



Evaluation of QR-010 on CFTR function in CF subjects with the F508del-*CFTR* mutation

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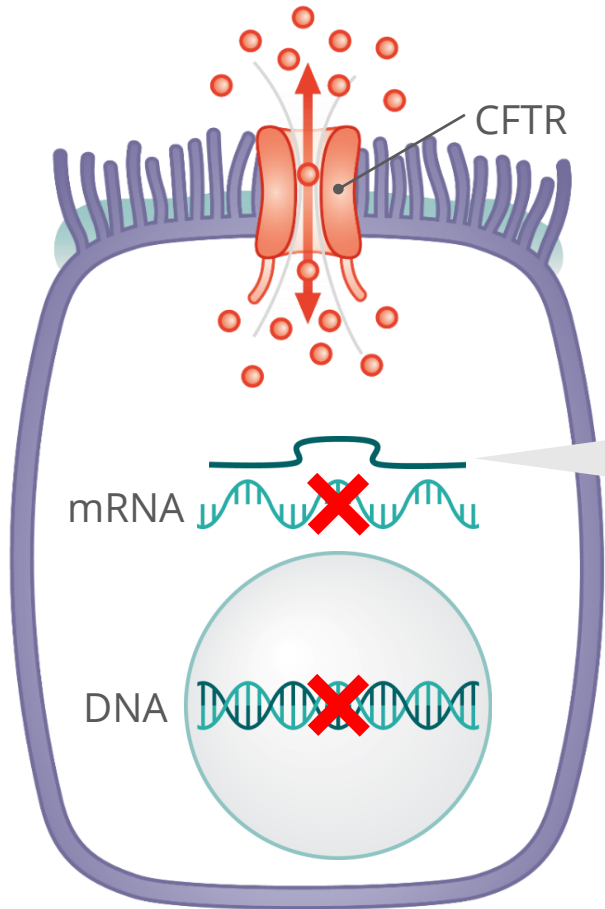
Background:

QR-010 is being developed as a novel RNA-based therapeutic for patients with CF carrying the F508del-*CFTR* mutation

Aim of this exploratory study:

Evaluate the ability of intranasal QR-010 to improve CFTR biologic activity in the respiratory epithelium, assessed by nasal potential difference, in adult homozygous and compound heterozygous F508del CF subjects

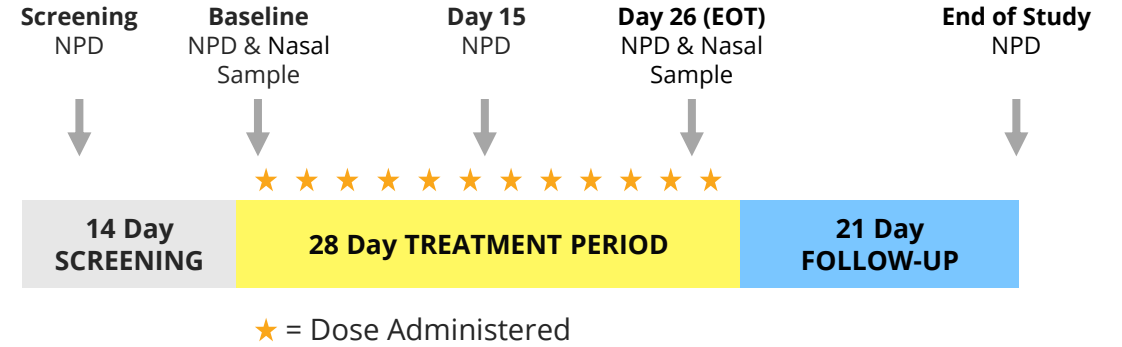
QR-010 - a novel antisense RNA oligonucleotide



QR-010

- Single stranded 33-mer RNA oligonucleotide
- P=S and 2'Ome chemically modified for stability and uptake
- Designed to bind to mRNA region around F508-encoding deletion and to restore CFTR function

Study design

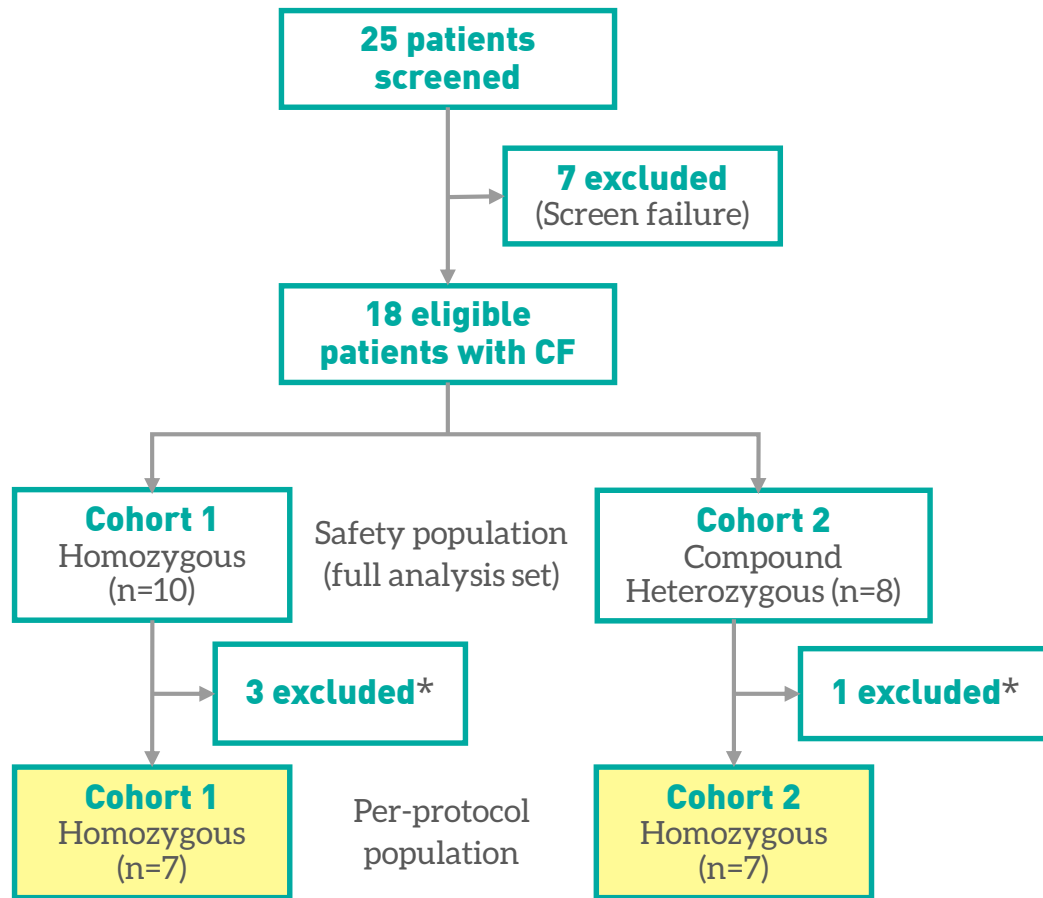


- Intranasal administration
- 5 expert participating sites in EU (CTN) and US (TDN)

Endpoints

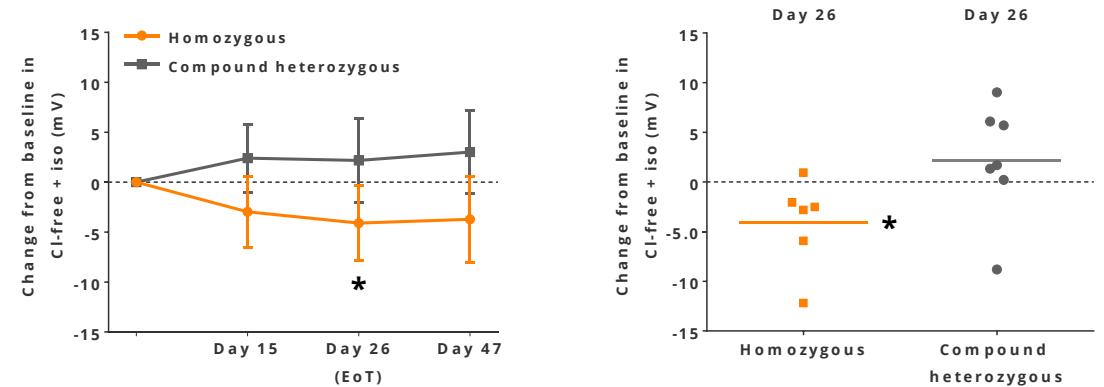
- Primary: total chloride transport assessed by NPD (CFTR biomarker)
- Secondary: sodium transport assessed by NPD
- Safety, SNOT-22 and NERS assessments

Subject Disposition

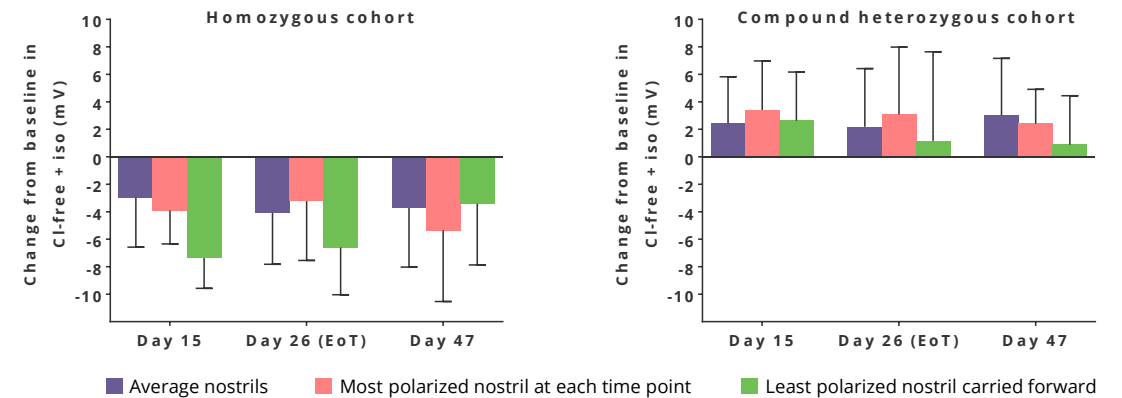


* Did not meet inclusion criteria; their total chloride transport value was more negative than -6.6 mV at baseline, as determined by central reader after subject-initiated treatment

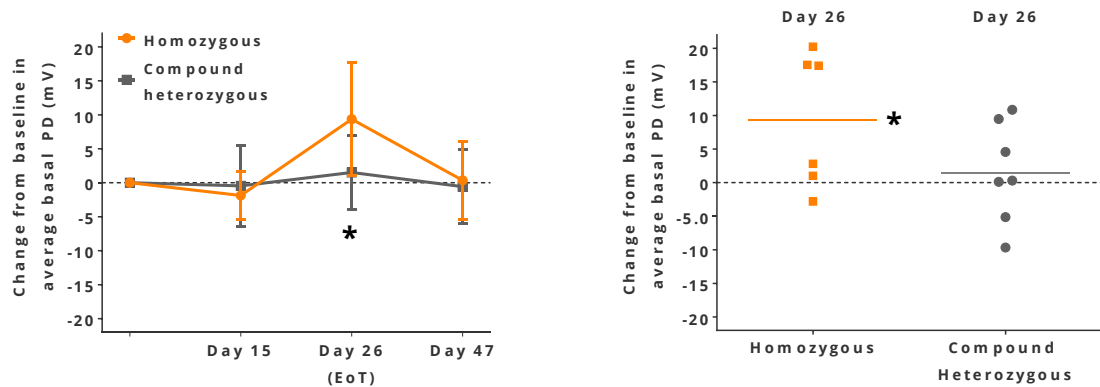
QR-010 improved total chloride transport in F508del homozygous subjects



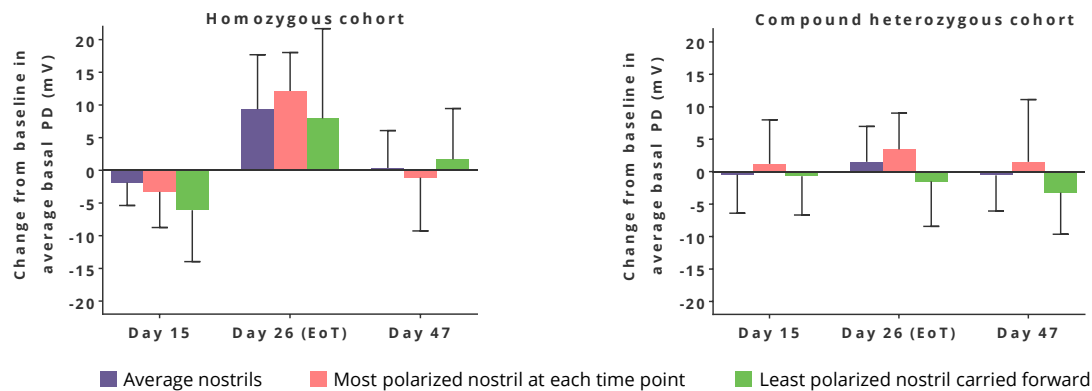
* Mean change Cl-free+iso at Day 26 = -4.1 mV [90% CI -7.8 ; -0.4], P = 0.04



QR-010 also improved sodium transport in F508del homozygous subjects



* Mean change average basal PD at Day 26 = +9.4 mV [90% CI 1.1 ; 17.7], P = 0.04



Conclusions

- ✓ Intranasal QR-010 improved CFTR biologic activity in F508del homozygous subjects
- ✓ This was shown by improved total chloride transport and was supported by improved sodium transport in the nasal epithelium
- ✓ The cohort of compound heterozygous subjects did not respond to the dose and QR-010 regimen tested in this study
- ✓ These data support development of QR-010 for F508del homozygous patients

Acknowledgements



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