

Novel neprilysin-derived BNP fragments in the plasma of heart failure patients suggest possible insights for a guided ARNi therapy

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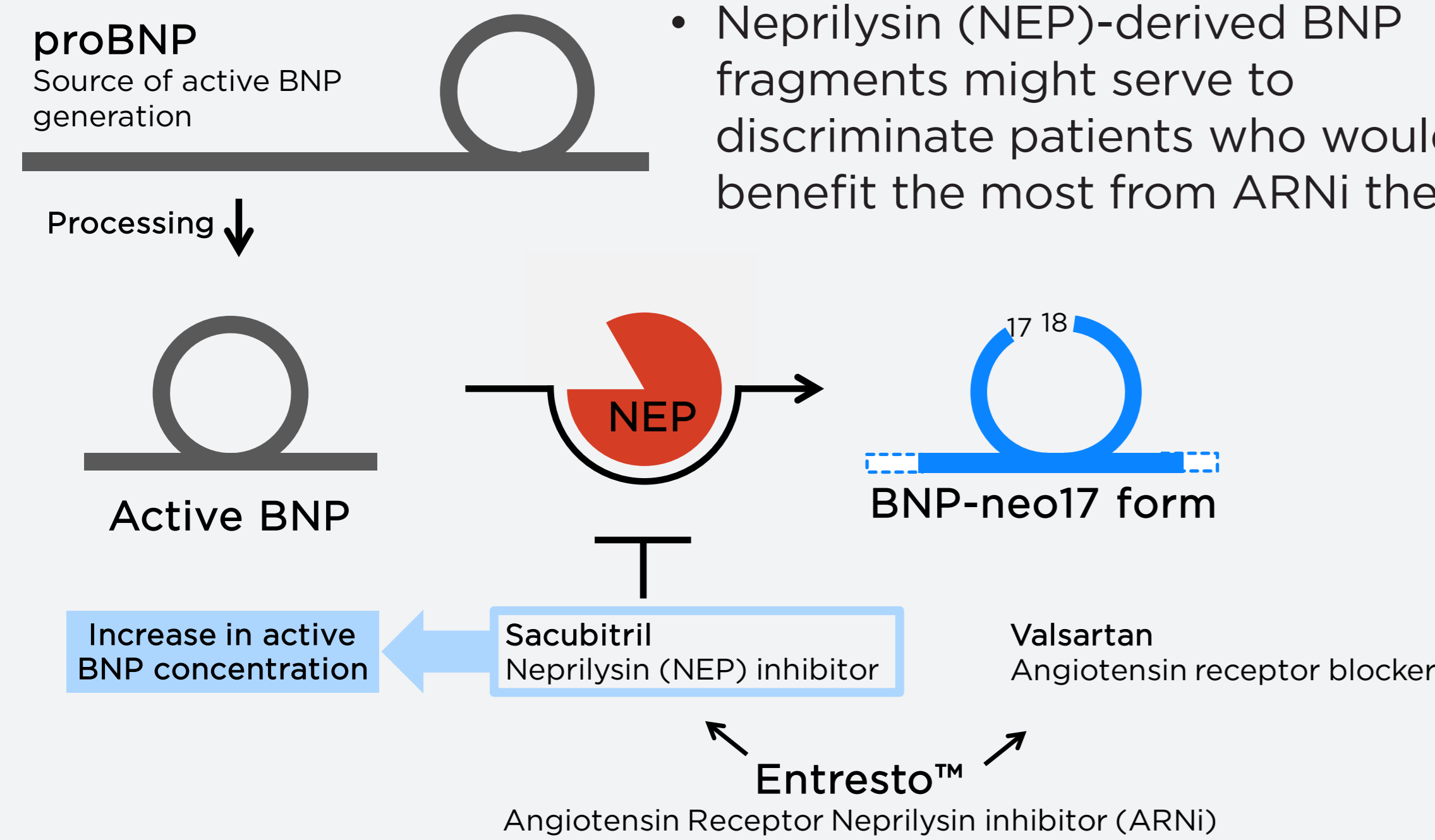
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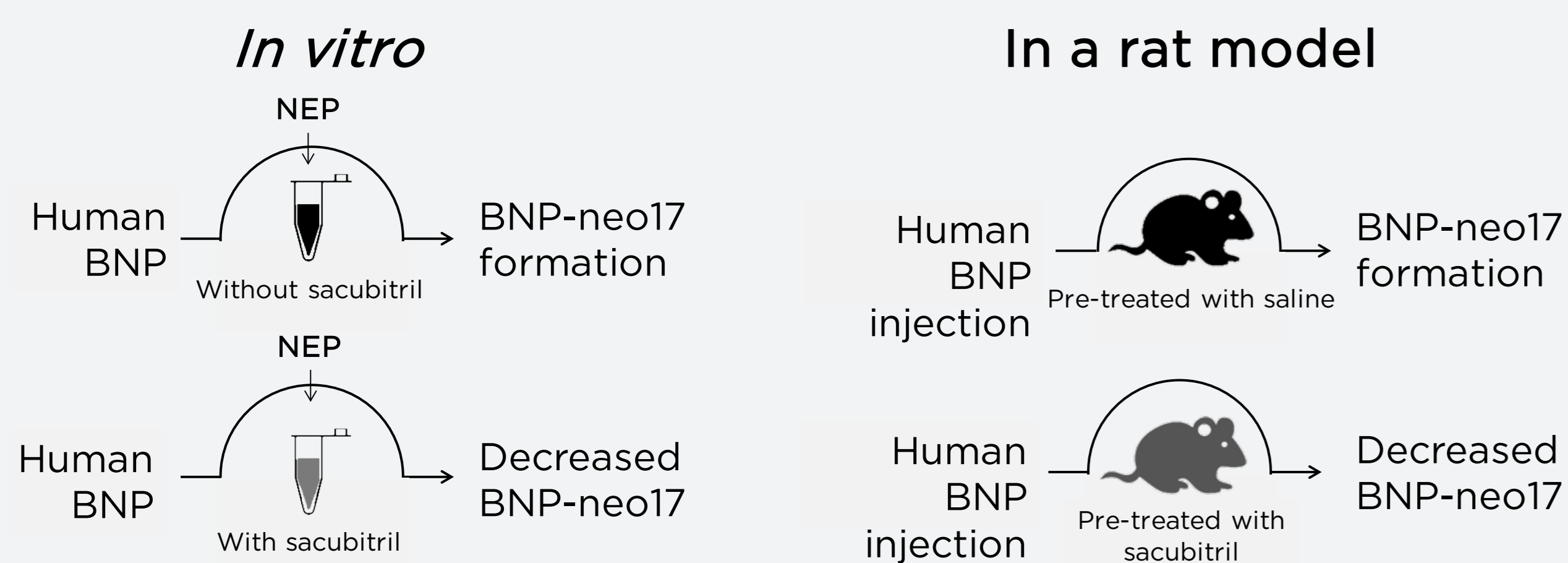
Background

What are neprilysin-derived BNP-fragments?

- The augmentation of active BNP levels is one of the possible mechanisms of cardiac function improvement by ARNi.
- Neprilysin (NEP)-derived BNP fragments might serve to discriminate patients who would benefit the most from ARNi therapy.



BNP-neo17 is generated from BNP by NEP



Aims of the study



- Explore BNP-neo17 in the plasma samples of heart failure (HF) patients
- Compare BNP-neo17 level to total BNP and N-terminal proBNP (NT-proBNP) levels

Methods

Patient information



- 32 patients
- Age 38-93 years (Median 72, IQR 59.8-78.7)
- Acute decompensated heart failure
- NYHA class II-IV
- EDTA-plasma samples
- None of the patients received ARNi therapy**

Immunoassays used

BNP-neo17 sandwich assay



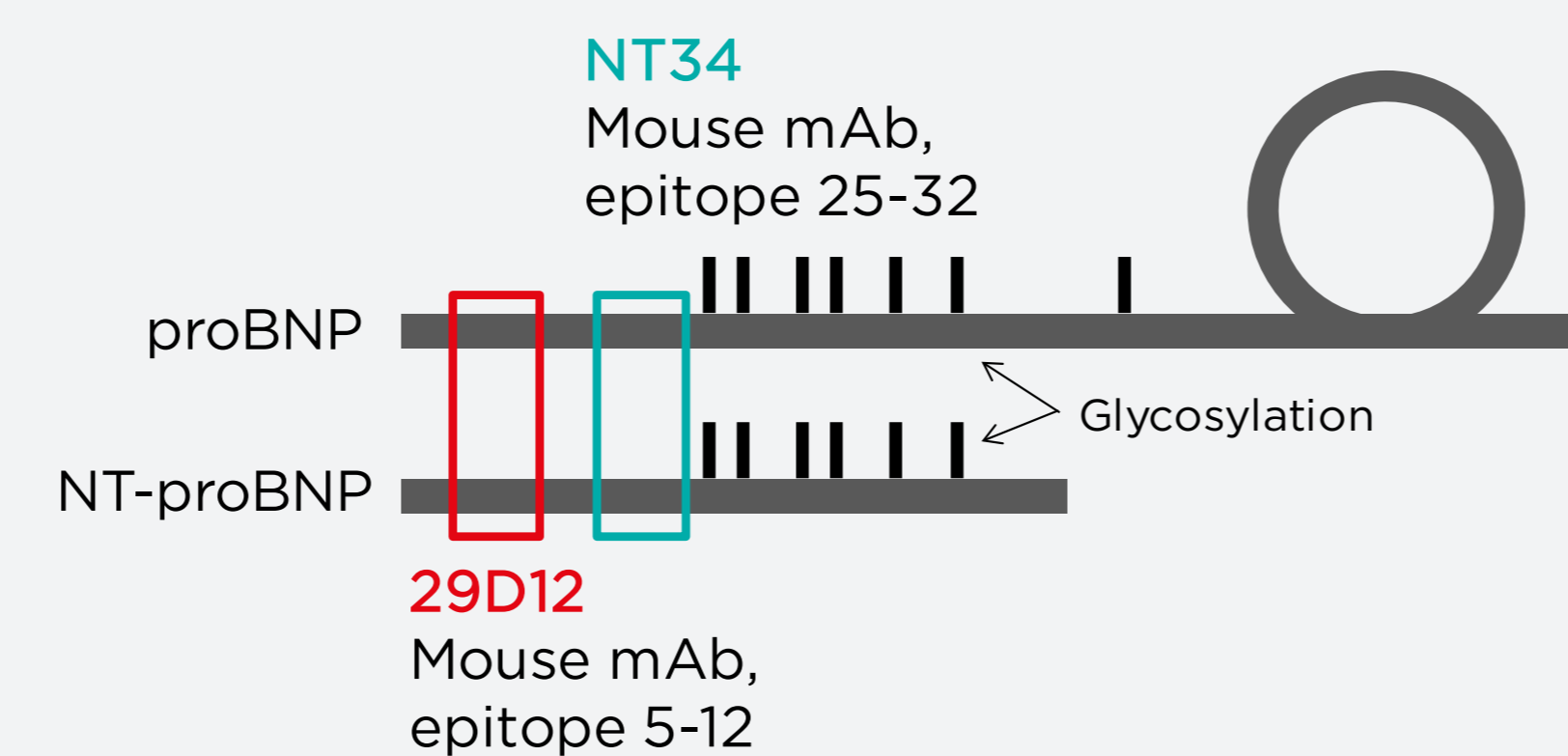
Total BNP assay (ET Healthcare Pylon BNP)

SES-BNP™ assay Detects both BNP and proBNP

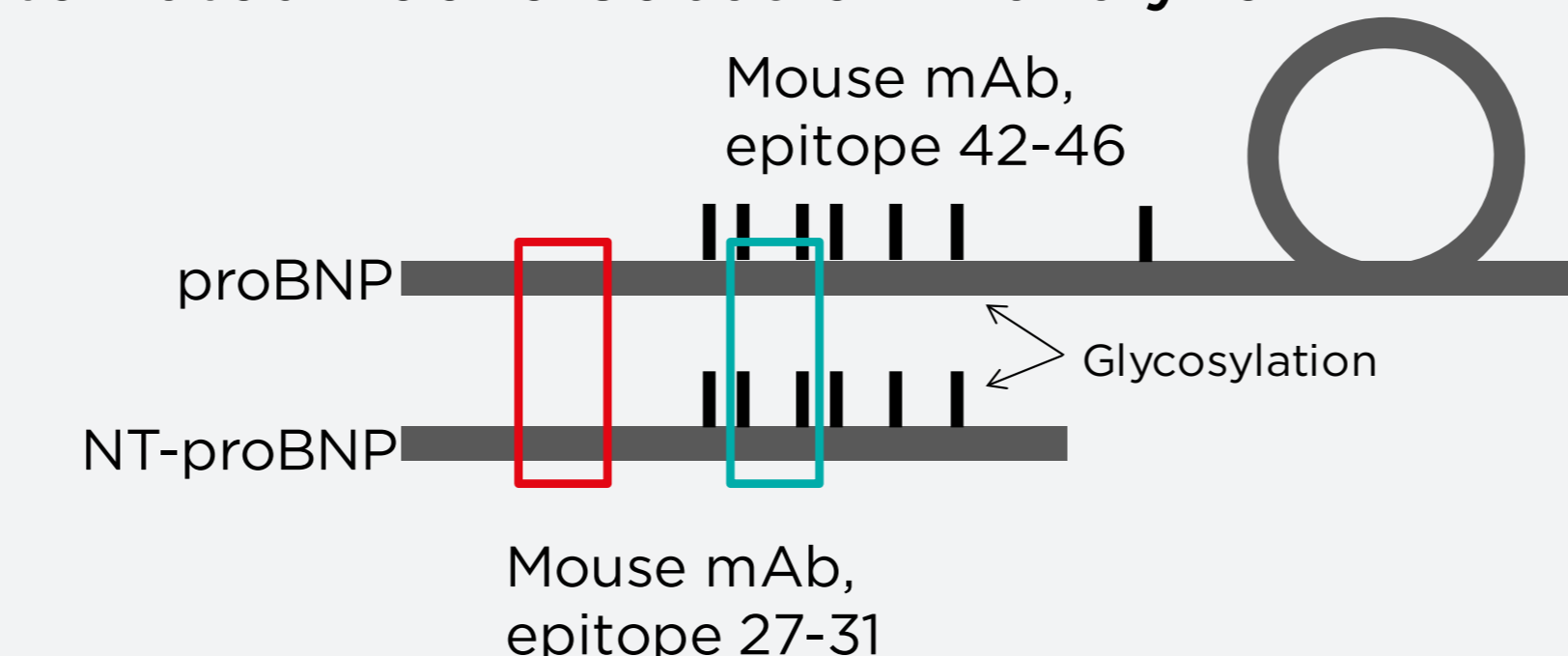
- mAb 24C5 (epitope 11-17)
- mAb AB-BNP-2 (specific to the immune complex BNP-24C5)

NT-proBNP assays

- In-house immunoassay



- Automated Roche Cobas e 411 analyzer



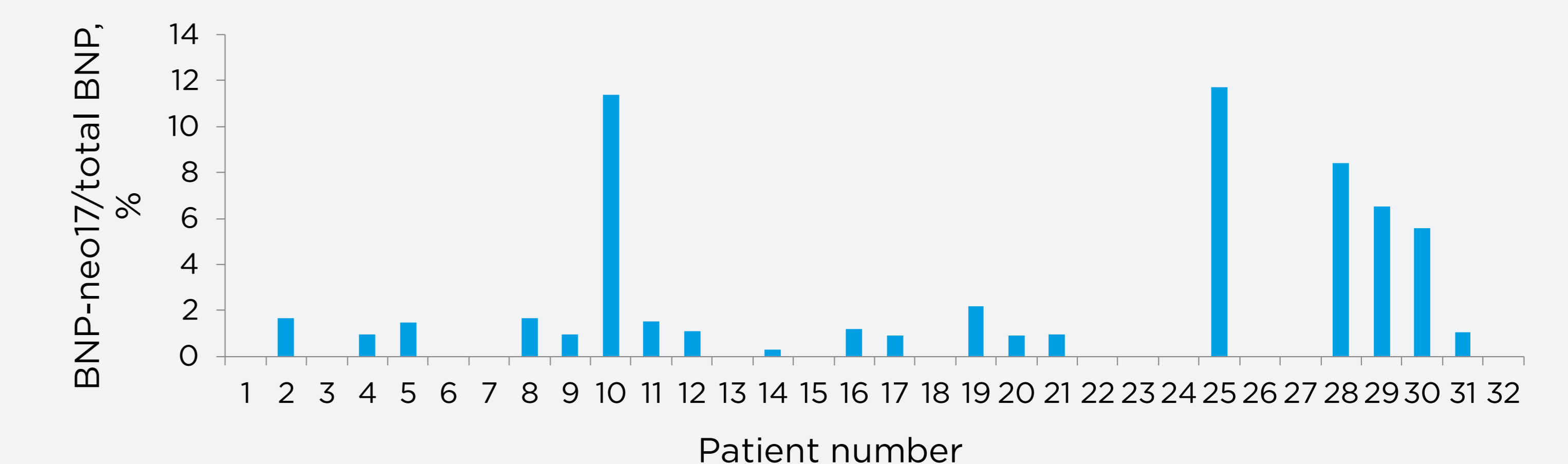
Results

Biomarker concentrations in plasma samples from HF patients

| Assay | Range, ng/L | Median | IQR |
|---------------------------------|----------------|---------|----------------|
| BNP-neo17 sandwich immunoassay | 1.7-37.3 | 7.7 | 6.2-14.0 |
| ET Healthcare Pylon BNP | 28.5-3384.5 | 322.2 | 161.3-737.0 |
| In-house 29D12-NT34 immunoassay | 711.2-156402.4 | 17313.1 | 6322.6-25598.0 |
| Roche Cobas e 411 analyzer | 195.3-95470.0 | 2582.0 | 847.7-5015.5 |

- BNP-neo17 was present in the circulation of HF patients
- BNP-neo17 was detected in 19 of the plasma samples (59.3%)

BNP-neo17 / total BNP ratio varies among individuals



Correlations between the levels of biomarkers

| | BNP-neo17 | BNP-neo17 total BNP |
|--------------------------------------|------------------------|------------------------|
| Total BNP | r=0.7838 P < 0.0001 | r=-0.17523 P=0.3374 |
| In house NT-proBNP assay 29D12-NT34 | r=0.7843 P < 0.0001 | r=-0.0888 P=0.6287 |
| Automated Roche Cobas e 411 analyzer | r=0.712 P < 0.0001 | r=-0.1026 P=0.5762 |

BNP-neo17/total BNP, %

Total BNP, ng/L

$r = -0.17523$
 $P = 0.3374$

- BNP-neo17 level correlates with total BNP or NT-proBNP levels.
- BNP-neo17/total BNP ratio does not correlate with total BNP or NT-proBNP levels.

Conclusions

- The NEP-derived BNP-neo17 is present in the circulation of HF patients. The percentage of BNP-neo17/total BNP varies among individuals independently of total BNP or NT-proBNP levels.**
- BNP-neo17 might serve as an independent biomarker that reflects the impact of NEP on the levels of active natriuretic peptides and thus could be used to guide ARNi or other NEP-inhibition based therapy.**