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Alnylam risks being an IgAN also-ran

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Today's mid-stage data on Alnylam's immunoglobulin A nephropathy (IgAN) candidate cemdisiran make for uneasy reading when put into context. The group said that in a phase 2 study in 31 patients with IgAN, cemdisiran reduced 24-hour proteinuria by 37% relative to placebo. True, this does appear to be better than the 29% placebo-adjusted figure posted by Calliditas's Tarpayo in its pivotal trial back in 2020, though the usual caution should be exercised when comparing data from different trials. But Tarpayo is a pill, whereas cemdisiran, a small interfering RNA, is injected subcutaneously once a month. Moreover, other projects, also oral, from Travere and Chinook might well outdo cemdisiran. Unfortunately it is hard to tell. Alnylam gave only the placebo-adjusted figure for proteinuria, whereas Travere used irbesartan, not placebo, as control, and Chinook's study was uncontrolled. Alnylam cautioned that its trial was descriptive only, and did not include statistical hypothesis testing – both Calliditas and Tarpayo were able to show statistical significance versus control in their much larger trials. Despite this Alnylam, along with partner Regeneron, is planning to take cemdisiran into phase 3.

Cross-trial comparison of selected IgAN projects

Drug	Company	Trial	N	Route	Time point	Reduction in proteinuria
Tarpayo/ Kinpeygo	Calliditas	Ph3 Nefigard (NCT03643965)	365	Once-daily pill	9mth	34% (29% pbo-adjusted*)
Sparsentan	Travere	Ph3 Protect (NCT03762850)	380	Once-daily pill	36wk	50% (38% adjusted for irbesartan control*)
Atrasentan	Chinook	Interim data from Ph2 Affinity (NCT04573920)	20	Once-daily pill	24wk	59% (no control arm)
Cemdisiran	Alnylam	Ph2 (NCT03841448)	31	Once monthly sc injection	32wk	37% pbo-adjusted

**Statistically significant. Source: clinicaltrials.gov, company releases.*