Retrospective Safety Evaluation of ADCON®-L For Inhibition Of Postoperative Peridural Fibrosis Following Spinal Root Decompression

[1]Joseph Maroon, M.D., [2]George Sypert, M.D., [3]Bruce Bartie, D.O., [4]Todd Moldawer, M.D., [5]James Greenspan, M.D., [6]Fred Ma, M.D., [6]Clark Tedford, Ph.D., [6]Emanuel Palatinsky, M.D., [7]Maureen Fournier, [7]Phil Lavin, Ph.D., [8]John Beghin, M.D., [9]David Rouben, M.D., [10]Jerome Kolavo, M.D., [11]Robert Shugart, M.D., [12]Bruce Mathern, M.D., [1]Tristate Neurosurgical Associates-UPMC, PA; [2]The Sypert Institute, FL; [3]St. Croix Orthopaedics, MN; [4]Southern California Orthopaedic Institute, CA; [5]North Country Neurosurgical Associates, NY; [6]Gliatech Medical Inc.; [7]Averion, Inc.; [8]Indiana Back Center, IN; [9]River City Orthopaedics Surgeons, P.S.C., KY; [10]Orthopaedic Associates of DuPage, IL; [11]Fort Wayne Orthopaedics, IN; [12]Mid-Atlantic Spine Specialists, VA

ABSTRACT

- **Objective:**
  Retrospective data collection of first time ADCON-L recipients for single level laminectomy.

- **Method:**
  - Ten study centers participated in data collection for surgeries that occurred between June 1, 1998 and October 30, 2000.
  - The safety profile of ADCON-L was evaluated by review of case reports on the postoperative outcome of patients treated with ADCON-L.
  - The data were also compared to the data obtained from patients in a previous prospective clinical study.

- **Number of Subjects:**
  847 ADCON-L patients

- **Diagnosis and Main Criteria for Inclusion:**
  First-time spinal root decompression, using ADCON-L to inhibit postoperative peridural fibrosis.

- **Statistical Methods:**
  - The primary analysis was based on 819 eligible patients
  - The adverse event incidence rates were determined using exact 95% confidence intervals computed for proportions

TABLE 1.
PARTICIPATING CLINICAL SITES

Site number	Investigator	Address	Number of patients
1	George Sypert, MD	The Sypert Institute, FL	200
2	Bruce Bartie, D.O.	St. Croix Orthopaedics, MN	125
3	Todd Moldawer, MD	Southern California Orthopaedic Institute, CA	109
4	James Greenspan, MD	North Country Neurosurgical Associates, NY	106

5	Joseph Maroon, MD	Tristate Neurosurgical Associates-UPMC, PA	103
6	John Beghin, MD	Indiana Back Center, IN	87
7	David Rouben, MD	River City Orthopaedics Surgeons, P.S.C., KY	46
8	Jerome Kolavo, MD	Orthopaedic Associates of DuPage, IL	39
9	Robert Shugart, MD	Fort Wayne Orthopaedics, IN	25
10	Bruce Mathern, MD	Mid-Atlantic Spine Specialists, VA	11

INTRODUCTION

- The purpose of this study was to collect information for use of ADCON-L when administered in adult patients undergoing first-time spinal root decompression in the lower back. The safety profile of ADCON-L was evaluated by a retrospective collection and review of case reports on the postoperative outcome of patients treated with ADCON-L. The final data collected from the study were compared with previous prospective pivotal clinical study data, including adverse events, medical events, and reoperation.

- Postoperative fibrosis is a natural consequence following lumbar surgery. When the formation of scar tissue is excessive, dense fibrosis may lead to clinically important sequelae due to adhesions between tissues or compression of anatomic structures[4,6]. Overall estimates of the rate of unsatisfactory results after lumbar disc surgery are as high as 65%[1,2,3,4]. Between 25,000 and 50,000 new patients have been estimated to be diagnosed with Failed Back Surgery Syndrome FBSS) each year in the USA[5]. Peridural scar formation after disc surgery contributes to an unfavorable outcome with recurring symptoms[4,6,7], possibly in up to 24% of all FBSS cases[8,9].

- ADCON-L is a flowable gel composed of a polyglycan ester and absorbable porcine-derived gelatin in phosphate buffered saline. It was designed for use in intraspinal lumbar surgical procedures as an absorbable barrier to peridural and perineural fibrosis.

TABLE 2.
SURGICAL PROFILE AND PATIENT DEMOGRAPHICS – ELIGIBLE PATIENTS

Levels of Primary Surgery	All Patients (N=819) N (%)
L4-L5 right	164 (20.0 %)
L4-L5 left	196 (23.9 %)
L5-S1 right	206 (25.2 %)
L5-S1 left	253 (30.9 %)
L4-L5 combined	360 (44.0 %)
L5-S1 combined	459 (56.0 %)
Time Since Primary Surgery	
Mean (SD) (weeks)	18.2 (20.0)
Median (weeks)	10.0
Min-Max (weeks)	0.0 – 140.0
Sex	**N (%)**
Male	527 (64.3 %)
Female	292 (35.7 %)
Age	
Mean (SD)	43.1 (11.8)
Median (years)	41.0
Min-Max (years)	20.0 – 87.0

TABLE 3.
ADVERSE EVENTS EXPERIENCED BY > 1% OF ELIGIBLE PATIENTS

Event Description	Patients (N=231)
Pain in Limb	70 (8.5 %)
Back Pain	68 (8.3 %)
Intervertebral Disk Herniation	32 (3.9 %)
Radiculitis NOS	26 (3.2 %)
Muscle Spasms	17 (2.1 %)
Pain NOS 11	(1.3 %)
Wound Drainage	9 (1.1 %)

FIGURE 1.
RELATIONSHIP OF ANY EVENT
TO ADCON®-L ADMINISTRATION

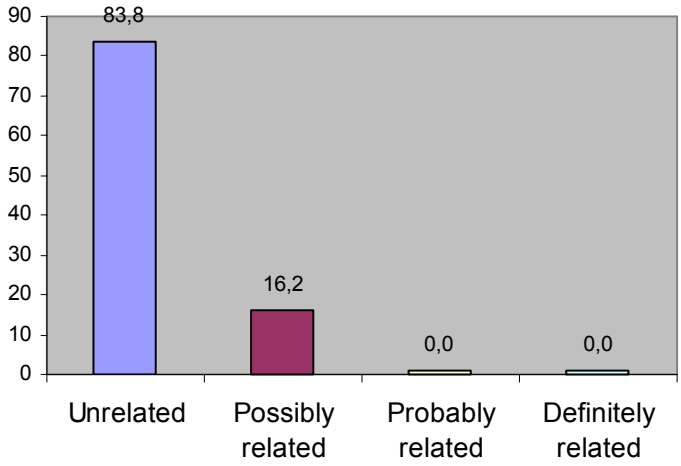


TABLE 4.
REVIEW OF COMPARABLE ADVERSE EVENTS IN THE EUROPEAN CLINICAL STUDY AT 6 MONTHS AND RETROSPECTIVE CLINICAL STUDY

Event Description	ADCON-L European Clinical Study (n=147)	ADCON-L Retrospective Evaluation (n=819)
Skin Rash	1 (0.7 %)	3 (0.1 %)
Radiculitis	8 (5.4 %)	26 (3.2 %)
Infection	0	2 (0.2 %)
Temperature Spike	1 (0.7 %)	5 (0.6 %)
CSF Leak/Pseudo-meningocele	2 (1.4 %)	5 (0.6 %)
Back Spasm	8 (5.4 %)	17 (2.1 %)
Deep Thrombophlebitis	0	1 (0.1 %)
Sensory Deficit	10 (6.8 %)	4 (0.5 %)
Motor Deficit	12 (8.2 %)	1 (0.1 %)
Anaphylactic/Anaphylactoid Reactions	0	0
Death	0	0

CONCLUSIONS

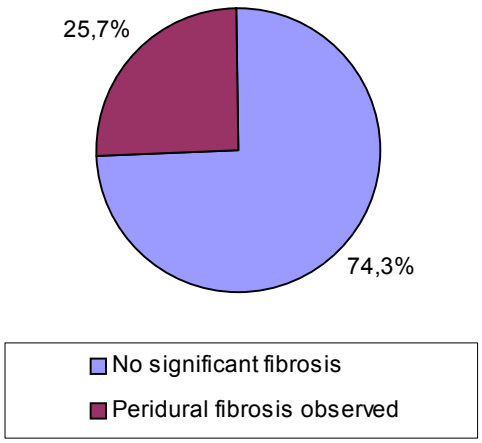
- No AE was considered “probably” or “definitely” related to ADCON-L
- 83.8% of any events (AE/ME) were considered “unrelated” to ADCON-L; 16.2% were considered “possibly” related.
- The incidence rate of CSF leakage or pseudomeningocele was 0.6% of the total eligible patient population
- Physicians’ observations at reoperation revealed that 74.3% of the cases at reoperation had no significant peridural fibrosis
- The most common reasons for reoperations (4.3% of population) were recurrent herniation and retained disc fragment

This study demonstrated that ADCON-L is safe, and the results are consistent with the previous prospective European Clinical Study

TABLE 5.
REOPERATION CHARACTERISTICS – ELIGIBLE PATIENTS

CHARACTERISTICS REOPERATION	PATIENTS N (%) 35 (4.3%)	
Reoperation Surgery Levels		
L4-L5 right	9	(25.7 %)
L4-L5 left	7	(20.0 %)
L5-S1 right	9	(25.7 %)
L5-S1 left‘	10	(28.6 %)
Indication for Reoperation		
Retained Disc Fragment	5	(14.3 %)
Residual Disc Material	3	(8.6 %)
Residual Radiculopathy	2	(5.7 %)
Local Mass	0	
Other Indication	31	(88.6 %)
Recurrent Herniation	23	(65.7 %)
Other Herniation	1	(2.9 %)
Dural Tear/CSF Leakage	4	(11.4 %)
Other	3	(8.6 %)
REOPERATIVE FINDINGS: SIGNIFICANT PERIDURAL FIBROSIS		
Yes	8	(22.9 %)
No	26	(74.3 %)
Missing	1	(2.9 %)
INTERVAL BETWEEN INITIAL SURGERY AND REOPERATION		
Mean (SD) (weeks)	29.2	(29.2)
Median (weeks)	18.0	
Min-Max (weeks)	1.0 – 123.0	

FIGURE 2.
SURGEONS' EXPERIENCE AT REOPERATIONS



REFERENCES

1. Benoist M, Ficat C, Baraf P, Cauchoix J: Spine 5:432-436, 1980.
2. Boden SC, Wiesel SW: The Spine, Third Edition, ed. Rothman and Simeone, pp. 1899-1906, 1992.
3. Fager CA, Freidberg SR: Spine 5:87-94, 1980.
4. North RB, Campbell JN, James CS, Conover-Walker MK, Wang H, Piantadosi S, Rybock JD, Long DM: Neurosurgery 28:685-691, 1991.
5. Burton CV: Orthop Clin North Am 16:417-444, 1985.
6. Cauchoix J, Ficat C, Girard B: Spine 3:256-259, 1978.
7. Finnegan WJ, Fenlin JM, Marvel JP, Nardini RJ, Rothman RH: J Bone Joint Surg (Am) 61:1077-1082, 1979.
8. Kotilainen E, Valtonen S, Carlson CA: Acta Neurochir 125:120-126, 1993.
9. Hurme M, Katerio K, Nykvist F, Aalto T, Alaranta H, Einola S: Acta Radiol 32:286-389, 1991.
10. Burton CV, Kirkaldy-Willis WH, Yong-Hing K, Heithoff KB: Clin Orthop 157:191-199, 1981.