

## S2 Appendix Statistical analysis

### Survival analysis

#### *Type of analysis*

- *Cox regression analysis*
- Left truncated (adjusted for age)

#### *Covariates included:*

- ERT type, eGFR at baseline, Sex, Phenotype, Sex \* phenotype
- Left truncated (adjusted for age)

#### *R syntax:*

- `coxph(Surv([Age at start of ERT], [Age at censoring], [status]) ~ [ERT type] + [eGFR at baseline] + strata([sex] + [phenotype] + [sex:phenotype]))`

### eGFR

#### *Type of analysis*

- *Linear mixed model*

#### *Covariates included*

- Time on ERT, eGFR baseline class, ERT type, Sex, Phenotype and interactions

#### *Definitions of covariates*

- eGFR baseline class: 0 = baseline eGFR  $\geq 60$  ml/min/1.73m<sup>2</sup>; 1 = baseline eGFR  $< 60$  ml/min/1.73m<sup>2</sup>

#### *R syntax*

- `LME(eGFR ~ [Time on ERT] * ([eGFR baseline class] * [ERT type] + [sex] * [phenotype]), random = ~ [Time on ERT] | [patient], control = "optim")`

## Proportion of patients with a decrease in LVMI one year after ERT

Response = A decrease or stable LVMI ( $\Delta\text{LVMI} \leq 0$ ) of the measurement closest to the one year time point after ERT

### Type of analysis

- *Logistic regression*

### Covariates included

- LVMI baseline class, LVMI at baseline, ERT type and interactions
- Including age, sex or phenotype as covariates did not led to an improvement of the model

### Definitions of covariates

- LVMI baseline class: 0 = baseline LVMI < 49 gram/m<sup>2.7</sup> (men) and LVMI < 44 gram/m<sup>2.7</sup> (men); 1 = baseline LVMI  $\geq$  49 gram/m<sup>2.7</sup> (women) and LVMI  $\geq$  44 gram/m<sup>2.7</sup> (women)

### R syntax

- GLM(response ~ [baseline LVMI class] \* ([ERT type] + [baseline LVMI]), random = ~ [Time on ERT] | [patient], control = "optim")

## Change in LVMI

$\Delta\text{LVMI}$  = the change in LVMI from baseline

### Type of analysis

- *Linear mixed model*

### Covariates included

- Time on ERT, LVMI baseline class, LVMI at baseline, ERT type, and interactions
- Including age, sex or phenotype as covariates did not led to an improvement of the model

### Definitions of covariates

- LVMI baseline class: 0 = baseline LVMI < 49 gram/m<sup>2.7</sup> (men) and LVMI < 44 gram/m<sup>2.7</sup> (men); 1 = baseline LVMI  $\geq$  49 gram/m<sup>2.7</sup> (women) and LVMI  $\geq$  44 gram/m<sup>2.7</sup> (women)

### R syntax

- LME( $\Delta\text{LVMI}$  ~ [baseline LVMI class] \* ([ERT type] + [baseline LVMI]), random = ~ [Time on ERT] | [patient], control = "optim")

### **Change in LysoGb3**

No differences were observed between non-classical men, classical women and non-classical women. Therefore they were considered as one group. Two separate analysis were performed for men with classical FD and the other patients because of the large differences in the range of lysoGb3 values between these groups

$\Delta$ LysoGb3 = the change in lysoGb3 from baseline

*Type of analysis*

- *Linear mixed model*

*Covariates included*

- Time on ERT, ERT type, lysoGb3 at baseline and interactions

*R syntax*

- $LME(\Delta LysoGb3 \sim ([Time\ on\ ERT] * [ERT\ type] + [Baseline\ lysoGb3]), random = \sim [Time\ on\ ERT] \mid [patient], control = "optim")$

### **Change in LysoGb3 in relation to antibody status**

Only men with classical FD were included since antibody development was limited to this group.

$\Delta$ LysoGb3 = the change in lysoGb3 from baseline.

*Type of analysis*

- *Linear mixed model*

*Covariates included*

- Time on ERT, ERT type, lysoGb3 at baseline, antibody status and interactions

Antibody status 0 = no antibodies present, 1 = antibodies present

*R syntax:*

- $LME(\Delta LysoGb3 \sim [Time\ on\ ERT] * [ERT\ type] * [Antibody\ status] + [Baseline\ lysoGb3], random = \sim [Time\ on\ ERT] \mid [patient], control = "optim")$