Hyaluronidase 101: From Science to Clinical Applications

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IgNS Immunoglobulin National Society

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Gregory received his Doctor of Pharmacy degree from Duquesne University in 2017. He then completed his PGY1 residency in pharmacy at the VA Pittsburgh Healthcare System in 2018. Since then, he has worked in home infusion and specialty pharmacy at Chartwell Pennsylvania, CarepathRx, and Accredo Health Group, as well as a Medical Science Liaison for Takeda Pharmaceutical Company. These experiences have shaped his exposure to plasma-derived therapies in terms of patient care, program management, therapeutic knowledge, and advisory board participation. He currently serves as a Coordinator of Clinical Outcomes and Patient Engagement at PANTHERx Rare Pharmacy.

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Accreditation Information continued…

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Gregory Caspero – Employee: PANTHERx Rare Pharmacy

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Learning Objectives

- Explain the mechanism of action of hyaluronidase within subcutaneous tissue
- Describe the historical use of hyaluronidase across various medical disciplines
- Discuss recent advancements in hyaluronidase-enabled immunoglobulin and biologic therapies, including current products and clinical trial data
- Identify and apply effective patient counseling strategies in clinical practice

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Patient Case

- JG is a 68-year-old Hispanic male

  - He was diagnosed with generalized myasthenia gravis (gMG) at age 62
  - Last weight: 242 lbs (110 kg)
  - Therapies for the disease have included pyridostigmine, prednisone, azathioprine, and IVIG
  - Most recently has been treated with efgartigimod alfa-fcab 1,100 mg IV once weekly x 4 weeks, then 4 weeks off therapy (each cycle)

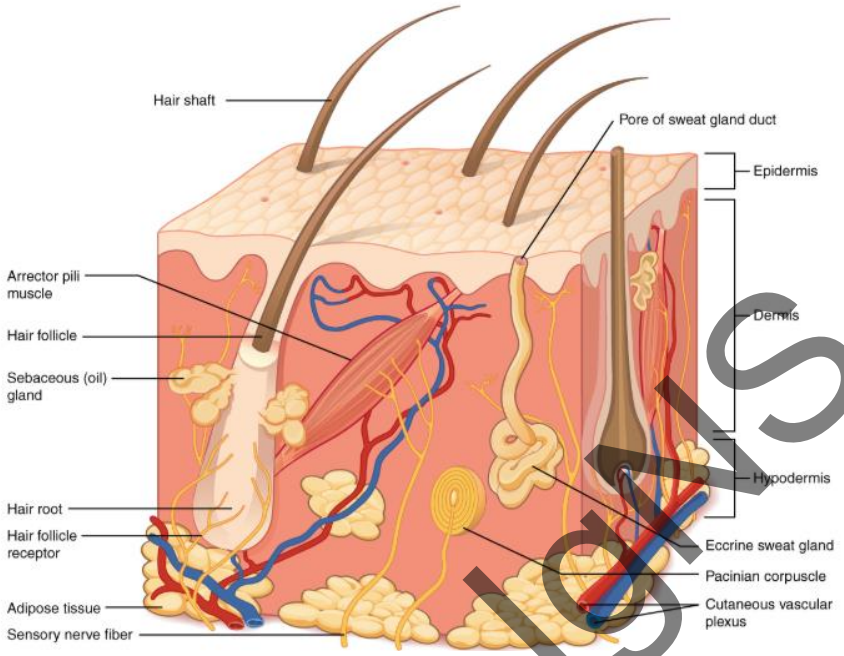
Patient Case

- JG is a 68-year-old Hispanic male
  - The patient would prefer to not have home health nurse come to his home for IV infusions
  - Appreciates that infusions are only 1 hour, but aware that there is a faster option available via online patient forum
  - Last MG-ADL score from 8/2025 was 5; fluctuated between 4-6 for the past 8 months
  - Discussed option of switching to efgartigimod alfa and hyaluronidase-qvfc with neuromuscular specialist

Learning Objectives

Explain the mechanism of action of hyaluronidase within subcutaneous tissue

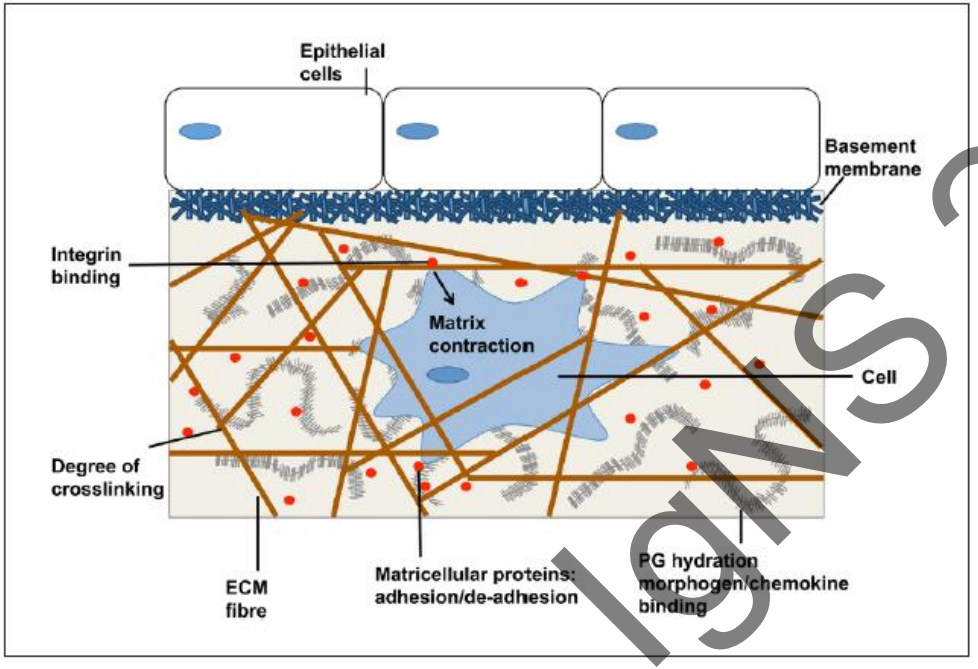
Subcutaneous Tissue



- Epidermis – protective, waterproof outer layer
- Dermis – structural support, sensation, skin elasticity
- Hypodermis – attaches skin to muscles and bone, stores fat, regulates temperature

Nunzio M, Biga LM, Bronson S, et al. 5.1 layers of the skin. Anatomy & Physiology 2e. September 1, 2025. Accessed September 4, 2025. https://open.oregonstate.education/anatomy2e/chapter/layers-skin/.

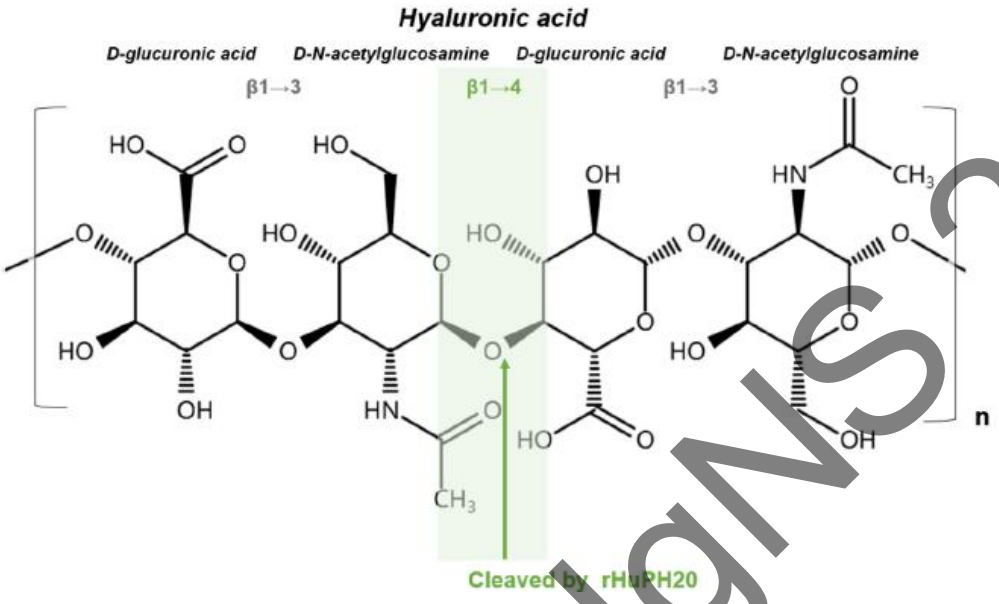
Extracellular Matrix (ECM)



- Collagens form as fibrils within the ECM
- Provide tensile strength
- Influence cell processes, such as adhesion and migration

Kular JK, Basu S, Sharma RI. The extracellular matrix: Structure, composition, age-related differences, tools for analysis and applications for tissue engineering. *Journal of Tissue Engineering*. 2014;5. doi:10.1177/2041731414557112

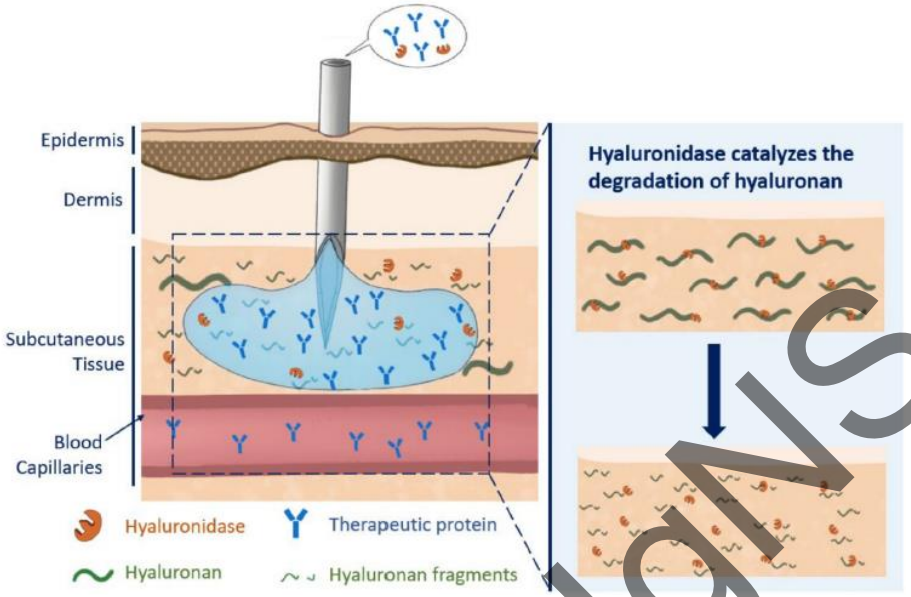
Hyaluronan



- Creates a barrier to bulk fluid flow through ECM
- High-molecular-weight molecule found in all mammals
- $t_{1/2}$ = 15-20 hours

Bookbinder LH, Hofer A, Haller MF, et al. A recombinant human enzyme for enhanced interstitial transport of therapeutics. *Journal of Controlled Release*. 2006;114(2):230-241. doi:10.1016/j.jconrel.2006.05.027
Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Hyaluronidase



- Family of glycosaminoglycan-degrading enzymes
- Used to disperse bacteria, sperm, toxins, and venoms
- Depolymerizes hyaluronan in the ECM within minutes

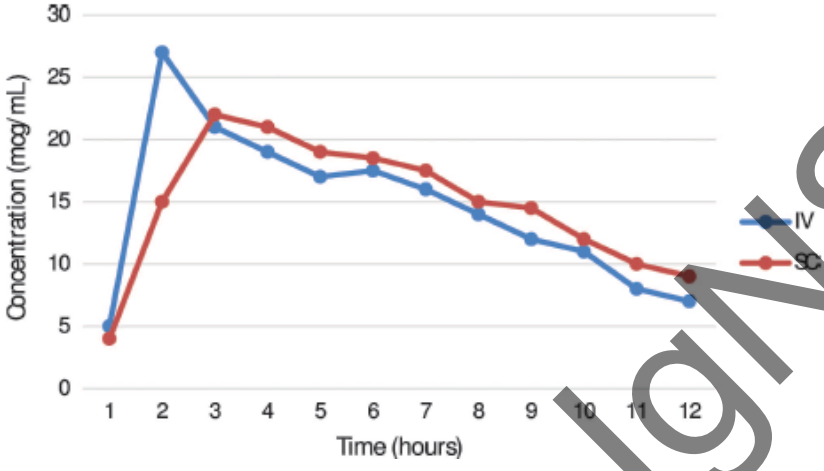
Bookbinder LH, Hofer A, Haller MF, et al. A recombinant human enzyme for enhanced interstitial transport of therapeutics. *Journal of Controlled Release*. 2006;114(2):230-241. doi:10.1016/j.jconrel.2006.05.027
Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Clinical Application

- Facilitate rapid SUBQ injection of large-volume solution
- Improve the absorption of co-administered therapeutics
- Enhances systemic bioavailability
- SUBQ tissue restored within 1-2 days after injection

Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Pharmacokinetics



- SUBQ-administered drugs:
  - Lower C_{max}
  - Delayed T_{max}
  - Higher AUC
  - Longer $t_{1/2}$
- Hyaluronidase helps to increase bioavailability of drug

Arthur AO. Innovations in subcutaneous infusions. *Journal of Infusion Nursing*. 2015;38(3):179-187. doi:10.1097/nan.0000000000000099

Why does this matter?

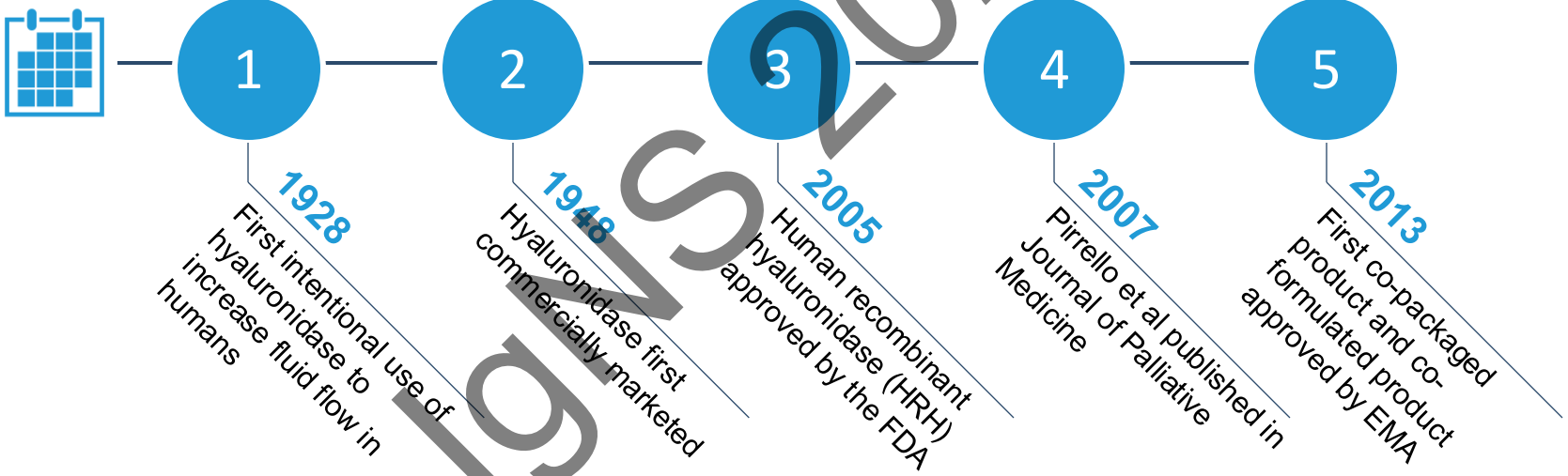
- Dosing volumes >2 mL can be administered
- Fixed doses with co-formulated products
- Administration method is more efficient
- Potentially less preparation steps, lower costs, and home infusion option
- Both patients and HCPs prefer over IV formulations

Bookbinder LH, Hofer A, Haller MF, et al. A recombinant human enzyme for enhanced interstitial transport of therapeutics. *Journal of Controlled Release*. 2006;114(2):230-241. doi:10.1016/j.jconrel.2006.05.027
Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Learning Objectives

Describe the historical use of hyaluronidase across various medical disciplines

History of Hyaluronidase

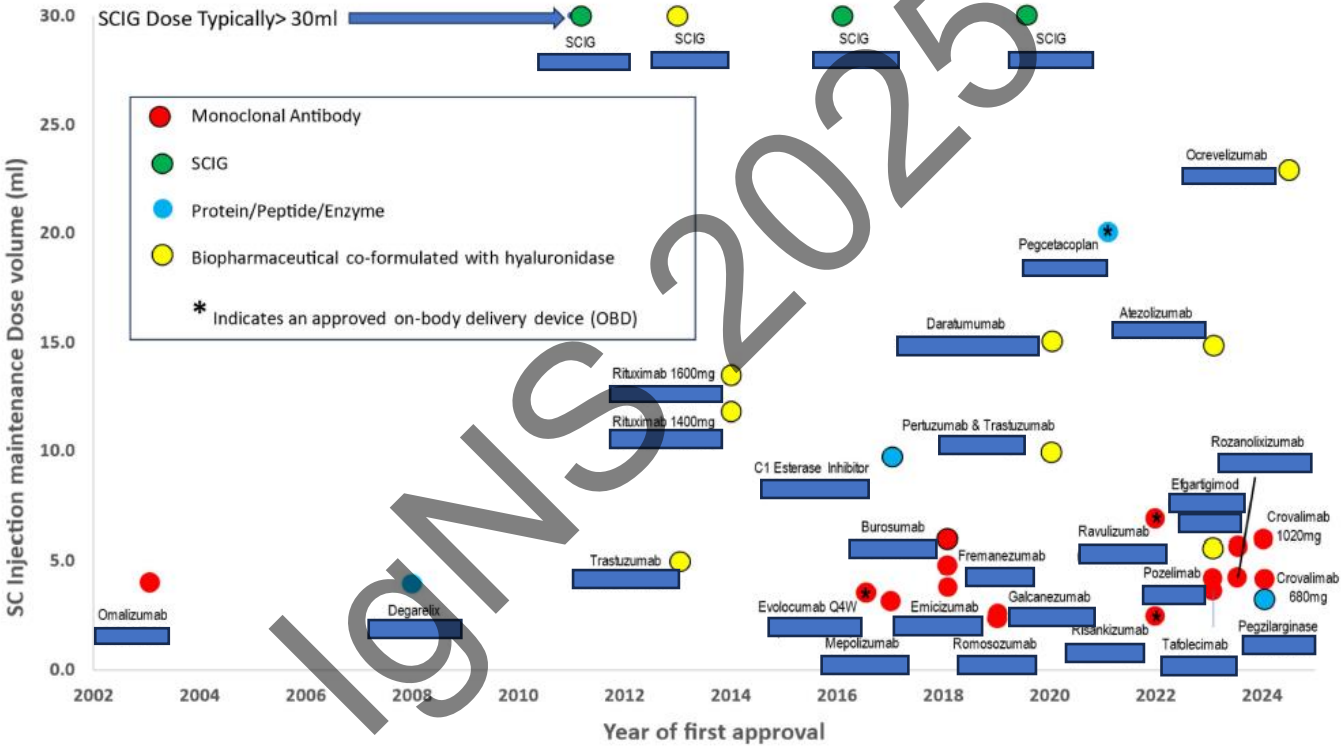


Arthur AO. Innovations in subcutaneous infusions. *Journal of Infusion Nursing*. 2015;38(3):179-187. doi:10.1097/nan.0000000000000099
Bookbinder LH, Hofer A, Haller MF, et al. A recombinant human enzyme for enhanced interstitial transport of therapeutics. *Journal of Controlled Release*. 2006;114(2):230-241. doi:10.1016/j.jconrel.2006.05.027
Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Learning Objectives

Discuss recent advancements in hyaluronidase-enabled immunoglobulin and biologic therapies, including current products and clinical trial data

Navigating Large-Volume SUBQ Admin. of Biopharmaceuticals



Green P, Schneider A, Lange J. Navigating large-volume subcutaneous injections of biopharmaceuticals: A systematic review of clinical pipelines and approved products. *mAbs*. 2024;16(1). doi:10.1080/19420862.2024.2402713

Use of SUBQ Biologic Formulations with Hyaluronidase

- Immune Globulin Infusion (Human), 10% with HRH
- Efgartigimod alfa and hyaluronidase-qvfc
- Atezolizumab and hyaluronidase-tqjs
- Ocrelizumab and hyaluronidase-ocsq
- Nivolumab and hyaluronidase-nvhy
- MK-3475A

Kim J, Kesselheim AS, Cliff ER, Rome BN. Medicare spending and use of subcutaneous biologic formulations with hyaluronidase. *The Oncologist*. 2025;30(6). doi:10.1093/oncolo/oyaf149

Immune Globulin Infusion (Human), 10% with HRH

FDA Approval

- September 2014 (for PI in adults)
- April 2023 (for PI in pediatrics aged 2-16 years)
- January 2024 (for CIDP)

Indication

- Maintenance therapy in adults with chronic inflammatory demyelinating polyneuropathy (CIDP)

Mechanism of Action

- MOA of immunoglobulins in treatment of CIDP in adults has not been fully elucidated, but may include immunomodulatory effects

PI = Primary Immunodeficiency
CIDP = Chronic Inflammatory Demyelinating Polyneuropathy

Immune Globulin Infusion (Human), 10% with Recombinant Human Hyaluronidase [package insert]. Cambridge, MA: Takeda Pharmaceuticals U.S.A., Inc.; 2025.

Immune Globulin Infusion (Human), 10% with HRH Overview

Administration	• Subcutaneous infusion into the abdomen or thighs with pump, SUBQ needles, 1-3 infusion sites, sequential administration (Hy, then Ig)
Strengths available	• Dual unit of 100 mg/mL Ig 10% and 160 U/mL of rHuPH20 • Ig comes as 25 mL, 50 mL, 100 mL, 200 mL, and 300 mL
Storage	• Refrigeration: 2° to 8°C for up to 36 months. • Room Temperature: up to 25°C for up to 3 months.

Immune Globulin Infusion (Human), 10% with Recombinant Human Hyaluronidase [package insert]. Cambridge, MA: Takeda Pharmaceuticals U.S.A., Inc.; 2025.

Immune Globulin Infusion (Human), 10% with HRH Dosing

- Induction: 2 g/kg over 2-5 days (IVIG)
- Maintenance: 1 g/kg every 3 weeks (IVIG or fSCIG)
- ***Switching from IVIG treatment:***
  - Patient must be on stable doses of IVIG
  - The starting dose and frequency of fSCIG is the same as the patient's previous IVIG treatment; the typical dosing interval range in the clinical trial was 2 to 4 weeks

Immune Globulin Infusion (Human), 10% with Recombinant Human Hyaluronidase [package insert]. Cambridge, MA: Takeda Pharmaceuticals U.S.A., Inc.; 2025.
Allen JA, Gelinas DF, Freimer M, Runken MC, Wolfe GI. Immunoglobulin administration for the treatment of CIDP: IVIG or SCIG? *Journal of the Neurological Sciences*. 2020;408:116497. doi:10.1016/j.jns.2019.116497

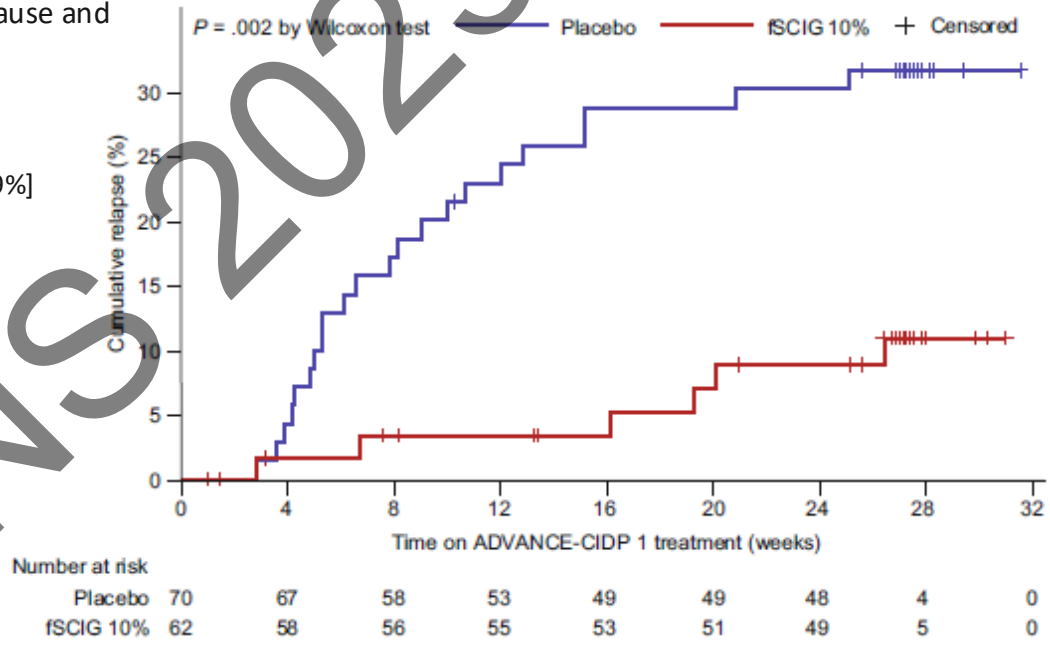
The ADVANCE-CIDP 1 Clinical Trial

Primary Outcome

- Relapse rate, assessed by % of patients with worsening functional disability, measured by Inflammatory Neuropathy Cause and Treatment (INCAT) disability scores
  - fSCIG 10%: 9.7% [95% CI 4.5%, 19.6%]
  - Placebo: 31.4% [95% CI 21.8%, 43%]
  - Absolute Difference: -21.8% [95% CI -34.5%, -7.9%]
  - *p* = .0045

Safety Outcomes

- Total Adverse Events
  - fSCIG 10%: 79%
  - Placebo: 57.1%
- Severe Adverse Events
  - 1.6% vs 8.6%
- Serious Adverse Events
  - 3.2% vs 7.1%



Bril V, Hadden RD, Brannagan TH, et al. Hyaluronidase-facilitated subcutaneous immunoglobulin 10% as maintenance therapy for chronic inflammatory demyelinating polyradiculoneuropathy: The ADVANCE-CIDP 1 randomized controlled trial. *Journal of the Peripheral Nervous System*. 2023;28(3):436-449. doi:10.1111/jns.12573

Efgartigimod alfa and hyaluronidase-qvfc

FDA Approval

- June 2023 (for gMG)
- June 2024 (for CIDP)
- April 2025 (for prefilled syringe formulation for self-injection)

Indication

- Chronic inflammatory demyelinating polyneuropathy (CIDP)

Mechanism of Action

- Efgartigimod alfa is a human IgG1 antibody fragment that binds to the neonatal Fc receptor (FcRn), resulting in the reduction of circulating IgG

Efgartigimod alfa and hyaluronidase-qvfc [package insert]. Boston, MA: argenx US, Inc.; 2025.

Efgartigimod alfa and HRH Overview

Administration	• Subcutaneous injection into the abdomen utilizing co-formulated product in either prefilled syringe (PFS) or vial
Strengths available	• Prefilled syringe: 1,000 mg efgartigimod alfa and 10,000 units hyaluronidase per 5 mL • Vial: 1,008 mg efgartigimod alfa and 11,200 units hyaluronidase per 5.6 mL
Storage	• Refrigeration: 2° to 8°C in original carton until time of use • Room Temperature: Up to 30°C for up to 30 days (PFS); 20° to 25°C for up to 3 days (vial)

Efgartigimod alfa and hyaluronidase-qvfc [package insert]. Boston, MA: argenx US, Inc.; 2025.

Efgartigimod alfa and HRH Dosing

- Single-Dose Prefilled Syringe
  - 1,000 mg efgartigimod alfa / 10,000 units hyaluronidase administered SUBQ over approximately 20 to 30 seconds as once weekly injections
- Single-Dose Vial
  - 1,008 mg efgartigimod alfa / 11,200 units hyaluronidase administered SUBQ over approximately 30 to 90 seconds as once weekly injections

Efgartigimod alfa and hyaluronidase-qvfc [package insert]. Boston, MA: argenx US, Inc.; 2025.

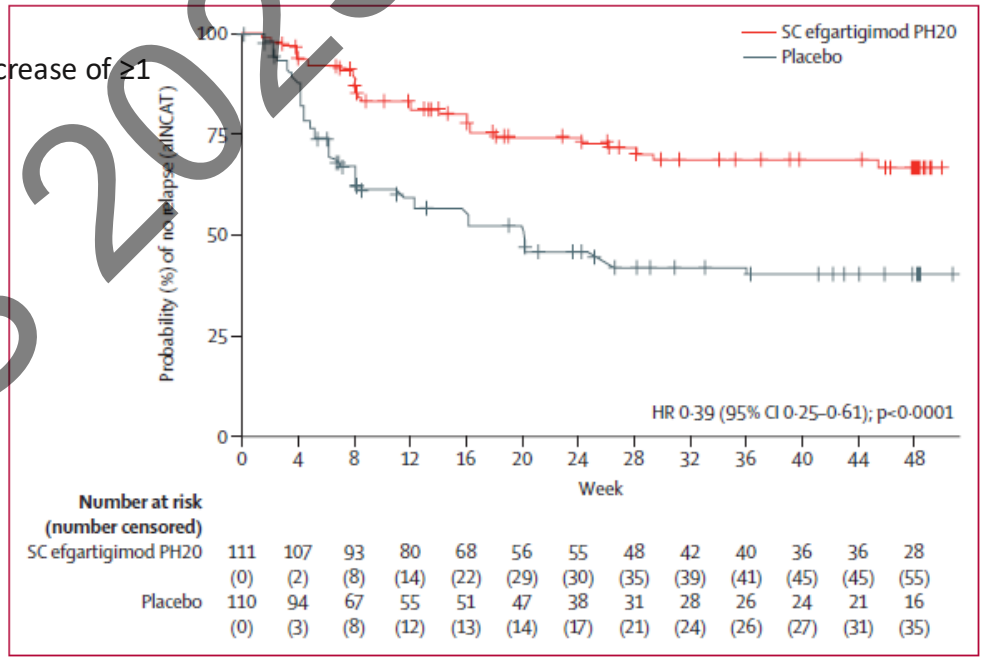
The ADHERE Clinical Trial

Primary Outcomes

- Stage A – Confirmed evidence of clinical improvement
  - 66% [95% CI 61-71.6]
- Stage B – Risk of relapse, measured by time to first aINCAT increase of ≥1 points
  - Hazard ratio 0.39 [95% CI 0.25-0.61]; $p < 0.0001$

Safety Outcomes

- Stage A – Treatment-emergent Adverse Events = 63%
- Stage A – Serious Treatment-emergent Adverse Events = 7%
- Stage B – Treatment-emergent Adverse Events
  - SUBQ efgartigimod PH20 = 64%
  - Placebo = 56%
- Stage B – Serious Treatment-emergent Adverse Events
  - SUBQ efgartigimod PH20 = 5%
  - Placebo = 5%



Allen JA, Lin J, Basta, I, et al. Safety, tolerability, and efficacy of subcutaneous efgartigimod in patients with chronic inflammatory demyelinating polyradiculoneuropathy (ADHERE): a multicentre, randomized-withdrawal, double-blind, placebo-controlled, phase 2 trial. *Lancet Neurology*. 2024;23(10):1013-1024. doi:10.1016/S1474-4422(24)00309-0

Atezolizumab and hyaluronidase-tqjs

FDA Approval	• September 2024 (for multiple cancers)
Indication	• Non-Small Cell Lung Cancer (NSCLC), Small Cell Lung Cancer (SCLC), Hepatocellular Carcinoma (HCC), Melanoma, Alveolar Soft Part Sarcoma (ASPS)
Mechanism of Action	• Atezolizumab is a monoclonal antibody that binds to PD-L1 and blocks its interactions with body PD-1 and B7.1 receptors

Atezolizumab and hyaluronidase-tqjs [package insert]. San Francisco, CA: Genentech, Inc.; 2025.

Atezolizumab and HRH Overview

Administration	• Subcutaneous injection into the thigh utilizing co-formulated product in single-dose vial
Strengths available	• 1,875 mg atezolizumab and 30,000 units hyaluronidase per 15 mL in a single-dose vial
Storage	• Refrigeration: 2° to 8°C in original carton until time of use

Atezolizumab and hyaluronidase-tqjs [package insert]. San Francisco, CA: Genentech, Inc.; 2025.

Atezolizumab and HRH Dosing

- 1,875 mg atezolizumab / 30,000 units hyaluronidase administered SUBQ over approximately 7 minutes every 3 weeks
- Different recommended dosage and administration than IV atezolizumab products
- No dose reduction is recommended

Atezolizumab and hyaluronidase-tqjs [package insert]. San Francisco, CA: Genentech, Inc.; 2025.

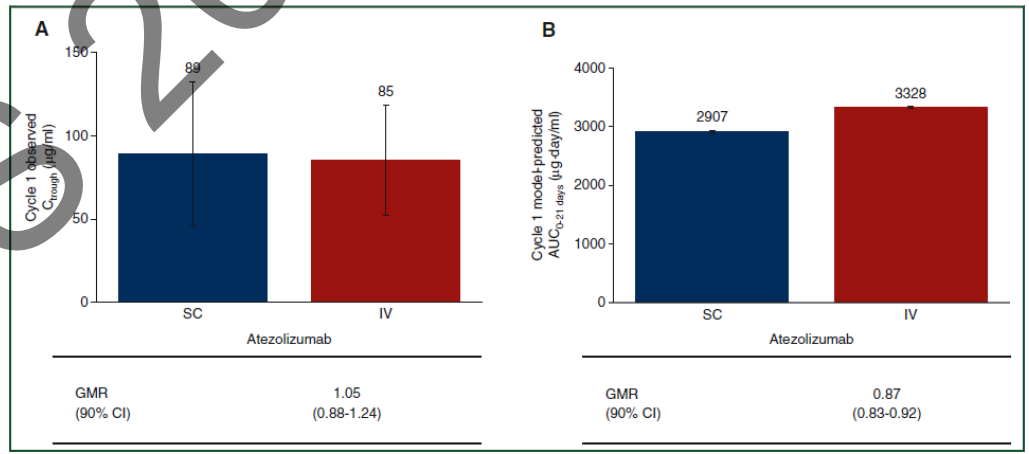
The IMscin001 Clinical Trial

Primary Outcomes

- Cycle 1 observed trough serum concentration (C_{trough})
  - SUBQ: 89 µg/mL vs. IV: 85 µg/mL
  - Geometric mean ratio: 1.05 [90% CI 0.88-1.24]
- Model-predicated area under the curve from days 0 to 21 ($AUC_{0\text{-}21\ d}$)
  - SUBQ: 2907 µg·day/mL vs. IV: 3328 µg·day/mL
  - Geometric mean ratio: 0.87 [90% CI 0.83-0.92]

Safety Outcomes

- Proportion of patients with ≥1 Adverse Event
  - SUBQ: 85.8% vs. IV: 83.9%
- Treatment-related Adverse Events
  - SUBQ: 37.7% vs. IV: 37.9%



Burotto M, Zvirbule Z, Mochalova A, et al. Imscin001 Part 2: A randomised phase III, open-label, multicentre study examining the pharmacokinetics, efficacy, immunogenicity, and safety of atezolizumab subcutaneous versus intravenous administration in previously treated locally advanced or metastatic non-small-cell lung cancer and pharmacokinetics comparison with other approved indications. *Annals of Oncology*. 2023;34(8):693-702. doi:10.1016/j.annonc.2023.05.009

Ocrelizumab and hyaluronidase-ocsq

FDA Approval

- September 2024 (for multiple sclerosis (MS))

Indication

- Relapsing forms of MS, in adults
- Primary progressive MS, in adults

Mechanism of Action

- Precise MOA is unknown, but presumed to involve binding to CD20

Ocrelizumab and hyaluronidase-ocsq [package insert]. San Francisco, CA: Genentech, Inc.; 2025.

Ocrelizumab and HRH Overview

Administration	• Subcutaneous injection into the abdomen utilizing co-formulated product in single-dose vial
Strengths available	• 920 mg ocrelizumab and 23,000 units hyaluronidase per 23 mL in a single-dose vial
Storage	• Refrigeration: 2º to 8ºC in original carton until time of use • Room Temperature: Up to 25ºC for up to 12 hours

Ocrelizumab and hyaluronidase-ocsq [package insert]. San Francisco, CA: Genentech, Inc.; 2025.

Ocrelizumab and HRH Dosing

- 920 mg ocrelizumab / 23,000 units hyaluronidase administered SUBQ over approximately 10 minutes every 6 months
- Different recommended dosage and administration than IV ocrelizumab products

Ocrelizumab and hyaluronidase-ocsq [package insert]. San Francisco, CA: Genentech, Inc.; 2025.

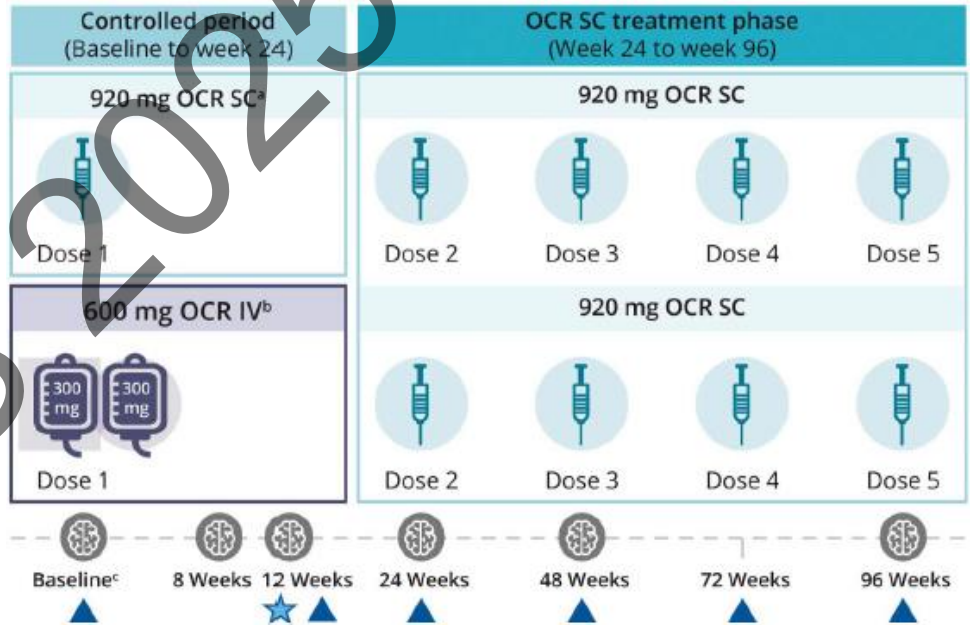
The OCARINA II Clinical Trial

Primary Outcome

- OCR area under the serum concentration time curve from day 1 to week 12 (AUC_{W1-12})
  - SUBQ: 3500 µg/mL·day vs. IV: 2750 µg/mL·day
  - Geometric mean ratio: 1.29 [90% CI 1.23-1.35]
- OCR area under the serum concentration time curve from day 1 to week 24 (AUC_{W1-24})
  - Geometric mean ratio: 1.27 [90% CI 1.21-1.34]

Safety Outcomes

- Proportion of patients with ≥1 Adverse Event
  - SUBQ: 86.4% vs. IV: 75.4%
- Serious Adverse Events
  - SUBQ: 2.5% vs. IV: 5.9%



Newsome SD, Krzystanek E, Selmaj KW, et al. Subcutaneous ocrelizumab in patients with multiple sclerosis: results of the phase III OCARINA II study. *Neurology*. 2025 May 13;104(9):e213574. doi:10.1212/WNL.0000000000213574

Nivolumab and hyaluronidase-nvhy

FDA Approval

- December 2024 (for multiple cancers)

Indication

- Renal Cell Carcinoma (RCC), Melanoma, NSCLC, Squamous Cell Carcinoma of the Head and Neck (SCCHN), Urothelial Carcinoma (UC), Colorectal Cancer, HCC, Esophageal Cancer, Gastric Cancer, Gastroesophageal Junction Cancer, and Esophageal Adenocarcinoma

Mechanism of Action

- Nivolumab is a human immunoglobulin G4 (IgG4) monoclonal antibody that binds to the PD-1 receptors and blocks its interaction with PD-L1 and PD-L2

Nivolumab and hyaluronidase-nvhy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2025.

Nivolumab and HRH Overview

Administration	• Subcutaneous injection into the abdomen or thigh utilizing co-formulated product in single-dose vial
Strengths available	• 600 mg nivolumab and 10,000 units hyaluronidase per 5 mL in a single-dose vial
Storage	• Refrigeration: 2° to 8°C in original carton until time of use

Nivolumab and hyaluronidase-nvhy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2025.

Nivolumab and HRH Dosing

Indication	Recommended Dosage	Duration of Therapy
Advanced renal cell carcinoma	600 mg nivolumab and 10,000 units hyaluronidase every 2 weeks or 1,200 mg nivolumab and 20,000 units hyaluronidase every 4 weeks	Until disease progression or unacceptable toxicity
Unresectable or metastatic melanoma		
Metastatic non-small cell lung cancer		
Squamous cell carcinoma of the head and neck		
Locally advanced or metastatic urothelial carcinoma		
Microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer		
Hepatocellular carcinoma		
Esophageal squamous cell carcinoma		
Adjuvant treatment of melanoma	600 mg nivolumab and 10,000 units hyaluronidase every 2 weeks or 1,200 mg nivolumab and 20,000 units hyaluronidase every 4 weeks	Until disease recurrence or unacceptable toxicity for up to 1 year
Adjuvant treatment of urothelial carcinoma		
Adjuvant treatment of resected esophageal or gastroesophageal junction cancer		

Nivolumab and hyaluronidase-nvhy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2025.

Nivolumab and HRH Dosing (cont.)

- Variety of dosing/frequency options depending on if product is used as monotherapy vs. in combination with other therapeutic agents
- Different recommended dosage and administration than IV nivolumab products
- No dose reduction is recommended

Nivolumab and hyaluronidase-nvhy [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2025.

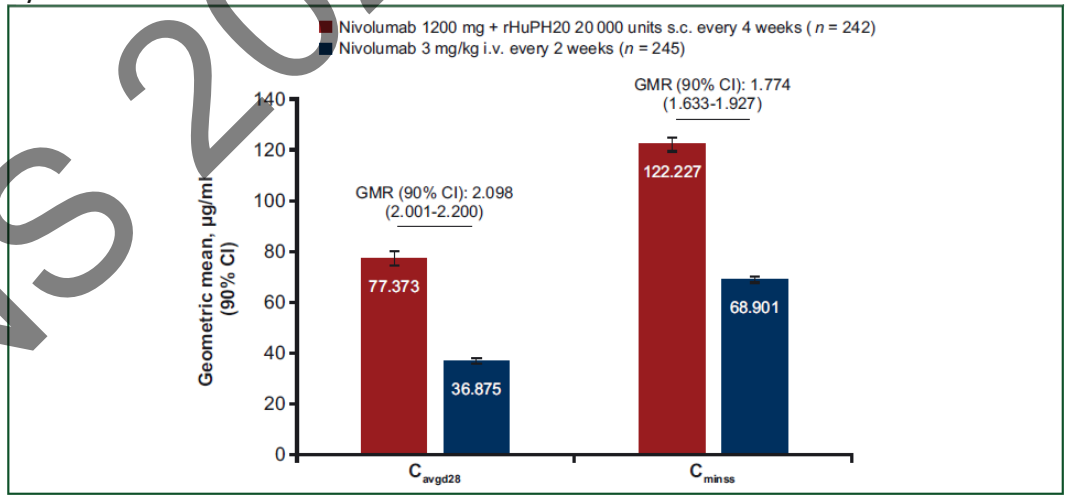
The CheckMate 67T Clinical Trial

Primary Outcomes

- Time-averaged serum concentration over the first 28 days (C_{avgd28})
  - SUBQ: 77.373 µg/mL vs. IV: 36.875 µg/mL
  - Geometric mean ratio: 2.098 [90% CI 2.001-2.2]
- Minimum steady-state serum concentration (C_{minss})
  - SUBQ: 122.227 µg/mL vs. IV: 68.901 µg/mL
  - Geometric mean ratio: 1.774 [90% CI 1.633-1.927]

Secondary Outcomes

- Objective response rate (ORR)
  - SUBQ: 24.2% vs. IV: 18.2%
  - Risk ratio: 1.33 [95% CI 0.94-1.87]



Albiges L, Bourlon MT, Chacón M, et al. Subcutaneous versus intravenous nivolumab for renal cell carcinoma. *Annals of Oncology*. 2025;36(1):99-107. doi:10.1016/j.annonc.2024.09.002

MK-3475A

- Pembrolizumab and berahyaluronidase alfa

FDA Approval

- To be determined
- PDUFA date set for September 2025

Indication

- All previously approved solid tumor indications for pembrolizumab

Mechanism of Action

- Pembrolizumab is a monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2

Felip E, Rojas CI, Schenker M, et al. Subcutaneous versus intravenous pembrolizumab, in combination with chemotherapy, for treatment of metastatic non-small-cell lung cancer: The phase III 3475A-D77 trial. *Annals of Oncology*. 2025;36(7):775-785. doi:10.1016/j.annonc.2025.03.012

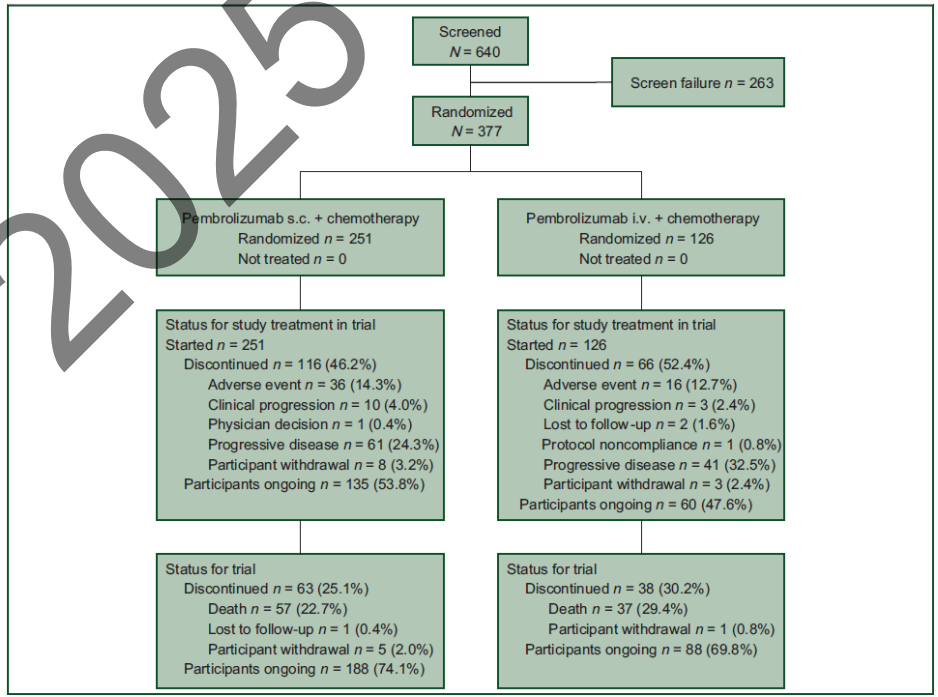
The 3475A-D77 Clinical Trial

Primary Outcomes

- Cycle 1 area under the curve ($AUC_{0\text{-}6\ weeks}$)
  - SUBQ: 1633.24 µg·day/mL vs. IV: 1437.58 µg·day/mL
  - Geometric mean ratio: 1.14 [96% CI 1.06-1.22]
  - $p < 0.0001$
- Steady-state trough concentration (C_{trough})
  - SUBQ: 39.23 µg/mL vs. IV: 23.49 µg/mL
  - Geometric mean ratio: 1.67 [94% CI 1.52-1.84)
  - $p < 0.0001$

Safety Outcomes

- Overall safety profile consistent between SUBQ and IV arms
- Injection-site reactions reported in 2.4% SUBQ participants



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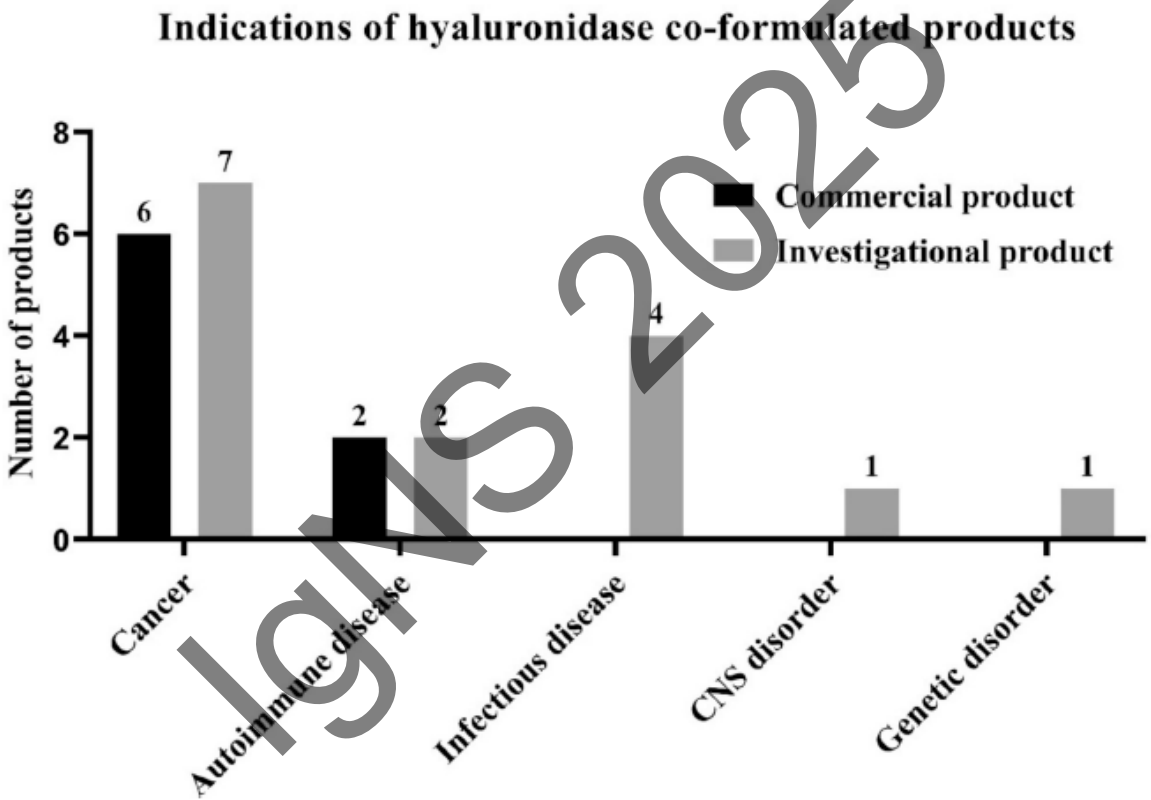
Clinical Pipeline of HRH Co-formulated Products

API (Target)	Indication	Clinical Stage
Nivolumab (PD-1) + Relatlimab (LAG-3)	Melanoma	Phase III
Pembrolizumab (PD-1)	Metastatic non-small cell lung cancer	Phase III
Amivantamab (EFGR and MET)	Non-small cell lung cancer	Phase II
BMS-986258 (TIM-3)	Advanced malignant tumors	Phase II
BMS-986179	Advanced Solid Tumors	Phase I/II
VH3810109 (CD4)	Human Immunodeficiency Virus (HIV)	Phase II
C1 esterase inhibitor [human] (C1 Esterase)	Hereditary Angioedema	Phase II
Argx-117 (C2)	Multifocal Motor Neuropathy	Phase I
B007 (C20)	CD20-positive B-cell non-Hodgkin Lymphoma	Phase I
VH3810109 (Undisclosed)	HIV	Phase I
VRC-HIVMAB091-00-AB (N6LS) (CD4)	HIV	Phase I
CAP256V2LS	HIV	Phase I
ALXN 1720 (C5)	Myasthenia Gravis	Phase I
Avelumab (PD-L1)	Pancreatic cancer	Phase I
SG301 (CD38)	Myeloma	Phase I

Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Clinical Pipeline of HRH Co-formulated Products (cont.)



Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069

Future Direction of Large-Volume SUBQ Injections

- TAK-881 – 20% IgG with HRH
- Co-formulated products
- Prefilled syringe (PFS)
- Docking stations for dual vial units
- On-body delivery system (OBDS)

Guo J, Weng J, Zhou F, Gu X. An industry perspective on hyaluronidase co-formulated biopharmaceutics. *Journal of Controlled Release*. 2025;381. doi:10.1016/j.jconrel.2025.02.069
Takeda's HyHub & Duo: FDA cleared devices. Takeda Pharmaceuticals: Global Homepage. July 21, 2025. Accessed September 4, 2025. https://www.takeda.com/newsroom/newsreleases/2025/hyhub/.

Learning Objectives

Identify and apply effective patient counseling strategies in clinical practice

Advantages of SUBQ Administration

- SUBQ drug delivery reduces infusion reactions seen with IV
- Limits the number of pre-medications required for certain drugs
- Infections of the local tissue may be experienced; less severe than seen with IV
- Patients and caregivers may be taught administration method
- Home infusion over infusion center

Arthur AO. Innovations in subcutaneous infusions. *Journal of Infusion Nursing*. 2015;38(3):179-187. doi:10.1097/nan.0000000000000099

Important Counseling Points

- Hyaluronidase is an enzyme
- It helps to break down hyaluronan, a component of the ECM
- SUBQ tissue restored within 1-2 days after injection
- These are natural processes
- Helping to provide another option to drug delivery compared to other available choices

Patient Case

- JG is a 68-year-old Hispanic male

  - Prescription comes to the pharmacy for efgartigimod alfa and hyaluronidase-qvfc 1,000 mg / 10,000 units PFS subcutaneously once weekly x 4 weeks, then 4 weeks off therapy (each cycle)
  - He is unfamiliar with the concept of hyaluronidase and asks for some counseling

Patient Case

- JG is a 68-year-old Hispanic male

- What are the main counseling points that we should highlight for this gentleman?
  - Hyaluronidase is an enzyme
  - MOA of Hyaluronidase
  - SUBQ tissue restored within 1-2 days after injection
  - These are naturally occurring processes in the human body
  - Provides another option for drug delivery
  - Bioavailability of efgartigimod alfa and hyaluronidase-qvfc
  - Explain the PFS administration and that nursing will assist upfront

Summary

Explain the mechanism of action of hyaluronidase within subcutaneous tissue

Describe the historical use of hyaluronidase across various medical disciplines

Discuss recent advancements in hyaluronidase-enabled immunoglobulin and biologic therapies, including current products and clinical trial data

Identify and apply effective patient counseling strategies in clinical practice

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Thank You!