Online Resource 4

How are growth hormone and insulin-like growth factor-1 reported as markers for drug effectiveness in clinical acromegaly research? A comprehensive methodologic review

Pituitary

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Checklist for reporting of acromegaly studies:

1. **Insulin-like growth factor 1**
    - Report method of sampling (single, fasting, mean of multiple samples).
    - Report IGF-1 assay, preferably including the international reference standard.
        - Handling of data obtained from 2 or more different assays.
    - Report criteria for biochemical control, cut-off for IGF-1?
    - Report ULN corrected IGF-1 levels.
    - Report % biochemical control and 95%-CI using the pre-defined criteria.
    - Report ULN corrected mean ± SD (or median [IQR] if non-normal distribution) of pre-defined subgroups.
    - Report % change from baseline with mean ± SD (or median [IQR] if non-normal distribution).
        - Individual baseline and measurements as supplemental material.
            - With an individual's age and gender when IGF-1 concentrations are given

2. **Growth hormone**
    - Report method of sampling (random, fasting, mean of multiple samples with interval).
    - Report GH assay, preferably including the international reference standard.
        - Handling of data obtained from 2 or more different assays.
    - Report criteria for biochemical control, cut-off for GH, if any.
    - Report % biochemical control and 95%-CI using the pre-defined criteria.
    - Report GH mean ± SD (or median [IQR] if non-normal distribution) of pre-defined subgroups.
    - Report % change from baseline with mean ± SD (or median [IQR] if non-normal distribution).
        - Individual baseline and measurements as supplemental material.

3. **Oral glucose tolerance test**
    - Report method of sampling and glucose dose.
    - Report GH assay, preferably including the international reference standard.
        - Handling of data obtained from 2 or more different assays.
    - Report GH cut-off for nadir to assess biochemical control, if any.
    - Report % biochemical control and 95%-CI using the pre-defined criteria.
    - Report GH nadir mean ± SD (or median [IQR] if non-normal distribution) of pre-defined subgroups.
    - Report % change from baseline with mean ± SD (or median [IQR] if non-normal distribution).
        - Individual baseline and measurements as supplemental material.

4. **Pharmacokinetics**
    - Report number of samples and time after dosing.
    - Report individual profiles or mean ± 95%-CI to show the inter-individual variability.
    - Report summary and individual statistics from a NCA (C_{max}, t_{max}, AUC, $t_{1/2}$) or, preferably, perform a more advanced statistical analysis (population PK/PD modeling).
    - Link the individual PK to individual response (e.g. linear/non-linear regression of AUC versus ΔIGF-1).
    - Search for and report covariates that explain the inter-individual variability in the PK.