
# VALOR Study Investigator Meeting

# Chile, Colombia, Mexico, Argentina Pre-Session

March 1, 2024

# Priovant Background

## Rarer High Morbidity/Mortality Indications Have Been Historically Neglected By JAKi Drug Development

JAK inhibitors approved or in industry-sponsored P3[1]

- Rheumatoid arthritis: **8**
- Psoriatic arthritis: **4**
- Ulcerative Colitis: **4**
- Myositis, uveitis, scleroderma, Behcet's, sarcoidosis, IgG4-RD, polychondritis, polymyalgia rheumatica: **0**

## Brepocitinib Is Distinctively Optimized For Highly Inflammatory Conditions With High Morbidity/Mortality

- Optimal suppression of type I IFN
- Suppression of type I IFN, type II IFN, IL6, IL12, IL23 with single asset
- Oral once-daily administration
- Success in 6 pbo-controlled P2 studies across rheumatic, dermatologic, and GI indications

## Priovant Created To Address This Need / Opportunity

- Dedicated to rarer autoimmune disease with higher morbidity/mortality and few available therapies of any mechanism/modality
- Initial focus on developing and commercializing brepocitinib for these indications
- Initial indication: dermatomyositis
  - ✓ Large unmet need
  - ✓ Strong clinical and mechanistic rationale
  - ✓ No approved targeted therapies of any modality; no other oral therapies in P3 development
- Strategy of moving directly into single P3 study to get an approved therapy as quickly as possible, given unmet need and strong rationale
  - ✓ VALOR: Largest interventional clinical study ever undertaken in dermatomyositis (N=225)

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1. Includes approvals / industry-sponsored development programs in any geography; excludes brepocitinib

# VALOR Study Today

- 155 subjects enrolled globally, with additional 30 currently in screening
- Tracking to wrap up screening sometime in May or early June
- Would love to help every site here enroll at least two qualified patients before enrollment concludes → 3-4 screenings over next 2-3 months (best to line up screenings for March/April)
- Need a concentrated effort from site teams and Priovant team, working directly / hand-in-hand for this to succeed
  - Patient identification and pre-screening process
  - Screening logistics
  - Study execution

# Priovant Support During Study Execution

| Before Screening | During Screening | During Study Treatment |
|---|---|---|
| **Direct partner to identify potential candidates and prepare for complex screening operations** | **Dedicated team to troubleshoot operational delays and ensure screening process goes smoothly and quickly** | **Frequent monitoring of patient journey through study, including steroid taper and rescue medication**<br>More on this tomorrow… |
| **Examples** | | |
| 1. Review of active patients in database to identify pathway to screening<br>2. Addressing protocol questions to confirm eligibility for screening<br>3. Confirmation that all necessary supplies and materials are on site for screening<br>4. Troubleshooting logistical challenges ahead of the visit (e.g., lab courier collection time is before visit) | 1. Tracking every sample to verify they are shipped and processed correctly, flagging to sites in real time if repeats are required<br>2. Management of data entry and readout of results to enable fast adjudication process (when applicable)<br>3. Calls with medical monitor to quickly align on next steps to randomizing patient as soon as possible | 1. Outreach as patient reaches start of steroid taper to align on approach<br>2. Meetings with medical monitor ahead of patient rescue to address questions and discuss correct set of next steps<br>3. Real-time discussions with medical and clinical operations teams as issues arise with study supplies, patient visit logistics, etc. |

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# Division Of Responsibities Between Priovant and Resolution

| Priovant Directly | Resolution |
| --- | --- |
| ➢ All topics related to patient identification, pre-screening, and scheduling of screening<br>➢ All topics related to screening process (logistics and substantive eligibility)<br>➢ Questions about protocol or patients in study<br>➢ Medical monitoring | ➢ On-site monitoring visits<br>➢ Ensure sites are appropriately maintaining regulatory documents<br>➢ Review data entry on ongoing basis for accuracy and completeness<br>➢ Assist in resolving pending action items and queries at site<br>➢ IP accountability |

# Priovant Team Here At IM

**Ade Adeboye**

**MEDICAL MONITOR**

**Courtney Cupples**

**FLUENT/BILINGUAL IN SPANISH**

Sergey Pavlenko

Matt Ackermann

Daniel Herz-Roiphe

Whitney Holmes

Noriko Iikuni

Scott Jones

Sabrina Pogrebivsky

Paul Mudd

Lindsey Rios

**Drew Webster**

**PROFESSIONAL PROFICIENCY IN SPANISH**

Ben Zimmer

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# Prescreening Best Practices

# Best Practices for Enrolling Patients over the next 3 months

We have seen high-enrolling sites use these key tactics to identify high-quality patients quickly

## Perform thorough database search

- Using EMR system or informatics division, identify patients who meeting the minimum criteria

1. Aged 18-75
2. BMI < 40
3. DM diagnosis
4. No active cancer diagnosis

Review the medical records of these patients

1. Current DM medications
2. Medical History
3. DM diagnosis date
4. Current DM symptoms
5. Current provider (if outside your own clinic)

## Review patients with Priovant MM

Based on the results of the database search, review the records and details of each pt with the Priovant Medical Monitor and Clinical Operations team

- Determine screening timeline
  - Medication washouts
  - Medication stabilization

- Determine any outstanding questions for patient/provider based on medical history

- Use Priovant team to make your patient review **faster, more efficient, and more likely to ID qualified pts**

## Provider/PI to contact patients

**Direct outreach from the PI** or their current provider can increase patient responsiveness to learning about the clinical trial and ultimately their participation.

Once the patient has expressed interest in participation, then the SC/scheduler can reach out to determine screening date

## Schedule pre-screening visit

For new pts, start with a pre-screening visit to:
- determine current skin/muscle symptoms
- confirm current medication
- gauge pt interest and how to best support their participation

# A complete understanding of medication history can prevent screening and randomization delays

## Gather information on previous and current DM medications early in the process

- DM medications need to be stable prior to screening and randomization
  - Corticosteroids – stable 4 weeks prior to baseline
  - ISTs/HCQ – stable 12 weeks prior to baseline
- If a patient changes a dose immediately prior to screening or during the screening period, this may unnecessarily delay randomization and the start of study drug
- **Confirm patient medications** during pre-screening visit or as the screening is being scheduled
- **Remind the patient:** Do not change any medications without discussing with the PI first
- **Ensure they have stopped any prohibited medications**
  - IVIG – 12-week washout
  - Most ISTs (if pt is taking 2) – 12-week washout
  - These washouts will determine screening timeline

Accurate and complete patient medication documentation early in the process will help mitigate delays in the enrollment process

# Patients often require a medication stabilization or washout

## Review DM conmeds with the Priovant team to determine the best screening timeline

- **Medication washouts and stabilizations can take place *during the screening window***
  - **Screening window is up to 8 weeks**
  - **Most washouts and stabilizations are to *randomization***
  - **Screenings should be scheduled prior to the completion of washouts/stabilizations**

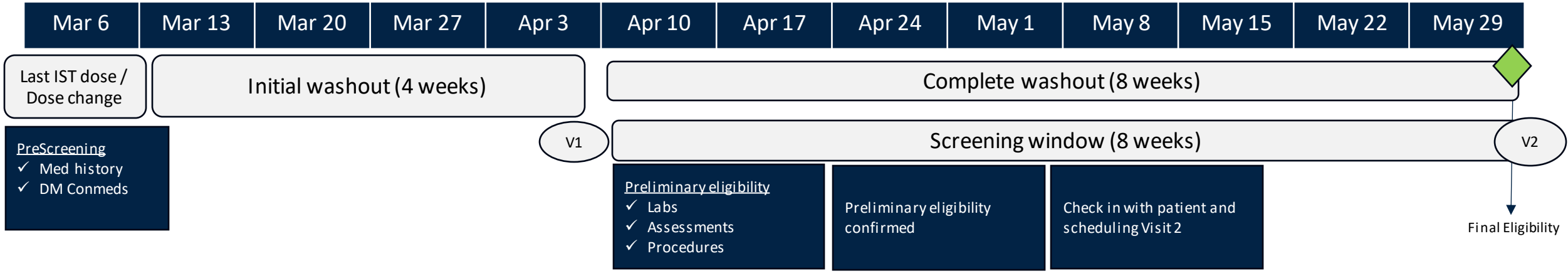
| **Corticosteroids need to be ≤ 20 mg at least 4 weeks prior to randomization** | |
|---|---|
| Pt is on steroid dose higher than 20 mg, but symptoms are inclusionary and pt is eager to screen | • Screening should be scheduled asap<br>• Date should be determined to allow to 4 weeks of taper to 20 mg<br>• Complete CS stabilization for the 4 weeks prior to V2 |
| Pt is on low-dose CS or no steroids, but PI wishes to increase or add steroids prior to starting trial | • CS dose change and screening should be scheduled asap<br>• Symptoms after CS dose change need to be inclusionary at screening and baseline<br>• Keep CS dose consistent for 4 weeks prior to V2 |

# Determine the best schedule for screening to prevent patient burden

## Best practice is to complete washout during screening window and confirm eligibility as early as possible

| **One Immunosuppressant Therapy is allowed as background; most washouts and stabile periods are 12 weeks prior to randomization** | |
|---|---|
| Pt is on MTX and Aza; symptoms and other history is inclusionary | • Determine which IST should be washed out immediately<br>• Initiate washout and schedule screening for 4 weeks after start of washout<br>• Schedule V2 for 8 weeks after screening (12-week washout) |
| Pt is on MMF but had a dose change recently. Pt has active disease and is eager to proceed to screening | • Screening should be scheduled for 4 weeks after the dose change<br>• Schedule V2 for 8 weeks after screening (12-week stabilization) |

Example Timeline

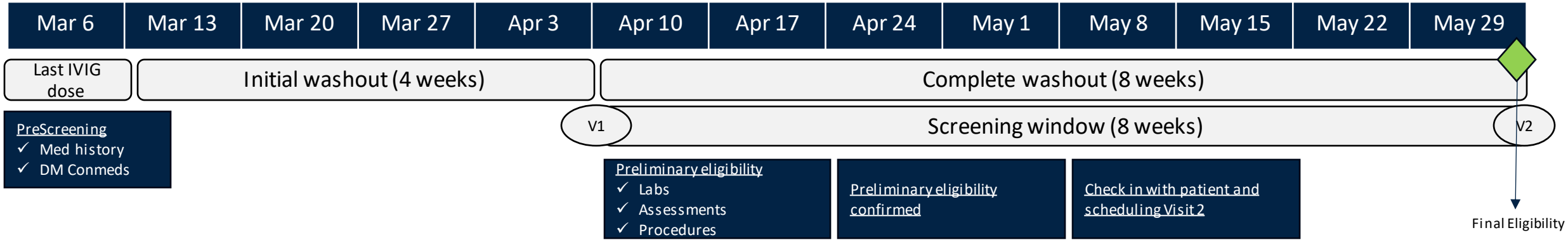


# Patients often require a medication stabilization or washout

## Review DM conmeds with the Priovant team to determine the best screening timeline

| **Prohibited meds can be washed out according to timeline in protocol; washouts are to randomization** | |
|---|---|
| Pt is currently on IVIG every 4 weeks but isn't responding fully. Pt is willing to try a washout, but is nervous about a 12-week washout. Last dose was 2 weeks ago. Symptoms are currently eligible. | • Washout should be communicated as a 4-week washout to screening<br>• Screening can be scheduled for a date in 2 weeks (4 weeks after the last dose). Pt should postpone next dose of IVIG to determine eligibility for trial.<br>• If pt is eligible, V2 can be scheduled 8 wks from screening (12 wks from last IVIG dose)<br>• If pt is not eligible, they can continue with IVIG |
| Pt is currently on Rituximab every 6 months, but disease is still active and they want to try an oral therapy. Last dose was 12 weeks ago. Symptoms are currently eligible. | • Screening should be scheduled for a date in 4 weeks (16 weeks from last RTX dose)<br>• If pt is eligible, V2 can be scheduled 8 wks from screening (24 wks from last RTX dose)<br>• If pt is not eligible, they can continue with RTX without having missed a dose |

Example Timeline



# Identify patients with active disease and discuss medications with PVT

## Key takeaways:

- Identify patients who meet the minimum criteria:
  - Age 18-75
  - BMI < 40
  - No active cancer diagnosis
  - DM diagnosis with active skin and muscle dx
- Gather accurate information about patient medications and medical history to prevent delays in screening and randomization
- Discuss current medications with the PVT team
  - Identify the ideal screening timeline based on current meds/washouts
    - Screenings can often happen earlier than expected
    - Optimize timing to allow pts to start IP as soon as possible
- PI/physicians should contact patients to discuss trial prior to scheduling

# Screening Logistics Best Practices

# Screening Best Practices are Essential for Enrollment Success

**The screening process for the VALOR study is complex and requires your close attention to our study guides and best practices, as a small deviation from the correct process could extend the screening period by several weeks and/or increase patient burden**

Top reasons for extended screening period:

1. Cancelled or delayed lab assessments
2. Delays in entering critical data into EDC shortly after screening visit
3. Surprise changes in medications or new information on medical history that impact timeline to randomization
4. Delays in scheduling key procedures required for the study (i.e., chest x-ray, CT)
5. Lack of preparation ahead of screening to ensure all necessary materials are available

**Over the last 12 months we have developed and refined a set of best practices to support our sites in mitigating these delays and accelerate the screening process.**

# Fast and Accurate Data Entry for a Seamless Screening Process

**Highest Priority Data (Entered Within 24 Hours)**

1. EULAR Idiopathic Inflammatory Myopathies
2. Medical History
3. MMT-8
4. CDASI
5. Dermatomyositis Prior and Concomitant Meds

**All other data must be entered within 72 hours**

**Timely data entry improves the screening process for several reasons:**

1. The faster the data is in, the faster we can confirm eligibility and bring the patient back in for randomization
2. Adjudication may be required to confirm eligibility, and all data must be entered to start this process
3. Our medical monitoring team needs to review the comprehensive list of DM medications and flag if a washout or dose stabilization impacts randomization timelines. Catching these early in the window can mitigate major impact to enrollment timelines.
4. Additional follow-ups may be required based on the subject's medical history (e.g., spirometry for ILD)
5. We can avoid unnecessary follow-ups for a patient if they are already excluded based on data entered in the EDC

**Delays in data entry will directly impact the length of time your patient will spend in the screening period**

# Cancelled and Delayed Lab Assessments are #1 Cause of Extended Screening Period

There are numerous operational complexities with lab collection and shipping that require your careful attention, as errors could cause multi-week delays to randomization

Below are the top issues we've seen across over 280 screenings:

| Issue | Mitigation Tactics |
|---|---|
| **QuantiFERON TB test is cancelled due to operational errors**<br>*The TB test is cancelled for >25% of patients* | • Use your site lab or a local lab to perform the QuantiFERON test instead<br>• Have lab tech, or whoever collects labs, watch prep video and read through extensive prep materials ahead of and during performing the QFT<br>• Send Priovant and ReSolution photos of the sample ahead of shipping to confirm all looks correct |
| **HBV DNA test is required to confirm Hepatitis B serology findings, but test has a long turnaround time to result** | • Rather than waiting for serology results to send in an HBV DNA sample, send it in with the rest of the screening samples<br>• Provide Priovant with the requisition # and airway bill so we can have ACM expedite the result |
| **Lab supplies are missing on the day of screening** | • Check supplies at least a week before the screening, including the individual tubes within the kits<br>• Flag to Priovant if something's missing so we can help identify a fast solution<br>• Do not deviate from the lab manual (e.g., using a different tube) without discussing with Priovant and your CRA first |
| **Courier not available for day-of collection of the samples**<br>*If samples are collected too late in the day, you may have to ship next day* | • Schedule courier in advance so that they can pick up the samples in the morning the next day<br>• Store the samples at the conditions outlined in the lab manual<br>• Ambient samples cannot be shipped on Fridays, or they will be cancelled at ACM. If ambient samples would have to be shipped on Friday, schedule a different time the following week to collect the ambient samples from the subject |

# Identifying One Primary Study Member to Master the Lab Sample Management Process Helps to Mitigate Risks

Due to the complexities of the lab sample collection for this study, you should dedicate one study team member to internalize the best practices and partner with Priovant to ensure the process goes smoothly

The dedicated lab team member should take the following approach to maximize success:

1. Spend 1:1 time with Priovant team ahead of patient screenings to review study-wide best practices and lessons learned from previous screenings
2. Review lab manual in detail ahead of patient visits, including instructions on how to process and ship each sample required for the visit
3. Print out the lab quick reference guide and use as a reference guide during the patient visit
4. Leverage Priovant team in real-time during patient visit to address questions around how to process, store, or ship samples

**In our experience, sites that have assigned the labs to one primary team member and invested in their training and preparation have significantly decreased the number of lab sample errors across all patient visits**

# Additional Best Practices That Support Accelerated Enrollment

We've gathered valuable insights across all of the patients screened to date and have identified the below best practices as additional areas of focus to minimize the time in screening and associated patient burden

| | |
|---|---|
| **Review meds and medical history ahead of screening** | If you identify any changes in medications (e.g., steroid dose) or medical conditions that may impact randomization timelines, flag this to the Priovant team.<br><br>We also encourage you to ask the patient at their screening visit if they've started any new medications, such as topical steroids |
| **Schedule Baseline in advance** | If all best practices are followed, screening only takes ~2 weeks, so it's best to get a V2 on the schedule as soon as possible.<br><br>While the patient is with you in clinic for the screening visit, you should confirm a date with them that works for the baseline visit. If lab re-draws are needed, a visit will already be on the calendar |
| **Schedule CXR / CT and spirometry in advance** | Review the protocol ahead of time and determine what procedures your subject will require. If needed, schedule the CT, CXR, or spirometry as part of the screening visit to avoid further delays |
| **Quick turnaround time with ECG** | Transmit the ECG the day of screening and enter results into the EDC as soon as their available. Banook should release the report within 24 hours of transmission |
| **Set up logistics in advance of screening** | Schedule any services you need (lab courier, patient travel, dry ice delivery) at least one week before the screening. This will give you sufficient buffer to flag if you have any issues |

# Lessons Learned from Top Enrollers – Dr. Medrano and Dr. Bozan

# Patient Enrollment Lessons Learned – VALOR Study

- **MSc. Gabriel Medrano Ramírez**

  Medicina interna –Reumatología

  Hospital General de México “Dr. Eduardo Liceaga”

  Hospital Angeles / CITER ( Centro de Investigación y Tratamiento de las Enfermedades Reumáticas )

  **México**

# Challenge

- Dermatomyositis is a rare disease.

- The average age- and sex-standardized
  - Annual incidence 2.8–3.0 cases per 100,000 adults.
  - Prevalence was 28.6 cases per 100,000 adults.

- In the US:
  - Incidence of DM has been 0.1 and 1.8 cases per 100 000 person-years

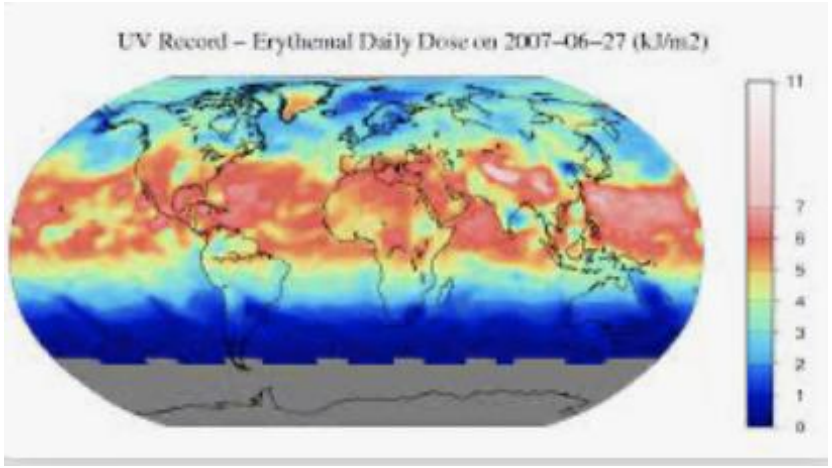


Osman, M., Martins, K.J.B., Wong, K.O. *et al.* Incidence and prevalence, and medication use among adults living with dermatomyositis: an Alberta, Canada population-based cohort study. *Sci Rep* **13**, 16444 (2023). https://doi.org/10.1038/s41598-023-43880-7
Meyer . Incidence and prevalence of inflammatory myopathies 2015 Jan;54(1):50-63. doi: 10.1093/rheumatology/keu289.

# Incidence and prevalence (cases/million)

| Author | Period | Country | I | P |
|---|---|---|---|---|
| **Medsger (1970)** | 1947-68 | EU | 2.7 – 10.8 | |
| **Benbassat (1980)** | 1960-76 | Israel | 0.8 – 2.1 | |
| **Hanissian (1982)** | | EU | 0.6 – 7.7 | |
| **Araki (1983)** | | Japan | | 2.4 |
| **Koh (1993)** | | Singapore | 7.7 | |
| **Symmons (1995)** | | Ireland | 1.9 | |
| **Weitoft (1997)** | 1984-93 | Sweden | 7.6 | |
| **Patrick (1999)** | 1989-91 | Australia | | 0.6 – 7.6 |
| **Darin (2000)** | 1979-94 | Sweden | | 25.0 |
| **Phillips (2000)** | 1988-98 | Australia | | 9.3 – 35.3 |
| **Badrising (2000)** | 1965-99 | The Netherlands | | 10 – 16 |
| **Felice (2001)** | 1992-2000 | EU | | 14.5 – 18 |

# UV Radiation and Dermatomyositis




ARTHRITIS & RHEUMATISM
Vol. 46, No. 7, July 2002, pp 1885–1893
DOI 10.1002/art.10358
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## Differences in Idiopathic Inflammatory Myopathy Phenotypes and Genotypes Between Mesoamerican Mestizos and North American Caucasians

Ethnogeographic Influences in the Genetics and Clinical Expression of Myositis

Ejaz A. Shamim,[1] Lisa G. Rider,[1] Janardan P. Pandey,[2] Terrance P. O'Hanlon,[1] Luis J. Jara,[3] Eduardo A. Samayoa,[4] Ruben Burgos-Vargas,[5] Janitzia Vazquez-Mellado,[6] Jorge Alcocer-Varela,[7] Mario Salazar-Paramo,[8] Abraham Garcia Kutzbach,[9] James D. Malley,[10] Ira N. Targoff,[11] Ignacio Garcia-De La Torre,[12] and Frederick W. Miller[1]

***Conclusion.*** **IIM in Mesoamerican Mestizos differs from IIM in North American Caucasians in the frequency of phenotypic features and in the immune-response genes predisposing to and protecting from myositis and anti–Mi-2 autoantibodies at 4 chromosomal loci. These and other data suggest the likelihood that the expression of IIM is modulated by different genes and environmental exposures around the world.**

# Success Factors of Site

-Public hospital
    -Concentration
    -Reference

-Private clinic
    -Reference

# Success Factors of Site

**Asociación Mexicana de Miopatías Inflamatorias A.C - AMMI**

Medicina y salud · 4,7 de 5 (24 opiniones) · $ · 0.8 km · Siempre abierto · 4,6 mil seguidores

-Redes sociales

En "AMMI" promovemos y difundimos información acerca de Dermatomiositis y Polimiositis, buscando concientizar al mundo sobre estos padecimientos.

4 publicaciones en las últimas 2 semanas

**Asociación Mexicana de Miopatías Inflamatorias A.C - AMMI** transmitió en vivo.
24 de agosto de 2019 ·

¿Qué es una #MiopatiaInflamatoria? ¿Cuál es la importancia del tratamiento correcto y oportuno?
Dr. Gabriel Medrano Ramirez, Reumatólogo
#TodosSomosAMMI


**Asociación Mexicana de Miopatías Inflamatorias A.C - AMMI**
17 de febrero a las 08:33 ·


**Asociación Mexicana de Miopatías Inflamatorias A.C - AMMI**
transmitió en vivo.
17 de febrero a las 08:30 ·

# Success Factors of Site

- Willingness to engage with Priovant team to navigate complex questions
- Quick turnaround time to bringing patient in for follow-up

- Review of patient profiles with medical monitor ahead of screening to maximize chance at enrollment.
- Close and fast contact to resolve doubts
  (Patient 38-105-1005)

# Additional Challenges to Enrolling the VALOR Study

- **Issue:** Low lymphocytes due to the disease are more frequent than expected
  - **Rationale:** FDA requires the ALC threshold to be ≥ 0.75. While the value can't be lowered and Priovant recognizes these patients have low ALC as part of their disease, Priovant is committed to partnering with sites to find a plan for the patients that maximizes their opportunity to enroll in the study
  - **Solutions:**
    - Protocol 6.0 allows for 3 total screenings, with two ALC tests per screening. Subjects with borderline ALC have a greater probability of an inclusionary value during one of those tests
    - Sites often monitor the ALC locally and wait to re-screen a patient until the value is inclusionary
    - Sites can work with Priovant's medical monitoring team to discuss how modifications in ISTs or other concomitant medications may result in a higher ALC

- **Issue:** In the ECG the QTCF, is not adjusted for men and women (ex: 450 st - 460 )
  - **Rationale:** Pfizer performed a formal QT study, which suggested that brepocitinib has a small effect on QT prolongation. Therefore, Priovant adopted a conservative approach with the criteria for QTcF interval
  - **Solutions:**
    - Protocol 7.0 allows for a repeat ECG, if deemed appropriate by the medical monitor

- THANK YOU

# VALOR Study Investigator Meeting

## New Site Session Presentation

**Dra. Francisca Bozan and Eleonor Peña**

CIEC-PMR

Probity Medical Research

# Centro Internacional De Estudios Clínicos

# Perspectiva de Investigadora Principal

- Dermatología y Reumatología con especial interés en el tema.
- Médicos formados en Hospital Clínico Universidad de Chile.
- Amplia red de conexión.
- Sistema de Salud Nacional.

CIEC-PMR
Probity Medical Research
Centro Internacional De Estudios Clínicos

# Perspectiva de Coordinadora

- Plan de trabajo estructurado.
- Conocimiento de la patología.
- Celeridad en los procesos.

CIEC-PMR
Probity Medical Research

**Centro Internacional De Estudios Clínicos**

# Key Takeaways from Top VALOR Study Enrollers

**The following best practices drive success in enrolling high-quality patients on fast timelines:**

- Willingness to engage with Priovant team to navigate complex questions
- Review of patient profiles with medical monitor ahead of screening to maximize chance at enrollment

**Ade Adeboye**

**MEDICAL MONITOR**

- Open to exploring alternative strategies in partnership with Priovant to avoid delays in screening (e.g., local TB test)
- Fast data entry, with critical data entered in EDC within 24-48 hours of screening
- High-quality execution of central labs, with minimal cancellations due to operational mistakes
- Quick turnaround time to bringing patient in for follow-up visits

# SC Breakout Session

# During Screening: Leading Issues that Delay Screening Process

Across over 280 screenings, we have gathered valuable insights on the leading causes of a long screening window, as well as tactics to mitigate these issues

1. **Lab test cancellations and confirmatory testing**
2. **Late and incomplete data entry**
3. **Delay in ECG upload and reporting results**
4. **No availability of CT / CXR scans and other assessment results**
5. **Lack of logistical preparation before screening**

**By working directly with the Priovant team throughout screening, we will help you proactively solve for the operational hurdles and avoid increasing patient burden and prolonging the screening window**

# Lab Test Cancellations and Confirmatory Testing

## QuantiFERON TB Test – Priovant Recommends Using Local Lab

1

**~28% of QuantiFERON TB tests sent to the central lab are cancelled due to operational errors**

We *highly* encourage sites to perform the QuantiFERON test at a local lab, if that option is available. If you perform the test locally, please follow the below steps:

1. Please ensure that an order is written for this patient's TB test in advance so that the sample can be collected on the day of screening
2. While on-site for the screening, patient should go the blood draw clinic to get their QuantiFERON TB samples drawn and processed
3. Please invoice the study for the costs of the test
4. Once available, please send redacted test results to Drew Webster (drew.webster@priovanttx.com) and Ade Adeboye (ade.adeboye.@priovanttx.com)

**Sites using local labs experience drastically lower cancellation rates and their patients do not need to return for a burdensome visit to repeat the TB test**

# Lab Test Cancellations and Confirmatory Testing

## Best Practices for QuantiFERON Tests Performed with ACM

1

If you are unable to perform the QuantiFERON test locally and need to use the central lab option, please ensure you follow the below best practices closely

**1**

All tubes are stored at room temperature and properly filled with **the blood meniscus falling within the black bar on the label**

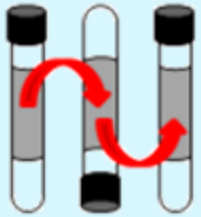
**Do not use butterfly needles** to draw blood for QuantiFERON TB tests – it has been shown to result in under-filled and hemolyzed samples. Use straight needles to collect these samples

Overfilled tube

Underfilled tube

**2**

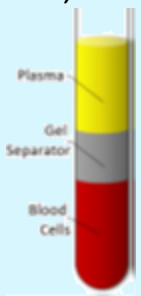
All tubes are **fully inverted 10 times after collection** (NOTE: do not vigorously shake tubes as that may cause gel disruption) and **incubated for 16-24 hours at 37 ± 1 º C**



**3**

All tubes are centrifuged at 2,000-3,000 RCF (g) **for 15 minutes.** If the gel plug did not separate from the plasma, re-centrifuge

After centrifugation
For 15 minutes
at 2000-3000g




**4**

All tubes are shipped in approved, ACM-provided NanoCoolers. **Do not ship samples in packaging other than that specified in the lab manual**


# Lab Test Cancellations and Confirmatory Testing

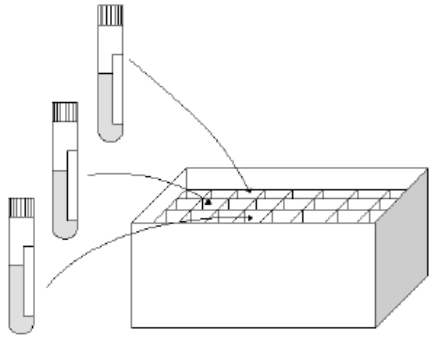
## Storage of Refrigerated and Frozen Samples to Avoid Cancellations

1

If you cannot ship samples the day of screening, you will need to store the frozen and refrigerated samples at the correct temperature until they can be shipped.

You can follow the below storage instructions for these samples, and they will remain stable until you're ready to ship:

1. Store the QuantiFERON TB sample (if you collect it centrally) at 2-8°C. The sample will be stable at this temperature for 28 days
2. Store the frozen samples (HBV DNA, CysC eGFR) in the ACM-provided aliquot storage box in the freezer. The box needs to be stored upright at -20°C or colder
   - Aliquot storage boxes should remain on site for the duration of the study. Do not ship the samples in this box to ACM
3. Do not ship any samples on Friday – Please store them at the above temperatures and ship on Monday



- Place aliquot tube into aliquot storage box.
- Place storage box containing aliquots in freezer.

**Note:** For ambient samples, these can be stored at room temperature, but only have a 72-hour stability. Please ensure they are shipped to ACM no later than the morning after screening

**Ensuring lab samples remain stable at the outlined conditions is critical to avoiding cancellation at ACM and need for repeat visits**

# Lab Test Cancellations and Confirmatory Testing

## Other Lab Best Practices

1

All other samples beyond the TB test must be collected centrally. To ensure there are no issues with these samples and we receive the results as fast as possible, please follow the below best practices:

1. Send in all confirmatory samples to ACM with all other frozen samples collected at screening. This includes HBV Confirmation (**Kit J**) and HIV/HCV Confirmation (**Kit B**)
    a. These confirmatory tests have long turnaround times, so sending them in with the rest of the samples, rather than waiting until we confirm they're required, will save up to a week of the screening window
2. Right after sending in the samples, please provide Priovant with all requisition numbers and airway bills for each sample (email to drew.webster@priovanttx.com). We will track the samples and ensure there are no issues with arrival and processing at ACM
3. Follow the lab manual closely, specifically with collection tube types and shipping instructions. Common mistakes made by other sites include:
    a. Using the incorrect tube type for the specific test, resulting in a cancellation at ACM. For example, many sites use the False Bottom Aliquot (FBA) tube for the coagulation test, rather than the frozen aliquot cryovial
    b. Sending refrigerated or ambient samples with a frozen gel pack, so they arrive at ACM frozen and are cancelled
    c. Not centrifuging samples completely, so they arrive at ACM "unspun" and are cancelled

**The lab collection process is complex, but following the best practices and communicating any questions to Priovant before shipping the samples will help avoid cancellations**

# Late and Incomplete Data Entry

## Data Should Be Entered in EDC within 24 – 72 Hours of Screening

2

The following forms should be prioritized and completed in the EDC on the day of screening, or within 24 hours of the visit:

1. EULAR Idiopathic Inflammatory Myopathies—Part I
2. Medical History – *Please include line item for DM diagnosis history*
3. MMT-8
4. CDASI
5. Dermatomyositis Prior and Concomitant Medications

Remaining data should be entered within 72 hours of the visit

**The critical forms contain essential information for subject eligibility and often requires follow-up from our medical monitoring team – Delays in data entry will directly impact the length of time your patient will spend in the screening period**

# Late and Incomplete Data Entry

## Common Data Entry Mistakes Leading to Delays

2

**eCRFs must be completed accurately to avoid delays in confirming eligibility as we approach randomization**

**Common Data Entry Mistake:** Medical History

The medical history should include Dermatomyositis. Please confirm that the subject has previous medical conditions on the “Medical History YN?” form, then add a log line for DM on the “Medical History” form

**Medical History YN?**

Requires Verification

| | |
|---|---|
| Does participant have any previous medical conditions reported? | Yes |

| Verbatim term | Start Date | Ongoing |
|---|---|---|
| DERMATOMYOSITIS | UN APR 2018 | ☑ |
| SOC 10040785 Skin and subcutaneous tissue disorders | | |
| HLGT 10014982 Epidermal and dermal conditions | | |
| HLT 10010760 Connective tissue disorders | | |
| PT 10012503 Dermatomyositis | | |
| LLT 10012503 Dermatomyositis | | |

# Late and Incomplete Data Entry

## Common Data Entry Mistakes Leading to Delays

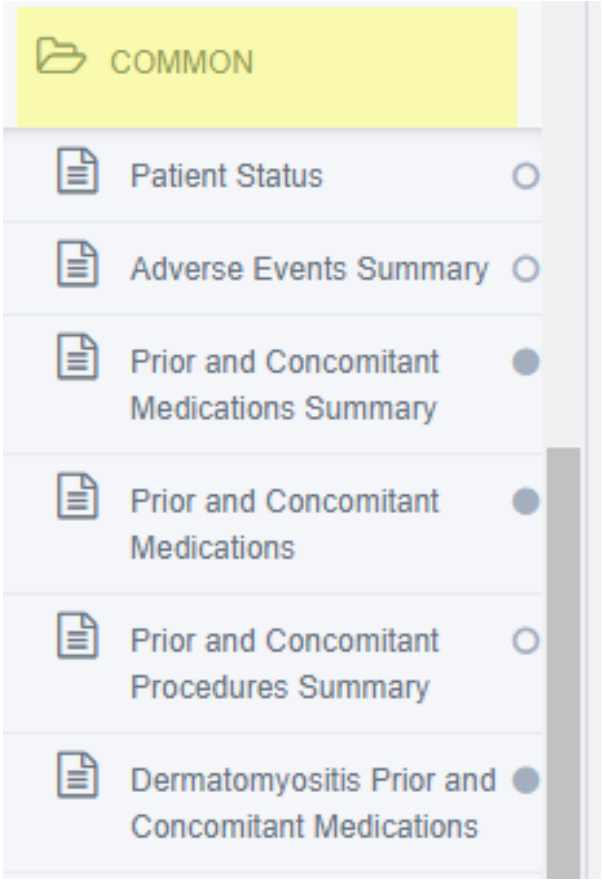
2

**eCRFs must be completed accurately to avoid delays in confirming eligibility as we approach randomization**

**Common Data Entry Mistake:** Completing Forms in “Common” Folder

There are additional critical forms for screening found in the “Common” folder.

Please complete as much information as possible in these forms



# Late and Incomplete Data Entry

## Common Data Entry Mistakes Leading to Delays

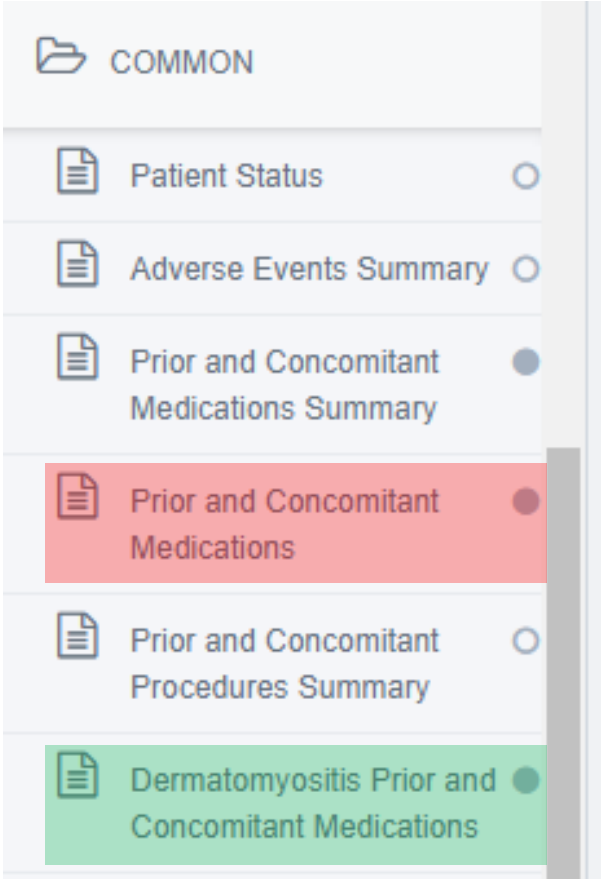
2

**eCRFs must be completed accurately to avoid delays in confirming eligibility as we approach randomization**

**Common Data Entry Mistake:** Enter DM Medications in Correct Location

All medications used to treat the subject's Dermatomyositis should be in the "Dermatomyositis Prior and Concomitant Medications" form.

All other medications should be entered into the "Prior and Concomitant Medications" form



# Late and Incomplete Data Entry

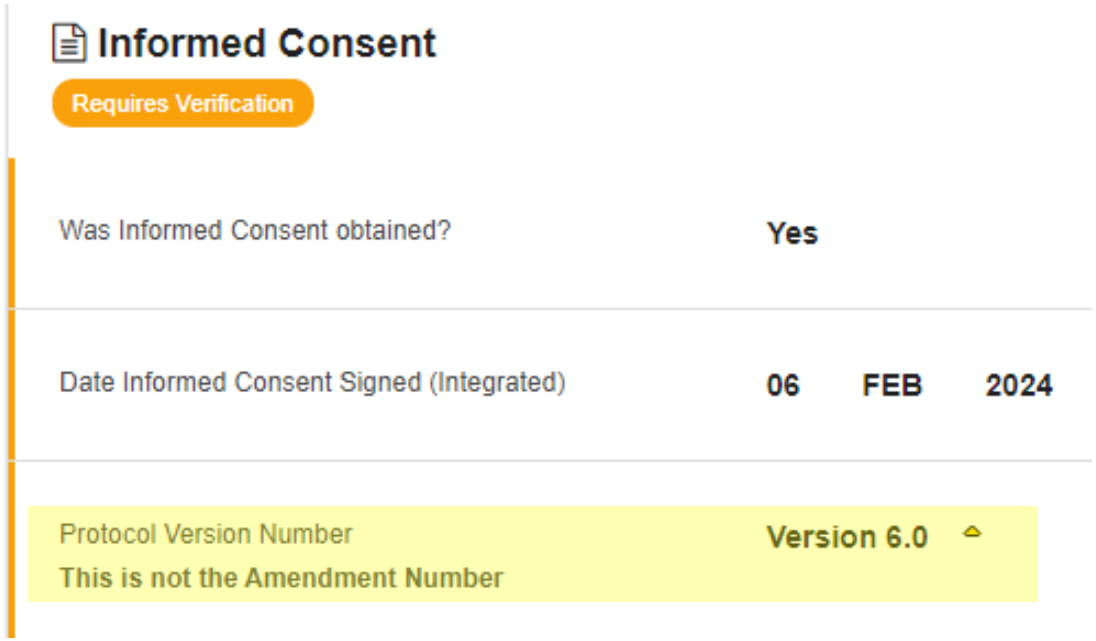
## Common Data Entry Mistakes Leading to Delays

2

**eCRFs must be completed accurately to avoid delays in confirming eligibility as we approach randomization**

**Common Data Entry Mistake:** Protocol Version in Consent Form

There are specific forms in the EDC that are linked to each protocol version. In order to trigger an accurate set of forms for your patient, please ensure you're entering the correct protocol version into the "Informed Consent" form



# Late and Incomplete Data Entry

## PROs in EDC Within 72 Hours of Screening



**PROs must be entered into the EDC or uploaded to BOX within 72 hours of the screening visit, as they are critical to confirming eligibility and supporting potential adjudication**

**VALOR Study PROs:**

I. PRO tools: PtGA skin, muscle, pain, swallow, flexibility, S
**II. PtGlobal Disease**
III. PP-NRS
IV. FACIT Fatigue
**V. HAQ**
VI. PTGI-C
VII. SF-36

The data entry guidance for the PROs varies depending on the patient visit

- **Screening and baseline visits (V1 and V2) –** Please enter the Health Assessment Questionnaire (HAQ) and Patient Global Assessment VAS (PtGA-VAS) into the EDC. All other PROs should be uploaded to the Premier BOX folder, and the Premier team will enter the PROs into the EDC on your behalf
  - Please check ahead of the screening to confirm you have access to BOX. If there are any issues on the day of screening, you can also email the PROs to ValorStudy_PatientAssessments_DataEntry@premier-research.com
- **Visits 3 – 12** – Please upload all PROs to the Premier BOX folder. The Premier team will enter the PROs into the EDC on your behalf

# Delay in ECG Upload and Reporting Results

## ECG Transmitted Day of Screening and Results in EDC ASAP

3

- On the day of screening, the subject's ECG will be collected using the study-provided Banook ECG machine
- Pleasure ensure that the ECG is successfully transmitted to the Banook Atrium portal, either through the USB transfer or directly from the machine via LAN connection, **on the same day as the screening**
- If you have any technical issues, you can contact the Banook Help Desk: https://www.banookgroup.com/hotline/
- If the issue is more serious, please reach out to the Priovant team directly (drew.webster@priovanttx.com) so that we can coordinate getting you an elevated level of support
- The Banook central report for the ECG will be available within 24 hours of upload. Please enter the results in the EDC exactly as they are shown on the report, particularly for abnormal findings. For example:

| | |
|---|---|
| Overall ECG Evaluation | Abnormal |
| If Abnormal, Specify | T WAVE INVERSION LOCALIZED IN SEPTAL LEADS (V1, V2)" |

**OTHER ABNORMALITIES NON CLINICALLY SIGNIFICANT OR FINDINGS**

T wave inversion localized in septal Leads (V1, V2)

| | | |
|---|---|---|
| Electro-stimulation spike on ECG recording | NO | YES |

Technical problem, if any : **No Technical problem**

| | |
|---|---|
| **Banook Group Conclusion:**<br>[] Within normal limits<br>[X] Abnormal<br>[] ECG not analysable<br>[] ECG not analysable but correct measurements | **Banook Group**<br>**Medical Reader**<br>**report approved on 17 Jan 2024 22:34:37 CET**<br>**Louisette Nassivera** |

# No Availability of CT / CXR Scans and Other Assessment Results

## Confirm CT / CXR Scan Needs Ahead of Screening

4

**CT Scan** – Subjects with DM symptom onset < 3 years ago require a full body CT scan with contrast (or PET CT) within the **12 months prior to screening**

**Chest X-Ray** – All subjects require a chest x-ray within the **6 months prior to screening** (3 months for Colombia sites on protocol 5.0)

If the subject received a CT scan within the last 6-months, **this will fulfill the chest x-ray requirement as well**

**CT / Chest X-ray Best Practices:**

- Given the CT / CXR requirements, please review your patient's file ahead of the screening to confirm if they have the required scans
- If there are no historical scans in the required time frame, please schedule the CT scan or chest x-ray as part of the screening visit, or as soon after the visit as possible
- Please enter the results of the scans in the EDC within 48-72 hours of screening, or within 24 hours of receiving the result
- If you have any questions about the results of the scan, you can reach out to our medical monitor directly via email (ade.adeboye@priovanttx.com)

**It is critical to be proactive and consider what scans your patient needs *before their screening*. It will save up to 2-3 weeks of time to randomization if you can perform the CT or CXR as part of the screening visit**

# Lack of Logistical Preparation Before Screening

## Confirm Lab Kit Supply At Least 2 Weeks Prior to Screening



Ahead of the screening, confirm that you have sufficient, non-expired lab kits and additional supplies to cover all specimen collections

**Visit Kits**

Kit A (Screening)

Kit B (HIV/HCV Confirmation)

Kit J (HBV Confirmation)

Kit D (Baseline/V2)

**Other Supplies**

- Validated 2-8°C Nanocooler
- Ambient Shipper
- Frozen Aliquot Box
- Thermosafe Coolers with dry ice markings
- Ambient/Frozen Airbills

If you need any of the above supplies, you can re-order them through ACM: https://labstar.acmgloballab.com. Note that lab kits may take up to 3-4 weeks to arrive on site

**Even if you don't have the necessary supplies in the 2 weeks prior to screening, do not cancel the visit. Reach out to Priovant and we will identify a solution that does not delay the patient's study participation**

# Lack of Logistical Preparation Before Screening

## Set Up Lab Sample Courier in Advance

5

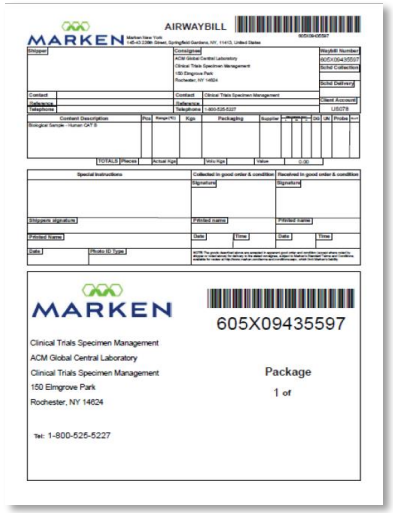
**If you do not set up courier pickup in advance of the screening visit, it will result in delayed pickup times and critically increase the likelihood that the samples will be cancelled at ACM**

### Chile Sites

**Courier:** Marken

**Coordinating Shipments:**

- When shipping specimens to ACM, a Marken airwaybill will be required. Marken provides pre-printed airwaybills upon site initiation
  - If more airwaybills are every needed, contact Marken at Marken.Chile@marken.com or +562-4107046/45/25/34
- You should schedule pickup the day of sample collection for ambient and frozen samples and the day after for the TB test
  - Pickups can only be coordinated Monday – Thursday, so store the samples at the temperature outlined in the lab manual if they're collected Friday
- When scheduling the frozen shipment, you must specifically request that Marken brings a cooler and dry ice




### Argentina and Colombia Sites

**Courier:** World Logistics Cargo

**Coordinating Shipments:**

- Ahead of screening, submit the collection request via email / phone:
  - All sites: pickupsamples@worldlogcargo.com
    - Argentina: Sol.avila@worldlogcargo.com
    - Colombia: operacionesibc@ltdexpress.net
  - By phone
    - Argentina: +54 9 11 6827-9009
    - Colombia: +57 313 2838658, +57 320 4932918, +57 320 4932925, +57 313 2827259
- Report the number of samples and the shipping temperature. Please indicate if your shipment will require dry ice
- Pickups are only 8 AM to 12 PM, so schedule your visit accordingly, or store samples at correct conditions until next day pickup
- You will print the Airwaybill using WLC's online system ahead of pickup
  - You will also need to provide a commercial invoice and CDC statement. WLC will send these in advance to be signed

# Lack of Logistical Preparation Before Screening

## Set Up Patient Travel and Other Reimbursements Ahead of Screening

5

**Setting up patient travel well in advance of the screening avoids high costs and ensures the patient receives the highest quality of transportation and accommodations**

### Chile and Colombia Sites

**Reimbursement through ClinEdge**

**Booking Travel for Screening Visit:**

Patient must provide consent before ClinEdge can book any travel or process reimbursements. To obtain consent, follow these steps:

1. Email patient-facing forms to patient
2. Patient completes forms and scans / emails back to site
3. Site confirms patient provided consent and completes the Site Travel Request Form
4. Site scans forms and emails to mystudytravel@clin-edge.com
5. Travel coordinator will reach out to site and patient to book travel

Please initiate this process with the subject as soon as the screening is scheduled so that ClinEdge has sufficient notice to secure preferable travel options for the patient

### Argentina Sites

**Reimbursement through institution**

**Booking Travel for Screening Visit:**

The patient will book their own travel and receive reimbursement directly from the institution

You will bill these patient reimbursements to the VALOR study as passthrough costs included in your study budget

# Baseline Visit Best Practices

## Proactively Schedule V2 While Patient is at Site for Screening

- If you follow all of the discussed best practices, our screening period only takes ~2 weeks. If no medication washouts or stabilizations are required, you can target a baseline visit (V2) for 14 days after the screening visit

- **While the patient is with you in clinic for the screening visit**, confirm a date with them that works for the baseline visit and get it on the schedule
  - If the patient needs any follow-up lab tests or procedures as part of screening, this visit can be re-purposed for those activities instead of the V2

**Scheduling the baseline visit with the patient during screening will avoid an unnecessarily long screening period and help them enter the study on the fastest possible timelines**

# Baseline Visit Best Practices

## Ensuring Accuracy of Patient Reported Outcomes

Some of the PROs are part of our primary endpoint or are critical assessments for understanding the patient's condition. We ask for your support in following some best practices while the patient fills out each PRO to ensure the forms are completed accurately:

1. Please remind the patient of the importance of completing these accurately. The patient should be aware of the concept of questionnaire fatigue.
2. Please sit with the patient while they complete each questionnaire. They should be provided to the patient one at a time.
3. Prior to completing each PRO, read the instructions out loud to the patient to ensure they understand the time point they need to consider for their answers
4. Once the PROs are completed, review them with the patient:
    - Have they left any questions blank?
    - Are there any discrepancies? For example:
        - Patient Global Assessment shows that they do not feel well, but patient said they can perform most activities without any difficulty on the HAQ
        - If a discrepancy is identified, you can verbally confirm "You indicated X on the HAQ; this means Y. Does this match how you have felt over the last week?" If the patient is surprised at the meaning of the score, they may have completed the form incorrectly.

**Patient accuracy of the assessments is critical, particularly the Health Assessment Questionnaire (HAQ), as it is part of the primary endpoint. Taking time to ensure the patient completes these questionnaires accurately during baseline and future visits will have a direct impact on the quality of the data**

# Baseline Visit Best Practices

## Physician Completed Questionnaires

**VALOR Study Physician Completed Questionnaires:**

I. EULAR/ACR Classification Criteria (only completed at V1)

II. Questionnaires Part of the Core Set Measures
- Physician Global Activity-VAS (PhGA-VAS)
- Manual Muscle Testing (MMT-8)
- Extramuscular Global Assessment-VAS (part of MDAAT)

III. Muscle Damage Index-VAS

IV. Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI)

V. Cutaneous Dermatomyositis Activity Physician's Global Assessment (CDA-IGA)

VI. Physician Global Impression of Severity (PhGI-S)

VII. Physician Global Impression of Change (PhGI-C) (completed starting at V3)

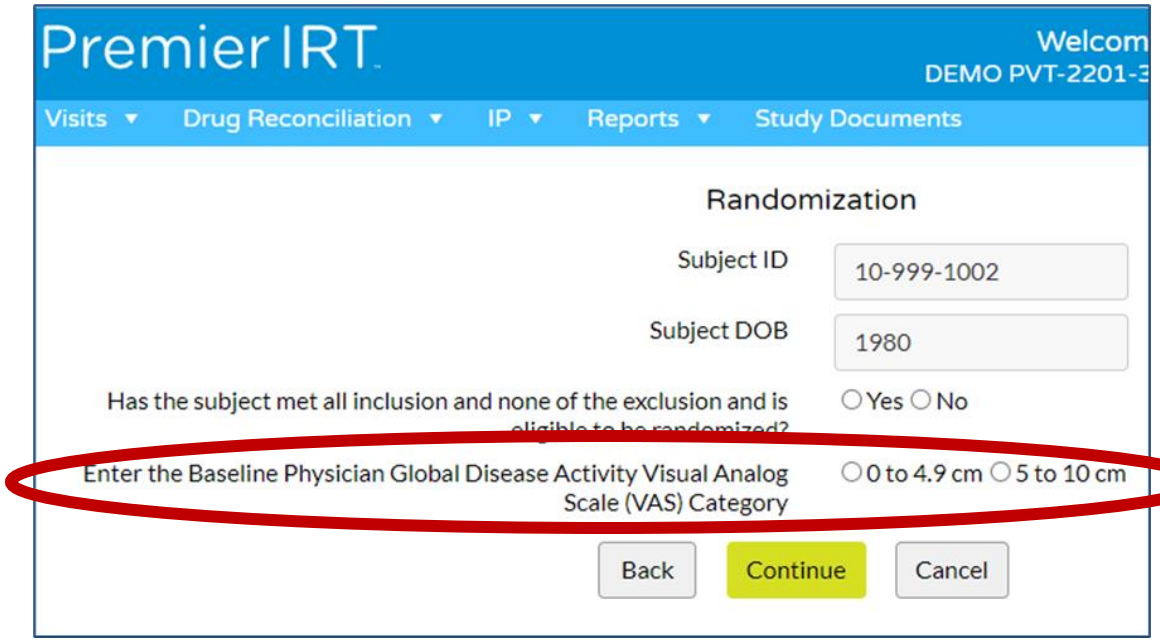
**Physician Completed Questionnaires Best Practices:**

- Maintain a consistent rater for each patient throughout the course of the study
  - Please consider this when selecting who your rater will be, as the rater will need to commit to being present for all patient visits
  - If you need to change the rater for any reason, please document the rationale in your source file
- Prior to the investigator exiting the study visit, review all questionnaires to ensure completeness (e.g. investigator name and signature, all rater components complete)
- You will enter every questionnaire in the EDC for all patient visits
  - Please record rater initials on each CRF in the EDC

# Baseline Visit Best Practices

## Stratification of Patient in IRT

**When randomizing subjects in the IRT, the BASELINE PhGA-VAS score must be entered**




- At randomization, the IRT prompts the site to enter in the Physician Global Disease Activity Visual Analog Scale (VAS) Category
- This applies to the assessment **at V2**, not at V1
- Prior to randomization, please use the study-provided ruler to measure the investigator's assessment and enter this into the IRT

- *This ensures that patients whose disease activity has gotten worse, or improved, since screening are stratified correctly into the study*

# Thank You!

**We are excited to kick off our partnership with your sites and work closely together to mitigate the operational challenges of enrollment in the VALOR study**

We are here to support you with whatever you need. Please reach out to me directly any time with any questions:

- Email: drew.webster@priovanttx.com
- Cell Phone (WhatsApp): +1 303 565 6358

# Interactive Assessment

Primary Objective: Emphasize the key components of the screening procedures covered today and assess whether additional trainings would be helpful on specific topics

**Please use the QR code to access the short assessment from your phone (or use the following link from your laptop):**

https://www.surveymonkey.com/r/FL86Z5V

We encourage you to participate, even if you are unsure of the answer.

We will review the answers live together, so don't hesitate to ask questions if you don't understand why a certain answer is correct.

# Pregunta 2

**¿Qué prueba de laboratorio ha sido la más difícil de realizar en los sitios, lo que resulta en múltiples visitas de pacientes durante el período de selección?**

a. Pruebas de seguridad
b. Prueba QuantiFERON TB
c. Panel de coagulación
d. Prueba de ADN de VHB
e. Panel de lípidos

# Pregunta 3

**Si realizas la selección un viernes, ¿qué deberías hacer con las muestras de laboratorio ambientales?**

a. Almacenar las muestras en el refrigerador durante el fin de semana y enviarlas el lunes
b. Enviar las muestras al laboratorio de inmediato
c. Programar otro momento para que el paciente venga a realizar los análisis de laboratorio ambientales
d. Almacenar las muestras a temperatura ambiente y enviarlas el lunes

# Pregunta 4

**Si realizas la selección un viernes, ¿qué deberías hacer con las muestras de laboratorio refrigeradas y congeladas?**

a. Almacenar las muestras a la temperatura indicada en el manual de laboratorio y enviarlas el lunes
b. Almacenar las muestras a temperatura ambiente y enviarlas el lunes
c. Enviar las muestras al laboratorio de inmediato

# Pregunta 5

## Al procesar la prueba QuantiFERON TB, debo asegurarme de que...

a. Agitar el tubo con mucha fuerza para asegurar que esté bien mezclado
b. No agitar el tubo en absoluto, ya que la agitación causa la interrupción del gel
c. Invertir suavemente el tubo 10 veces

# Pregunta 6

**Si centrifugo la prueba de TB durante 15 minutos y el tapón de gel no se separa, debería...**

a. Re-centrifugar la muestra durante otros 15 minutos, repitiendo hasta que se separe
b. Enviar la muestra de todos modos, ya que el manual de laboratorio dice que 15 minutos es todo lo necesario
c. Invertir el tubo varias veces para finalizar el proceso de separación

# Pregunta 7

**¿En qué tipo de embalaje debería enviarse la muestra de la prueba QuantiFERON TB?**

a. NanoCooler
b. Cualquier embalaje disponible, siempre que se coloque una bolsa de hielo en la caja
c. Una caja refrigerada de otro studio

# Pregunta 8

**¿Qué deberías hacer primero si no tienes los kits de laboratorio que necesitas unos días antes de la selección?**

a. Ordenar nuevos kits de laboratorio en el portal de ACM
b. Contactar al equipo de Priovant y ReSolution
c. Crear tu propio kit usando suministros disponibles en el sitio
d. Usar tubos de otros kits de laboratorio del estudio VALOR

# Pregunta 9

**Si tengo una pregunta sobre la elegibilidad del paciente, debería contactar a:**

a. Mi CRA
b. Monitor médico de Priovant

# Pregunta 10

**¿Cuándo deberías ingresar la clasificación EULAR, MMT-8, CDASI, Historia Médica y Medicamentos de Dermatomiositis en el EDC?**

a. Dentro de las 72 horas
b. El día de la selección, o dentro de las 24 horas
c. Dentro de 1 semana de la selección
d. En cualquier momento dentro del período de selección de 4 u 8 semanas

# Pregunta 11

## ¿Cuál es el proceso para ingresar el HAQ y PhGA-VAS en el EDC?

a. Los ingresarás para todas las visitasPrueba QuantiFERON TB
b. El equipo Premier los ingresará para todas las visitas
c. Para las visitas 1 y 2, los ingresarás. Para las visitas 3 a 12, los cargarás a Box y el equipo Premier los ingresará
d. Solo los ingresarás para la selección. El equipo Premier los ingresará para todas las demás visitas

# Pregunta 12

**Si tengo un problema con la transmisión del ECG y no he tenido éxito usando el Centro de Ayuda de Banook, debería...**

a. Contactar a mi CRA
b. Contactar a Priovant
c. Volver a realizar el ECG en el paciente
d. Usar mi máquina local de ECG en su lugar


priovant
therapeutics