Perioperative and Early (90-Day) Clinical Safety and CT Imaging Data from an Investigational Laparoscopically-Implanted Splenic Neuromodulation System for the Treatment of Refractory Rheumatoid Arthritis

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Background:

- Relatively few patients with Rheumatoid Arthritis (RA), achieve sustained remission or low disease activity with current Anti-Rheumatologic Therapy.

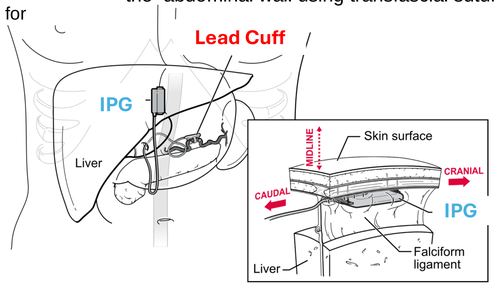
  [Smolen; Lancet 2016;Oct 22:388(10055):2023-2038)
- **Electric stimulation of Splenic Artery Nerves** is being studied as a form of bioelectronic immuno-modulation therapy for refractory RA under an FDA IDE.
- Patients with RA are at **increased risk of Surgical Site Infections** (SSIs) due to their RA and the immuno-suppressive effects of anti-rheumatologic therapy
- To reduce the risk of SSIs and systemic complications, this neuromodulation system uses a unique design that allows the system to be **implanted laparoscopically**

Study Methods:

- **Preoperative evaluation**
  - The Rheumatologist identified and evaluated patients to determine if their disease activity and clinical status were appropriate for this study.
  - The surgeon evaluated these patients and their CTA to determine if they were an appropriate surgical candidate.
  - **No other procedure specific preparation was required.**
- **Postoperative Follow-up:**
  - **All patients were:**
    - Evaluated with a postoperative plain film of the abdomen.
    - Monitored overnight and discharged when clinically appropriate.
    - Followed for one month, to assess for perioperative complications.
  - Therapy was initiated, one month postoperatively, and patients followed for two additional months while receiving therapy.
  - Three months after implantation patients underwent a CTA to assess for system movement and tissue changes induced by:
    - The implant procedure,
    - The presence of the system in the body, or
    - The delivery of Splenic Nerve Stimulation Therapy.

High level Overview of The Laparoscopic Implant Procedure

- The lesser sac is opened and the splenic artery isolated in an area where it is separate from the pancreas.
- The **cuff** is then applied to the splenic artery.
- The lead body is tunneled through the gastro-hepatic ligament into the subhepatic space.
- The connector end of the lead is exteriorized and connected to the Implantable Pulse Generator **(IPG)**.
- The **IPG** and proximal lead are then introduced into the abdominal cavity and the IPG is placed in a pocket formed within the falciform fat pad on the inner aspect of the abdominal wall using transfascial sutures.



Results – Operative Outcomes

- All patients were successfully implanted with the system and completed three months of follow-up
- No intraoperative adverse events were reported.
- All patients were observed in the hospital, per protocol, and discharged on postoperative day one.
- No perioperative complications were reported.
- Splenic nerve stimulation was started one month after surgery, and patients followed for two additional months, while receiving therapy (Total follow-up three months).
- After three months with the system implanted, patients were evaluated clinically and with CTA.
- There were no complications during the three-months of postoperative follow-up. Specifically, **wound infections and impaired wound healing were not observed.**
- The CTAs, as interpreted by board certified radiologists, demonstrated:
  - Normal postoperative findings
  - That the position of the neuromodulation systems remained stable,
  - No evidence of splenic artery pathology (stenosis, thrombosis or pseudoaneurysms).
  - No evidence of pathology in the pancreas, spleen or other abdominal viscera or the imaged portions of the thorax.

Demographic Factors (N = 5)	
Age (years), Median [Min, Max]	52 [49, 67]
BMI, Median [Min, Max]	26.2 [23.8, 26.8]
RA functional class III*	60%
Failed ≥ 2 Biologic Agents	100%

*__Class III__ able to perform usual self care but limited in vocational and avocational activities

Hochberg et. al. Arthritis Rheum 1992;35(2):498-502

Novel Aspects of the System and Implant Procedure

- **The implant procedure:**
  - Is performed using standard laparoscopic techniques and commercially manufactured instruments.
  - Allows for implantation of the system via trocars, eliminating contact between the skin and the system.
- **The Lead** contains electrodes in a self-retaining, self-sizing cuff that is placed around the Splenic artery and the surrounding nerve plexus.
- The implant procedure includes a novel site for the **Implantable Pulse Generator** [IPG] in the preperitoneal plane within the falciform fat pad of the abdominal wall which:
  - Allows for wireless recharging and programing
  - Eliminates the need to create skin flaps for a subcutaneous pocket and the wound healing issues related to these pockets.

Conclusions:

- **These safety data from this Early Feasibility Study support expanding the clinical investigations of this first in human bioelectronic based splenic nerve stimulation therapy system that is implanted entirely within the abdominal cavity using a minimally invasive surgical technique.**

- This system has been developed by, and the clinical trial is being sponsored by Galvani Bioelectronics
- This is an investigational system, that is not commercially available and is currently being studied in an Early Feasibility Study under an FDA Investigational Device Exemption