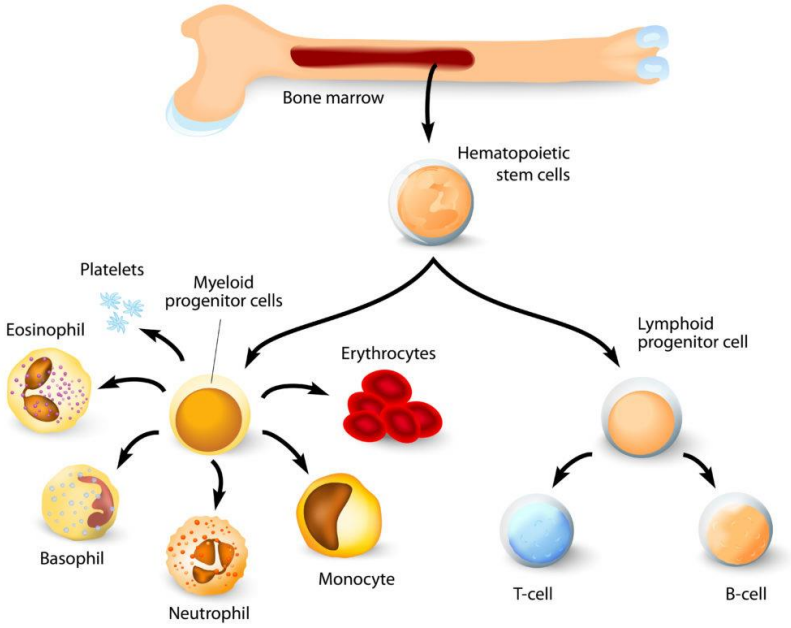
Safety

- Acute serious liver injury, elevated transaminases and cardiac troponin-I levels, thrombocytopenia

Lisocabtagene maraleucel (*Breyanzi*)

Relapsed/refractory high-grade B-cell non-Hodgkin lymphoma

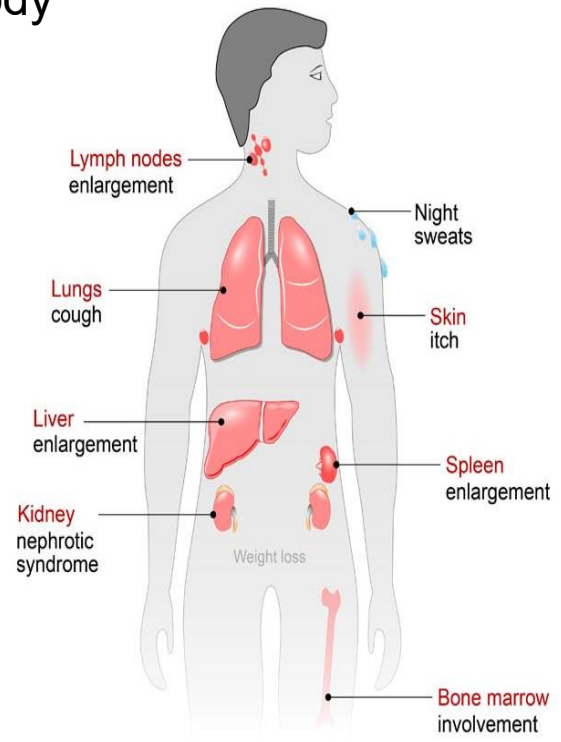
- Diffuse large B-cell lymphoma (DLBCL) most common type
- Others include primary mediastinal (PMBCL) and follicular grade 3B (FL3B)
- Abnormal cells larger than healthy B cells and spread out when examined under a microscope
- Develops at any age, including children, but more common in older people
- 5,500 people diagnosed with DLBCL each year in the UK
- About 600 people a year in England with a high-grade B-cell NHL relapse after 2 or more previous treatments



Lisocabtagene maraleucel (*Breyanzi*)

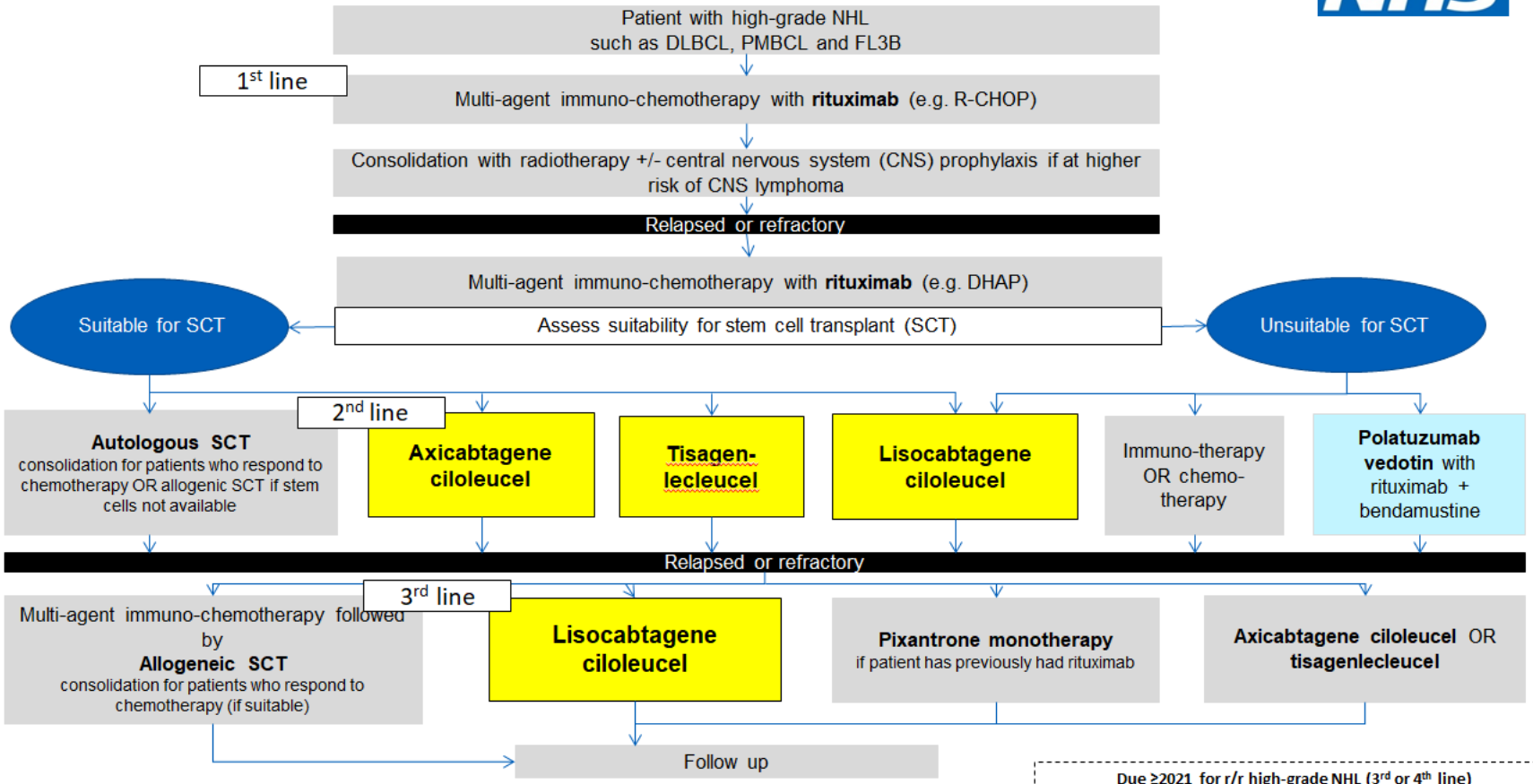
Symptoms

- Painless lumps (often in neck, armpit or groin) usually grow over a few weeks
- Sometimes develops in lymph nodes inside the body
- DLBCL can develop outside lymph nodes (extranodal disease), affects 1 in 5 with DLBCL
- Exact symptoms depend on where in the body:
  - stomach or bowel – abdominal discomfort or pain, diarrhoea or bleeding
  - chest – cough or breathlessness
- Around 1 in 3 people with DLBCL have fevers, night sweats and unexplained weight loss
- Fatigue and loss of appetite quite common, some experience severe itching



Lisocabtagene maraleucel (*Breyanzi*)

Proposed pathway for high-grade non-Hodgkin lymphoma (NHL)

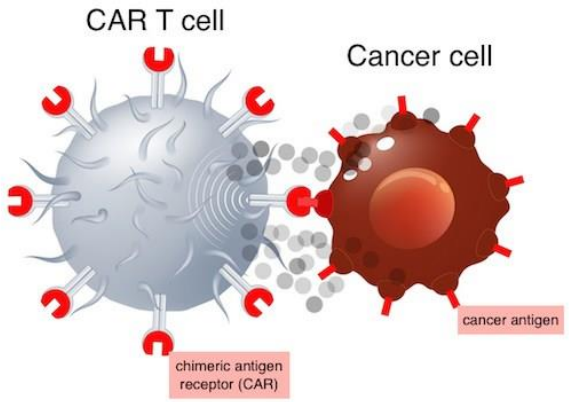


https://pathways.nice.org.uk/pathways/non-hodgkins-lymphoma/treating-follicular-lymphoma

Due ≥2021 for r/r high-grade NHL (3rd or 4th line)
AUTO-3, avelumab, selinexor

Lisocabtagene maraleucel (*Breyanzi*)

- **Lisocabtagene maraleucel** is an autologous chimeric antigen receptor (CAR)-T cell therapy made by Celgene
- Patient's own mononuclear cells collected by leukapheresis and CD8+ and CD4+ T lymphocytes modified genetically *ex vivo* using a lentiviral vector encoding an anti-CD19 CAR protein
- After lymphodepleting chemotherapy, single dose of CAR T-cells infused back to the patient and attach to CD19 on cancer cells causing cell death
- Filed for approval to EU July 2020
- Licensed in the US February 2021 to treat adults with relapsed or refractory large B-cell lymphoma after ≥2 lines of systemic therapy, including DLBCL not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, PMBCL and FL3B



How does it differ from other CAR-Ts?

- Manufacturing process involves selection of a defined composition of CD8 and CD4 T cells from leukapheresis, followed by independent CD8 and CD4 activation, transduction, expansion, formulation, and cryopreservation
- Major difference to other CAR-T therapies is CD4 and CD8 T cells are separately transduced and expanded, and administered in equal target doses
- Axicabtagene ciloleucel and tisagenlecleucel manufactured on bulk T cells
- No comparative studies between CAR-T products, so unknown if differences affect clinical outcomes

Lisocabtagene maraleucel (*Breyanzi*)

Delivery mode Intravenous infusion Central venous access may be needed	**Dose and duration of therapy** Single dose of 100×10^6 CAR-T cells – defined composition of 50×10^6 CD8+ CAR-T cells and 50×10^6 CD4+ CAR-T cells
Starting material and presentation Peripheral blood mononuclear cells harvested by leukapheresis Dispersion for infusion	**Pre- treatment** Lymphodepleting chemotherapy (fludarabine & cyclophosphamide) 2-7 days prior to infusion of lisocabtagene

Lisocabtagene maraleucel (*Breyanzi*)

Handling and storage Supplied frozen – requires thawing Storage requirements and shelf life unknown *Genetically modified microorganism (GMM) class = TBC*	**Infrastructure requirements** Apheresis facilities (including trained staff), and facilities for storage, temperature monitoring and thawing of cryopreserved product Critical care facilities needed and co-ordinator role
Patient monitoring and follow up Monitored as inpatient for 10 days for neurological toxicities and CRS; management with supportive therapies (e.g. tocilizumab) as appropriate. Further follow up will be clinical review by treating clinician.	**Service implications** As per other commissioned CAR-T therapies. Commissioned services must be accredited and demonstrate experience in use of CAR-T and immune effector cell (IEC) therapies. Co-ordinator role needed.

Lisocabtagene maraleucel (*Breyanzi*)

Efficacy

Pivotal PI TRANSCEND-NHL-001 trial (n=268)

- ORR 73% and CR rate 53% at 24 months in 255 evaluable patients
- Median PFS 6.8 months and median OS 21.1 months

Interim data from 12 patients in the PII TRANSCENDWORLD trial (n=116)

- All achieved a response with 6 (50%) achieving CR and 5 achieving PR
- 58% maintained response levels at 3 months
- Primary outcome data due by August 2021

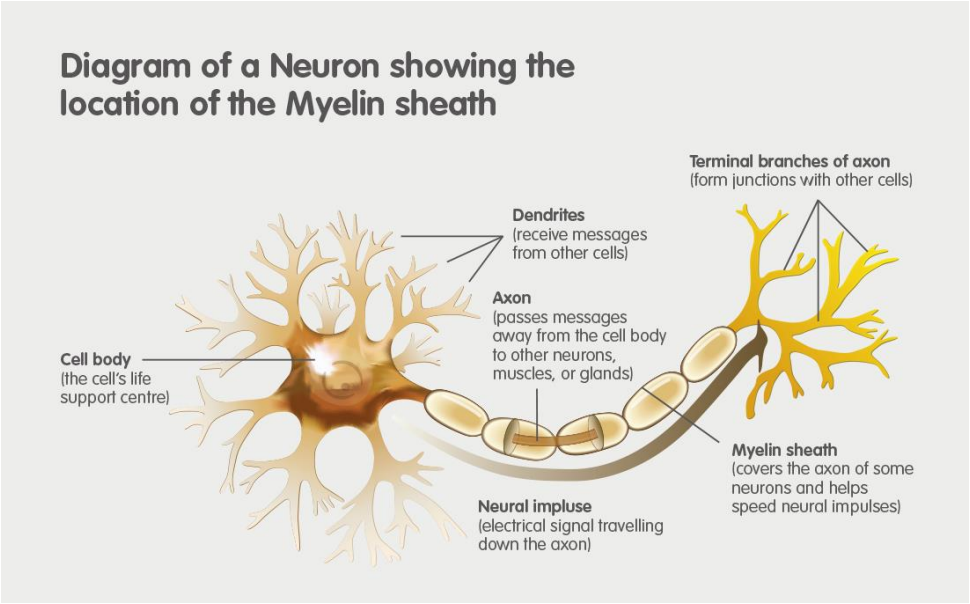
Safety

- Serious (grade 3) adverse events 79%, mostly cytopenias
- Cytokine release syndrome 47% (median onset 5 days); 2% grade ≥3
- Neurological adverse events 47%

Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

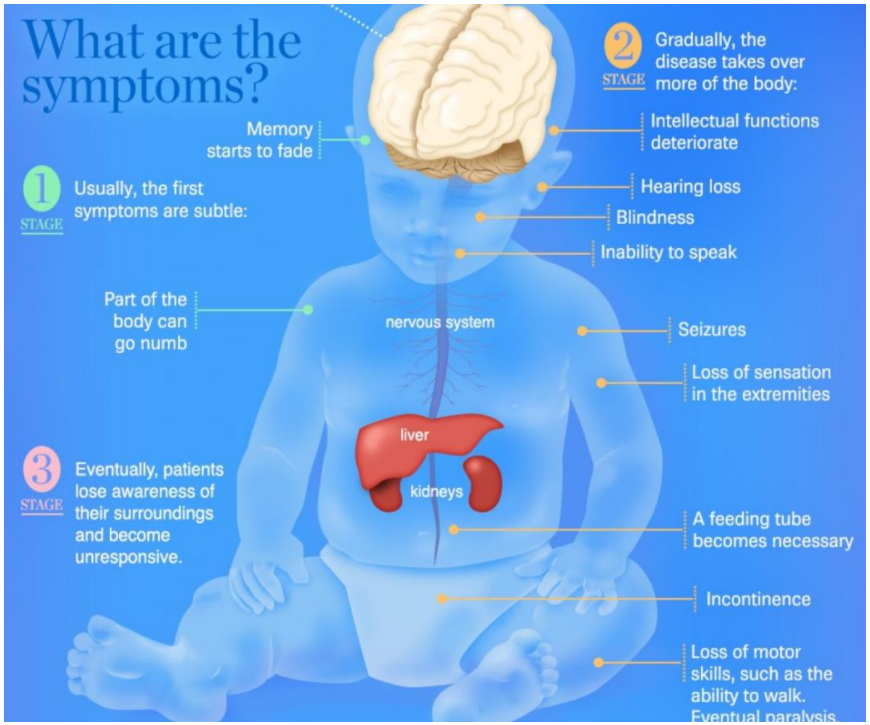
Metachromatic leukodystrophy (MLD)

- Rare inherited disorder
- Mutation in a gene needed to make arylsulfatase A (ARSA) enzyme
- Sulfatides build up and damage the myelin sheath in the nervous system, causing walking difficulties, gradual mental deterioration and eventual death
- About 50 people living with MLD in England (prevalence ~1 per million)
- Birth incidence 1 in 40,000; about 2-4 new cases annually



Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

- **Late-infantile MLD** (most common, affects 50-60%) – children begin having difficulty walking after first year. Often mistaken for cerebral palsy. Also deterioration in other developmental skills, e.g. loss of speech.
- **Juvenile MLD** (early-juvenile & juvenile) onset between 3 and 10 years of age, usually begins with impaired school performance
- **Adult-onset MLD** rarest form, commonly begins after age 16. Often initially misdiagnosed as a psychiatric disorder because of personality changes.



Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

Treatment pathway Currently, no effective treatments

Late infantile MLD

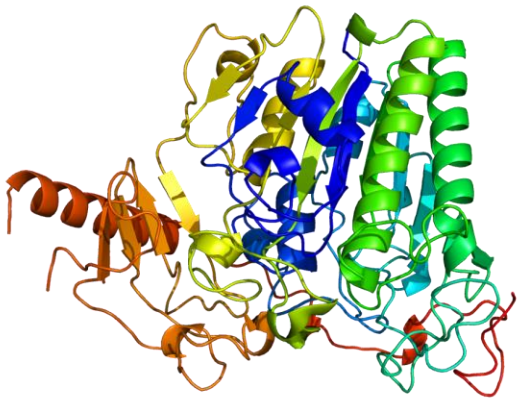
- Haematopoietic stem cell transplant (HSCT) ineffective and associated with risks, e.g. graft vs. host disease
- Management is palliative and supportive, e.g. preventing complications
- Best supportive care at specialist centres aims to stabilise patients with input from other specialties (e.g. neurology, cardiology, dietetics, physiotherapy, etc.)

Juvenile and adult MLD

- Less rapid progression so HSCT is an option but limited efficacy
- Done before symptom onset, HSCT can stabilise cerebral demyelination and arrest/slow progression
- HSCT has no effect on the peripheral nervous system – patients have developed severe, peripheral neuropathy-related motor deficits several years after HSCT

Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

- **Autologous CD34+ cells encoding ARSA gene** is an autologous gene therapy where the patient's CD34+ stem cells modified *ex vivo* using a lentiviral vector to insert a functional ARSA gene
- Cells re-infused after myeloablative therapy, in bone marrow make normal white blood cells that produce working ARSA – this breaks down sulfatides in surrounding cells, controlling symptoms
- Made by Orchard Therapeutics
- Licensed in the UK December 2020 for treating MLD characterised by biallelic mutations in the ARSA gene leading to reduction of ARSA enzymatic activity:
  - in children with <u>late infantile or early juvenile forms</u>, without clinical manifestations of the disease,
  - in children with the <u>early juvenile form</u>, with early clinical manifestations of the disease, who still have the ability to walk independently and before the onset of cognitive decline



ARSA enzyme

Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

Delivery mode Intravenous infusion through central catheter (completed within 2 hours of thawing) Maximum 5mL/kg/hour (1 bag/hour)	**Dose and duration of therapy** Single treatment with 3 to 30 × 10^6 cells/kg
Starting material and presentation CD34+ stem cells harvested by leukapheresis or from bone marrow ~1 month before gene therapy Presented in a fixed volume with a cryoprotectant in cryopreservation bags	**Pre- treatment** Myeloablative conditioning (i.v. busulfan 11.2 to 16.8mg/kg every 6h for 4 days – last dose >24h before *Libmeldy*) and supportive care Veno-occlusive disease, seizures, allergy and infection prophylaxis

Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

Handling and storage Requires thawing before infusion. Shelf-life: 6 months. Once thawed, maximum 2 hours at room temperature. *Genetically modified microorganism (GMM) class = TBC*	**Infrastructure requirements** Apheresis facilities (including trained staff), and facilities for storage and temperature monitoring of cryopreserved product – already available at selected centres. Aseptic facilities may be required for dose preparation.
Patient monitoring and follow up Period of hospitalisation ~60 days and vital signs monitored. Rescue infusion with back-up cells if graft fails. Follow up is clinical review by treating clinician. Regular testing for vcn and number of cells still expressing the new gene (not yet available).	**Service implications** May need a nurse specialist/co-ordinator. Possibly additional costs for staff training, patient counselling and with preparation, storage and disposal. Patients may require some care in an isolation unit after treatment.

Autologous CD34+ cells encoding ARSA gene (*Libmeldy*)

Efficacy

- Interim results from ongoing PI/II trial of non-cryopreserved formulation (n=20)
- 18 normal motor development, stabilisation of motor dysfunction or significant delay in disease progression after 3-7.5 years
- Significant treatment differences in gross motor function scores after 3 years vs. untreated patients (clinically meaningful minimum 10%)
  - 71% in late infantile patients
  - 40% in early juvenile patients
- Single-arm PIII trial (n=10) of cryopreserved formulation ongoing – data due 2022
- Integrated data analysis after median 3 years (n=29) – none of 16 patients in the late infantile subgroup died vs. 12 of 19 (63%) untreated patients (natural history study)

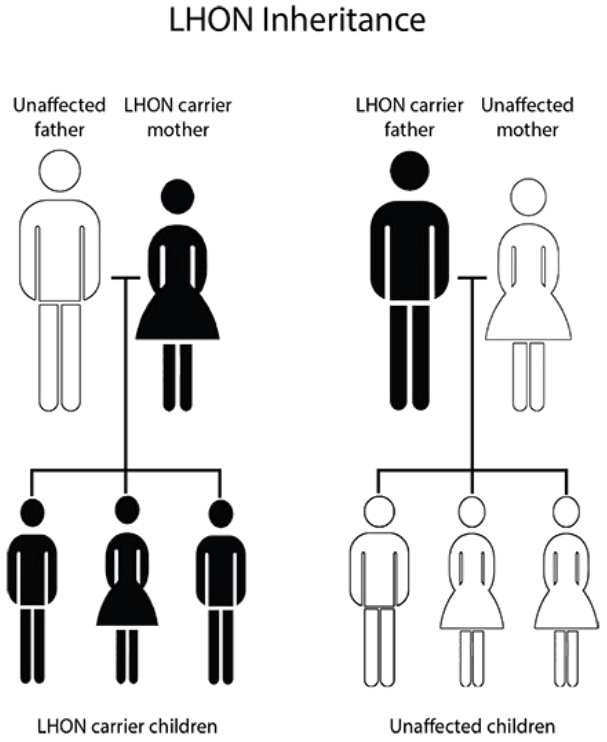
Safety

- Common side events (cytopenia and mucositis) related to pre-conditioning regimen
- *Libmeldy* well tolerated with no oncogenic transformation
- Anti-ARSA antibodies in some patients

Lenadogene nolparvovec (*Lumevoq*)

Leber's hereditary optic neuropathy (LHON) with ND4 gene mutation (G11778A)

- Rare maternally inherited mitochondrial genetic disease
- Degeneration of retinal ganglion cells results in irreversible vision loss
- Presents mainly in adolescents and young adults - triggers unknown
- 1,400 to 1,500 people lose their sight every year in the US and Europe due to LHON
- In England, 1,120 people living with LHON and approx. 30 new cases/year (with an ND4 mutation)



Lenadogene nolparvovec (*Lumevoq*)

Clinical presentation

- Sudden painless blurring and clouding of vision usually first symptoms
- May begin in one eye or simultaneously in both eyes – if starts in one eye, other eye usually affected within several weeks or months
- Rate of progression can vary 3-4 months to over 2 years
- Vision in both eyes worsens with severe loss of sharpness and colour vision
- Mainly affects central vision

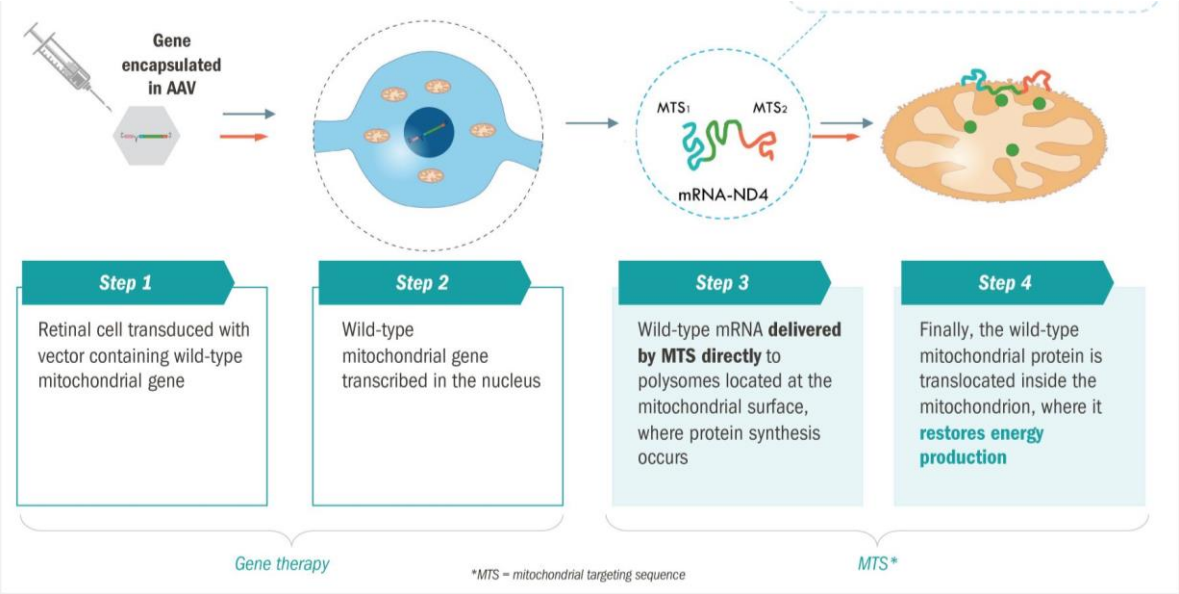
Normal Vision

LHON Vision

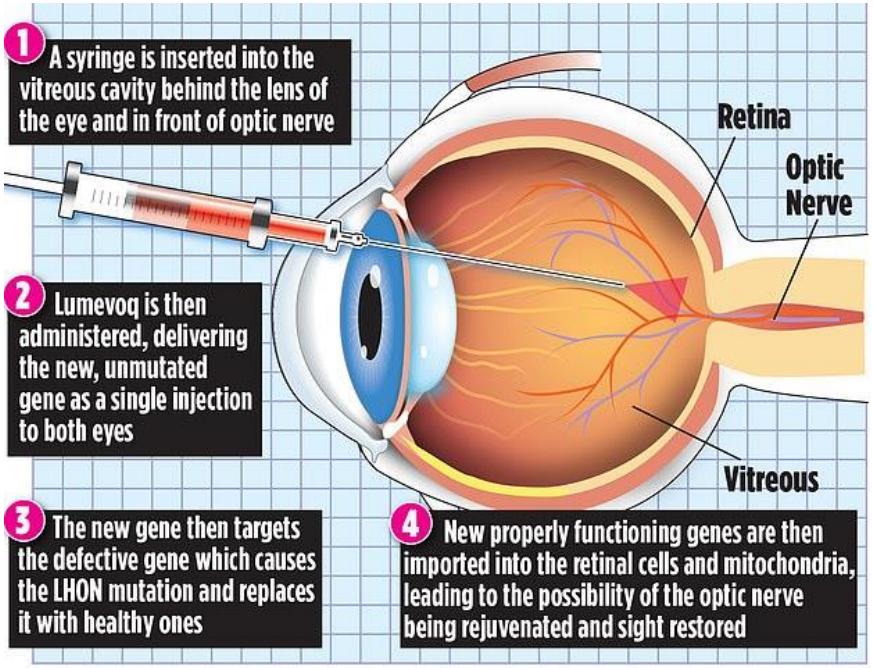
Lenadogene nolparvovec (*Lumevoq*)

Treatment pathway

- Supportive – visual aids, occupational rehabilitation, genetic counselling and screening for complications
- Avoid smoking and excessive alcohol, maintain low intraocular pressure
- Idebenone only medicine licensed in EU/UK (not routinely commissioned in England)
- Antioxidant food supplements
- Lenadogene would be first gene therapy to treat a mitochondrial disease



Lenadogene nolparvovec (*Lumevoq*)



- **Lenadogene nolparvovec** is an *in vivo* gene therapy using an adeno-associated virus 2 (AAV2) vector to deliver normal copies of human ND4 gene directly to the mitochondrial membrane of retinal ganglion cells
- Gene produces functional protein, restoring energy production
- Made by GenSight Biologics
- Filed for approval in the EU September 2020 for treatment of vision loss in patients with LHON due to a mutated ND4 mitochondrial gene

Lenadogene nolparvovec (*Lumevoq*)

Delivery mode Intravitreal injection by surgeon	**Dose and duration of therapy** Single injection containing 9^{10} viral genomes into each eye
Presentation Likely cryofrozen concentrate as per other gene therapies for the eye	**Pre- treatment** Ocular anaesthetic, mydriatic and intra-ocular pressure lowering agents immediately precede treatment

Lenadogene nolparvovec (*Lumevoq*)

Handling and storage Needs thawing and reconstitution prior to administration (in trial, this was performed by cell and gene therapy team in hospital) *Genetically modified microorganism (GMM) class = TBC*	**Infrastructure requirements** Aseptic facilities required for dose preparation (Class II vertical laminar flow biological safety cabinet) Surgical facilities required for administration
Patient monitoring and follow up Containment and genetically modified organism (GMO) waste management of fluid from eyes (e.g. tears) likely to be needed Further follow up will be clinical review by treating clinician (e.g. at 1, 3, 6 and 12 months, then annually)	**Service implications** Expected to be significant increase in number of patients referred for diagnosis (as genetic testing newly available nationally), so implications for consultant numbers, service capacity, etc. Additional costs for staff training, patient counselling and with preparation, storage and disposal of the gene therapy

Lenadogene nolparvovec (*Lumevoq*)

Efficacy

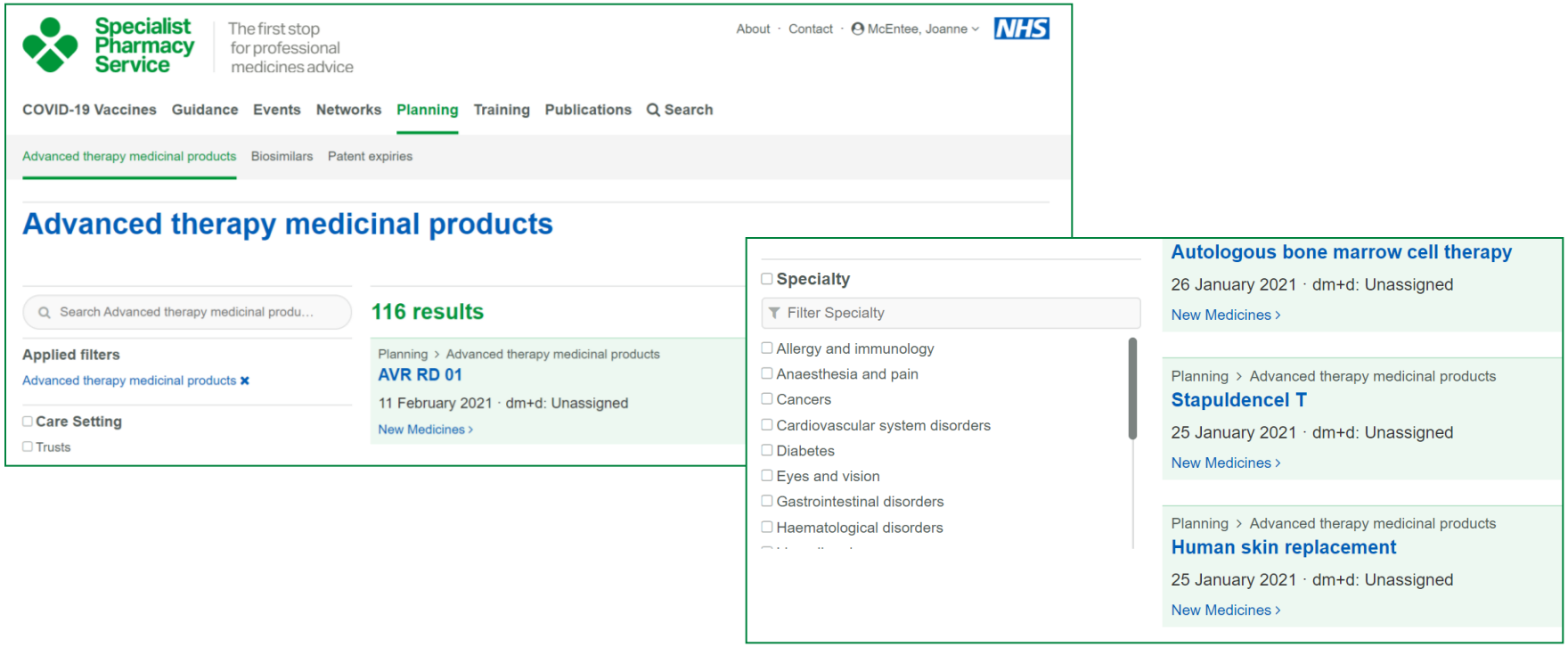
- In RESCUE trial (n=39) lenadogene-treated eyes improved at week 48 by +13 ETDRS letters vs. +11 in placebo-treated eyes
- In REVERSE trial (n=37) lenadogene-treated eyes improved at week 48 by +11 ETDRS letters vs. +11 in placebo-treated eyes
- 96 week data show +26 vs. +23 (RESCUE) and +15 vs. +13 (REVERSE)
- Pooled 48-month trial and natural history data – difference between treated (n=76) and untreated patients (n=208) clinically meaningful (+16.5 ETDRS letters)
- PIII REFLECT trial (n=90) investigating efficacy and safety of bilateral injection of lenadogene planned to complete in June 2024 (recruiting at Moorfields Eye Hospital, London)

Safety

- Appears safe and well tolerated
- Common ocular adverse effects related to injection procedure
- Intraocular inflammation accompanied by increased intraocular pressure in some patients
- 5-year follow-up study recruiting 74 patients from RESCUE and REVERSE ongoing

WHERE TO FIND MORE INFORMATION ON ATMPs

www.sps.nhs.uk/home/planning/advanced-therapy-medicinal-products/



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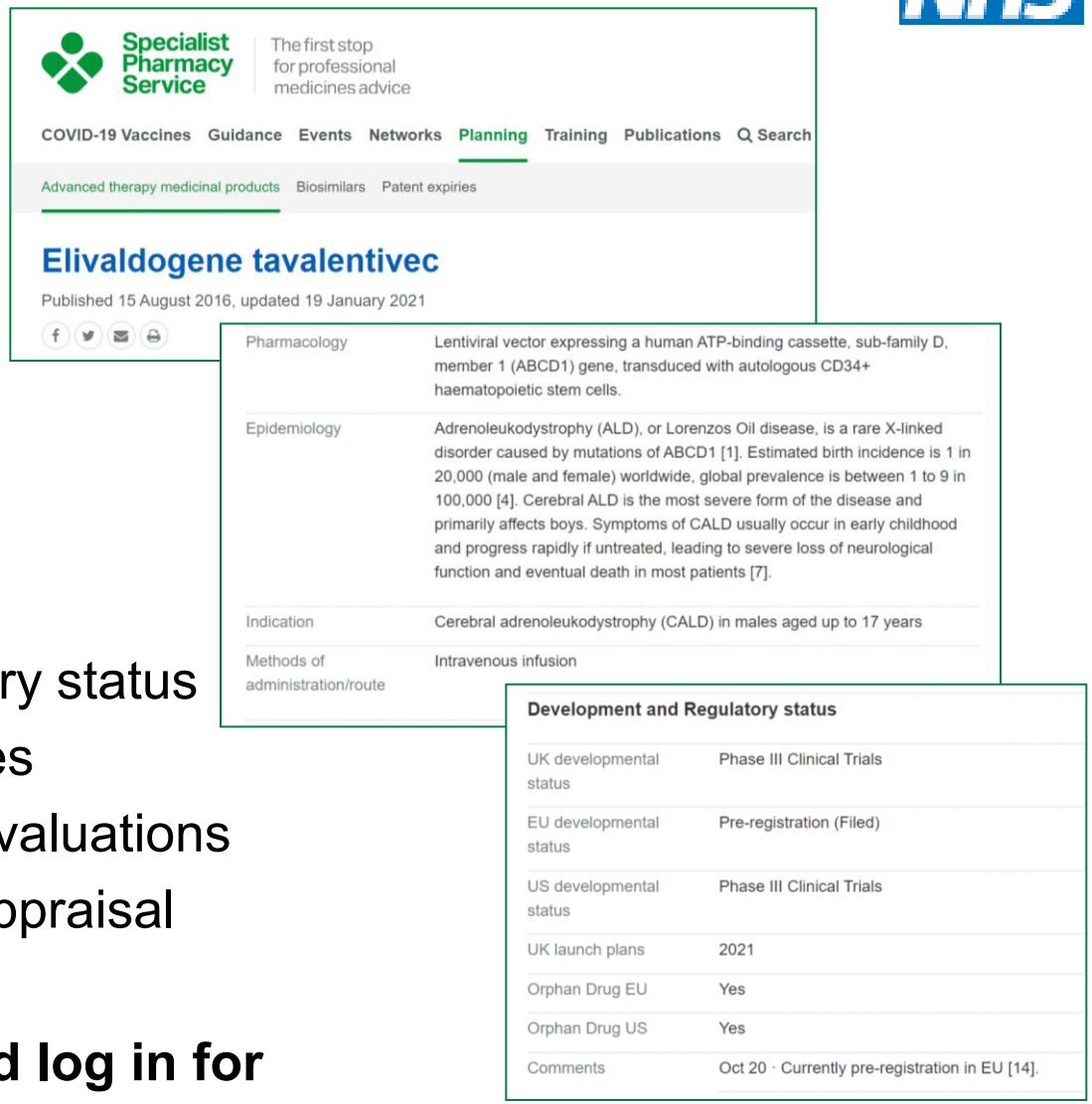
NHS

- Brand name
- Company name
- Pharmacology
- Epidemiology
- Indication
- Method of administration
- Development and regulatory status
- Trial data including UK sites
- Links to evidence-based evaluations
- Link to NICE technology appraisal



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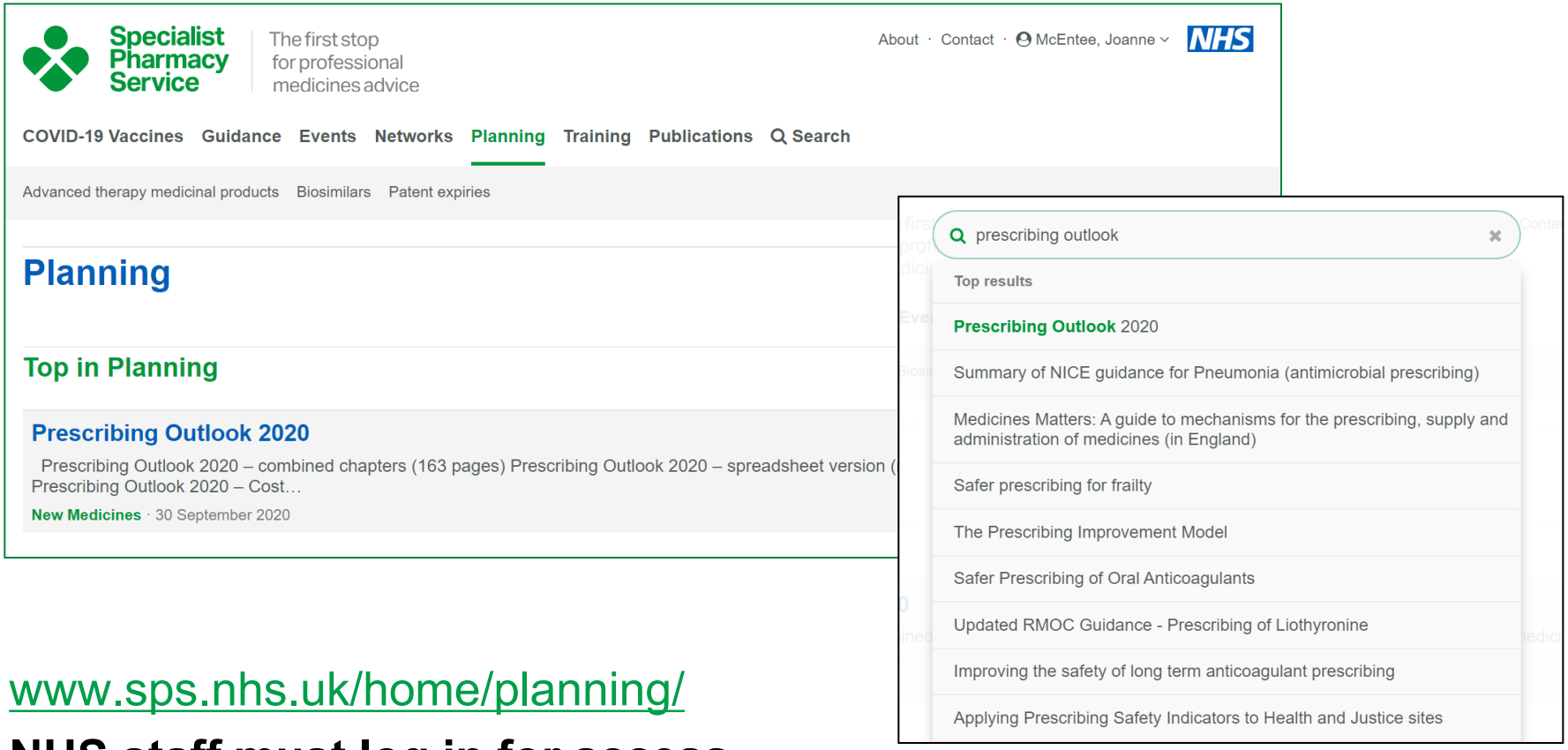
PRESCRIBING OUTLOOK



www.sps.nhs.uk/home/planning/

NHS staff must log in for access

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Prescribing Outlook

New Medicines and National Developments

Focussing on anticipated UK availability of new medicines, licence extensions, and published new guidance in 2020, 2021 or 2022

Advanced Therapy Medicinal Products (ATMPs)

A resource for the NHS to help with budget setting, prescribing planning and medicines management.

September 2020

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www.sps.nhs.uk

Contents

Key to financial assumptions and risk

Financial assumptions

To asses cost impact, assumptions are made about potential cost, place in therapy and whether the new medicine will displace, compete with or be added to existing therapy, but quantifying uptake is difficult. Cost of launched products is published NHS cost, and an indication made if a patient access scheme (PAS) may apply.

Financial risk

Risk categories are:

Estimated* additional cost per year/course	Cost saving	Low	High
Per patient	Likely positive budget impact	<£10,000	>£10,000
Per 100,000 people	Likely positive budget impact	<£30,000	>£30,000
For England (assuming 55 million people)	Likely positive budget impact	<£15 million	>£15 million

*Estimates are made on anticipated additional cost vs. comparators (where available), prevalence of the condition and eligible population based on study inclusion cr
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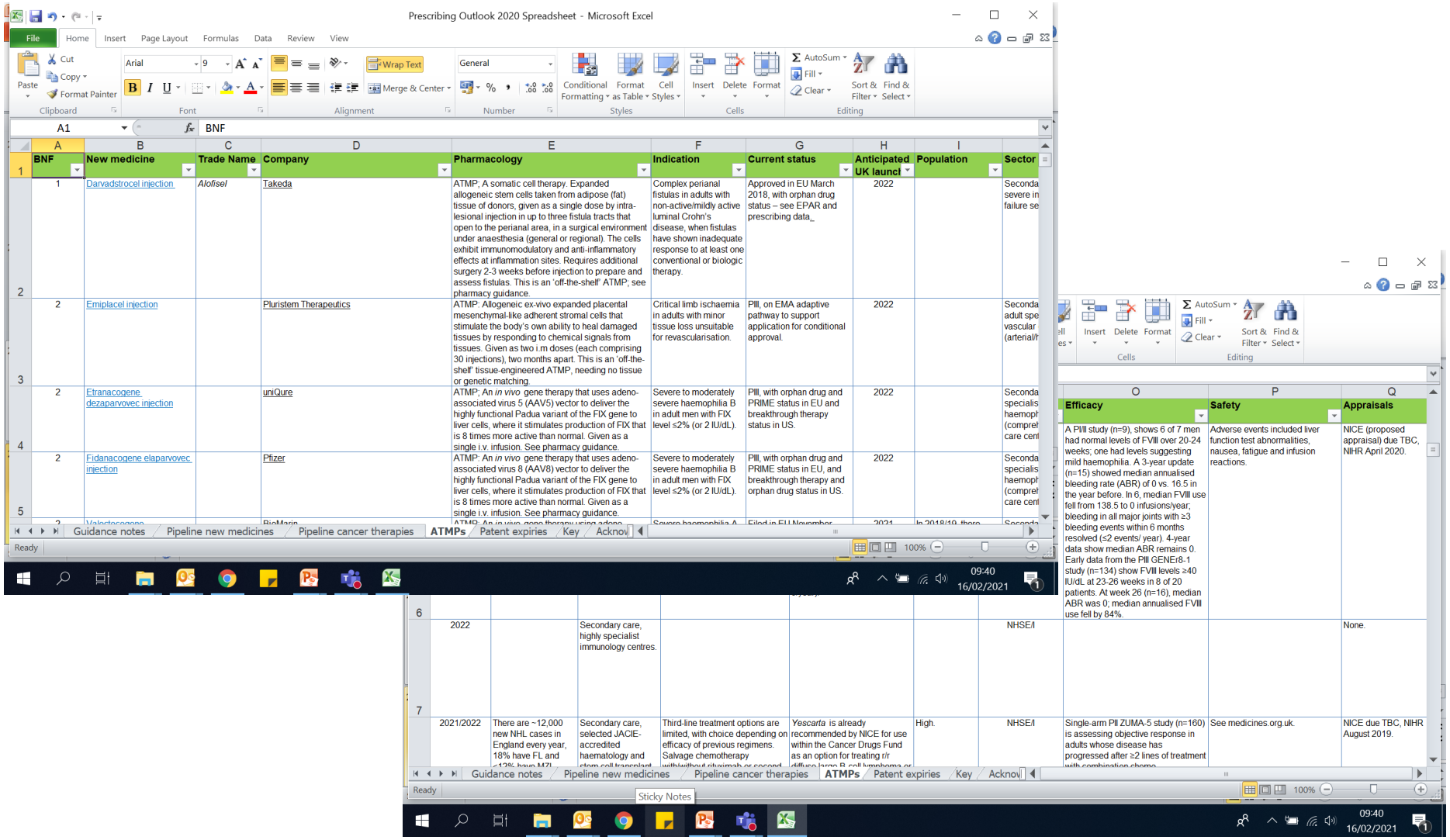
To be used in conjunction with this
Foreword, Acknowledgements, Gui

New medicine	Lenadogene nolparvovec **injection** *[Lumevoq]*; GenSight Biologics
Pharmacology	ATMP; An *in vivo* gene therapy using an adeno-associated virus 2 (AAV2) vector to deliver normal copies of human wild-type 11778 (ND4) gene directly to the mitochondrial membrane of retinal ganglion cells. Given as a single intravitreal injection into each eye by a surgeon. See pharmacy guidance.
Indication	Leber's hereditary optic neuropathy (LHON) due to G11778A mutation in the ND4 gene.
Current status	PIII, with orphan drug status in EU and US.
UK availability	2021
Population	Prevalence in England is ~4 in 100,000 people, with ~80 new cases each year, predominantly in males. The 11778 (ND4) mutation accounts for ~50% of all LHON reported cases. Most patients (~97%) progress to a bilateral visual acuity of 20/200 or worse within 1 year of disease onset. Vision loss is usually permanent; those with the G11778A mutation have a ~4% chance of spontaneous visual recovery. Most people do not go completely blind, but become registered as visually impaired.
Sector	Secondary care, specialist ophthalmology centres (likely selected centres).
Implications	Idebenone, the only licensed treatment available, is not routinely commissioned by NHSE/I. Lenadogene nolparvovec (LN) would be the first potentially curative treatment but with few long-term data. Results of a third PIII trial are awaited after initial trials did not show benefit vs. placebo.
Financial assumptions	LN is likely to be very expensive, but less than voretigene neparvovec costing £613,410/patient (simple discount PAS available). Assuming LN costs £300,000/patient and all patients within 1 year of onset of vision loss are treated (~30/year), the additional annual cost would be £16,000 per 100,000 people.
Financial risk	High.
Commissioner	NHSE/I
Efficacy	Primary outcome of improvement in ETDRS visual acuity in the treated eye vs. placebo eye was not met in two PIII trials in patients with onset of vision loss ≤1 year, attributed to an unexpected improvement in placebo-treated eyes. In RESCUE (n=39), at week 72, treated eyes improved by -0.413 LogMAR (+21 ETDRS letters) from nadir vs. week 48 improvement of -0.257 LogMAR (+13 ETDRS letters); p=0.89. In REVERSE (n=37) at week 48, change was -0.219 and -0.211 LogMAR in treated and untreated eyes, respectively (p=0.88). Data from the PIII REFLECT trial (n=90) using bilateral injection of LN, are due 2024.
Safety	Most common ocular adverse effects are related to injection procedure, except for intraocular inflammation with increased intraocular pressure in some patients. A follow-up study is ongoing.
Appraisals	NICE due TBC.


Prescribing Outlook 2020 Spreadsheet - Microsoft Excel
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A1 BNF
BNF | New medicine | Trade Name | Company | Pharmacology | Indication | Current status | Anticipated UK launch | Population | Sector
1 | Darvadstrocel injection | Alofisel | Takeda | ATMP; A somatic cell therapy. Expanded allogeneic stem cells taken from adipose (fat) tissue of donors, given as a single dose by intra-lesional injection in up to three fistula tracts that open to the perianal area, in a surgical environment under anaesthesia (general or regional). The cells exhibit immunomodulatory and anti-inflammatory effects at inflammation sites. Requires additional surgery 2-3 weeks before injection to prepare and assess fistulas. This is an 'off-the-shelf' ATMP; see pharmacy guidance. | Complex perianal fistulas in adults with non-active/mildly active luminal Crohn's disease, when fistulas have shown inadequate response to at least one conventional or biologic therapy. | Approved in EU March 2018, with orphan drug status – see EPAR and prescribing data_ | 2022 | | Seconda severe in failure se
2 | Emiplacel injection | | Pluristem Therapeutics | ATMP: Allogeneic ex-vivo expanded placental mesenchymal-like adherent stromal cells that stimulate the body's own ability to heal damaged tissues by responding to chemical signals from tissues. Given as two i.m doses (each comprising 30 injections), two months apart. This is an 'off-the-shelf' tissue-engineered ATMP, needing no tissue or genetic matching. | Critical limb ischaemia in adults with minor tissue loss unsuitable for revascularisation. | PIII, on EMA adaptive pathway to support application for conditional approval. | 2022 | | Seconda adult spe vascular (arterial/t
2 | Etranacogene dezaparvovec injection | | uniQure | ATMP; An *in vivo* gene therapy that uses adeno-associated virus 5 (AAV5) vector to deliver the highly functional Padua variant of the FIX gene to liver cells, where it stimulates production of FIX that is 8 times more active than normal. Given as a single i.v. infusion. See pharmacy guidance. | Severe to moderately severe haemophilia B in adult men with FIX level ≤2% (or 2 IU/dL). | PIII, with orphan drug and PRIME status in EU and breakthrough therapy status in US. | 2022 | | Seconda specialis haemoph (compret care cent
2 | Fidanacogene elaparvovec injection | | Pfizer | ATMP: An *in vivo* gene therapy that uses adeno-associated virus 8 (AAV8) vector to deliver the highly functional Padua variant of the FIX gene to liver cells, where it stimulates production of FIX that is 8 times more active than normal. Given as a single i.v. infusion. See pharmacy guidance. | Severe to moderately severe haemophilia B in adult men with FIX level ≤2% (or 2 IU/dL). | PIII, with orphan drug and PRIME status in EU, and breakthrough therapy and orphan drug status in US. | 2022 | | Seconda specialis haemoph (compret care cent
Guidance notes | Pipeline new medicines | Pipeline cancer therapies | ATMPs | Patent expiries | Key | Acknow
Ready
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Efficacy | Safety | Appraisals
A PIII study (n=9), shows 6 of 7 men had normal levels of FVIII over 20-24 weeks; one had levels suggesting mild haemophilia. A 3-year update (n=15) showed median annualised bleeding rate (ABR) of 0 vs. 16.5 in the year before. In 6, median FVIII use fell from 138.5 to 0 infusions/year; bleeding in all major joints with ≥3 bleeding events within 6 months resolved (≤2 events/ year). 4-year data show median ABR remains 0. Early data from the PIII GENEr8-1 study (n=134) show FVIII levels ≥40 IU/dL at 23-26 weeks in 8 of 20 patients. At week 26 (n=16), median ABR was 0; median annualised FVIII use fell by 84%. | Adverse events included liver function test abnormalities, nausea, fatigue and infusion reactions. | NICE (proposed appraisal) due TBC, NIHR April 2020.
6 | 2022 | | Secondary care, highly specialist immunology centres. | | | | NHSE/I | | | None.
7 | 2021/2022 | There are ~12,000 new NHL cases in England every year, 18% have FL and | Secondary care, selected JACIE-accredited haematology and | Third-line treatment options are limited, with choice depending on efficacy of previous regimens. Salvage chemotherapy | *Yescarta* is already recommended by NICE for use within the Cancer Drugs Fund as an option for treating r/r | High. | NHSE/I | Single-arm PII ZUMA-5 study (n=160) is assessing objective response in adults whose disease has progressed after ≥2 lines of treatment | See medicines.org.uk. | NICE due TBC, NIHR August 2019.
Sticky Notes

Specialist Pharmacy Service

NHS

Thank you for listening

Any questions?

Q&A

Please add any question you have into the Q&A box

Please fill in feedback survey, your input is really valuable to us

Upcoming webinars,

Patient and public perspectives on advanced therapies

12pm, 24th March, Dr Lee Aiyegbusi, CPROR Deputy Director, University of Birmingham