

Patient- and Clinician-Reported Meaningfulness of Treatment-Related Change Following Investigational Sirolimus Topical Gel 3.9% in Microcystic Lymphatic Malformations: Qualitative Findings From the Phase 3 SELVA Trial Show Clinical Benefit and High Treatment Satisfaction

Maria Gnarra Buethe¹, Kristen Kahle², James Treat³, Denise Adams³, Sally Cohen-Cutler³, Michael Kelly⁴, Megha M. Tollefson⁵, Amy Theos⁶, Jeffrey Martini², Wes Kaupinen², Emily Cook², Andrea Zaenglein⁷, Kiersten Ricci⁸, Elizabeth Nieman⁹, Ionela Iacobas¹⁰, Michael White¹¹, Neeraja Swaminathan¹², Stacie Hudgens¹³, Joyce M.C. Teng¹⁴

¹University of California, Irvine; ²Palvella Therapeutics; ³Perelman School of Medicine at the University of Pennsylvania, Children’s Hospital of Philadelphia; ⁴Cleveland Clinic; ⁵Mayo Clinic and Mayo Clinic Children’s Rochester; ⁶University of Utah; ⁷Penn State/ Hershey Medical Center; ⁸Cincinnati Children’s Hospital Medical Center; ⁹University of North Carolina at Chapel Hill, Department of Dermatology; ¹⁰Texas Children’s Hospital/Baylor College of Medicine; ¹¹Emory University School of Medicine, Aflac Cancer & Blood Disorders Center; ¹²Monroe Carrell Jr. Children’s Hospital at Vanderbilt; ¹³Clinical Outcomes Solutions; ¹⁴Stanford University, Lucile Packard Children’s Hospital

SYNOPSIS: Microcystic lymphatic malformations (mLM) are rare, serious, lifelong vascular anomalies associated with substantial physical and psychosocial burden; no FDA-approved therapies currently exist. In the pivotal Phase 3 SELVA trial of sirolimus topical gel 3.9%, an embedded qualitative interview study captured patient, caregiver, and clinician perspectives to contextualize clinical efficacy endpoints and evaluate treatment satisfaction. At entry, participants described substantial physical, emotional, and social burden; by Day 168, patients, caregivers, and clinicians independently reported consistent symptom improvement, corroborating a 95.3% response rate on the primary mLM-IGA endpoint and 100% treatment satisfaction on the TSQM. These qualitative and quantitative findings converged to demonstrate clinically meaningful, patient-centered benefit.

OBJECTIVE

To contextualize clinical trial efficacy endpoints through the patient/clinician experience and evaluate treatment satisfaction following investigational sirolimus topical gel 3.9%.

METHODS

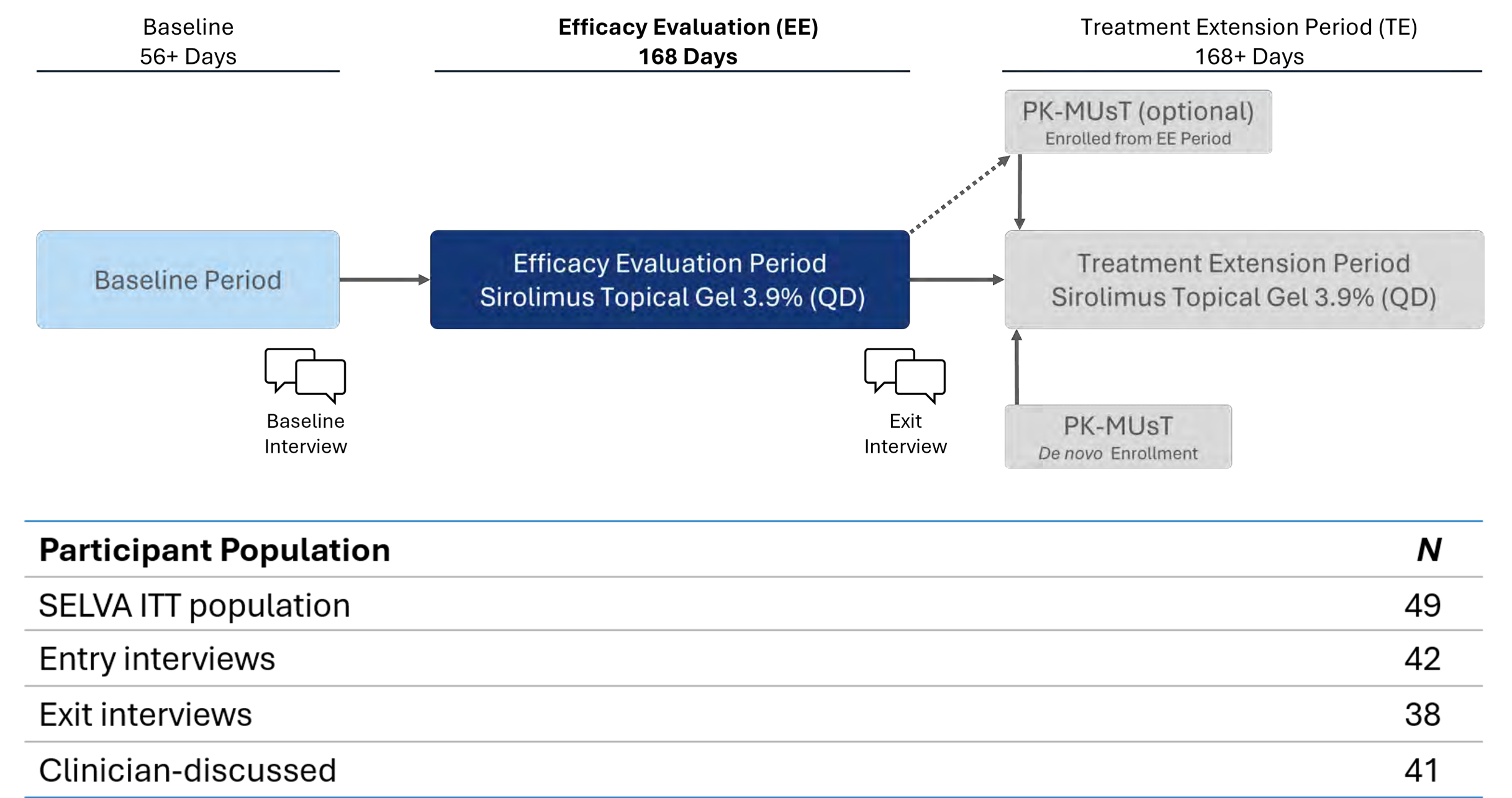


Figure 1. SELVA study design and qualitative interview participant characteristics. Semi-structured entry (baseline) and exit (Day 168) interviews were conducted with SELVA trial participants and/or caregivers (for participants <12 years), alongside independent clinician exit interviews; interviews were analyzed thematically. Participant-reported Patient Global Impression of Severity and Change (PGI-S and PGI-C, respectively), collected at multiple timepoints throughout the Efficacy Evaluation period, and the Treatment Satisfaction Questionnaire for Medication (TSQM-9), administered at Day 168, were compared against qualitative interview findings to evaluate the meaningfulness of reported changes.

ENDPOINT SUMMARY

Efficacy Endpoint	Scale Trajectory (Baseline → Day 168)	Mean Change at Day 168 (95% CI)	p-value
Primary Endpoint: mLM-IGA ^a Overall		+2.13 (1.88, 2.38)	$p < 0.001$
Key Secondary Endpoint: Blinded mLM-MCSS ^b		-3.36 (-4.34, -2.38)	$p < 0.001$
Secondary Endpoint: Live Clinician mLM-MCSS ^b		-4.6 (-5.20, -3.92)	$p < 0.001$
Secondary Endpoint: PGI-C ^a		+1.9 (1.66, 2.16)	$p < 0.001$
Secondary Endpoint: CGI-S ^c		-1.7 (-1.91, -1.39)	$p < 0.001$
Secondary Endpoint: PGI-S ^c		-1.0 (-1.26, -0.74)	$p < 0.001$

Table 1. Summary of efficacy endpoints, changes from baseline to Day 168. Statistically significant improvements were observed across all primary and secondary efficacy endpoints ($p < 0.001$ for each), converging with qualitative interview findings from participants, caregivers, and clinicians (Figure 2).

^aDynamic change scale (7-point scale ranging from -3 to +3; positive values indicate improvements from baseline)
^bSum of 3 static severity scales (Height, Leaking/Bleeding, Vesicle Appearance: each scale rated 1 to 5, total score 3-15; negative values indicate improvements from baseline)
^cStatic severity scale (5-point scale ranging from 1 to 5; negative values indicate improvements from baseline)

RESULTS

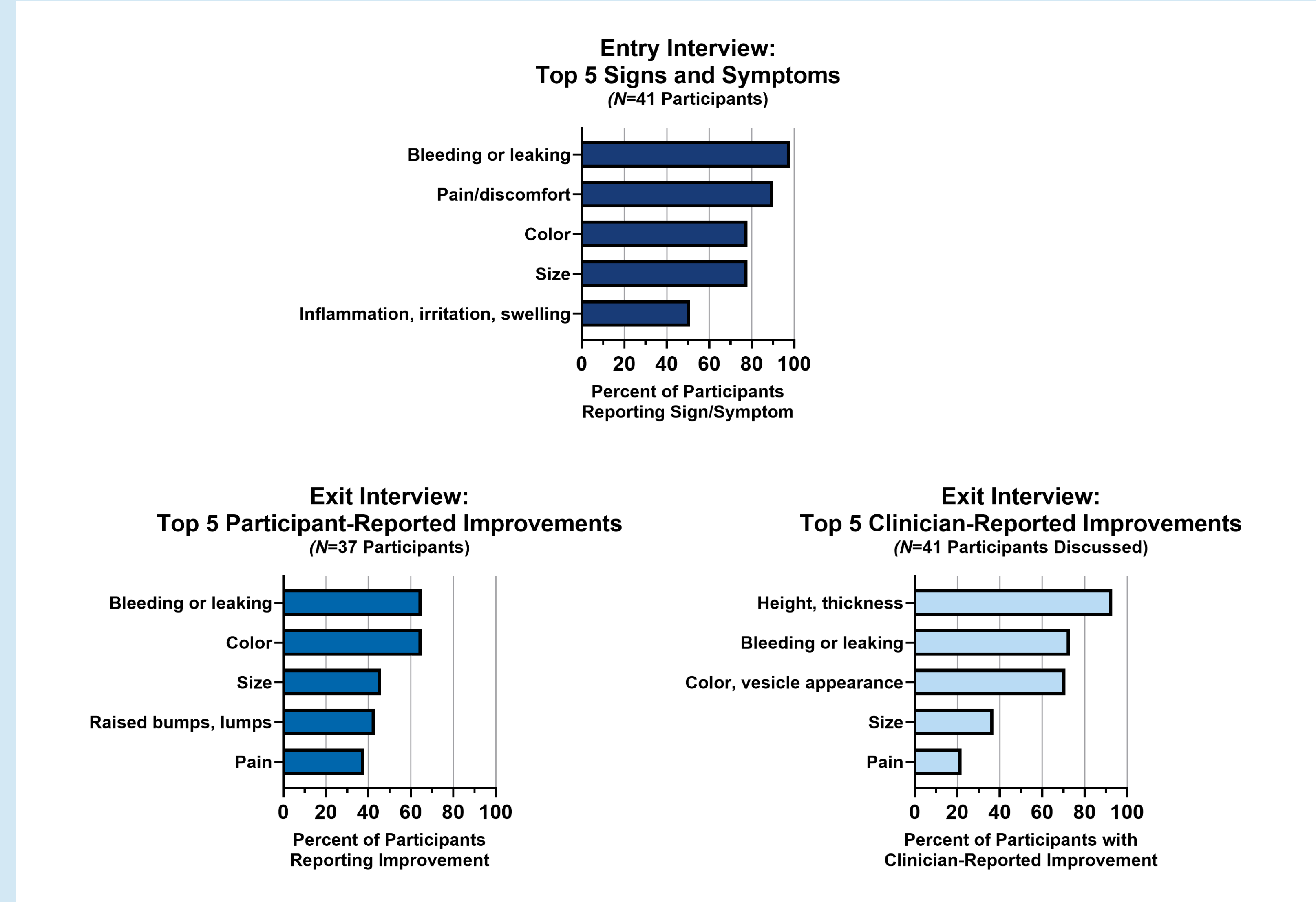


Figure 2. Debilitating baseline burden, convergent improvement: patient, caregiver, and clinician-reported change at Day 168. At entry (baseline), the most frequently reported signs and symptoms were bleeding or leaking, pain/discomfort, color, size, and inflammation/irritation/swelling (Top). At Day 168 (exit), participants and/or caregivers most commonly reported improvement in bleeding or leaking, color, size, raised bumps/lumps, and pain (Bottom Left); clinicians, interviewed independently, most often reported improvement in height/thickness, bleeding or leaking, color/vesicle appearance, size, and pain (Bottom Right).

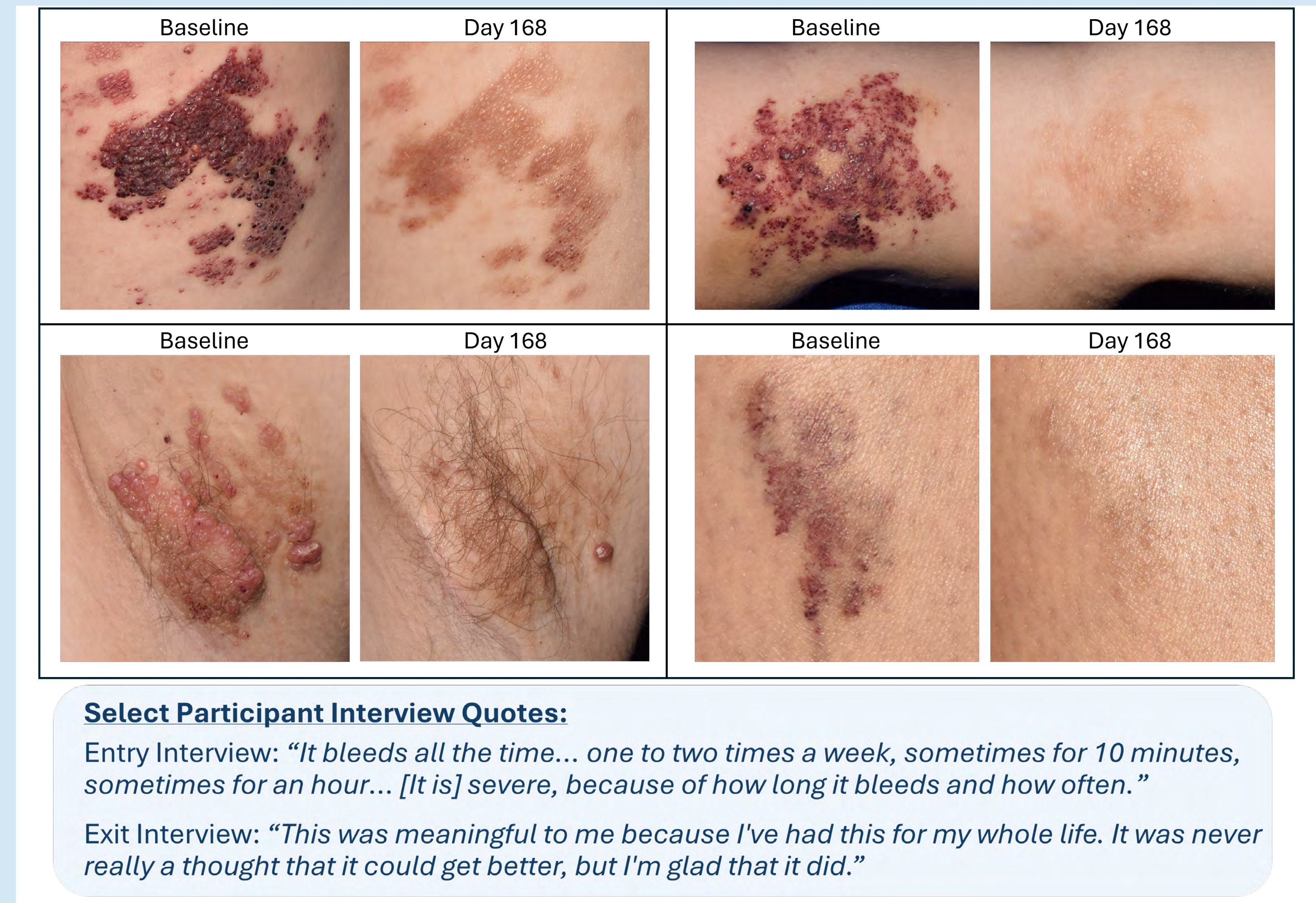


Figure 3. Select clinical photographs demonstrating treatment response in microcystic lymphatic malformations. Paired baseline and post-treatment images from participants demonstrate clinical improvement following treatment with investigational sirolimus topical gel 3.9%. Baseline images (left panels within each pair) show characteristic clusters of vesicular and plaque-like lesions, with varying degrees of erythema, hemorrhagic vesiculation, and lymphatic leakage. Post-treatment images (right panels) demonstrate marked improvement, including flattening of lesions, reduction in vesicle burden, and decreased erythema and discoloration across multiple anatomic sites.

TREATMENT SATISFACTION

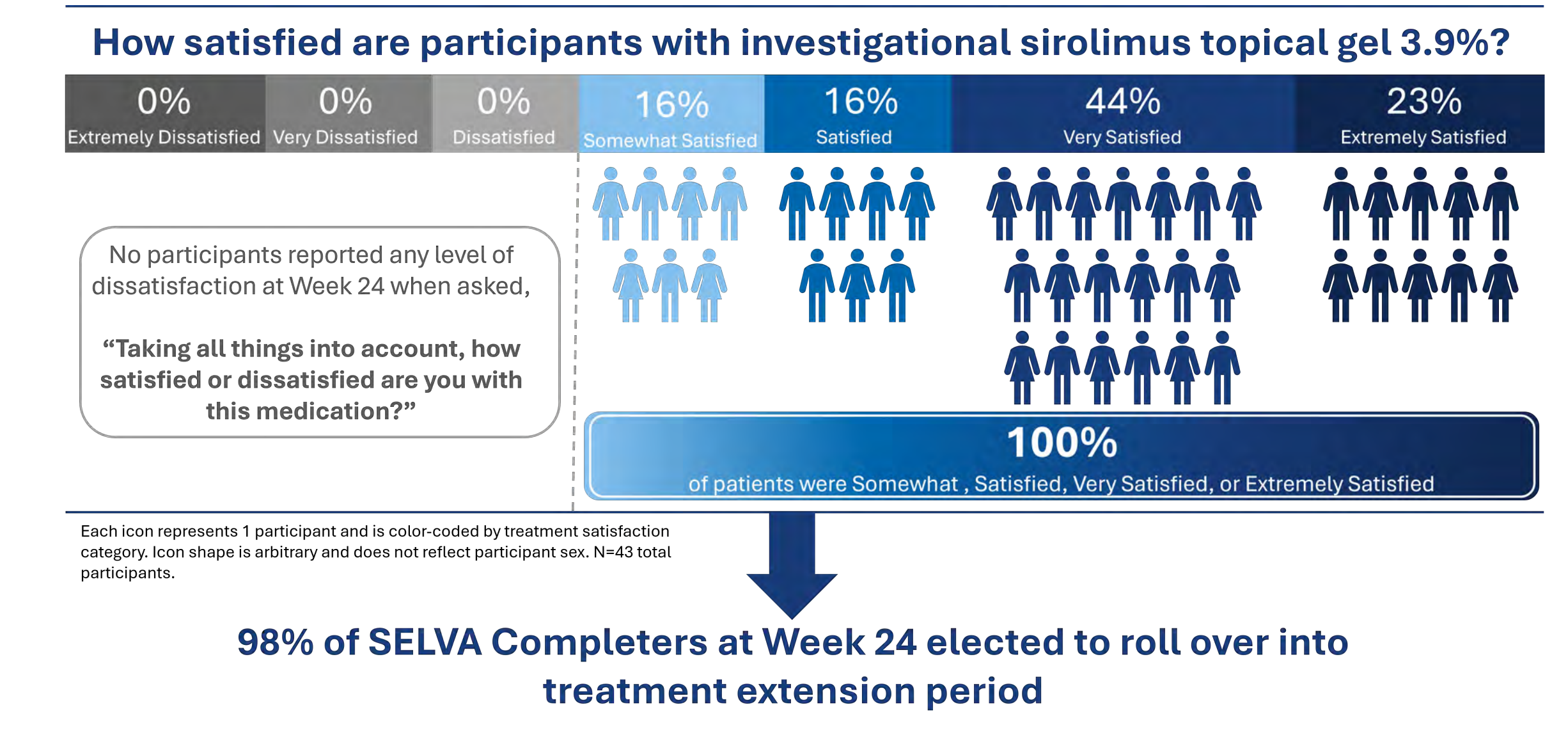


Figure 4. Treatment satisfaction among all participants receiving investigational sirolimus topical gel 3.9%. Satisfaction was assessed as a supportive endpoint using the Treatment Satisfaction Questionnaire for Medication (TSQM-9). Results from item 9: “Taking all things into account, how satisfied or dissatisfied are you with this medication?” are shown. Each icon represents an individual participant and is color-coded according to overall satisfaction category; icon shape is arbitrary and does not reflect participant sex. The distribution of responses demonstrates favorable treatment satisfaction across the overall study population.

CONCLUSIONS

- At entry, mLM presented as a chronic, debilitating disease, with participants, caregivers, and clinicians reporting substantial physical burden.
- Quantitative efficacy endpoints and qualitative interview findings converged across patient and clinician perspectives, with statistically significant improvement on all SELVA efficacy endpoints ($p < 0.001$) corroborated by concordant reported symptom-level improvement.
- At Day 168, 95.3% of participants achieved a clinically meaningful response on the primary mLM-IGA endpoint and 100% reported treatment satisfaction on the TSQM-9.
- Improvements were described as meaningful given the chronic, progressive nature of mLM and the historical absence of effective therapies; 98% of participants who completed the Efficacy Evaluation period elected to continue into the Treatment Extension period.
- These concordant findings support the interpretability of the SELVA efficacy endpoints and support investigational sirolimus topical gel 3.9% as a potential first FDA-approved therapeutic option for mLM, a rare, serious, and historically underserved disease.