Change in NT-proBNP and Clinical Outcomes in the Vericiguat Global Study in Subjects with Heart Failure with Reduced Ejection Fraction (VICTORIA)

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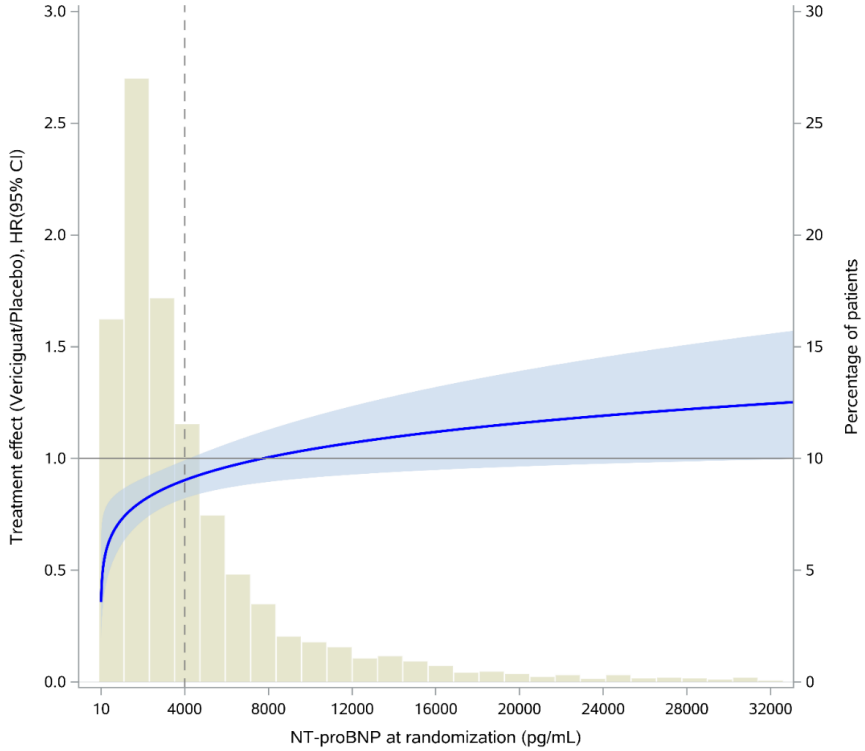
Background: Changes in NT-proBNP & Clinical Outcomes in VICTORIA

NT-proBNP at Randomization and Clinical Outcomes



Prior studies have evaluated the change in NT-proBNP and a meta-analysis has demonstrated that reduction in NT-proBNP is associated with a reduction in HF hospitalizations

Objectives

- Assess whether vericiguat produces changes in sequential measures of NT-proBNP versus placebo
- Explore the relationship between changes in NT-proBNP between randomization and 16 weeks and the primary outcome of CV death or HF hospitalization according to study treatment.

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Vadugnathan *JACC-HF* 2020; Ezekowitz *JACC-HF* 2020

Methods: NT-proBNP, Statistics and Outcomes

- VICTORIA: RCT of 5050 patients with HFrEF and LVEF <45%

  Screening natriuretic peptides:

  Sinus rhythm: NT-proBNP ≥1000 pg/ml (or BNP ≥300 pg/ml)

  Atrial fibrillation: NT-proBNP ≥1600 pg/ml (or BNP ≥500 pg/ml)

- NT-proBNP measured at Randomization, 16, 32, 48 weeks in a core lab (n=4805 patients)
- Primary outcome: Time to CVD or first HFH
- Association between NT-proBNP change from baseline to 16 weeks and primary outcome (assessed by a landmark Kaplan-Meier survival analysis in 16-week survivors).
- Time-varying treatment effect related to NT-proBNP assessed via a joint modeling framework* through 48 weeks.

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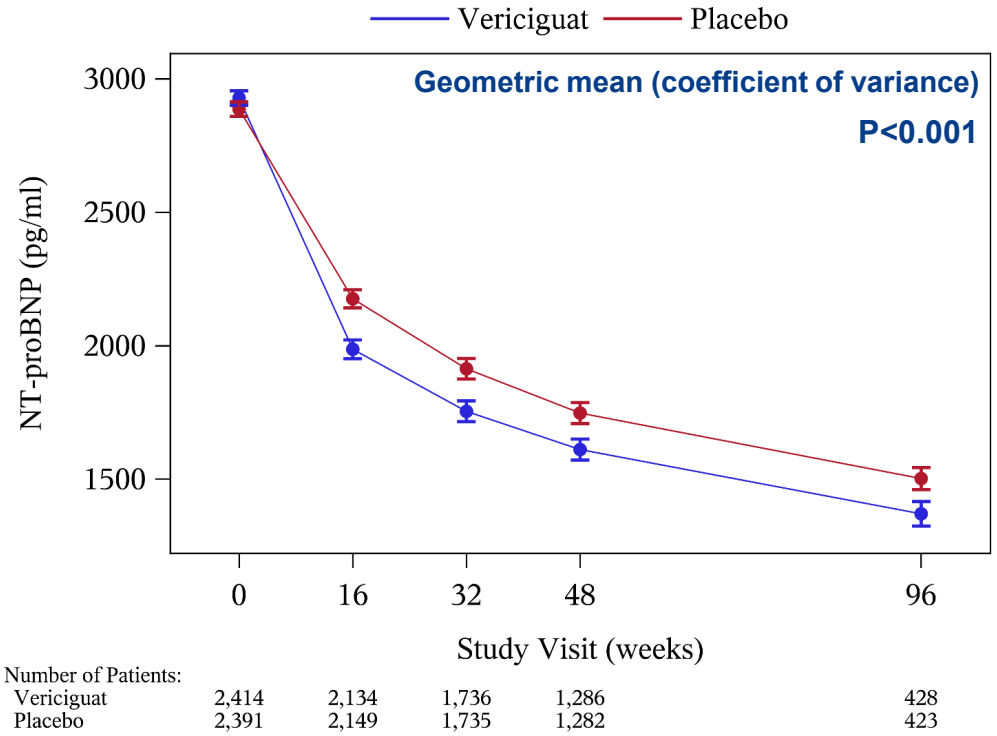
VICTORIA trial funded by Bayer and Merck / MSD

*van Oudenhoven et al Stat Med 2019

Results: NT-proBNP changes over time



Overall relative change over 96 weeks was 14%

Extent of relative changes in NT-proBNP from randomization to Week 16 by treatment.

Week 16 Change	Vericiguat (n=2047), %	Placebo (n=2053), %	Vericiguat vs. Placebo OR (95% CI)	P-value
Any reduction	66.5	57.8	1.45 (1.28-1.65)	<0.001
Reduction ≥50%	25.3	21.0	1.27 (1.10-1.47)	0.001
20%-50% Reduction	27.2	22.9	1.26 (1.09-1.45)	0.002
Change <20%	24.0	24.9	0.95 (0.82-1.10)	0.478
Increase ≥20%	23.4	31.1	0.68 (0.59-0.78)	<0.001
Increase >50%	13.8	18.7	0.70 (0.59-0.82)	<0.001

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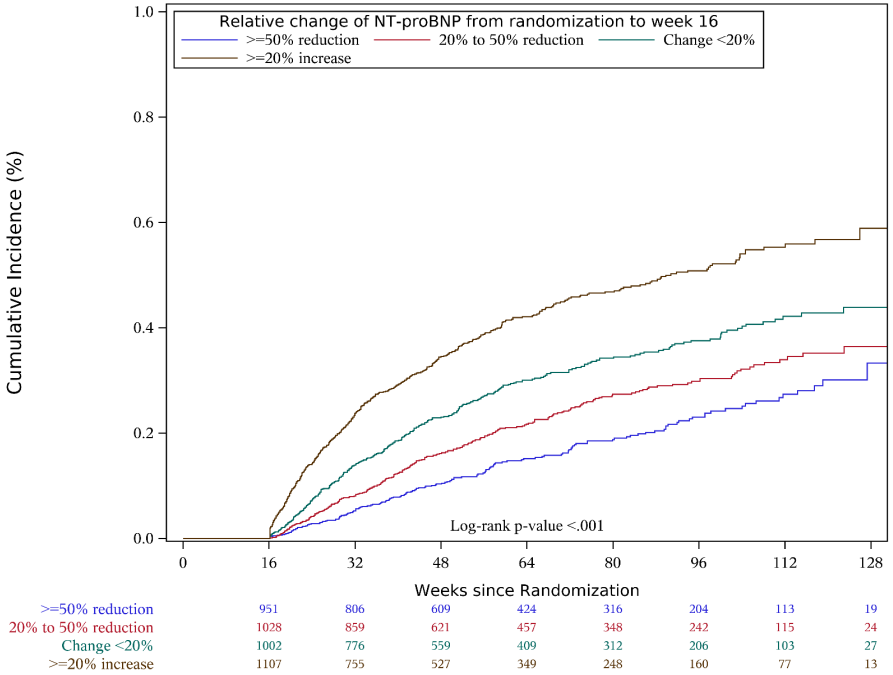
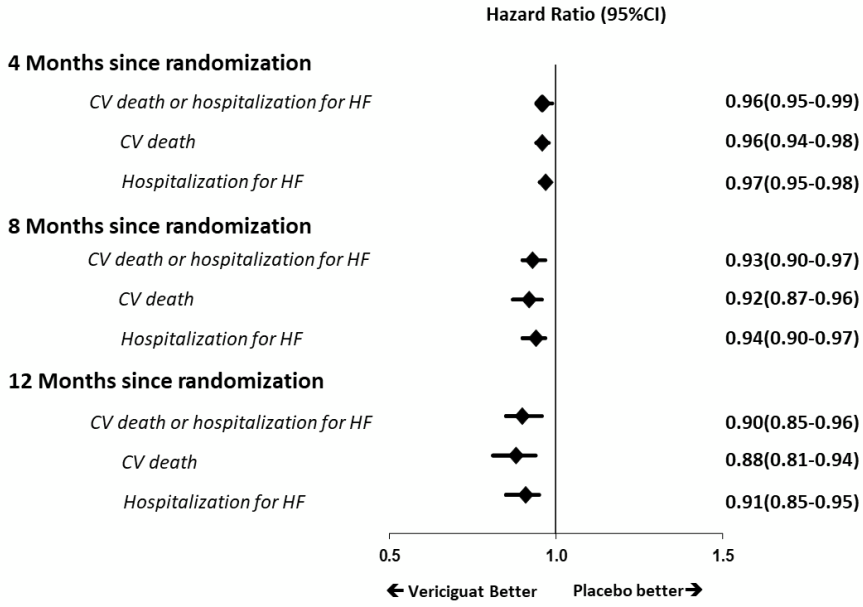
Results: Changes in NT-proBNP and Outcomes

CVD / HFH: *All Patients*



Time-varying treatment effect of vericiguat related to NT-proBNP



Time-varying treatment effect of vericiguat compared to placebo related to NT-ProBNP over time

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Summary/Conclusions

- In patients with worsening HFrEF, vericiguat caused a greater early and sustained decrease in NT-proBNP compared to placebo.
- At 16 weeks, more vericiguat treated patients had declines and fewer had increases in NT-proBNP compared to placebo.
- Relative changes in NT-proBNP were related to the primary composite outcome in *all* patients surviving to Week 16.
- Based on a joint modeling framework, vericiguat's treatment benefit on outcomes was associated -in part- to changes in NT-proBNP over time.