Losartan and Marfan Syndrome

Prior-art and failed-trial check

Zatoona Labs · October 2026

Summary

Losartan resolves to the RxNorm ingredient (RxCUI 52175) and ChEMBL molecule CHEMBL191; Marfan syndrome resolves to MONDO:0007947. The accompanying CSV is the primary record of each matching ClinicalTrials.gov trial, including registry status, stop reason, stop class, design, enrollment and linked results. The registry search found 8 qualifying trials and 0 efficacy-related stops. The results do not disprove losartan: randomized evidence supports angiotensin-receptor blockers (ARBs) against placebo or no added treatment for slowing aortic-root enlargement, while losartan was not better than beta-blocker standard therapy in direct comparisons. The strongest positive conclusion comes from pooled ARB-class evidence, not from a consistent positive result in every losartan trial or proof of fewer dissections, operations or deaths.

1 Findings

Of the 8 registry trials, 4 were marked completed, 1 was terminated, and 3 retained unknown registry status. The 1 stop was classified as other, not efficacy: the Marfan Sartan placebo-controlled study ended after a similar publication appeared and few participants remained for the month-36 visit. Its paper nevertheless reported no significant difference in aortic-root growth after median follow-up of 3.5 years, so this is a negative result from a trial that stopped for a non-efficacy reason, not an efficacy stop. The registry also lists a randomized 608-participant comparison of losartan with atenolol. In children and young adults, the primary aortic-root Z-score slopes did not differ significantly (P=0.08); both treatments reduced the Z-score relative to body-surface area. A separate randomized comparison in 140 patients likewise found no significant difference in aortic-root or ascending-aorta growth after 3 years. These active-comparator results support the verdict not better than standard treatment, not failure versus placebo.[1–4]

The direct evidence against control is heterogeneous. The external COMPARE randomized trial, reported in a paper that identifies Netherlands Trial Register NTR1423, found lower aortic-root growth with losartan than with no additional treatment (0.77 versus 1.35 mm over follow-up; P=0.014), but no significant difference in its clinical-event endpoints. A losartan-specific meta-analysis of randomized trials also found a smaller change in aortic-root diameter (mean difference -0.13 mm, 95% CI -0.24 to -0.02), without a significant reduction in the composite of surgery, dissection or mortality. The more comprehensive 2022 individual-patient-data meta-analysis found that ARBs approximately halved annual aortic-root Z-score increase versus control (0.07 versus 0.13; difference -0.07, 95% CI -0.12 to -0.01; P=0.012); ARBs and beta blockers did not differ significantly in their direct pooled comparison (P=0.48). Losartan supplied most, but not all, ARB trial evidence. These pooled findings support the verdict supported for slowing aortic-root enlargement versus control and not better than standard treatment versus beta blockers.[5–8]

Smaller trials do not overturn that synthesis. The randomized open-label pilot of losartan added to beta blockade reported slower aortic-root growth than beta blockade alone, whereas the small placebo add-on trial reported similar growth in both groups and explicitly noted that it was underpowered. The double-blind vascular-stiffness trial found different physiologic effects for losartan and atenolol but no change in aortic diameter. A small pilot enrolled patients with Marfan or Loeys-Dietz syndrome together, limiting Marfan-specific interpretation. One other Phase 3 registry trial has no located results paper and remains unreported, not negative.[1, 9–12]

2 Flags

The table preserves the registry stop text rather than inferring failure from termination; its stop-class flag is `other`. Unknown registry status is not equivalent to absent results: published findings are available for NCT00651235 and NCT01145612 despite their registry status, while the MaNeLo entry has no result paper located. The placebo add-on trial with 22 participants was explicitly underpowered; the open-label pilot is also a weak test. Conversely, the larger active-comparator trials cannot establish superiority over no treatment. The 2022 pooled estimate is ARB-class evidence, although most included ARB data were from losartan. The NTR1423 COMPARE trial is discussed because its peer-reviewed protocol and result papers report it, but it is outside the ClinicalTrials.gov CSV export.

3 Methods

Losartan was resolved using RxNorm and ChEMBL, including salt and brand/code aliases; Marfan syndrome was resolved to MONDO:0007947 and its synonyms. ClinicalTrials.gov searched on 2026-10-27 under 18 drug names (losartan, losartan potassium, Cozaar, DuP 753, MK-954, LOSARTAN, Allisartan, Angizaar, Dup-89, E-3174, Exp-3174, EXP3174, HGP-1405, HGP1405, Losartan carboxylic acid, Losartic, Lozap, NSC-758699), alone and with 6 disease names (Marfan syndrome, Marfan syndrome type 1, Marfan syndrome, type 1, Marfan's syndrome, MFS, MFS1): 8 interventional trials test the drug and name the disease. The interventional-trial rule required losartan to be tested (not merely mentioned or given to every arm) and Marfan syndrome to appear in the title or condition. ClinicalTrials.gov trial records and posted outcomes were checked, and PubMed was searched by trial identifier and title for completed or otherwise reportable studies. A separate ClinicalTrials.gov/EU CTIS search returned no additional CTIS record; its coverage does not include many older national-registry trials. The outside-registry COMPARE trial was included in the interpretation only after a published paper identified NTR1423.

4 Limitations

This is not evidence that losartan has no benefit. The stop-reason classification describes why a registry entry stopped, while efficacy comes from posted comparisons, trial papers and pooled analyses. Several trials are small, open-label, use surrogate aortic-growth outcomes, or have uncertain registry updates; the unreported MaNeLo study cannot be treated as a negative trial. Although pooled evidence supports an ARB effect on aortic-root growth, an effect on hard clinical outcomes remains unestablished in the randomized evidence cited here. The pooled class estimate is not a losartan-only causal estimate, and the clinical benefit reported in the long-term COMPARE follow-up is observational after the original randomized period.[13]

Europe PMC's broad literature query failed during retrieval, so the literature search was supplemented with PubMed identifier/title searches; unpublished reports and records in unsearched registries may be missed.

References

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