






Nephrology Journal Club

@NephJC

10 Tweets • 2023-01-28 •  [See on Twitter](#)

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 #TenTweetNephJC 

This week CARDINAL - the largest ever RCT in patients with Alport Syndrome  

#TenTweetNephJC


- 1. Intro**
- 2. So I didn't join – what was the study?**
- 3. I tweet methods**
- 4. I tweet results**
- 5. A figure paints a 1000 words**
- 6. Give me something clever to repeat**
- 7. Was there consensus in the chats?**
- 8. Quote of the fortnight!**
- 9. I want more info**
- 10. Final thoughts**



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What did I miss?

In 2013 BEACON RCT of the Nrf2 activator Bardoxolone looked to slow CKD in patients with diabetic nephropathy. Unfortunately it  CCF, leading to early termination.

But could it do better in a younger Alport cohort at less CV risk?

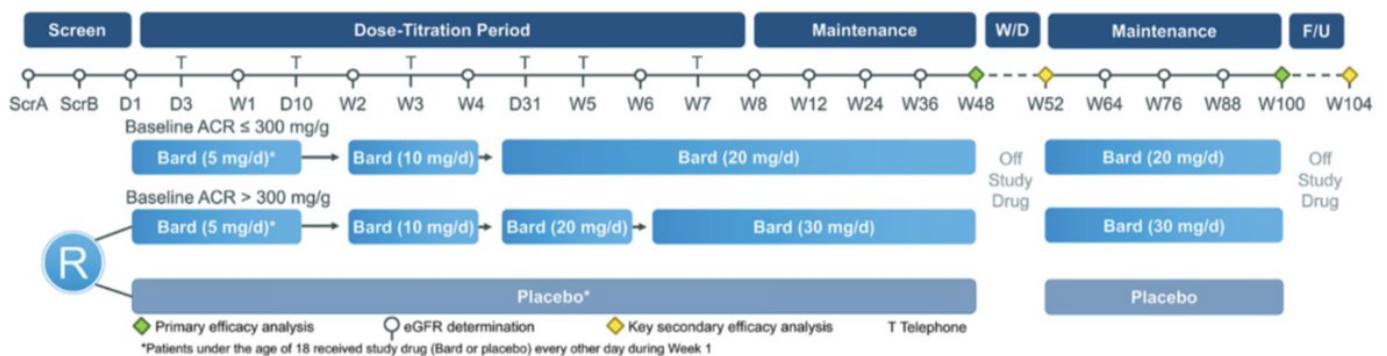
<https://pubmed.ncbi.nlm.nih.gov/36411058>

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1 tweet methods

- ✓ Histologic or genetic diagnosis of Alport Syndrome
- ✓ Age 12–70 yrs, eGFR of 30–90, no cardiac disease
- ✓ 1:1 randomization to bardoxolone or placebo. Two washouts periods week 48-52, and after week 100
- ✓ Primary outcomes: eGFR at week 48 & week 100



Abbreviations: Bard=bardoxolone methyl; eGFR=estimated glomerular filtration rate; F/U=follow-up; R=randomization; W/D=withdrawal

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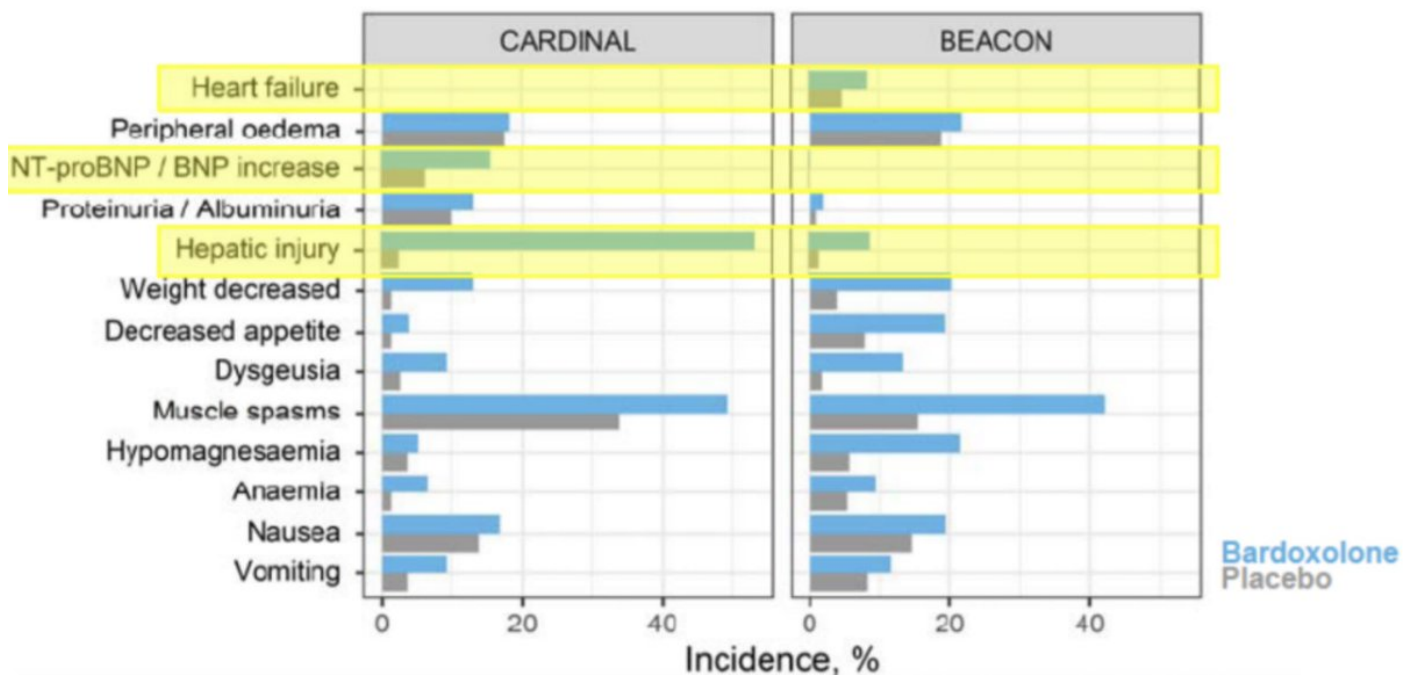
1 tweet results

- ◆ 155 randomized!
- ◆ Mean: age 40, eGFR 63, uACR 142mg/g
- ◆ 'positive' primary outcome: week 100 'on treatment' bardoxolone arm = higher eGFR by 7.4 (P<0.001)
- ◆ But after drug washout effect disappeared, indicating no impact on actual disease progression

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A figure paints 1000 words

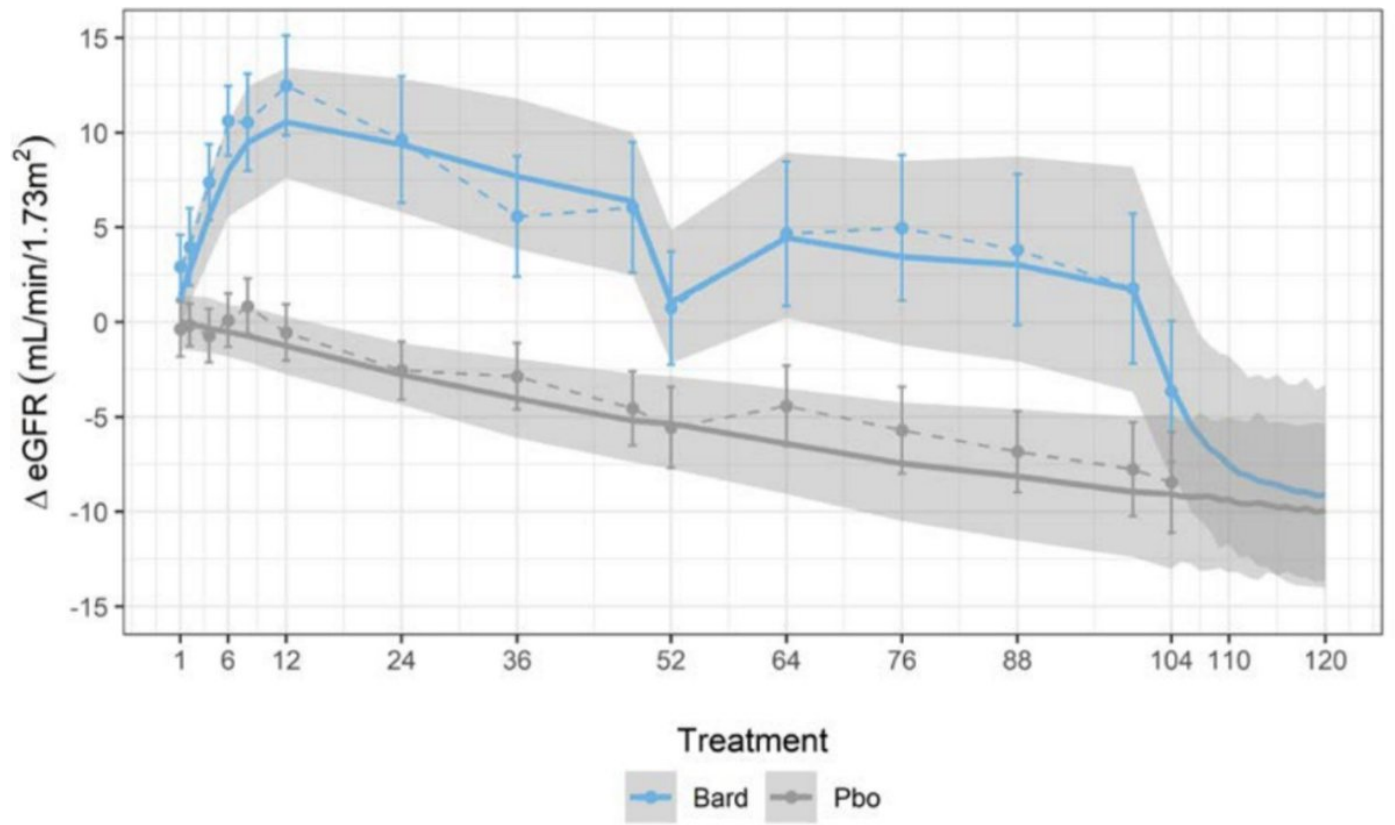
Bardoxolone side-effects in CARDINAL and BEACON, from the FDA



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Give me something clever to say

“Bloods drawn at >14 days were accepted in washout period, but the FDA thought washout should have been >8 weeks. Look how eGFR gains modelled by FDA were fully lost when drug is stopped; it’s just a temporary pharmacodynamic effect.”



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Chat consensus?

1 Use of bardoxolone for Alport never had any supportive preclinical data

2 FDA made right decision rejecting approval application

3 Future generally looking brighter in Alport; for now focus on early diagnosis, early ACEi, finding an RCT of better drug

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Quote(s) of the fortnight!

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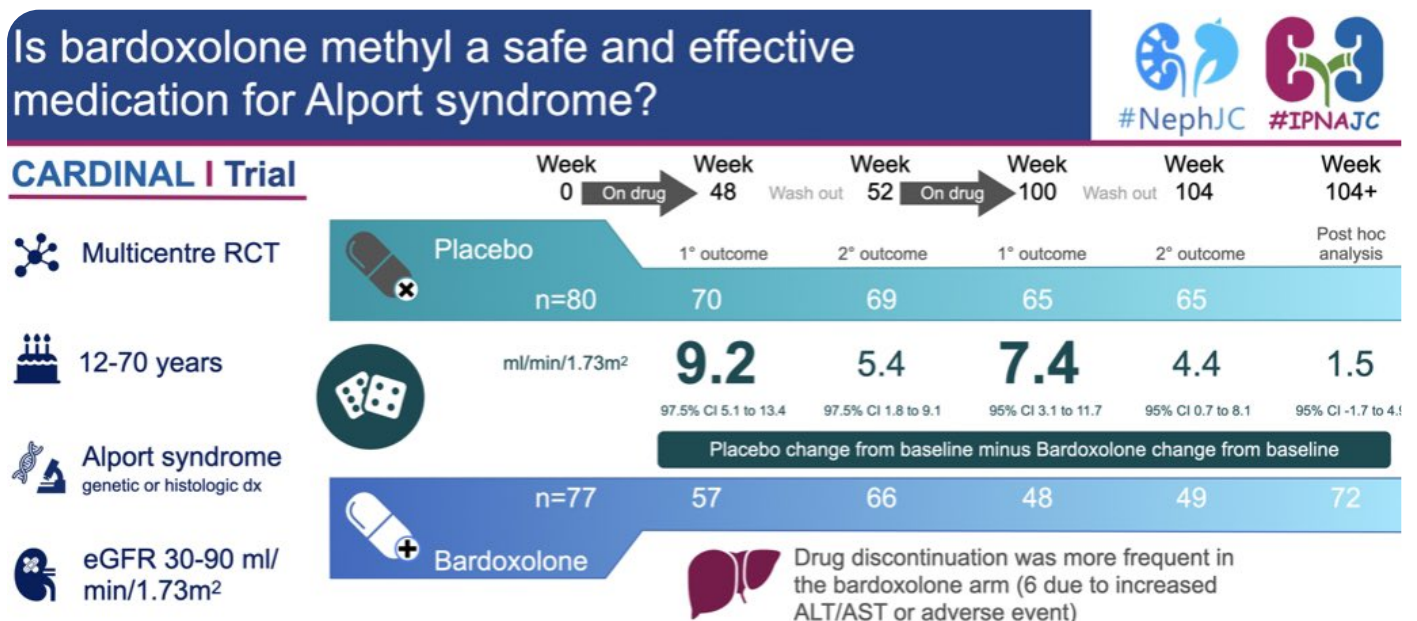
I want more info

✓ Follow @rheault_m & @AlportSyndFndn

✓ NephJC summary from @priti899 and @jamielwilows

✓ VA by @md_abdulqader83

<http://www.nephjc.com/news/bardoxolone>



Conclusion: Patients with Alport syndrome receiving standard care, treatment with bardoxolone methyl resulted in preservation in eGFR relative to placebo; off-treatment results using all available data were not significantly different.

Warady BA et al., *CJASN* 2022; 17: 1763–1774

Twitter @md_abdulqader83

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Final thoughts

* Further bardoxolone trials in ADPKD & diabetes awaited - look critically at washout period & side-effect profile

➔ Up next 7/8 Feb - is chlorthalidone actually better than HCTZ? Bring your biases!

Tweetorial by @jamiexwillows

[https://www.nejm.org/doi/full/10.1056/NE](https://www.nejm.org/doi/full/10.1056/NEJMoa2212270)

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