Pros and Cons of Polidocanol Endovenous Microfoam

Kathleen Gibson, MD
Lake Washington Vascular Surgeons, Bellevue, WA

AIM Symposium
New York, New York
November 16, 2015

Varithena Overview

• 14 years of systematic pharmaceutical development
• Multiple clinical trials leading up to the FDA approval of Varithena rigorously proved its safety in treating patients with GSV incompetence
• No other clinical trial of foam sclerosants has included before and after MRIs to prove neurologic safety
• Two large Phase III trials showed that Varithena treatment provided significant improvement in both patient symptoms from varicose veins and in appearance of the leg

Varithena Development

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1996/1997</td>
<td>Cabrera publishes on use of foam sclerotherapy</td>
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<td>1997</td>
<td>Alain Monfreux also publishes on use of foam</td>
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<td>2003</td>
<td>Varisolve trial put on hold by FDA-bubbles seen in heart on echo during treatment</td>
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<td>2006</td>
<td>Phase III trial in Europe</td>
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<td>2008</td>
<td>Varisolve Phase II “MRI” trial</td>
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<td>2009</td>
<td>Savvy trial-develop new PRO</td>
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<td>2009</td>
<td>Pilot Phase III: PEM vs low dose PEM</td>
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<td>2012</td>
<td>VANISH 1 and VANISH 2 pivotal trials</td>
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<tr>
<td>11/25/2013</td>
<td>FDA approves Varithena</td>
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<td>8/2014</td>
<td>Product release</td>
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Varithena Indications

• Treatment of incompetence of the great saphenous vein (GSV)
• Treatment of accessory saphenous veins (AASV, PASV)
• Treatment of visible varicosities that are tributaries of the GSV, AASV, or PASV
• Not indicated for treatment of the small saphenous vein (SSV) or perforator veins as these veins were not included in the pivotal trials

Technique

• Requires two people—one for ultrasound, one for injection
• Proper vein mapping of the GSV-mark on skin with perforators in calf and thigh marked
• Mark side branches you intend to treat
• Patient in supine position, hip flexed
• Access above knee GSV with ultrasound guidance using either an angiocatheter, or a micropuncture needle, followed by a micropuncture sheath. Aspirate and flush,
• Secure sheath or angiocath with injection tubing (in kit)
Micropuncture sheath in place

Endovenous Microfoam Ablation

Varithena Microfoam

Side branch treatment

Pros to Varithena v. Physician Compounded Foam

- No reports of neurologic injury (stroke, TIA) in any patient in clinical development or since FDA approval
- All reports of strokes in the literature have occurred with physician compounded foam
- Demonstrated significant improvements in well validated patient reported outcome measures
- Only foam sclerosant that is FDA approved

How is Varithena different?

- More consistent bubble size
- Small bubble diameters
- Increased foam stability
- Diminished circulating bubbles (dog pulmonary artery study)
Glass Plate Method of Foam Analysis

Comparison of Bubble Size Distribution: O₂:CO₂ (65:35), 1:7 (liquid:gas) made by Varithena™, DSS, and Tessari methods.

Foam Dwell Time (DT) by Turbiscan:
Analysis by Foam Generation Method and Liquid:Gas Ratio

Cons to Varithena over Physician Compounded Foam
- Expense
- Need to “batch” patients in order to maximize use of canister (this is an issue in comparison to all of the other technologies)
- One week self life once canister activated
- Reimbursement challenges—non-payment “hurts more” with expensive products

Comparison to Endothermal Ablation
- Can be used, as used for endothermal ablation for treating incompetent GSV or AASV-no tumescent needed
- Not approved for treatment of the SSV
- Closure rates (surrogate marker) lower than traditionally reported for thermal techniques (no head to head studies yet)
- Able to treat branches at same time
- Excellent treatment for recurrent varicose veins, tortuosity
- Higher DVT rate may be due to stringency of duplex in trial
- Reimbursement issues—unlisted CPT, J codes
Comparison to MOCA and Venaseal
- Similar issues with reimbursement, use of an unlisted CPT code
- Treats similar segments (except SSV), but also side branches
- Like these techniques, tumescence not required
- Unlike Venaseal (but like MOCA), compression used afterwards
- No head to head trials have been done

Patient Scheduling Considerations
- On the whole, faster than EVLT/RF
- Each can of Varithena contains enough foam to treat three patients
- Shelf life of can is one week once opened
- If purchasing cans yourself, need to take consider wasted foam-expensive, so schedule patients in batches of three if feasible
- Remember the weekend when counting days until can expires

Reimbursement strategies
- Need to document failure of conservative management, impact on ADLs, anatomy on ultrasound for these patients just as you would an endovenous RF or laser ablation
- Carefully crafted letter of medical necessity imperative, as always
- Pre-authorization a must unless patient is cash paying

Reimbursement
- Technique does not have its own CPT code at this point
- For billing, current recommendation is to “cross-walk” endovenous RF or laser plus phlebectomy CPT codes (36478 or 36475 plus 37785 or 37765) or use an unlisted procedure code: 37799
- Product can either be purchased by practice and an unlisted J-code billed or drug can be prescribed to an approved specialty pharmacy
- Varithena has a “Solutions Center” on its website to assist with pre-authorization and reimbursement issues

Advantages over thermal ablation?
- No sedation needed
- Faster
- Especially advantageous for recurrent varicose veins/tortuosity/neovascularization
- “All in one” therapy
- Little to no intra-procedural pain

Summary
- Varithena can be performed without sedation and requires no tumescent anesthesia to treat the GSV, accessory branches, and tributaries
- Technique straightforward for physicians familiar with catheter-based skills and sclerotherapy
- Patient scheduling needs to take into account amount of drug in can and shelf life of product
- Product currently being used by multiple US physicians and company can provide resources for reimbursement issues
Thank you!