TREAT-NMD Activity A07: Accelerate preclinical phase of new therapeutic treatment developement

Work package 7.4: Develop standardised protocols and procedures for harmonising and accelerating pre-clinical studies (including standardised data analysis)

SOP Title	**The recovery score to evaluate therapy efficiency in NMD: a common, quantitative and comparative scoring system**.
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1.   OBJECTIVE

The success of a therapy is judged from the reduction or disappearance of the symptoms and the normalization of biological markers, specific or not. This is rarely an "all-or-none" situation and it is important to express the benefits obtained in a way allowing a quantitative evaluation of the therapeutic success. Calculation of the **"recovery score"** as proposed here offers a mean to attain this goal. Moreover, it allows comparisons with other therapies and with results obtained by various laboratories.

2.   SCOPE AND APPLICABILITY

Calculation of the recovery score applies to any parameter that can be measured quantitatively: isometric force, serum creatine kinase, percentage of centronucleated fibers, to give a functional, biochemical or morphological example. It is based on the measurements of the parameter studied on **three different specimens*:**

* specimen here refers to either whole animal or to ex vivo samples (blood, tissue etc)

1. the "treated" specimen, i.e. a specimen submitted to the treatment and coming from a NMD-affected animal
2. the "untreated" specimen, i.e. a specimen coming from a NMD-affected animal
3. the "normal" specimen i.e. a specimen from a normal animal

➢ The difference between "normal" and "untreated" gives how much the parameter is affected by the NMD disease
➢ The difference between 'treated' and "untreated" gives the effect of the treatment.

The "recovery score" aims at expressing the effect of a treatment, not by the mere difference between "treated" and "untreated", but **RELATIVELY** to the extent of the deficiency between normal and NMD-affected animals; it gives directly how much (in %) of the deficit has been recovered by the treatment.

$$\text{Recovery score} = \frac{[\text{ treated }[- [\text{ untreated }]}{[\text{ normal }] - [\text{ untreated }]} \times 100$$

Note that the numerical values to be entered into the formula are absolute values, without sign.

3. CAUTION

The recovery score is based on two references specimen : the "untreated" and the "normal" specimen. The parameter studied must be measured on these two reference specimen in the same experimental conditions as the "treated" one (littermates, same genetic background, same experimental session, etc)

4. EVALUATION and INTERPRETATION

The recovery score ranges from 0%, when the treatment has no effect to 100% when the "treated" specimen displays the same parameter value as the "normal" one.

The recovery score is independent of the "sign" of the parameter studied. In pathological situations like NMD's, some parameters increase – e.g. the level of serum creatine kinase - , while other decreases – e.g. the muscle force. An efficient treatment will make the creatine kinase to decrease and the muscle force to increase. This may generate confusion of terms in reporting results, a situation prevented by the use of the recovery score.

The recovery score allows

▪ to compare how the treatment differently affect the various parameters of a pathological entity;

▪ to compare how different treatments affect a given parameter

▪ to compare results from different laboratories.

The recovery score is an objective way of assessing the effect of a treatment on a given parameter. It could be complemented by an agreed "scale of clinical interest" among the parameters studied.

5. REFERENCES

Deconinck, N., Tinsley, J., De Backer, F., Fisher, R., Kahn, D., Phelps, S., Davies, K. and Gillis, J. M. (1997). Expression of truncated utrophin leads to major functional improvements in dystrophin-deficient muscles of mice. Nat Med 3**,** 1216-1221.

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