Cardiovasc Intervent Radiol (2023) 46:1283–1284
https://doi.org/10.1007/s00270-023-03516-9

GENESIS 2 Trial: Unveiling the Potential of Genicular Artery Embolization

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Received: 4 July 2023 / Accepted: 12 July 2023 / Published online: 2 August 2023

Genicular artery embolization (GAE) has garnered significant attention as a minimally invasive procedure for the treatment of chronic knee pain. The GENESIS 2 Trial, a landmark study in this domain, will provide crucial insights into the efficacy of GAE [1]. This commentary aims to highlight the design and implications of the trial for the interventional radiology community and patients.

Several prospective trials of GAE have been reported to date, starting with the landmark study by Okuno et al. [2]. The majority of these have been single-arm trials. While a significant benefit was shown with GAE, there remains a placebo effect in any study addressing pain. Acceptance into treatment guidelines, embolic device approval by government bodies, and approval for procedure payment mandates proven benefit in randomized trials in which a control group is present. Recent randomized trials involving a control group have been mired with questionable methodology or technique. It is paramount that operator experience in GAE is present from the start of the trial. Additionally, mid- and long-term outcomes (6–24 months) allow one to truly assess the benefit of GAE, as the placebo effect tends to wane over time.

GENESIS 2 employs a multicenter, prospective, randomized controlled design, ensuring robustness in its methodology. The study includes a substantial sample size (110 participants) and employs rigorous selection criteria to ensure the inclusion of patients with refractory chronic knee pain. The participants are randomly assigned to two groups: the GAE group, receiving the intervention, and the control group, receiving a placebo procedure. The primary outcomes assessed are pain relief, functional improvement, and quality of life measures. Additionally, the trial evaluates the safety profile of GAE.

Several potential trial pitfalls from prior studies are addressed in the GENESIS 2 trial. The authors have formed a multidisciplinary team, including members from orthopedic surgery interventional radiology and neuroscience. The neuroscience component assesses the neuropsychological aspect of chronic pain. The interventional radiologists have extensive experience in embolization, particularly with GAE. Finally, the outcomes are assessed at multiple timepoints, with the primary endpoint at 6 months. Secondary outcomes include an assessment at 24 months as well. Participants will be allowed to crossover from the placebo to the treatment arm at 6 months, after the primary outcome measure.

It is important to acknowledge some potential drawbacks associated with GENESIS 2. These limitations should be considered when interpreting the results and planning future research:

1. Lack of blinding: The GENESIS 2 Trial employs a placebo-controlled design, but blinding of treating physicians and outcome assessors is not possible due to the nature of the intervention.
2. Generalizability of findings: The trial's inclusion and exclusion criteria may have resulted in a relatively homogenous study population, limiting the generalizability of the findings to a broader patient population. Specifically, the trial results should not be applied to people with Kellgren–Lawrence grade 4 osteoarthritis.

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3. Lack of comparative data: Although the Genesis 2 Trial includes a control group receiving a placebo procedure, it does not directly compare GAE to other established treatment modalities, such as invasive surgical interventions or alternative non-surgical interventions. In general, other current minimally invasive interventions are mostly considered investigational and not the standard of care. Therefore, comparative trial of GAE versus these treatments would be premature.
4. While the trial may report a favorable safety profile with no major adverse events, the sample size and follow-up duration may not be sufficient to capture extremely rare or long-term complications associated with GAE. Larger studies and longer-term follow-up will be necessary to better understand the potential risks and complications of the procedure. Multi-center registries could potentially fill this role.

If positive, the GENESIS 2 trial will be a significant milestone in the advancement of interventional radiology for chronic knee pain management. GAE presents itself as a promising alternative for patients who have exhausted traditional therapeutic approaches or are unsuitable candidates for invasive surgeries. With its minimally invasive nature and low complication rates, GAE offers the potential for reduced hospital stays, faster recovery times, and improved patient satisfaction. Furthermore, the impact of GAE on pain relief and functional outcomes signifies a paradigm shift in the management of chronic knee pain, potentially reducing the need for long-term analgesic medication use. As interventional radiology continues to evolve, GAE holds promise in offering a minimally invasive solution that can potentially alleviate the burden on patients and healthcare systems alike.

Funding None.

Declarations

Conflict of interest Consultant for Varian Medical Systems, Boston Scientific Corporation, Teleflex, Delcath, Terumo.

Ethical Approval Not applicable.

Informed Consent Not applicable.

Consent for Publication Yes, I give consent for publication.

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