Development Pathways and Considerations for Subcutaneous Biologic Formulations

SUBCUTANEOUS
DRUG DEVELOPMENT
& DELIVERY
CONSORTIUM

CRS 2025
ANNUAL MEETING
& EXPOSITION

PHILADELPHIA, PA
JULY 13-18, 2025

NEXT-GENERATION
DELIVERY INNOVATIONS

Agenda

Clinical Development and Regulatory Strategies for SC Drug and Device Development	Charles Theuer M.D. Ph.D.	1:10 – 1:50
Formulation Considerations for Subcutaneous Biologics Development	Dany Doucet Ph.D.	1:55 – 2:35
Device Considerations for Combination Product Development …is it all about the dose delivery?	Ron Pettis Ph.D.	2:40 – 3:20
Large-Volume Subcutaneous Development: Considerations and Strategic Approaches	*** cancelled **	
Panel Discussion / Q&A	All	3:30 – 4:00

SC Consortium Vision and Mission Informs Strategic Imperatives

The SC Consortium is a diverse group of **key stakeholders** in the broader SC community, collaborating to **address and advance the most pressing research questions** in SC drug delivery and development in a **precompetitive manner**

Vision

Our vision is to **transform patient care** and **improve patient outcomes** by leading **fundamental advancements in subcutaneous drug development and delivery**

Mission

Our mission is to **collaboratively advance the most pressing issues and opportunities in subcutaneous dosage and delivery** in a **precompetitive manner**

Strategic Imperatives

1. **Establish** and **maintain** the SC Consortium as the **go-to industry collaboration hub** for **advancing** the science, technology, and best practices for SC drug development and delivery
2. **Characterize** top unmet needs in SC drug development and delivery and **develop tools and positions** that address unmet needs
3. **Engage** and **influence** key stakeholders (e.g., regulatory bodies) around key opportunities related to SC Consortium activities

Since its inception in 2018, the SC Consortium has **continuously grown and engaged** a **diverse group of pharmaceutical and medical device organizations** interested in contributing to and benefiting from **pre-competitive collaboration** on **critical issues related to SC drug delivery and development.**

100+ Experts in the field

22 Innovative Companies

6 Problem Statements

1 Vision & Mission

SUBCUTANEOUS DRUG DEVELOPMENT & DELIVERY CONSORTIUM

AMGEN · AstraZeneca · BD · Biogen · Halozyme · Boehringer Ingelheim · Pfizer · YPSOMED SELFCARE SOLUTIONS · GSK · Johnson&Johnson · MERCK · SHL MEDICAL · sanofi · NOVARTIS · GILEAD · novo nordisk® · matchstick · Roche · Bristol Myers Squibb · KORU MEDICAL SYSTEMS · Nemera

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Six Consortium Focus Areas & 2025 Problem Statements

Members collaborate within the SC Consortium's **sub-teams** to address **industry-level problem statements** (which are re-visited each year), driving research activities and advancing solutions to critical challenges in SC drug development and delivery

2025 Problem Statements

Bioavailability

Subcutaneous (SC) bioavailability of biologics is **unpredictable and variable.** There is a **gap in translation of data from in-vitro to preclinical to clinical** with regards to **bioavailability after SC administration**.

Clinical Design & Regulatory Strategy

There is still a lack of a cross-industry position on the most **appropriate development pathway** that will be addressed by the CDRS sub-team to form a basis for a health authority interaction on the topic.

High Dose High Volume (HDHV)

Gaps exist in the industry regarding **understanding and implementation of best practices** for **CMC development of HDHV products,** encompassing the challenges of both formulation and design of medical devices

Immunogenicity

There is a lack of **patient-derived real-life clinical data** to understand the **clinical relevance of immunogenicity** via the SC route of administration. Further, there are no harmonized, industry-wide accepted in vitro or preclinical in vivo models for immunogenicity through which multiple proteins have been tested

User Preference & Experience (UP/UE)

User preferences, including key perceptions and tradeoffs to inform **optimal SC product design** are not clearly understood by SC developers. Publicly available quantitative data is deficient and qualitative opinions are insufficient.

Sustainability

There is a lack of **collaboration, guidance, and integration of sustainability concepts** across the full value stream for SC products. Hence, implementation is limited and often relies on solutions developed at the local product or company level

In Memory of

Brian Carpenter

Charles River Associates

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Devoted and loving husband, father, and son

“Steady and calming presence”

“Patient and skilled listener - someone who could truly understand, analyze, and synthesize complex and sometimes divergent needs”

“Thank you Brian“

Involved with establishing the SC Consortium (2018)

“Most pleasant to work with“

“A true partner”

“Amazing ability to communicate ideas, next steps, and conclusions with incredible clarity and thoughtfulness”

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The Carpenters:
Brian
Dalton
Mallory
Blake

Workshop Overview

Charles Theuer MD PhD, Halozyme Therapeutics

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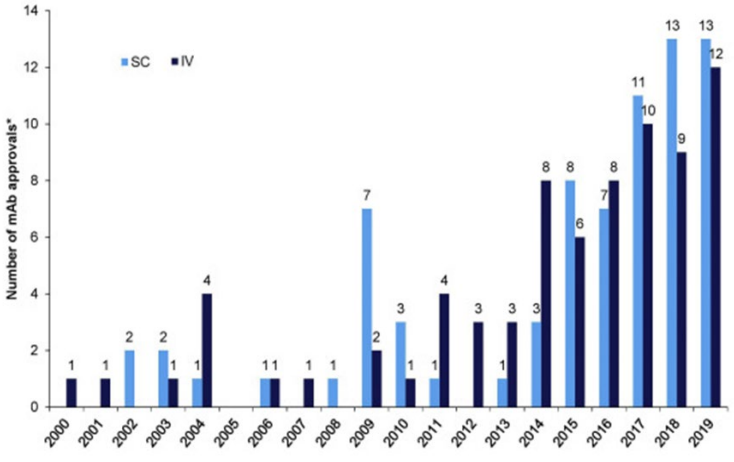
Trend Towards SC versus IV Route of Administration for Biologics

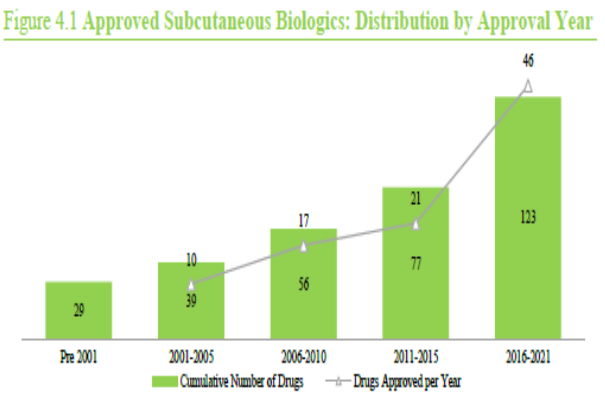


~50% of the newly approved biologics are administered SC[1]

Further trends:

- Extended dosing interval
- Coadministration
- Coformulation

This may contribute to increased need for higher doses per treatment



Distribution of approved subcutaneous biologics based on year of approval (for SC formulation), US and EU)[2]

1. Subcutaneous (SC) versus intravenous (IV) monoclonal antibody (mAb) approvals in the US from 2000 to 2019 (M. Sanchez-Felix, AdvDrugDelRev, 2020)
2. Subcutaneous Biologics, Technologies and Drug Delivery Systems (4rd Edition), 2022 – 2035, Roots Analysis

Trend to High Volume SC Administration

Increasing doses SC (for mAb's)

≤ 300 mg	300 – 600 mg	600 -1000 mg	>1000 mg

Standard formulation standard Autoinjector (AI) up to 2 mL of up to 200 mg/mL solultion

High concentration solution (*) with high-force 2 mL AI

Ultra-High concentration suspension with high-force 2 mL AI

Hyaluronidase coformulation with vial, syringe, or pre-filled syringe (PFS) or High Volume AI

Formulation & Clinical Bridging Strategy drive device options:

- Manual syringe
- High Force Autoinjector
- Reusable Autoinjector
- High Volume Autoinjector
- On-Body or Off-Body Device

(*) with VRA = viscosity-reducing agent

Standard formulation with vial-based 25 mL On-Body-Device or Off-Body Device

High concentrated solutions (*) with cartridge10/20 mL On-Body-Device or Off-Body Device

Clinical Development and Regulatory Strategies for SC Drug and Device Development

Charles Theuer MD PhD, Halozyme Therapeutics

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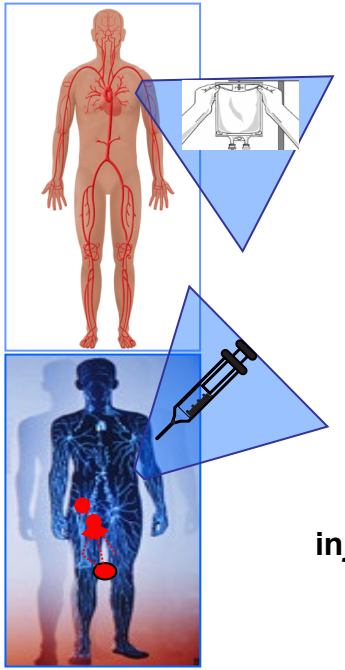
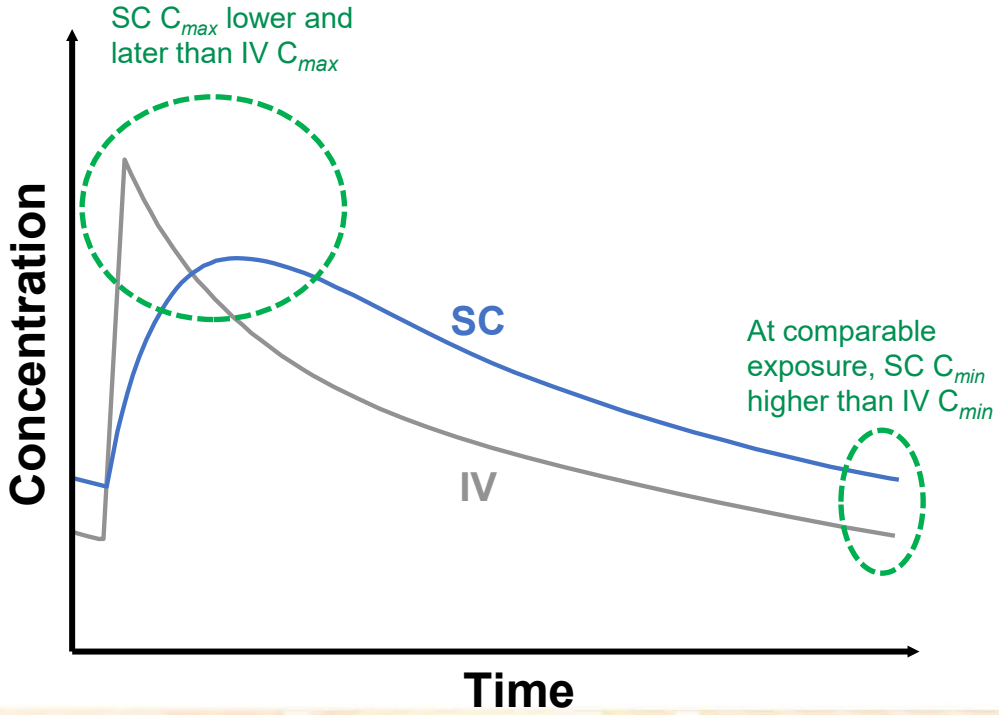
- *From IV to SC; how to arrive at the right SC dose regimen*
- From SC to SC; how to bridge from SC dose to another SC dose
- SC dosing from the start
- From SC to SC with a new Device
- From approved SC back to IV

Impact of Subcutaneous *vs.* Intravenous Delivery on PK profile of Monoclonal Antibodies[1]



1. Adapted from McLennan DN *et al*. Drug Discovery Today 2005.

Impact of Subcutaneous vs. Intravenous Delivery on PK profile of Monoclonal Antibodies[1]



- Impact of C_{max} and C_{min} on **efficacy & safety profile**
- **For high-dose mAbs: Technical feasibility** of high-concentration formulations and **high volume injection**

1. Bittner B, Schmidt J. Advancing Subcutaneous Dosing Regimens for Biotherapeutics: Clinical Strategies for Expedited Market Access. BioDrugs. 2024 Jan;38(1):23-46.

Approved IV to SC Bridging: Leverage Preclinical and Clinical Data During Development

Supporting preclinical (and clinical) data

- Assess impact of administration route on PD parameters, incl. relevance of C_{max}
- Demonstrate SC toxicology and local tolerability
- Assess the impact of different formulations on the PK profile

Aims of the clinical development program

- Demonstrate PK non-inferiority between the IV and SC formulations to ensure comparable efficacy
- Show that the safety and immunogenicity profile of the SC formulation is consistent with that of the IV formulation
- Provide supportive efficacy data

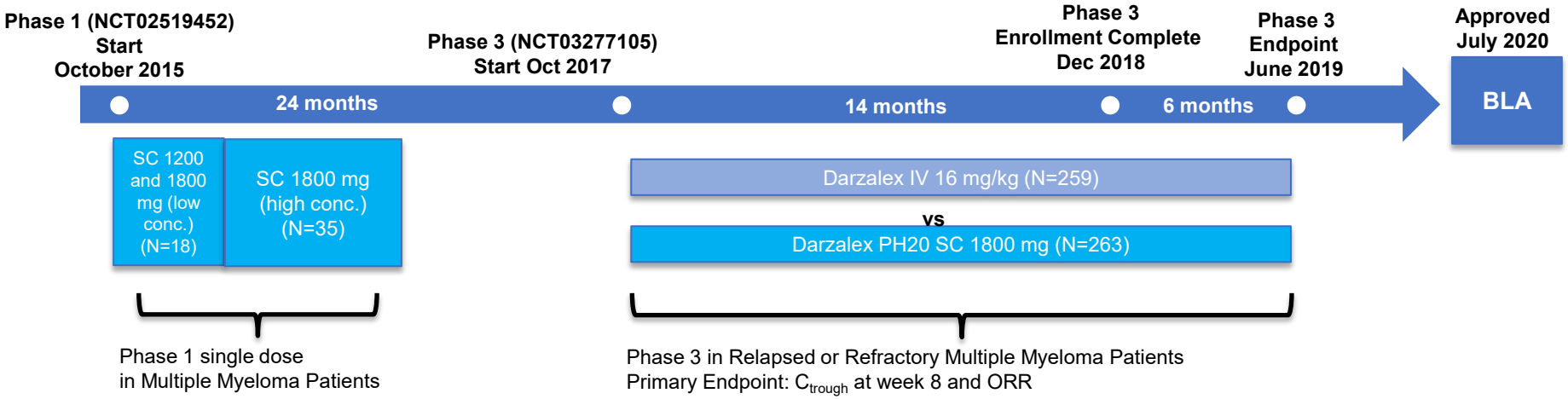
Approval Pathway for SC when IV Product is Already Approved

- Phase 1 PK endpoint study to select SC dose
  - One or two dose levels in patients or healthy volunteers to determine the absorption coefficient (K_a) for SC dosing
  - PK modeling using clearance characteristics established from IV dosing used to select the SC dose that will produce non-inferior exposure (e.g., match AUC and/or C_{trough})

- Phase 3 non-inferiority study to demonstrate non-inferiority of SC versus IV
  - PK or PD endpoint (90% CI of the geometric mean ratio contained within the standard bioequivalence margins (0.80 - 1.25)
  - Short time to endpoint (as short as 21-28 days)

- PK modeling using SC exposures from non-inferiority study used to allow for a broad label for the SC product that includes existing IV indications

SC Delivery of Monoclonal Antibodies - Development Pathway Based on Prior Availability of an IV Formulation: Daratumumab[1-3]



IV, intravenous; SC, subcutaneous; PH20, containing recombinant human hyaluronidase PH20

1. Usmani SZ, Nahi H, Mateos MV, et al. Subcutaneous delivery of daratumumab in relapsed or refractory multiple myeloma. Blood. 2019;134(8):668-677.
2. Mateos MV, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. Lancet Haematol. 2020;7(5):e370-e380
3. https://clinicaltrials.gov/study/NCT03277105

Comparison of Daratumumab IV and SC[1]

	Daratumumab IV	Daratumumab PH20 SC
Pharmaceutical form	20 mg/mL vial diluted into 500 – 1000 mL for infusion	Ready-to-use 120 mg/mL vial for fixed dose direct manual injection
Delivery technology	n/a	rHuPH20 2,000 U/mL
Need for IV access	Yes	No
Dose	16 mg/kg	1800 mg in 15 mL
Time required for administration	3.25-6.5 hours	3-5 minutes
Exposure (ratio of SC to IV)	C_{trough} = 1.08 (90% CI 0.96-1.21)	
Rate of Infusion-related reactions	34%	13%
Rate of life-threatening toxicity (G4)	11%	8%
Objective Response Rate	37%	41%

IV, intravenous; SC, subcutaneous containing rHuPH20, recombinant human hyaluronidase

1. Mateos MV, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. Lancet Haematol. 2020;7(5):e370-e380

SC Delivery of Monoclonal Antibodies - Development Pathway Based on Prior Availability of an IV Formulation: Atezolizumab[1,2]

IV, intravenous; SC, subcutaneous; PH20, containing recombinant human hyaluronidase PH20

1. Felip E, Burotto M, Zvirbule Z, et al. Results of a dose-finding phase 1b study of subcutaneous atezolizumab in patients with locally advanced or metastatic non-small cell lung cancer. Clin Pharm Drug Dev 2021; 10:1142-1155.
2. Burotto M, Zvirbule Z, Mochalova A, et al. Part 2: a randomized Phase III open-label, multicentre study examining the pharmacokinetics, efficacy, immunogenicity, and safety of atezolizumab subcutaneous vs. intravenous administration in previously treated locally advanced or metastatic NSCL cancer and pharmacokinetics comparison with other approved indications. Annals of Oncology 2023; 35:693-702.

Comparison of Atezolizumab IV and SC[1]

	Atezolizumab IV	Atezolizumab SC
Pharmaceutical form	60 mg/mL vial diluted for infusion at a fixed dose	Ready-to-use 125 mg/mL vial for fixed dose direct manual injection
Delivery technology	n/a	rHuPH20 2,000 U/mL
Need for IV access	Yes	No
Dose	1200 mg Q3W	1875 mg in 15 mL Q3W
Time required for administration	30-60 minutes	7 minutes
Exposure (ratio of SC to IV)	C_{trough} = 1.05 (90%CI 0.88-1.24)	
Rate of Infusion-related reactions	3.2%	0%
Rate of severe/life-threatening toxicity (G3/4)	32%	21%
Objective Response Rate	10%	12%

IV, intravenous; SC, subcutaneous containing rHuPH20, recombinant human hyaluronidase PH20

1. Burotto M, Zvirbule Z, Alvarez R, et al. Brief Report; Updated data from IMscin001 Part 2: a randomized 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. J Thor Onc (2024) 19:1460-1466

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SC Delivery when SC Product is Approved: Polyclonal IgG Using Single Cohort Cross-over Study of Fewer than 50 Patients[1]

- HyQvia (10% IgG)

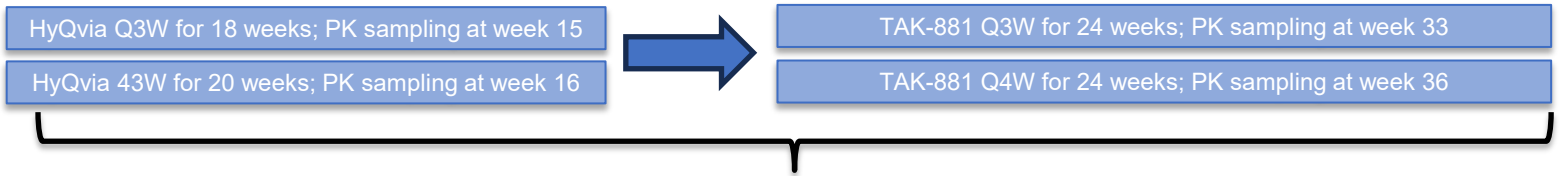
  Approved for the treatment of patients with primary immunodeficiency and for CIDP

  – Large volume of infusion of up to 1,200 mL approved for patients with CIDP

  – Typical infusions of 300 – 600 mL given at 5 mL/min, facilitated by rHuPH20

- TAK-881 (20% IgG)

  Concentrated IgG solution facilitated by rHuPH20 in Phase 3 testing to shorten infusion time



Primary endpoint: steady-state baseline-uncorrected area under the curve of total IgG during the dosing interval ($AUC_{0\text{-}\tau,ss}$)

SC, subcutaneous containing rHuPH20, recombinant human hyaluronidase PH20

1. Yukaitis CJ, et al. Comparability of pharmacokinetics between HyQvia and TAK-881 in CIDP: a phase 3 design. Presented at EAN-2025

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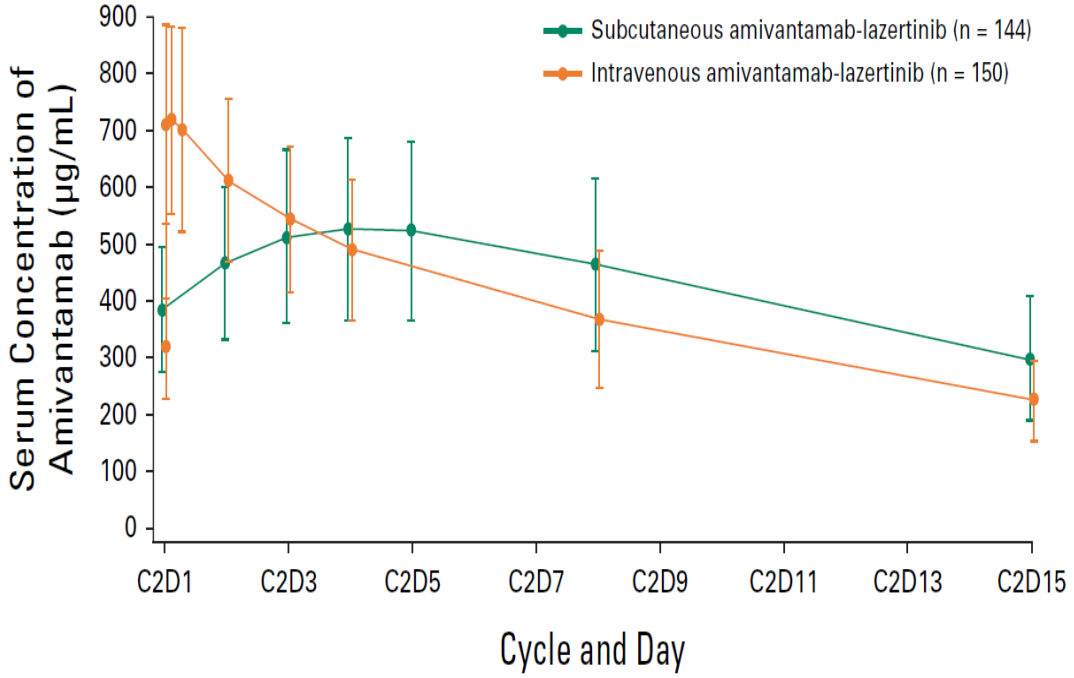
Potential Advantages of SC Dosing From the Start[1]

- Phase 1 SC Dose Escalation Study
  - Expect to escalate to a dose level associated with higher overall exposure if toxicity is driven by C_{max}
- Recommend Phase 2 Dose will entirely reflect advantages of SC dosing
  - This could include lymphatic trafficking, longer duration on therapy due to better tolerability, higher exposure for PK parameters associated with efficacy



1. Leighl, N.B. et al. J Clin Oncology, 42: 3593-3605 (2024)

Benefits of SC Delivery of a Bispecific Antibody[1]: Lessons Learned from IV vs SC Non-Inferiority Trial Make a Case for SC Dosing from the Start

PALOMA-3 Results (Amivantamab PH20 vs Amivantamab IV (each with lazertinib in EGFR-Mutated NSCLC)

- Shorter infusion time: SC median less than 5 minutes vs. up to 5 hours IV on each of two days
- 5-fold reduction in infusion related reactions: 13% for SC vs. 66% for IV
- **Longer Duration of Therapy (HR = 0.86, P>0.05)**
- **Higher Exposure: geometric mean ratio of $C_{troughC4}$ = 1.43 (90% CI, 1.27-1.61)**
- **Lymphatic Trafficking**
- Longer duration of response: median 11.2 months SC vs. 8.3 months IV among confirmed responders (response rate was comparable (30% SC vs. 29% IV)
- Longer progression free survival: median 6.1 months SC vs. 4.3 IV
- Exploratory Endpoint: Longer overall survival for SC compared to IV (HR= 0.62, P=0.02)

1. Leighl, N.B. et al. J Clin Oncology, 42: 3593 (2024)

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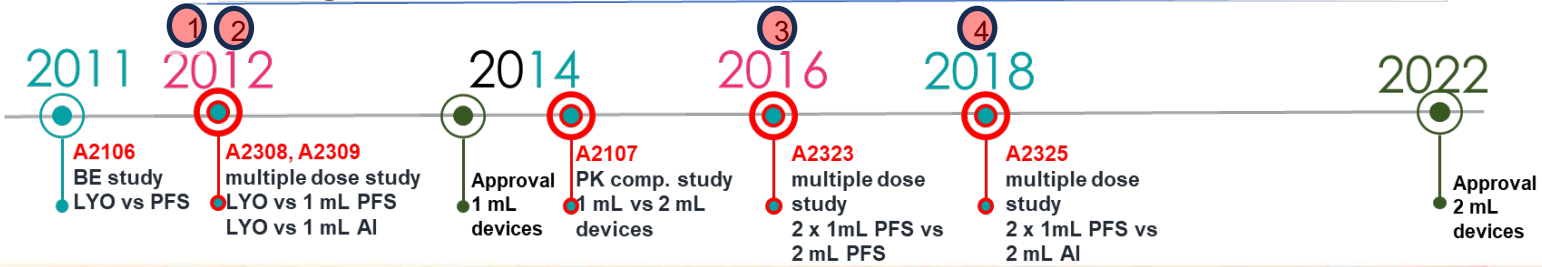
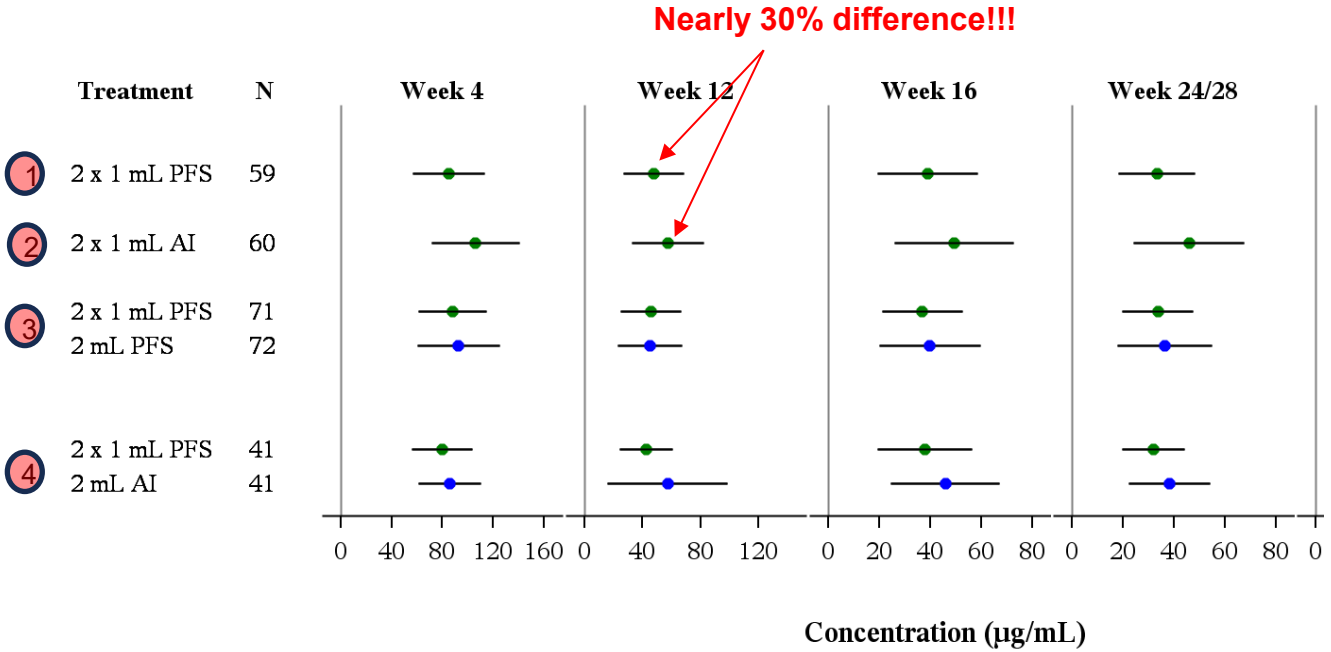
Consider timely bridging strategies!

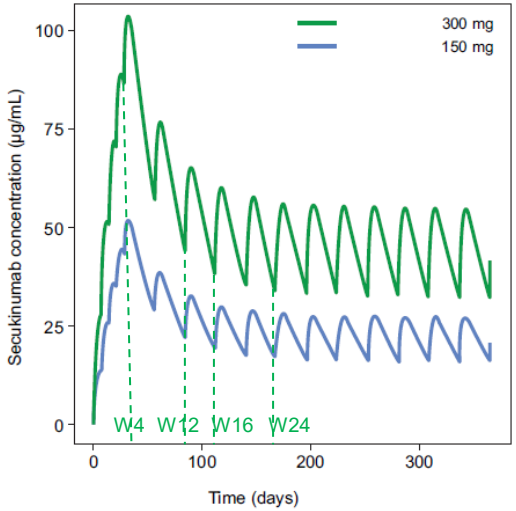
Are so many studies and is so much time needed? Probably not anymore

	From	To	Clinical study	HV/Patients	Number of subjects / arms	HA request	Comment
	300 mg, < 1 mL LYO,	300 mg, 2 x 1 mL PFS	7A2106 single dose BE	HV	141 / 2	N	with excipients change from LYO to PFS
1	150, 300 mg 1 or 2 x 1 mL LYO	150, 300 mg 1 or 2 x 1 mL PFS	7A2308 multiple dose Phase 3	Pso	174 / 3	Y	
2	150, 300 mg 1 or 2 x 1 mL LYO	150, 300 mg 2 x 1 mL AI Delta	7A2309 multiple dose Phase 3	Pso	177 / 3	Y (FDA only)	
	300 mg, 2 x 1 mL PFS or 2 x 1 mL AI Delta	300 mg, device prototypes	7A2107 single dose – PK comparability	HV	122 / 6	N	Abdomen/thigh, injection time comparison
3	300 mg, 2 x 1 mL PFS	300 mg, 2 mL PFS	7A2323 multiple dose Phase 3	Pso	214 / 3	Y	Abdomen/thigh comparison
4	300 mg, 2 x 1 mL PFS	300 mg, 2 mL AI YpsoMate	7A2325 multiple dose Phase 3	Pso	122 / 3	Y (FDA only)	Abdomen/thigh comparison



Things can go wrong in Cross-Study Comparisons with Sparse PK[1]



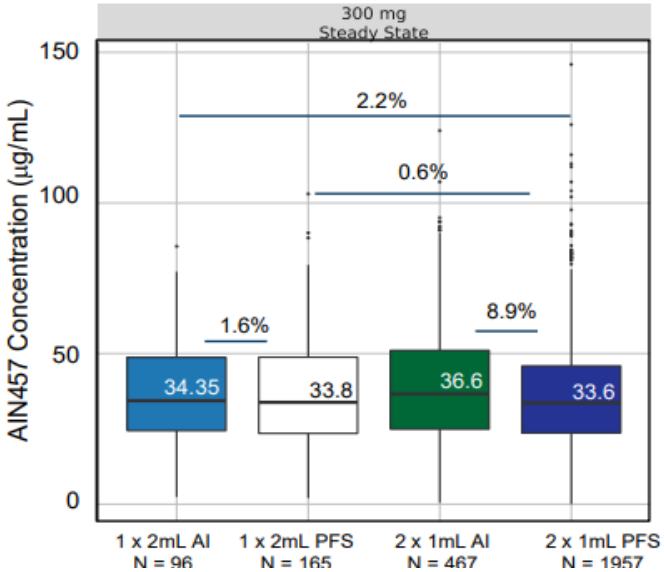


Simulated concentration profiles 300 and 150 mg with subcutaneous dosing regimens derived from phase 3 trials. Patients were simulated to receive secukinumab at baseline; weeks 1, 2, and 3; and then every 4 weeks from week 4 to week 48.

1. Bruin G, et al. A case study of bridging from a lyophilizate formulation to an autoinjector for patient self-administration *Development of Biopharmaceutical Drug-Device Products, 2020, Chapter 34*, Springer

Combined Ph 3 Studies with Psoriasis (PsO) and Psoriatic Arthritis (PsA)

No impact of Drug-Device-Combination-Product on PK, clinical efficacy, and safety



Studies	N	2x1mL PFS	2x1mL AI	1x2mL PFS	1x2mL AI
A2308	135	X			
A2309	147		X		
A2323	323	X		X	
A2325	181	X			X
F2312	236	X			
F2318	320		X		
F2342	570	X			
F2366	773	X			

4 PsO Phase 3 studies

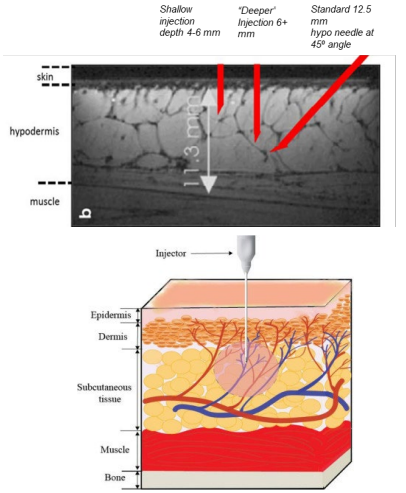
4 PsA Phase 3 studies

Are Injection Depth Differences between PFS and AI Significant Factors for PK?

Position: Comparability between PFS vs. AI injection depth in SC administration (e.g., 1.0 - 2.0 mL) for SC administration of mAb's may not raise significant PK questions and could be justified without a PK study measuring bioequivalence.

Supporting Information:[1]

- Standard 12.5 mm PFS needle inserted at a 45° angle reaches the same depth as a typical AI needle insertion depth (5-7.5 mm). Geometrical comparability is supportive.
- Delivery to SC tissue with either delivery device typically reaches the same SC biospace. Potential factors affecting PK (catabolism, intercellular diffusion and lymphatic drainage) for short delivery times will not meaningfully impact C_{max} (typically occurring after 5-7 days) or AUC.
- CDRH allows a wide acceptance criterion for AI injection depth in upper and lower specification limit (e.g., ± 2mm) based on potential tolerances of component parts suppliers. Minor differences in manual and AI injection depth should not be a critical factor.



Dingding et al, Transport and Lymphatic Uptake of Biotherapeutics Through Subcutaneous Injection, Journal of Pharmaceutical Sciences, Volume 111, Issue 3, 2022

[1] Hu P, Wang J, Florian J, Shatzer K, Stevens AM, Gertz J, Ji P, Huang SM, Zineh I, Wang YC. Systematic Review of Device Parameters and Design of Studies Bridging Biologic-Device Combination Products Using Prefilled Syringes and Autoinjectors. AAPS J. 2020 Feb 27;22(2):52. doi: 10.1208/s12248-020-0433-8. PMID: 32107671. https://pubmed.ncbi.nlm.nih.gov/32107671/

Are Injection Time Differences between PFS and AI Significant Factors for PK?

Position: Comparability of injection time for manually administered mAb (1.0-2.0 mL) PFS vs. AI for SC administration may not raise significant PK questions and an *in vitro* assessment without a PK study might be justified.

Supporting Information:[1-2]

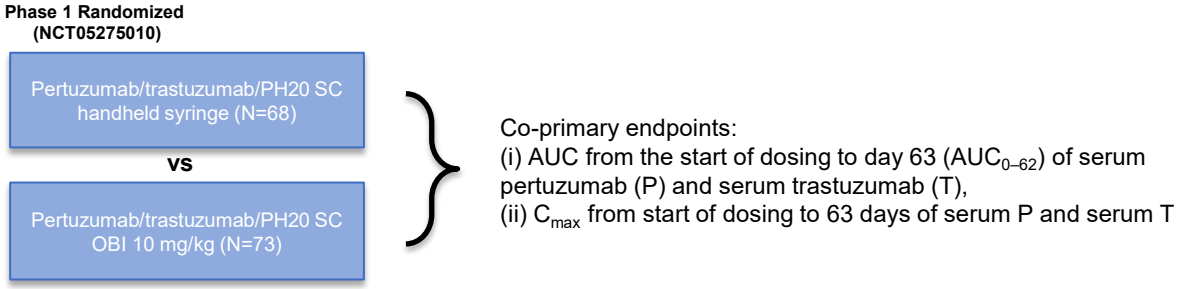
- Manual administration time depends on a user-specific "comfortable" application of force on the syringe plunger and can vary from 5-10 seconds for a 1 mL PFS.
- AI injection time is more consistent and typically varies (<10 seconds) for 1 mL volume depending on the AI technology.
- There are no studies or data to suggest that different injection times of this duration are a significant factor for BA/BE for typical mAbs where Cmax occurs 5-7 days post-dose. Studies support the case that injection times are insignificant for BE.[1,2]

[1] Portron A, et al. Study to Assess the Effect of Speed of Injection on Pain, Tolerability, and Pharmacokinetics After High-volume Subcutaneous Administration of Gantenerumab in Healthy Volunteers. Clin Ther. 2020;42(1):108-120.e1. doi: 10.1016/j.clinthera.2019.11.015.

[2] Bruin G, et al. Comparison of pharmacokinetics, safety and tolerability of secukinumab administered subcutaneously using different delivery systems in healthy volunteers and in psoriasis patients. Br J Clin Pharmacol. 2020;86(2):338-351. doi: 10.1111/bcp.14155..

More Recent SC to SC Device Trials are Simpler[1]

- Pharmacokinetic bioequivalence of the fixed-dose combination of pertuzumab (P), trastuzumab (T) and recombinant human hyaluronidase PH20 administered subcutaneously using a handheld syringe or an on-body delivery system in 1:1 randomized trial of male healthy volunteers



- The null hypothesis was to be rejected, and bioequivalence concluded, if the bounds of the 90% CI of the GMR of $AUC_{0–62}$ and C_{max} values for P and H administration by the OBI relative to the administration by the handheld syringe with hypodermic needle were entirely contained within the standard bioequivalence margins (0.80; 1.25) for all co-primary endpoints. 130 evaluable subjects provided 80% power at a 5% significance level, assuming a between-subject coefficient of variation of 40% and a “test” to “reference” ratio of 0.95

1 Wynne C et al. Pharmacokinetic bioequivalence of the fixed-dose combination of pertuzumab and trastuzumab administered subcutaneously using a handheld syringe or an on-body delivery system. J Cancer Res Clin Oncol 2025 Jun 14;151(6):188

Pertuzumab/trastuzumab/PH20 SC : pertuzumab 600 mg, trastuzumab 600 mg, 20,000 U PH20, recombinant human hyaluronidase PH20; OBI: on-body injector

More Recent SC to SC Device Trials are Simpler[1]

- Bioequivalence was demonstrated
- Automating a 5–8 min manual injection with an OBI could reduce healthcare provider workload by minimizing hands-on time and ensuring consistent drug delivery.

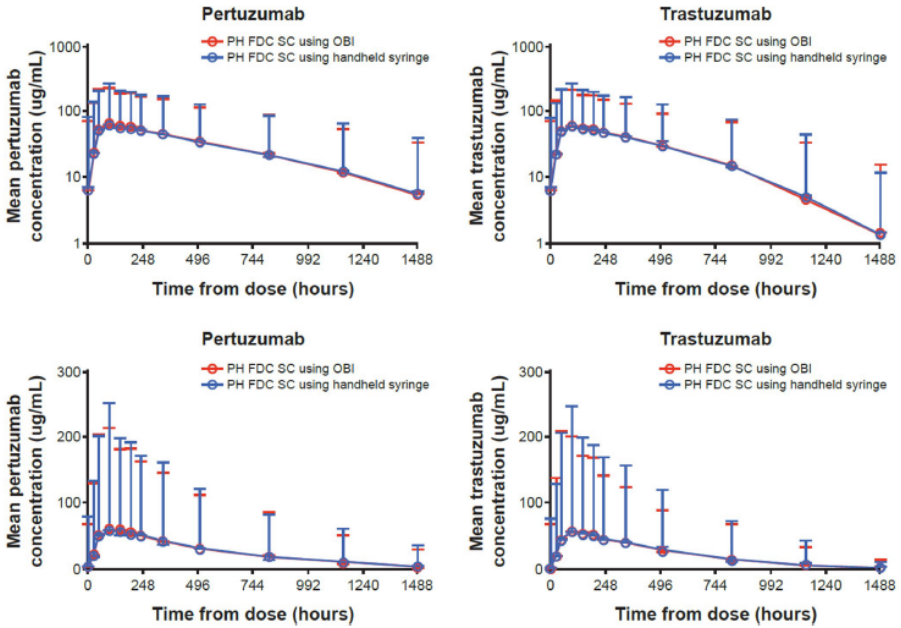


Fig. 2 Mean (±SD) serum concentration–time plots by treatment arm (log and linear scales). *FDC* fixed-dose combination; *H* trastuzumab; *OBI* on-body injector; *P* pertuzumab; *SC* subcutaneous; *SD* standard deviation

1 Wynne C et al. Pharmacokinetic bioequivalence of the fixed-dose combination of pertuzumab and trastuzumab administered subcutaneously using a handheld syringe or an on-body delivery system. J Cancer Res Clin Oncol 2025 Jun 14;151(6):188

PH FDC SC: pertuzumab 600 mg trastuzumab 600 mg/20,000 U rHuPH20, recombinant human hyaluronidase PH20; OBI: on-body injector

Agenda

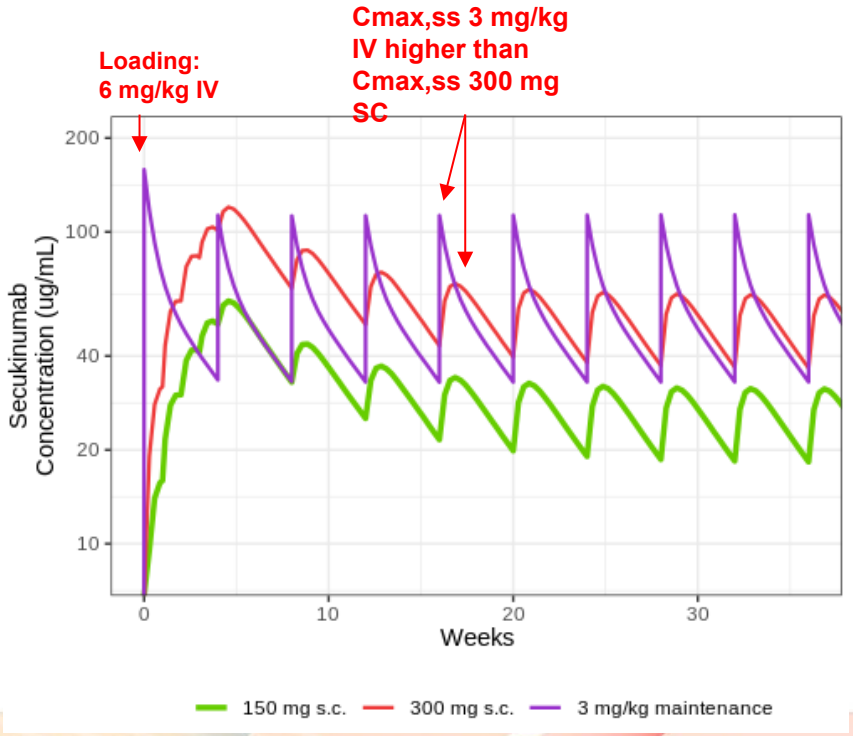
- From IV to SC; how to arrive at the right SC dose regimen
- From SC to SC; how to bridge from SC dose to another SC dose
- SC dosing from the start
- From SC to SC with a new Device
- *From approved SC back to IV*

From Approved SC to IV: How to arive at the Right IV Regimen?

Cosentyx, an IL-17A mAb

Brief development history (2019)

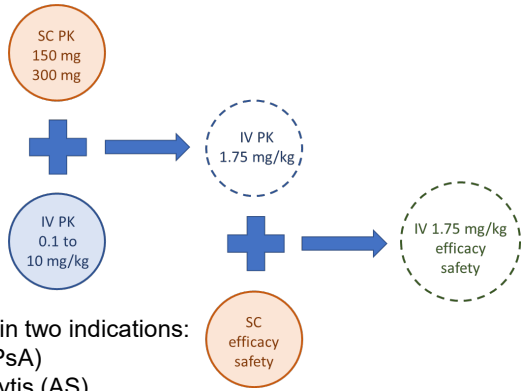
- Cosentyx was approved for doses of 150 mg SC and 300 mg SC in Spondyloarthritis (SpA) (2015)
- Two Phase III studies were conducted to test a new IV regimen (6 mg/kg IV loading, then 3 mg/kg IV, q4w) in SpA
- This regimen was discussed (and we thought agreed!) with FDA
- 2021: The IV studies were positive and confirmed the expected efficacy and safety profile like SC
- But FDA's Pre-BLA feedback:
  "... IV regimen appears to result in higher Cmax ..." and "We are concerned that your IV regimen may not have sufficient information to support the benefit-risk assessment ..., particularly for more rare and latent AEs"
- FDA also hinted at a potential next step using Model-Informed Drug Development (MIDD)



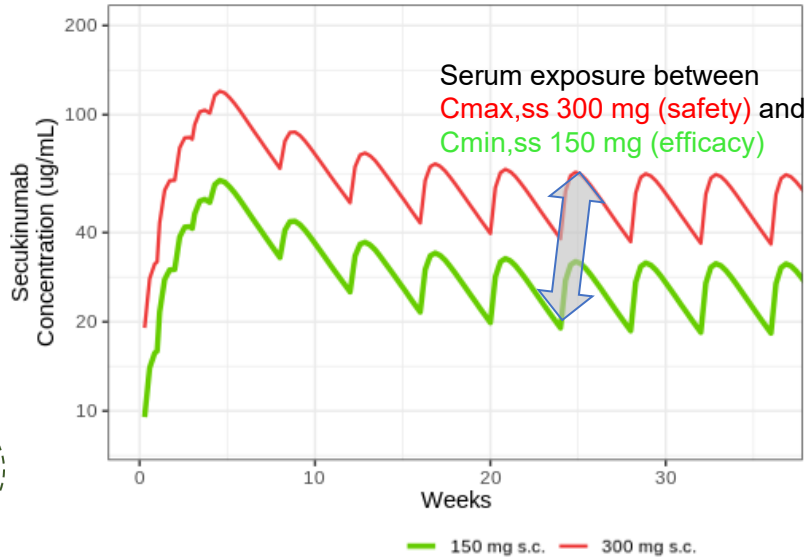
2022 - How can Model Informed Drug Development (MIDD) help our Case?[1]

1. Identification of a new, lower IV regimen that approximates the exposure of the s.c. regimens
2. Extrapolation of the efficacy and safety from the SC regimens to a lower IV regimen on the basis of: Same exposure with IV and SC will lead to same efficacy/safety

SC PK data available across three indications:
- Psoriatic Arthritis (PsA)
- Ankylosing Spondilytis (AS)
- nonradiographic-axial Spondyloarthritis (nr-axSpA)

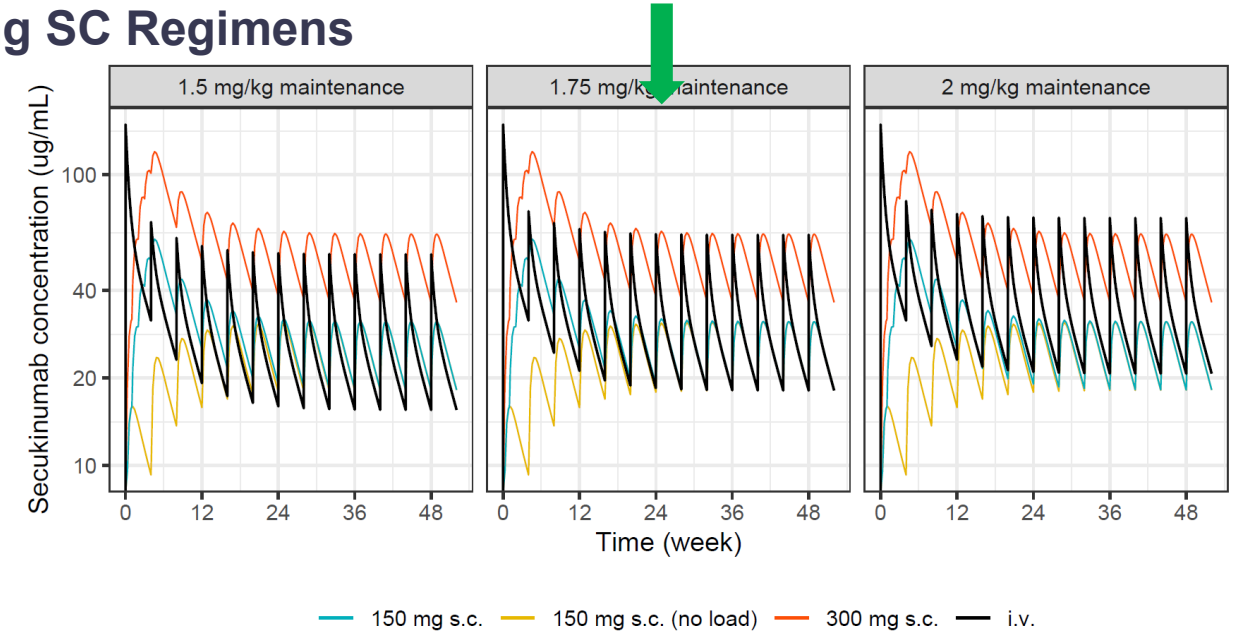


IV PK data available in two indications:
- Psoriatic Arthritis (PsA)
- Ankylosing Spondilytis (AS)



1. Dumortier, T., Valenzuela, G., Churchill, M., Mijatovic, J., Bruin, G., Pricop, L., Richards, H., Renard, D., Singhal, A. and Marathe, A. (2025), Model-Informed Drug Development-Based Bridging from Subcutaneous to Intravenous Secukinumab Dosing: Approval in Psoriatic Arthritis and Axial Spondyloarthritis. Clin Pharmacol Ther. https://doi.org/10.1002/cpt.3716

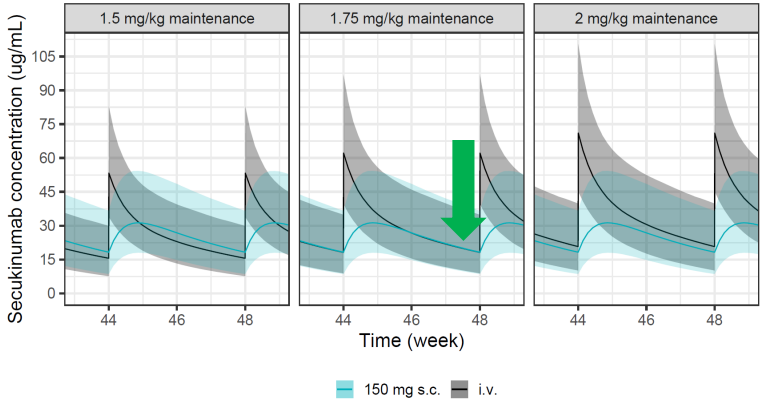
Predicted PK Profiles of three IV Regimens that Approximate the 150 mg and the 300 mg SC Regimens

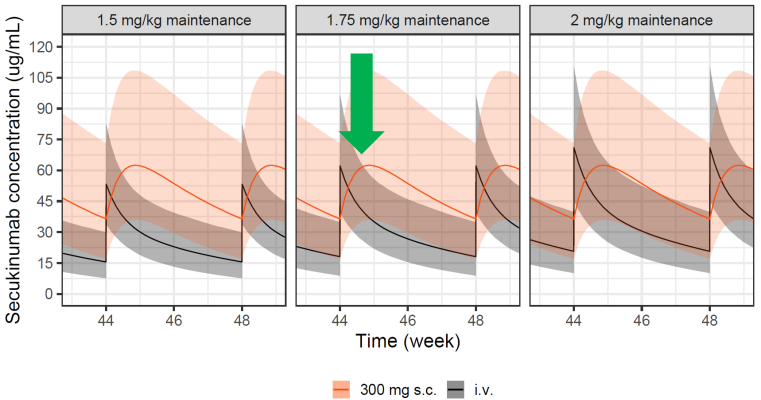


The three IV regimens comprise a 6 mg/kg loading dose at Week 0 followed by a maintenance with 1.5, 1.75, or 2 mg/kg administered q4w starting on Week 4.

The lines represent the median of the secukinumab concentration-time profiles predicted for 3000 PsA and 3000 axSpA subjects for each secukinumab regimen, as obtained from the final popPK model.

Distribution of PK Profiles at Steady-State for three IV regimens and the 150 and 300 mg SC q4w Regimen





The lines represent the median of the secukinumab concentration-time profiles simulated for 3000 PsA and 3000 axSpA subjects for each secukinumab regimen, obtained from the final popPK model. The ribbons correspond to the 90% prediction interval.

Maintenance regimen	Median (90% PI)		
	Cmin,ss (µg/mL)	Cavg,ss (µg/mL)	Cmax,ss (µg/mL)
1.5 mg/kg i.v. q4w	15.6 (7.6, 29.9)	25.1 (13.7, 45.7)	53.3 (34.0, 83.0)
1.75 mg/kg i.v. q4w	**18.1 (8.9, 34.8)**	**29.2 (16, 53.4)**	**62.1 (39.6, 96.9)**
2 mg/kg i.v. q4w	20.7 (10.2, 39.7)	33.4 (18.2, 61.0)	71.0 (45.3, 110.7)
150 mg s.c. q4w	18.2 (8.6, 36.5)	25.1 (12.3, 50.6)	31.3 (18.0, 54.3)
300 mg s.c. q4w	36.4 (17.2, 73.2)	50.1 (24.6, 101.2)	62.6 (36.1, 108.7)

Conclusions

- Bridging from IV to SC currently involves PK-based (single) dose finding and non-inferiority Phase 3 studies with short time to endpoint, allowing broad labels
- Bridging from SC to SC may involve a streamlined single cohort trial of fewer than 50 patients
- SC dosing from the start may mitigate C_{max} based toxicities to optimize exposures associated with response
- Bridging to to-be-marketed Drug-Device-Combination-Products might be possible by leveraging historical (PK) data and/or by using platform device technology
- Clinical bridging trials will likely be smaller and increasingly complemented by MIDD approaches