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OnabotulinumtoxinA for Systemic Sclerosis-associated Raynaud's Phenomenon: A Multi-Institutional Study on Accessibility and Effectiveness

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INTRODUCTION

Raynaud's phenomenon (RP), a common presenting symptom of systemic sclerosis (SSc), is a painful and debilitating condition of the digits caused by increased vascular reactivity.[1,2] Recurrent digital ulcers and critical ischemic events may result in osteomyelitis or necessitate partial amputations.[1] Despite this and RP's profound impact on quality of life (QOL), there are currently no Food and Drug Administration (FDA)-approved therapies to treat this condition.[1] Additionally, severe RP is often challenging to treat, and numerous agents may be required to adequately control disease.[3] Accumulating evidence demonstrates that onabotulinumtoxinA (Botox®) hand injections may be an effective treatment choice for refractory RP.[1,2,4-6] Herein, we present our experience with the accessibility and effectiveness of onabotulinumtoxinA for 51 patients with SSc-associated RP, making this the largest cohort of its kind to date.

Following Institutional Review Board exemption by Mass General Brigham, we conducted a retrospective study from two large academic institutions to determine the accessibility and effectiveness of onabotulinumtoxinA for SSc-associated RP. We identified patients with SSc-associated RP for whom insurance approval for onabotulinumtoxinA was attempted between 2014-2020. Data regarding success in insurance coverage, disease severity, impact on quality of life, previously failed therapies, and effectiveness for RP were collected.

51 patients for whom onabotulinumtoxinA was prescribed were identified and included in the study. The median number of previously failed therapies for RP was 3 (range: 0–10). 80% (41/51) of PAs were initially denied, the most common reason being "not covered for SSc/off-label use" (32/41, 78%). Among the patients who were initially denied coverage, 41% (17/41) ultimately acquired coverage after a median 37.5 days (range: 4–434). All of these 17 patients had private insurance (Figure 1). This contrasts with 0% (0/8) of Medicare patients who ultimately obtained insurance approval. In total, 53% (27/51) of patients ultimately received coverage. Although all patients (9/9) who had failed 6 or more therapies ultimately received onabotulinumtoxinA coverage, only 60% (26/43) of patients who failed between 2 and 5 therapies received coverage.

Decreased QOL was documented in 35% (18/51) of patients; among these patients, 39% (7/18) still failed to obtain coverage. 82% (42/51) of patients had documented tissue loss, defined as ulcers, autoamputation, and/or gangrene. Among these patients, 45% (19/42) were still ultimately denied coverage.

92% (34/37) of patients with documented tissue loss who ultimately received onabotulinumtoxinA (either via insurance approval [n=20] or via free supply [n=14]) showed improvement after onabotulinumtoxinA treatment. Furthermore, 82% (36/44) of all treated patients had sufficient benefit to warrant continued treatment.

This study highlights the challenges of prescribing off-label onabotulinumtoxinA, despite clinical effectiveness, for SSc-associated RP. Our results indicate that the vast majority of patients with documented tissue loss who received onabotulinumtoxinA showed improvement. While onabotulinumtoxinA is an

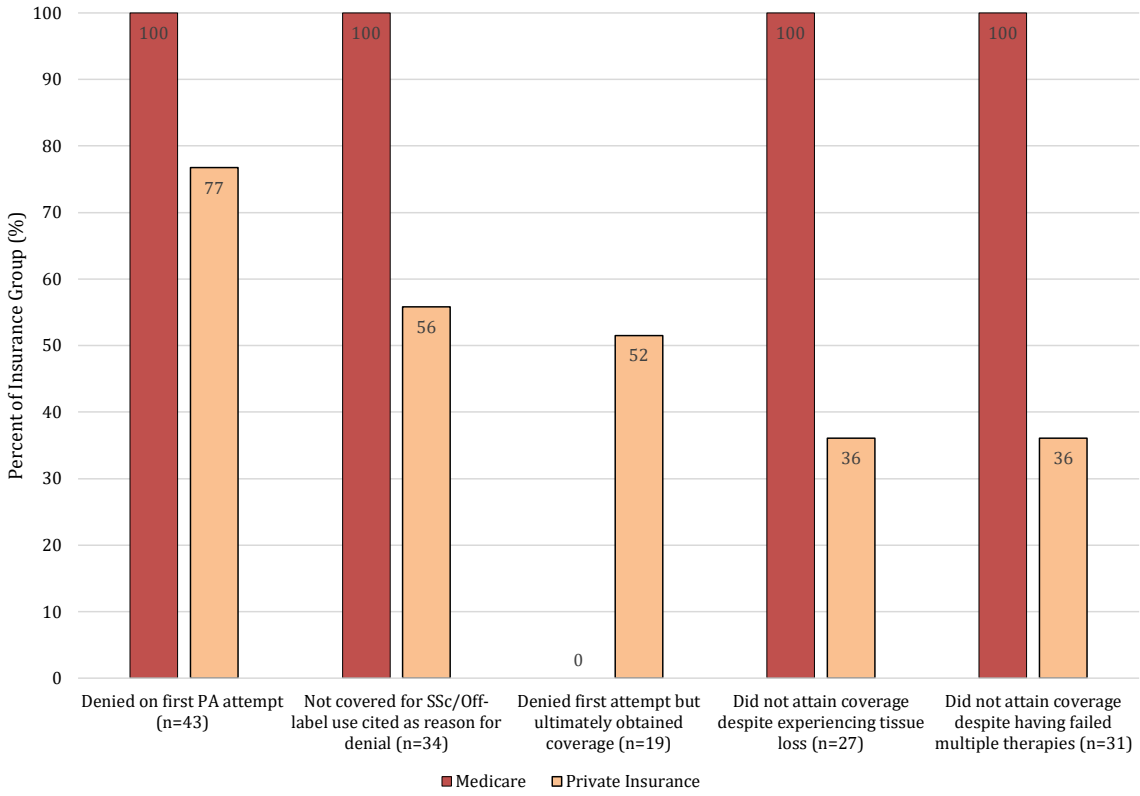
TABLE 1.

Coverage of OnabotulinumtoxinA for SSc-Associated RP According to Demographics, Clinical Features, and Treatment Response

	N (%)	Covered (%*)	Not Covered (%*)
Age (years)			
<21	N/A	--	--
21-30	N/A	--	--
31-40	3 (56)	3 (100)	0 (0)
41-50	9 (18)	5 (56)	4 (44)
51-60	19 (37)	12 (63)	7 (37)
61-70	14 (27)	5 (36)	9 (64)
71+	6 (12)	2 (33)	4 (67)
Gender			
Male	7 (14)	5 (71)	2 (29)
Female	44 (86)	22 (50)	22 (50)
Race			
White	41 (80)	20 (49)	21 (51)
Hispanic or Latino	3 (6)	2 (67)	1 (33)
Black or African American	2 (4)	1 (50)	1 (50)
Asian	1 (2)	1 (100)	0 (0)
Other	1 (2)	1 (100)	0 (0)
Not specified or unknown	3 (6)	2 (67)	1 (33)
Insurance			
Private or commercial	43 (84)	27 (63)	16 (37)
Medicare	8 (16)	0 (0)	8 (100)
Smoking Status			
Never Smoker	35 (69)	19 (54)	16 (46)
Former Smoker	14 (27)	8 (57)	6 (43)
Current Smoker	1 (2)	0 (0)	1 (100)
Unknown	1 (2)	0 (0)	1 (100)
Provider documented decreased QOL			
Yes	18 (35)	11 (61)	7 (39)
No	33 (65)	16 (48)	17 (52)
Tissue Loss			
Yes	42 (82)	23 (55)	19 (45)
No	7 (14)	2 (29)	5 (71)
Unknown	2 (4)	2 (100)	0 (0)
No. previously failed therapies			
0	1 (2)	0 (0)	1 (100)
1	5 (10)	3 (60)	2 (40)
2	9 (18)	3 (33)	6 (67)
3	10 (20)	7 (70)	3 (30)
4	9 (18)	5 (56)	4 (44)
5	6 (12)	2 (33)	4 (67)
6	2 (4)	2 (100)	0 (0)
7	3 (6)	1 (33)	2 (67)
8	2 (4)	2 (100)	0 (0)
9	1 (2)	1 (100)	0 (0)
10	1 (2)	0 (0)	1 (100)
Not specified or unknown	2 (4)	1 (50)	1 (50)
Tissue loss improvement after onabotulinumtoxinA			
Yes	34 (67)	20 (59)	14 (41)
No	3 (6)	2 (67)	1 (33)

*The percentages in covered vs. not covered use the N in column 2 as the denominator.

FIGURE 1. Summary of insurance coverage approval based on insurance type.



effective treatment for SSc-associated RP, this therapy remains an off-label use, and patients, particularly those with public health insurance, have limited success in acquiring insurance coverage for this treatment. This difference in coverage based on insurance status, despite treatment effectiveness, highlights an important access issue. Furthermore, there are no FDA-approved treatments for RP as it is an orphan disease, making it challenging to study in controlled clinical trials. Given the clinical benefits of off-label onabotulinumtoxinA for refractory SSc-associated RP, insurance approval should ideally not hinge on FDA approval alone. A reevaluation of the policies that determine coverage of therapies for RP is warranted.

DISCLOSURES

The authors have no conflicts of interest to declare.

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