

Therapeutic Advances in Neurology

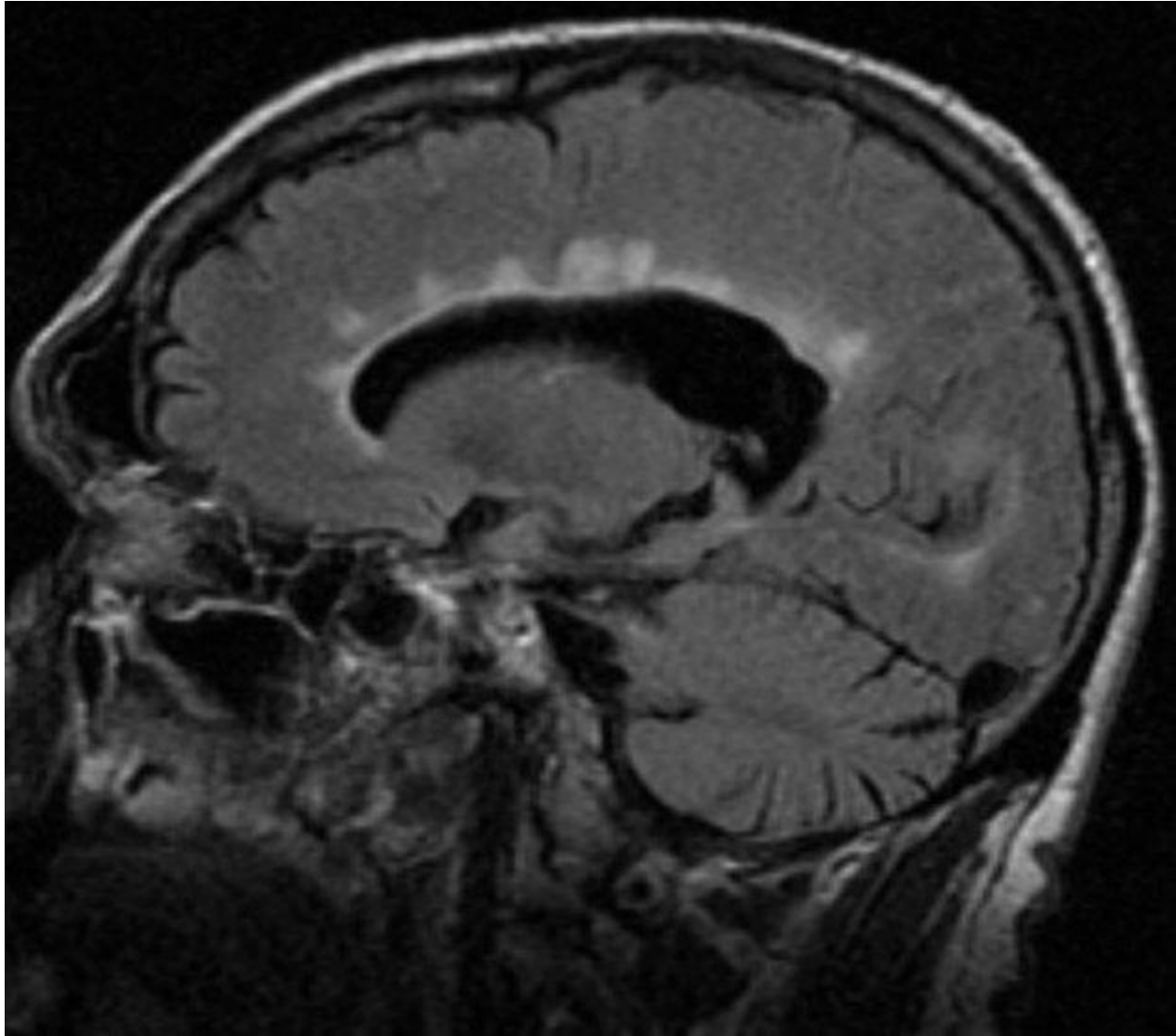
Peter Fernandes

Consultant Neurologist UHS

Disclosures

No commercial disclosures

Disclosures



NEUROLOGY: The armchair intellectual



...For you see, with the onset of dysarthria, an ipsilateral Horner's syndrome, and diminished sensation to the contralateral body, we can isolate this stroke to the posterior circulation, specifically a lateral medullary infarct.

What can you do about it now?

Nothing. Still, fascinating, isn't it?



Royal College
of Physicians

6 CPD
credits

Update in medicine

20 June 2023 | Bournemouth

CPD code: TBC

08.00 Registration and refreshments

09.10 **Welcome and introduction**
Dr Chris Roseveare, RCP regional adviser – Wessex

Session 1 – Acute neurology
Chair – Dr Chris Roseveare

09.15 **Latest therapeutic advances in neurology**
Dr Peter Fernandez, consultant neurologist,
University Hospitals Southampton NHS Trust

09.20 **Managing seizures in the patient with 'known' epilepsy**
Dr Lucy Kinton, consultant neurologist and regional specialty advisor,
University Hospitals Southampton NHS Trust

Program



Prednisolone
Tablets

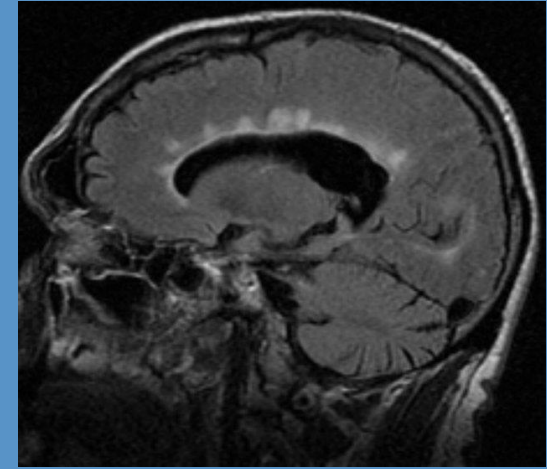
5mg

For oral use

28 tablets

WOCKHARDT





What's new in neurology?



CGRP FORUM
EDUCATION AND RESEARCH

Educational Partners and Supporters (others pending)

AMGEN **biohaven** *Lilly* **NOVARTIS**
pharmaceuticals



Lecanemab for Alzheimer's Disease

Business | Prognosis

Biogen Rally Adds \$11 Billion in Value on Alzheimer's Win

- The drug lecanemab was shown to slow the disease's progression
- Shares soared 40% in the biggest gain since November 2020

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Alzheimer's drug lecanemab hailed as momentous breakthrough

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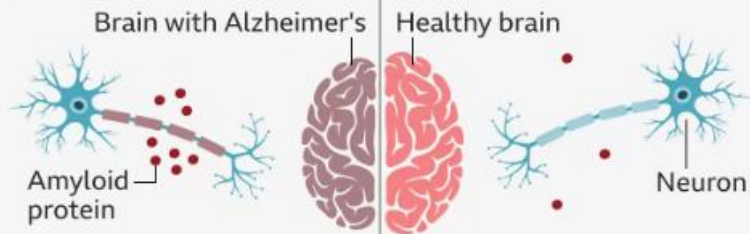


GETTY IMAGES

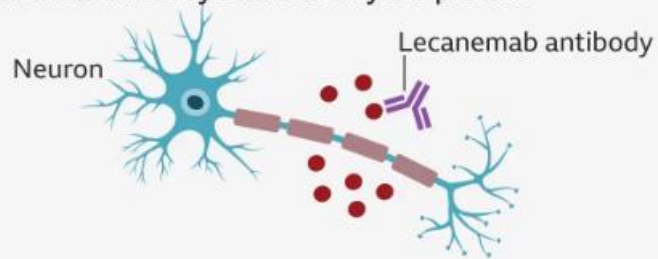
1 Year Biogen Chart



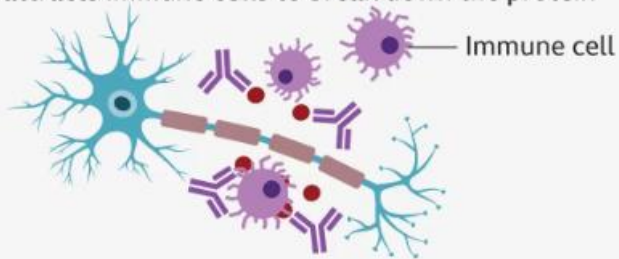
① Amyloid protein collects around brain neurons in Alzheimer's



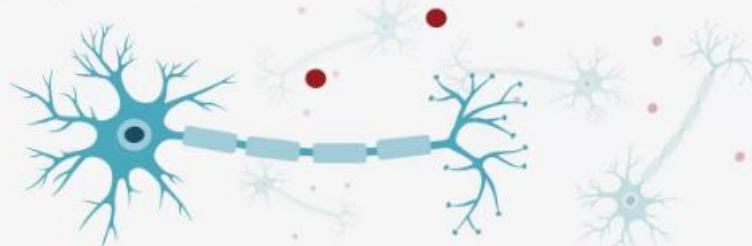
② Lecanemab antibody sticks to amyloid protein



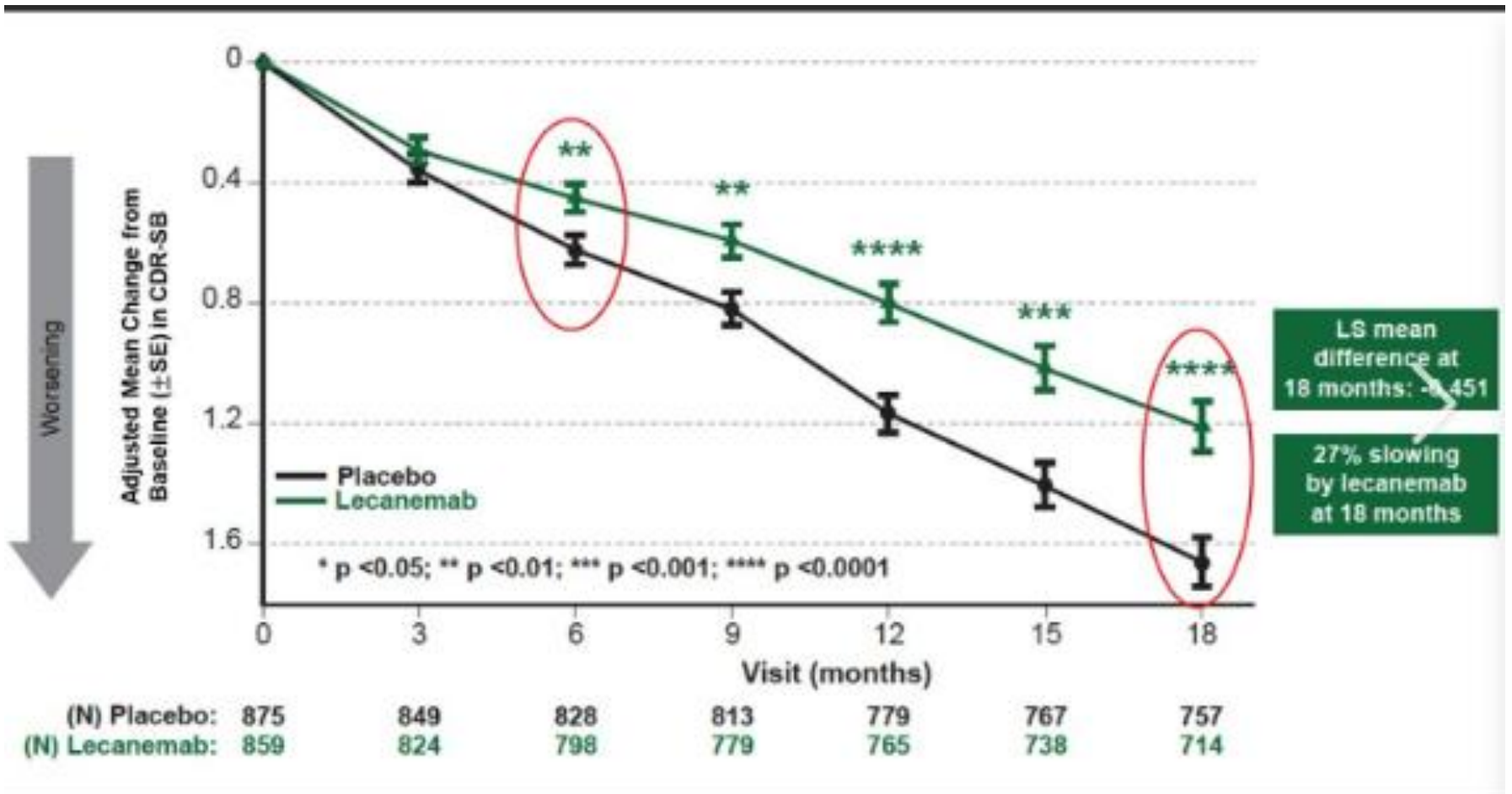
③ Antibody attracts immune cells to break down the protein



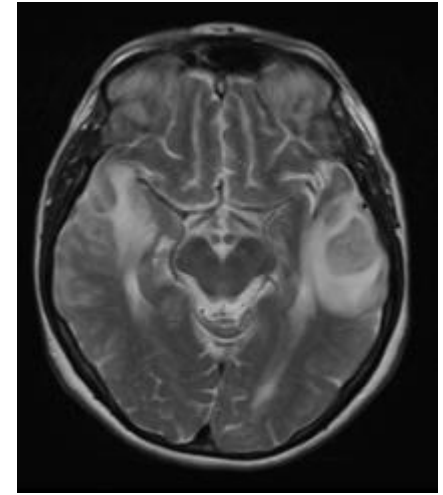
④ Less protein around the neuron



CLARITY-AD (NEJM 2022)



However ...



- Concerns over risk of side effects
 - Infusion reactions (26% vs. 7%)
 - ARIA-E (13% vs. 2%; symptomatic 3% vs. 0%)
- 0.45 points on CDR-SB scale is not very much
 - Only 1-1.5 points is clinically noticeable
 - Everyone still got worse
- Can we afford this/is it worth it?
 - PET scanning/CSF testing necessary beforehand
 - 2-weekly infusions
 - Regular MRI scanning (3x in first year, more often if ARIA)
 - \$26,500/year for (potentially) 900,000 patients in UK with AD



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Dementia: Lifestyle changes that could lower your risk

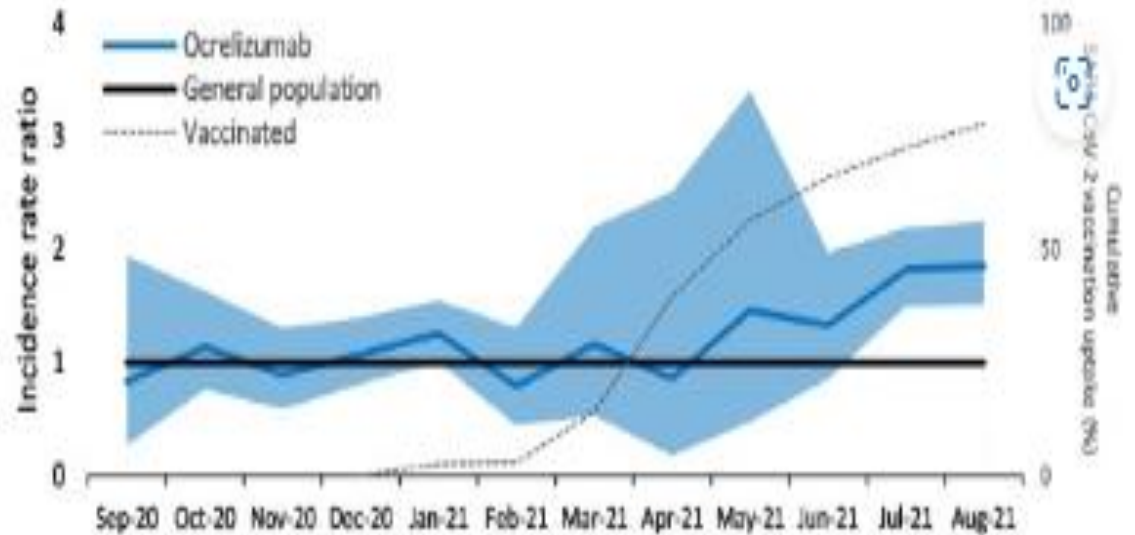
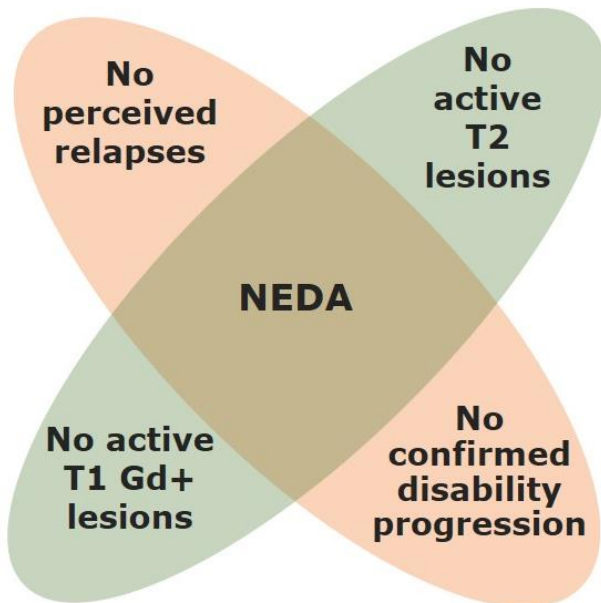
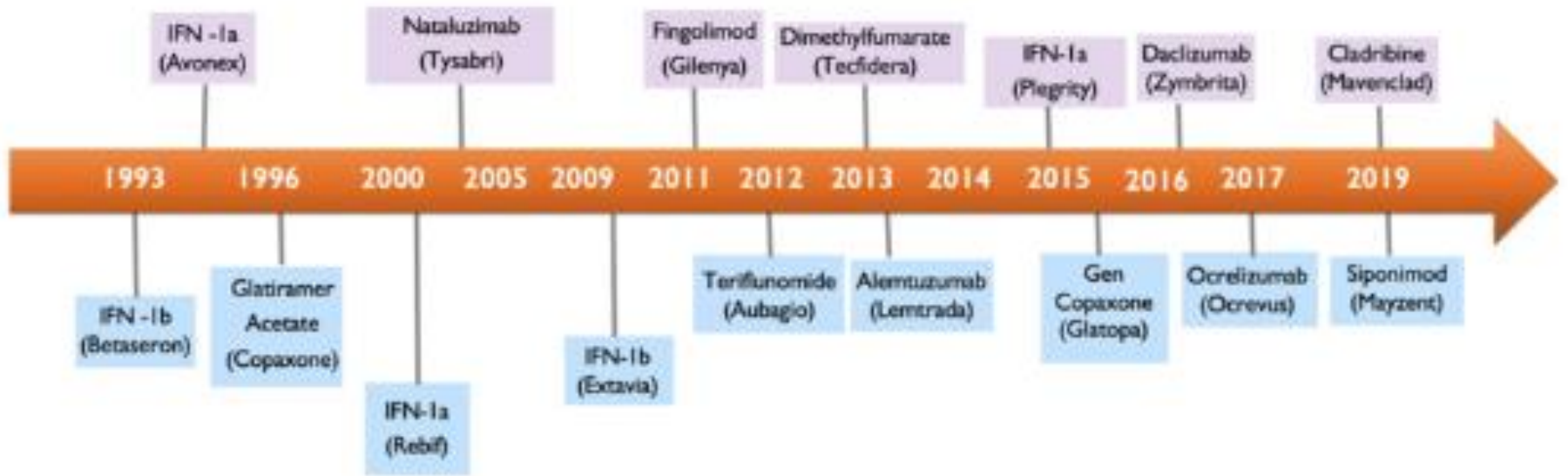
The study followed 196,383 people from the age of 64 for about eight years.

It analysed people's DNA to assess their genetic risk of developing the disease.

The study showed there were 18 cases of dementia per 1,000 people if they were born with high risk genes and then led an unhealthy lifestyle.

But that went down to 11 per 1,000 people during the study if those high-risk people had a healthy lifestyle.

Disease Modifying Treatments for Multiple Sclerosis



Spinal Muscular Atrophy (SMA)

SMA (SMN1 mutation)

- Most common genetic cause of infant mortality
- Incidence of 1:10,000 births (100 cases each year)
- Majority are type I (6/100,000) or type 2 (3/100,000)

Table 1. Clinical and molecular features of SMA sub-types

	Type of SMA				
	0	I	II	III	IV
SMN2 copy number*	1	2	3	3-5	3-5
Age of onset	<i>In utero</i>	Majority by 6 months	6-12 months	After 18 months (IIIa: <3 years, IIIb: >3 years)	Adulthood
Key clinical features	Widespread motor and sensory neuronal loss Contractures High incidence of congenital cardiac defects	Neonatal hypotonia Poor feeding and head control Respiratory insufficiency Never develop ability to roll or sit unaided	Sit unsupported Never walk Respiratory muscle weakness	Walk unaided, even if briefly	Progressive proximal weakness Lower limb predominance
Natural history	Peri-natal death	50% death by 12 months 90% death by 24 months without invasive ventilation	Life expectancy 30-50 years depending on respiratory function	Loss of ambulation very variable (from childhood to late life) Respiratory involvement uncommon Life expectancy near normal	Slow progression Ambulation maintained Normal lifespan

Treatments

- Spinraza
 - Intrathecal ASO that increases protein levels by upregulating alternative splicing of sister gene
 - £450,000/year
- Zolgensma
 - Gene therapy (viral vector)
 - £1.8m (once-only)
- Risdiplam
 - Oral small molecule that binds to RNA splice site of sister gene
 - £130,000/year

SPRINT study (pre-symptomatic gene therapy)

1

2

Majority by 6 months

Neonatal hypotonia

Poor feeding and head control

Respiratory insufficiency

Never develop ability to roll or sit unaided

50% death by 12 months

90% death by 24 months

without invasive ventilation

100%

(14/14) of patients with 2 copies of *SMN2* could sit independently (30 seconds or more) as measured by Bayley-III

71%

(10/14) of patients stood without assistance (10 seconds or more) as measured by WHO-MGRS

- 5/10 patients achieved this milestone within an age-appropriate time

71%

(10/14) of patients walked without assistance (5 steps or more) as measured by WHO-MGRS

- 6/9 patients achieved this milestone within an age-appropriate time

Migraine

Re-purposed migraine treatments

Acute

Triptans

NSAIDs

Anti-emetics

(metoclopramide/domperidone)

Opiates

Prophylactic

Amitriptyline/Nortriptyline

Propranolol/Metoprolol

Topiramate

Venlafaxine

Duloxetine

Riboflavin

Magnesium

Aspirin

Pizotifen

Verapamil

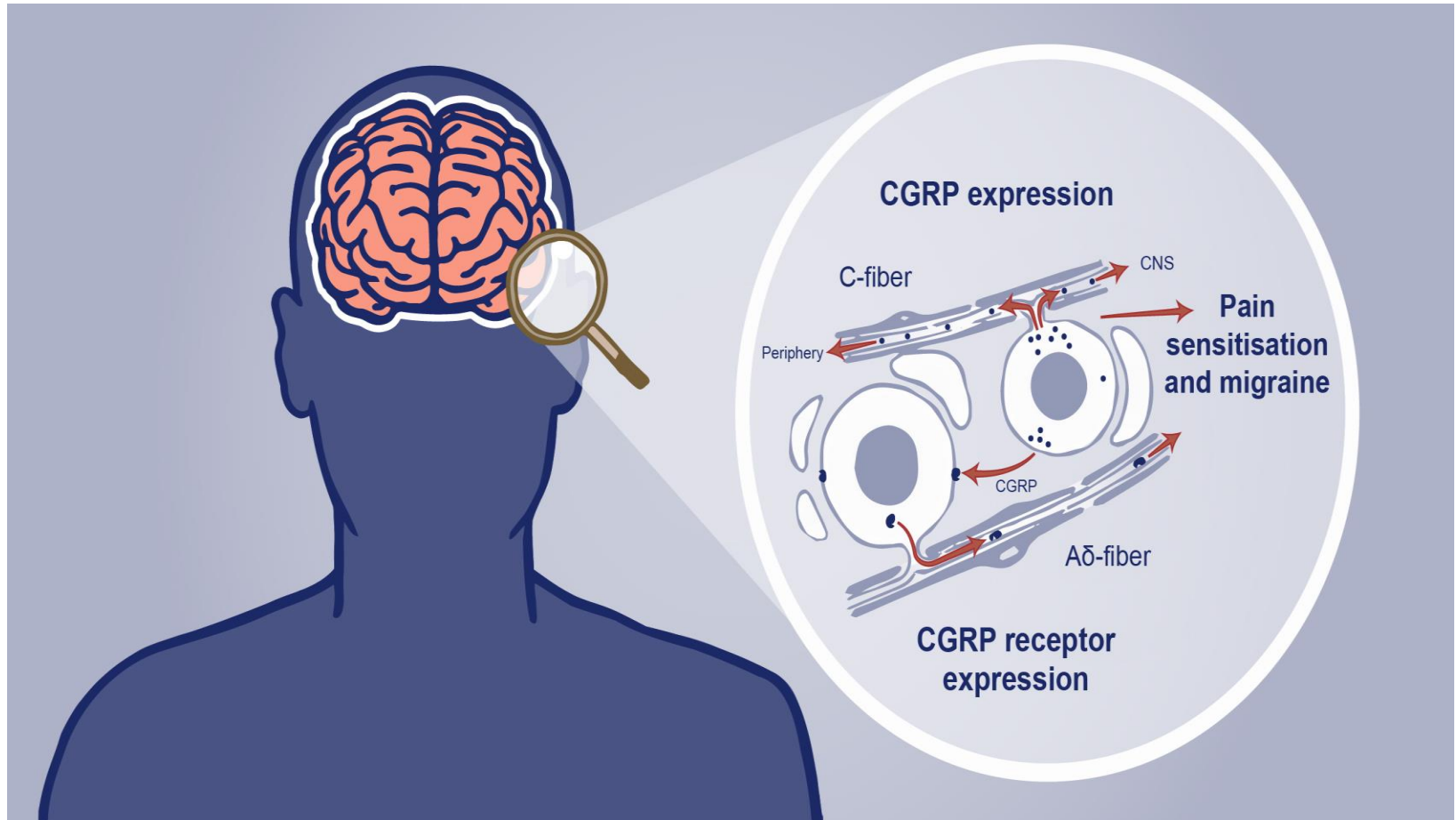
Valproate

Gabapentin

Botox (chronic migraine)

(“Learning to cope” therapy)

CGRP

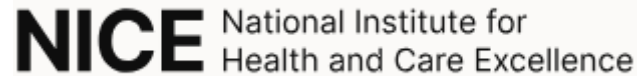


- Nerves/blood vessels release CGRP during a migraine; reducing CGRP seems to be helpful

Anti-CGRP monoclonal antibodies

- Erenumab (fremanezumab, galcanezumab, eptinezumab)
 - Once monthly SC injection
- Injectable preventative treatment
- Effectiveness
 - -3.7days/month (vs. -1.8 days/month for placebo) so reduces by 1.9 days/month
 - 30% had a 50% reduction in headache days per month (vs. 17% in placebo)
- Side effects:
 - Hypertension (including hypertensive crisis)
 - Angioedema & anaphylaxis
 - Rash

Erenumab



- Approved if:
 - At least 4 migraine days per month
 - Failed at least 3 preventative treatments
 - Promise to stop if not working
- £5000/year
 - = £100 per migraine day avoided (more in responders)
 - 8% of men and 18% of women have had a migraine in the last year
 - 8% have chronic migraine (5m in the UK)

CGRP receptor antagonists (“gepants”)

- Rimegepant (atogepant)
 - Oral preventative AND acute treatment (but only licensed for preventative)
- Effectiveness
 - -4.3 days/month (vs. -3.5 days for placebo) so reduces by 0.8 days/month
 - 49% had a 50% reduction in headache days per month (vs. 41% for placebo)
- Side effects:
 - Rash
 - Mild abdominal symptoms (pain, dyspepsia, nausea)

Rimegepant

NICE National Institute for
Health and Care Excellence

- Approved if:
 - At least 4 migraine days per month (but less than 15)
 - Failed at least 3 preventative treatments
 - Stop if not working
 - Only for prevention (not acute)
- £2400/year
 - = £160 per migraine day avoided (more in responders)

Questions?

