신경근육질환의 최신지견

신 하 영
연세의대 신경과학교실

Neuromuscular disease

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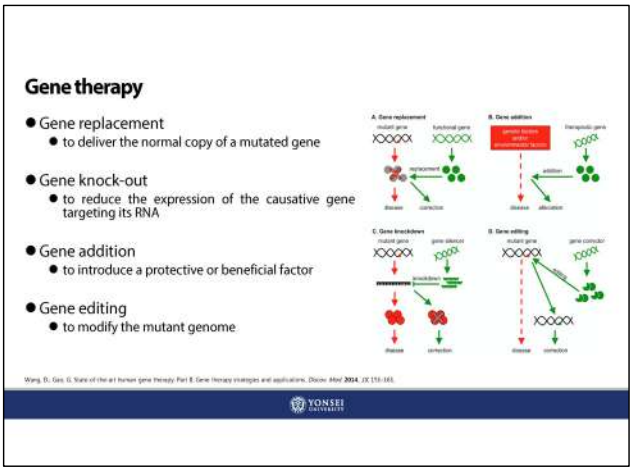
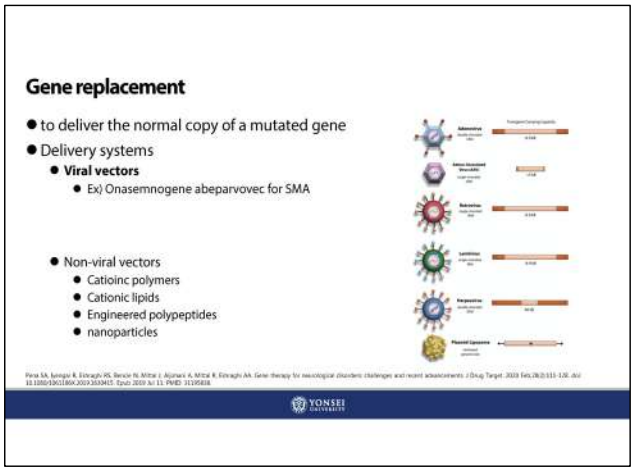
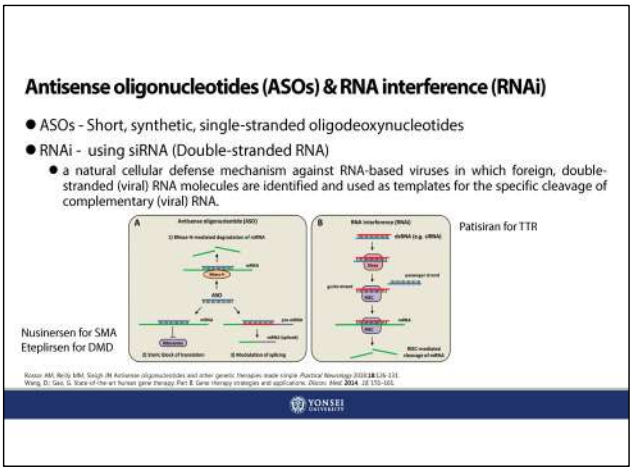
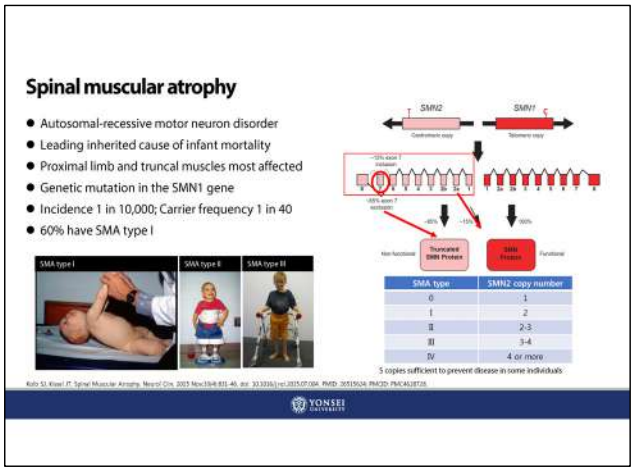
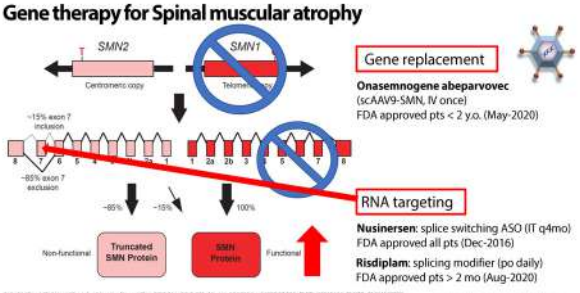








Gene therapy for Spinal muscular atrophy



Gene replacement

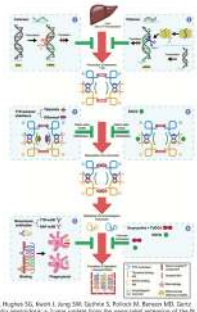
Onasemnogene abeparvovec
(scAAV9-SMN, IV once)
FDA approved pts < 2 y.o. (May-2020)

RNA targeting

Nusinersen: splice switching ASO (IT q4mo)
FDA approved all pts (Dec-2016)

Risdiplam: splicing modifier (po daily)
FDA approved pts > 2 mo (Aug-2020)

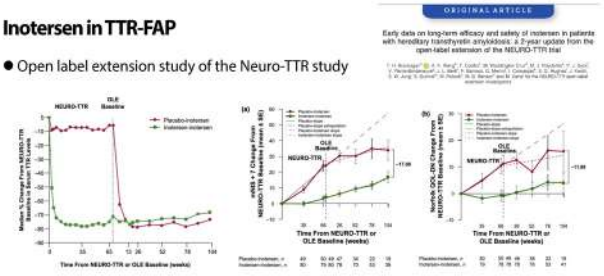
TTR-FAP



- Transthyretin – transportation of thyroxine & retinol-binding protein
  - Produced by **liver (90%)**, choroid plexus, retina.
- Transthyretin familial amyloidosis polyneuropathy
  - AD inherited disorder involving multiple organs
  - TTR mutations → misfolding and deposition of amyloid
  - Frequent cardiac and eye involvement
- Therapy
  - **Inotersen** – antisense oligonucleotide, inhibits hepatic production of TTR
  - **Patisiran** – RNA interference therapeutic agent, inhibits hepatic synthesis of TTR
  - **Tafamidis** & **Diflunisal** - The TTR tetramer stabilizers

Inotersen in TTR-FAP

- Open label extension study of the Neuro-TTR study



ORIGINAL ARTICLE

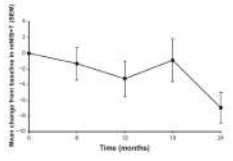
Early data on long-term efficacy and safety of inotersen in patients with hereditary transthyretin amyloidosis: a 2-year update from the open-label extension of the NEURO-TTR trial

Patisiran in TTR-FAP

- 24 month Phase II Open label extension study
  (Apollo Phase III went out 18 mos)
  27 pts entered the study
  - 26/27 pts reported AEs (96%)
    majority mild-to-moderate
    - M/C: Mild flushing and infusion related reactions
  - At 24 mos, mean mNIS+7 decrease from baseline was 6.95 points.
  - Other clinical parameters demonstrated stability over 24 mos

RESEARCH Open Access

A phase II, open-label, extension study of long-term patisiran treatment in patients with hereditary transthyretin-mediated (hATTR) amyloidosis



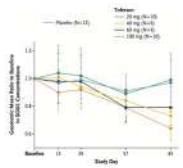
SOD1 ALS

- SOD1 mutation: up to 2% of all cases of ASL
  - a toxic gain of function has been considered to be the most likely mechanism in ALS caused by SOD1 mutations.
- Phase 1-2 trial of ASO Tofersen for SOD1 ALS

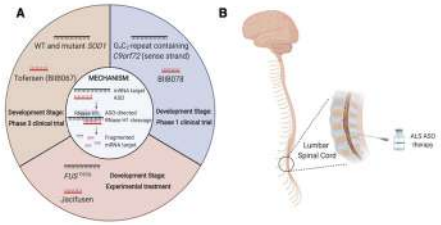
The NEW ENGLAND JOURNAL of MEDICINE

Phase 1–2 Trial of Antisense Oligonucleotide Tofersen for SOD1 ALS

- N=50
- Tofersen
  - ASO: RNase H–dependent degradation of SOD1 mRNA
  - intrathecal injection for 12 weeks (5 doses)

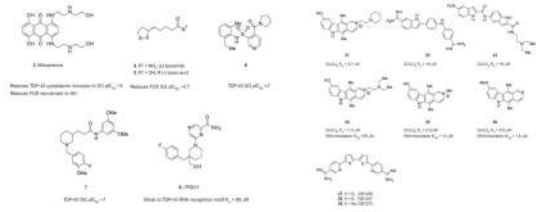


ASOs Targeting mutant ALS genes

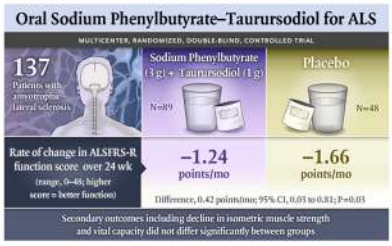


Emerging small-molecule therapeutic approaches for ALS

- TDP-43
- C9orf72



Trial of Sodium Phenylbutyrate-Taurursodiol for ALS



Participants
Definite ALS
Within 18 mos after Sx onset
sVC > 60% of predicted value

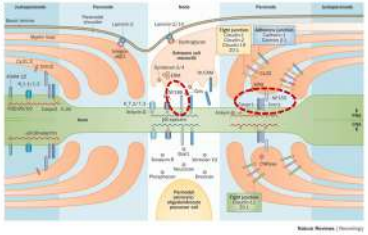
Sodium phenylbutyrate : mitigating endoplasmic reticulum stress

Taurursodiol: mitigating mitochondrial dysfunction

Both reduce neuronal death in experimental models.

CIDP – Nodopathies and Paranodopathies

- <10% of CIDP patients harbor auto-abs directed toward the paranodal & nodal complex.
  - Paranodal complex
    - Neurofascin-155
    - Contactin-1
    - Contactin-associated protein 1
  - Nodal complex
    - Neurofascin-140/186
- IgG4 is the predominant isotype
- **'Nodo-paranodopaties'**



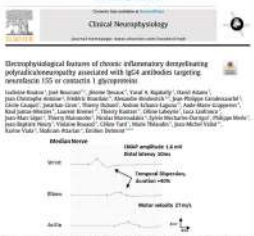
CIDP – Nodopathies and Paranodopathies

Antibody Target	Clinical Features	Percentage of Chronic Inflammatory Demyelinating Polyradiculoneuropathy Cases*	Target	Treatment Response
Neurofascin 155 (NF155)	Subacute onset, symmetric motor more than sensory, sensory ataxia, tremor (also of head/voice), distal-predominant, cranial neuropathies reported	5–10%	Paranodal transmembrane cell adhesion molecule located on Schwann cell membrane	Good response to rituximab and plasma exchange; partial response to corticosteroids; IV immunoglobulin (IVIg) refractory
Neurofascin 140 (NFH40)/ neurofascin 186 (NF186)	Subacute onset, symmetric sensory and motor, sensory ataxia, cranial neuropathies, nephrotic syndrome reported	2%	Axonal membrane protein involved in clustering of sodium channels located at the nodes of Ranvier; interacts with gliomedin and neuronal cell molecules	Good response to rituximab; partial response to IVIg and corticosteroids
Contactin-1 (CNTN1)	Subacute onset, symmetric motor more than sensory, sensory ataxia, nephrotic syndrome reported	5%	Paranodal, axonal cell adhesion molecule	Good response to rituximab; partial response to corticosteroids; IVIg refractory
Contactin-associated protein 1 (CASPR1)	Subacute onset, symmetric distal predominant, severe neuropathic pain	<1%	Paranodal, axonal cell adhesion molecule	Good response to rituximab; IVIg refractory

Antibodies to neurofascin, contactin-1, and contactin-associated protein 1 in CIDP

- 342 sera from CIDP patients tested
- 19 pts (5.5%) had antibodies against NF155 (n=9), CNTN1 (n=3), Caspr1 (n=6), NF140/186 (n=1).
- Predominant Ab isotypes were IgG4 (n=13)
- Non IgG4 isotype (n=6: NF155=3; Caspr1=3)
  - These patients had no distinct clinical features or response to treatments compared with seronegative patients.
- **IgG4** seropositive vs. 64 seronegative CIDP patients
  - Subacute onset in 69% seropositive and 28% seronegative.
  - Tremor (69% vs. 12%), sensory ataxia (85% vs. 35%): more common in seropositive.
  - Seropositive patients had lower response to IVIg compared to seronegative pts.

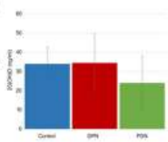
Electrophysiologic features of CIDP with IgG4 abs against NF155 or CNTN1



- EDx data from 13 NF155 and 9 CNTN1 +ve pts.
- All NF15 and CNTN1 pts fulfilled EFNS/PNS EDx criteria for definite CIDP.
- CNTN1 and NF155 EDx profiles were similar and both had more pronounced electrophysiologic changes than seronegative pts.
- Median nerve motor CV <24 m/s, or ulnar motor CV <26 m/s or ulnar motor distal latency >7.4 ms were predictive of positive antibodies with a sensitivity 59% and specificity 93%

Vitamin D in Painful Diabetic Neuropathy

- Study of 43 patients with T1DM
  - 20 painless neuropathy (DPN)
  - 23 painful neuropathy (PDN)
  - 14 non-diabetic controls
- No significant differences for DPN and PDN regarding labs, neurological deficits, EDx, IENFD, and CCM.
- Serum 25(OH)D levels were lower in PDN compared to DPN (p=0.03)
- The odds ratio for painful diabetic neuropathy for vitamin D deficiency <20 ng/mL was 9.8 (p=0.003).



Alam U, Petropoulos IN, Ponirakis G, Ferdousi M, Asghar O, Jeziorska M, Marshall A, Boulton AJM, Efron N, Malik RA. Vitamin D deficiency is associated with painful diabetic neuropathy. Diabetes Metab Res Rev. 2020 Jun 7:e3361. doi: 10.1002/dmrr.3361. Epub ahead of print. PMID: 32506740.

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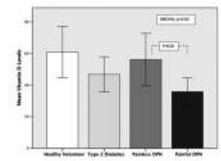
Vitamin D in Painful Diabetic Neuropathy

- Study of 45 patients with T2DM
  - 14 painless neuropathy (DPN)
  - 17 painful neuropathy (PDN)
  - 14 T2DM without neuropathy
  - 14 healthy controls



- A systematic review and a meta-analysis
  - 13 studies, 2814 T2DM patients
  - Serum 25(OH)D in T2DM with neuropathy group was lower than T2DM without neuropathy group (p<0.00001)
  - Serum 25(OH)D deficiency was a risk factor for neuropathy in T2DM patients (RR=1.07)
  - The concentration of 25(OH)D was positively related to risk of T2DM with neuropathy

Shillo P, Selvarajah D, Greig M, Gandhi R, Rao G, Wilkinson ID, Anand P, Tesfaye S. Reduced vitamin D levels in painful diabetic peripheral neuropathy. Diabet Med. 2019 Jan;36(1):44-51. doi: 10.1111/dme.13798. Epub 2018 Sep 20. PMID: 30102801.
Zhang B, Zhao W, Tu J, Wang X, Hao Y, Wang H, Zhao Y, Mizuno K, Tseng Y, Bu H. The relationship between serum 25-hydroxyvitamin D concentration and type 2 diabetic peripheral neuropathy: A systematic review and a meta-analysis. Medicine (Baltimore). 2019 Nov;98(48):e18118. doi: 10.1097/MD.0000000000018118. PMID: 31770219; PMCID: [illegible].

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Vitamin D in Painful Diabetic Neuropathy

- Does vitamin D supplementations improve peripheral diabetic neuropathy?
  - 60 T2DM with painful diabetic neuropathy
  - Weekly 50000 IU of vitamin D3 for 12 weeks orally,

Table 3
The before and after intervention laboratory and clinical findings.

Variables	Before Trial Mean (±SD)	After Trial Mean (±SD)	P-value
Fasting plasma glucose (mg/dL)	164.65 (±55.43)	159.70 (±53.93)	0.522
HbA1c (%)	8.13 (±1.60)	7.69 (±1.31)	0.021
25 (OH) vitamin D3	26.00 (±17.26)	55.52 (±31.94)	0.001
Calcium (mg/dL)	8.95 ± 0.86	9.73 ± 0.52	0.14
MNSI: Questionnaire (Score)	6.05 (±1.45)	4.63 (±2.10)	0.001
MNSI: Physical Examination (Score)	4.87 (±1.29)	3.88 (±1.45)	0.001

Ghadiri-Anari A, Mozafari Z, Gholami S, Khodaei SA, Aboutorabi-Zarchi M, Sepehri F, Nadjarzade A, Rahmanian M, Namiranian N. Dose vitamin D supplementations improve peripheral diabetic neuropathy? A before-after clinical trial. Diabetes Metab Syndr. 2019 Jan-Feb;13(1):890-893. doi: 10.1016/j.dsx.2018.12.014. Epub 2018 Dec 20. PMID: 30641826.

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Developments in therapeutics

- Complement inhibitor
  - Eculizumab (q2w)
  - Ravulizumab (q8w, on phase III clinical trial for MG)
  - Zilucoplan
    - a small (3.5 kDa), 15-amino acid macrocyclic peptide
    - binds to C5 with high affinity and specificity.
    - prevents the cleavage of C5 into complement components C5a and C5b.

Howard JF, Nowak RJ, Wolfe GI, et al. Clinical Effects of the Self-administered Subcutaneous Complement Inhibitor Zilucoplan in Patients With Moderate to Severe Generalized Myasthenia Gravis: Results of a Phase 2 Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial. JAMA Neurol. 2020;77(5):582-592. doi:10.1001/jamaneurol.2019.5125
Vincent, A. Unravelling the pathogenesis of myasthenia gravis. Nat Rev Immunol 2, 797–804 (2002). https://doi.org/10.1038/nri916
Conti-Fine BM, Milani M, Kaminski HJ. Myasthenia gravis: past, present, and future. J Clin Invest. 2006;116(11):2843–2854. doi:10.1172/JCI29894

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Developments in therapeutics

- Zilucoplan Phase II study
  - Randomized, double-blind, placebo-controlled, multicenter
  - Key eligibility: adult AChR Ab positive generalized MG (MGFA II-IVa), QMG score 12 or more
  - a daily SC self-injection of placebo, 0.1-mg/kg zilucoplan, or 0.3-mg/kg zilucoplan for 12 wks

Howard JF, Nowak RJ, Wolfe GI, et al. Clinical Effects of the Self-administered Subcutaneous Complement Inhibitor Zilucoplan in Patients With Moderate to Severe Generalized Myasthenia Gravis: Results of a Phase 2 Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial. JAMA Neurol. 2020;77(5):582-592. doi:10.1001/jamaneurol.2019.5125

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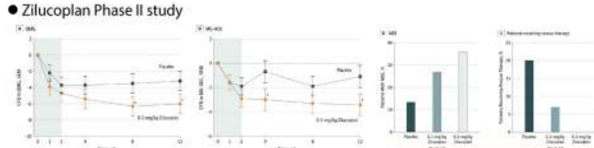
Developments in therapeutics

- Zilucoplan Phase II study



Safety
- No treatment related SAEs
- 8 serious AEs – none considered related to the study drug
- Two pts discontinued before week 12
  - One placebo treated due to worsening MG
  - One with zilucoplan (0.3 mg/kg) due to prolonged hospital admission for diverticulitis exacerbation
- No meningitis

Minimal symptom expression (MSE), defined as Myasthenia Gravis Activities of Daily Living score of 0 or 1 at 12 weeks.

Howard JF, Nowak RJ, Wolfe GI, et al. Clinical Effects of the Self-administered Subcutaneous Complement Inhibitor Zilucoplan in Patients With Moderate to Severe Generalized Myasthenia Gravis: Results of a Phase 2 Randomized, Double-Blind, Placebo-Controlled, Multicenter Clinical Trial. JAMA Neurol. 2020;77(5):582-592. doi:10.1001/jamaneurol.2019.5125

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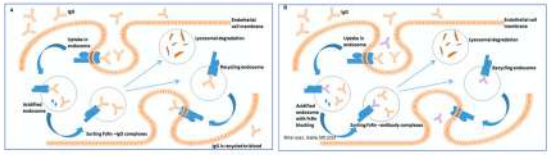
Developments in therapeutics

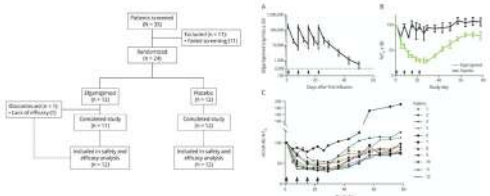
- Antagonism of the neonatal Fc receptor (FcRn)



Gable KL, Guptill JT. Antagonism of the Neonatal Fc Receptor as an Emerging Treatment for Myasthenia Gravis. Front Immunol. 2019 Jan 30;10:3052. doi: 10.3389/fimmu.2019.03052. PMID: 31998310; PMCID: PMC6965431.

Developments in therapeutics

- Efgartigimod, randomized phase II study in generalized MG
  - an IgG1 Fc portion mutated to increase FcRn affinity at physiologic and acidic pH
  - Key eligibility: adult AChR Ab positive gMG (MGFA II – IVa), MG-ADL score 5 or more



Howard JF Jr, Bril V, Burns TM, Mantegazza R, et al. Randomized phase 2 study of FcRn antagonist efgartigimod in generalized myasthenia gravis. Neurology. 2019 Jun 4;92(23):e2661-e2673.

Developments in therapeutics

- Efgartigimod, randomized phase II study in generalized MG

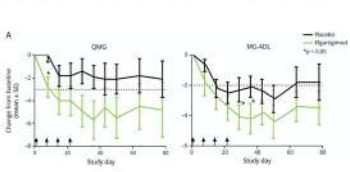


Table 2 Treatment-emergent safety outcomes in all treated patients (overall reported in ≥2 patients)

TEAE/patient count	Placebo (N = 13)	Efgartigimod (N = 12)	Total (N = 25)
TEAEs (total)	13 (65.0)	12 (60.0)	25 (62.5)
Headache	3 (15.0)	4 (33.3)	7 (25.0)
Nausea	1 (5.0)	1 (8.3)	2 (8.0)
Diarrhea	1 (5.0)	1 (8.3)	2 (8.0)
Abdominal pain upper	1 (5.0)	1 (8.3)	2 (8.0)
Arthralgia	2 (15.4)	0 (0.0)	2 (8.0)
Small lymphocyte count decrease	0 (0.0)	2 (16.7)	2 (8.0)
B-lymphocyte decrease	0 (0.0)	2 (16.7)	2 (8.0)
Monocyte count decrease	0 (0.0)	2 (16.7)	2 (8.0)
Neutrophil count increase	0 (0.0)	2 (16.7)	2 (8.0)
Hyalgia	0 (0.0)	2 (16.7)	2 (8.0)
Pruritus	2 (15.4)	1 (8.3)	3 (12.0)
Rhinorrhea	1 (5.0)	1 (8.3)	2 (8.0)
Tooth abscess	2 (15.4)	0 (0.0)	2 (8.0)
Toothache	2 (15.4)	0 (0.0)	2 (8.0)

Howard JF Jr, Bril V, Burns TM, Mantegazza R, et al. Randomized phase 2 study of FcRn antagonist efgartigimod in generalized myasthenia gravis. Neurology. 2019 Jun 4;92(23):e2661-e2673.

Developments in therapeutics

- Argenx announces positive topline results from phase III ADAPT trial of Efgartigimod in patients with generalized MG

Argenx press release and investor statement, Sep. 2020

Developments in therapeutics

- Antagonism of the neonatal Fc receptor (FcRn)

Therapeutic Name	Company	Molecule Summary	SAD/MAD Dosing*	Maximum % IgG lowering from baseline in phase 1
Efgartigimod (ARGX-113)	Argenx BVBA	Humanized IgG1 Fc fragment	**SAD** IV 0.2, 2, 10, 25, 50 mg/kg **MAD** **IV: 10, 25 mg/kg** every 4 or 7 days	70, 75 mg/kg IV, 79%
Nipocalimab (M281)	Momenta	Human deglycosylated IgG1 monoclonal Ab	**SAD** IV 0.3, 3, 10, 30, **60 mg/kg** **MAD** **IV: 15, 30 mg/kg** weekly[1]	55, 30 mg/kg IV, 66%
Rozanolixizumab (UCB7665)	UCB Biopharma	Humanized IgG4 monoclonal Ab	**SAD** SC 1, 4, 7 mg/kg **SC: 1, 4, 7 mg/kg** **MAD** NA, SAD only	4 mg/kg SC: 28% 7 mg/kg SC: 45%
RVT-1401 (HL 101)	Immunovant Sciences GmbH	Human IgG1 monoclonal Ab	**SAD** SC: 0.05, 1.0, 3 mg/kg, 340, 680, 700 mg IV: 1.5 mg/kg, 100 mg, 340, 765, 1,000 mg **MAD** **SC: 340, 680 mg** weekly	340 mg SC: 65% 680 mg SC: 79%

Gable KL, Guptill JT. Antagonism of the Neonatal Fc Receptor as an Emerging Treatment for Myasthenia Gravis. Front Immunol. 2019 Jan 30;10:3052. doi: 10.3389/fimmu.2019.03052. PMID: 31998310; PMCID: PMC6965431.

Classification of inflammatory myopathies

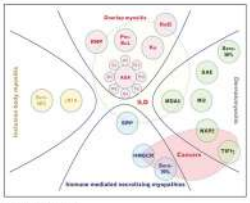
- The five most recognized types of inflammatory myopathies
  - Dermatomyositis
  - Immune-mediated necrotizing myopathy
  - Overlap myositis (including antisynthetase syndrome)
  - Sporadic inclusion-body myositis
  - Polymyositis.

Greenberg, S.A. Inclusion body myositis: clinical features and pathogenesis. Nat Rev Rheumatol 15, 257–272 (2019). https://doi.org/10.1038/s41584-019-0186-x

Selva-O'Callaghan A, Pinal-Fernandez I, Trallero-Araguás E, Milisenda JC, Grau-Junyent JM, Mammen AL. Classification and management of adult inflammatory myopathies. Lancet Neurol. 2018 Sep;17(9):816-828. doi: 10.1016/S1474-4422(18)30254-0. PMID: 30129477.

Autoantibodies of inflammatory myopathies

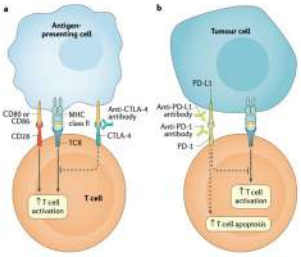
Myositis-Specific Antibody	Muscle	Skin	Lung	Cancer
Dermatomyositis				
Mi-2	X	X		
TIF-1γ	X	X		X
NXP-2	X	X		X
MDA-5		X	X	
Antisynthetase				
Jo-1	X		X	
PL-7	X		X	
PL-12			X	
Immune-mediated necrotizing myopathy				
Signal recognition particle (SRP)	X			
3-Hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase	X			
Antibody-negative immune-mediated necrotizing myopathy	X			X



Goyal NA. Immune-Mediated Myopathies. Continuum (Minneap Minn). 2019 Dec;25(6):1584–1585. doi: 10.1212/CON.0000000000000783. PMID: 31794460.
Benveniste O, Stenzel W, Allenbach Y. Advances in serological diagnostics of inflammatory myopathies. Curr Opin Neurol. 2016 Oct;29(5):642–53. doi: 10.1097/WCO.0000000000000376. PMID: 27538058.

Immune Checkpoint Inhibitor (ICI)

- ICIs – cancer immunotherapy agents effective against a wide range of cancers
- Targets
  - CTLA-4: ipilimumab
  - PD-1: nivolumab
  - PD-L1: pembrolizumab, cemiplimab, atezolizumab, durvalumab, avelumab
- CTLA-4, PD-1, & PD-L1 are involved in the regulation of T cell activation



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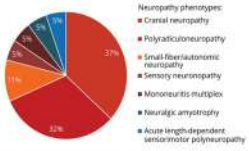
irAEs associated with ICIs

- Exposure may increase risk of immune-related adverse events (irAEs)
  - The result of immune response against self-antigens
- Neurological irAEs are reported in up to 3% of patients.
- Peripheral Neuropathies associated with ICIs
  - Cranial neuropathies including facial nerve palsy
  - Trigeminal neuralgia
  - Sensory neuronopathy
  - Sensory axonal polyneuropathy
  - Small fiber/autonomic neuropathy
  - Demyelinating neuropathies: GBS, CIDP
  - Neuralgis amyotrophy
  - ANCA vasculitis



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Dubey D, David WS, Amato AA, Reynolds KL, Cement NE, Chute DF, Cohen JV, Lawrence DP, Moinuddin MS, Sullivan RJ, Guidon AC. Varied phenotypes and management of immune checkpoint inhibitor-associated neuropathies. Neurology. 2019 Sep 10;93(11):e1083-e1103. doi: 10.1212/WNL.0000000000008091. Epub 2019 Aug 12. PMID: 31409698.

irAEs associated with ICIs

- irMyositis
  - The most commonly reported neurological irAEs associated with ICIs
  - More commonly occurs in elderly patients at a mean age of 70 years (Male > female)
  - Onset within the first 2 months after ICIs
  - Myalgia: neck, back, or proximal limbs, preceding weakness.
  - Weakness, predominant proximal, and symmetrical
    - Often axial weakness with dropped head
    - Frequent ocular involvement
    - Facial weakness and involvement of bulbar muscles 50% of cases
    - Respiratory muscle failure possible
  - CK elevation (CK can be normal)
  - Muscle biopsy
    - necrotizing myopathic changes with a variable degree of necrotic myofibers associated with inflammatory infiltrates.

Ramos-Casals M., Brahmer, J.R., Callahan, M.K. et al. Immune-related adverse events of checkpoint inhibitors. Nat Rev Dis Primers 6, 38 (2020). https://doi.org/10.1038/s41572-020-0160-6
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irAEs associated with ICIs

- irMG
  - The most commonly reported neurological irAEs associated with ICIs
  - Fluctuating and fatigable (30%) muscle weakness, involving ocular, bulbar, and/or respiratory muscles
  - Typically, generalized MG at onset with rapid progression to myasthenic crisis
  - Myositis and myocarditis overlap possible
  - Anti-AChR antibodies positive (57%-83%)
    - No correlations anti-AChR titers and irMG severity
  - HyperCKemia possible pointing to an overlap syndrome

Ramos-Casals M., Brahmer, J.R., Callahan, M.K. et al. Immune-related adverse events of checkpoint inhibitors. Nat Rev Dis Primers 6, 38 (2020). https://doi.org/10.1038/s41572-020-0160-6
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Treatment of irAE associated with ICIs

- Administration corticosteroids (oral or IV) had a significant association with favorable clinical outcomes (76% vs 24%; p=0.023).[1]
- Consensus guidelines use corticosteroids in patients with severe neurological irAE.[2]
- Although GBS patients are not usually treated with corticosteroids they are associated with favorable outcome and should be considered first line treatment.[3]

1. Dubey D, David WS, Reynolds KL, Chute DF, Clement NF, Cohen JV, Lawrence DP, Moinuddin MS, Sullivan RJ, Guidon AC. Severe Neurological Toxicity of Immune Checkpoint Inhibitors: Growing Spectrum. Ann Neurol. 2020 May;87(5):659-669. doi: 10.1002/ana.25700. Epub 2020 Mar 10. PMID: 32086972.
2 Psimaras D, Velasco R, Birzu C, Tamburin S, Lustberg M, Bruna J, Argyriou AA. Immune checkpoint inhibitors-induced neuromuscular toxicity: From pathogenesis to treatment. J Peripher Nerv Syst. 2019 Oct;24 Suppl 2:S74-S85. doi: 10.1111/jns.12339. PMID: 31593660.
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EDx during the COVID-10 pandemic

Received: 18 May 2020 | Revised: 19 May 2020 | Accepted: 20 May 2020
DOI: 10.1002/mus.26990

AANEM PRACTICE TOPIC

MUSCLE&NERVE WILEY

Guidance for resumption of routine electrodiagnostic testing during the COVID-19 pandemic

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EDx during the COVID-10 pandemic

- Patient scheduling
  - Lengthen intervals between EDx appointments based on space and guidelines for distancing
- Arrival
  - Social distancing, check-in from car and only come in when ready
- Safety
  - All wear masks, all patient perform hand hygiene and all provides with PPE including gloves, masks, and eyewear
- Screening
  - Symptom checklist day prior to appointment, second screen when entering building; postpone testing in positive or suggestive patients until at least 10 days have passed
- Outpatient
  - Avoid observers (Med students, visiting trainees); continue in those in whom EDx training requirement must be met with precautions, preassembled single-use kit for each patients

Hematoma risk after needle EMG in patients using NOAC

- Assess safety of needle EMG in patients on non-vit K oral anticoagulants (NOACs)
  - NOACs: dabigatran, rivoroxaban, apixaban, edoxaban
- Compare to the risk between warfarin and NOACs

- Monitored patients on warfarin or NOACs for 2 hours after needle EMG
- Ultrasound on all 'high risk' muscles

- 58 pts (NOACs: 29; Warfarin: 29)
  - 9 pts (3.3%) with hemorrhagic complications
    - 7 NOACs
    - 2 Wafarin
  - 6/9 – clinically relevant non-major bleeding
    - 5 NOACs, 1 warfarin
    - Acute bleeding need pressure (rivoroxaban)
    - 5 with hematoma needing ice

TABLE 2. Type of Complication and Muscle Groups Tested

Type of Hematoma	Muscle (Number)
Acute bleeding	Tibialis anterior (1)
Clinical hematoma	Tibialis anterior (2), iliopsoas (1), biceps (1), extensor digitorum communis (1)
Ultrasound hematoma	Lumbar paraspinal (1), flexor pollicis longus (1), iliopsoas (1)

- 3 with asymptomatic hematoma on US

Nagarajan E, Dyer N, Bailey E, Bollu PC, Yelam A, Gisanaman M, Govindarajan R. Hematoma Risk After Needle Electromyography in Patients Using Newer Oral Anticoagulants. J Clin Neurophysiol. 2019 Nov 8. doi: 10.1097/WNP.0000000000000641. Epub ahead of print. PMID: 31725032.

Hematoma risk after needle EMG in patients using NOAC

- Risk of bleeding with NOACs in EDx is low, and similar to that of warfarin
  - Bleeding risk between 0.62-1.45% (per muscle tested)

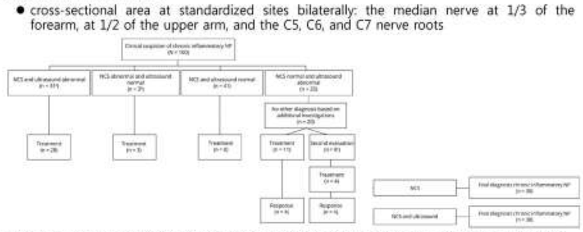
- Although no events in either study required ongoing management, 66% (6/9 events) met criteria for clinically relevant non-major bleeding

- Overall, most hematomas related to needle EMG are self-limited, and without serious clinical consequences
  - However, patients should always be counseled regarding risk

Nagarajan E, Dyer N, Bailey E, Bollu PC, Yelam A, Gisanaman M, Govindarajan R. Hematoma Risk After Needle Electromyography in Patients Using Newer Oral Anticoagulants. J Clin Neurophysiol. 2019 Nov 8. doi: 10.1097/WNP.0000000000000641. Epub ahead of print. PMID: 31725032.

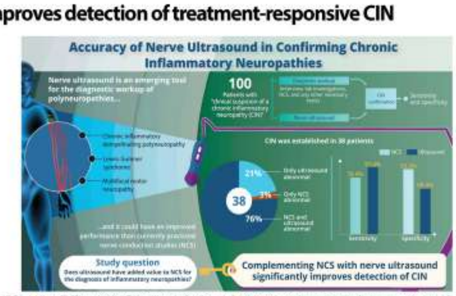
U/S improves detection of treatment-responsive CIN

- Ultrasound assessment
  - cross-sectional area at standardized sites bilaterally: the median nerve at 1/3 of the forearm, at 1/2 of the upper arm, and the C5, C6, and C7 nerve roots



Herraets IJT, Goedee HS, Telleman JA, van Eijk RPA, van Asseldonk JT, Visser LH, van den Berg LH, van der Pol WL. Nerve ultrasound improves detection of treatment-responsive chronic inflammatory neuropathies. Neurology. 2020 Apr 7;94(14):e1470-e1479. doi: 10.1212/WNL.0000000000008978. Epub 2020 Jan 29. PMID: 31959710.

U/S improves detection of treatment-responsive CIN



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