DOSE - RESPONSE MODELING OF RECOMBINANT HUMAN ERYTHROPOIETIN (rhEPO) IN CHRONIC RENAL FAILURE (CRF) PATIENTS

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Purpose : To build a pharmacodynamic model which describes and predicts hemoglobin (Hgb) change during rhEPO therapy and to use it for dosage adjustment.

Methods : 62 CRF patients with Hgb<8g/dl were treated with rhEPO. Hgb was measured every 2wks. Fifty-four patients without transfusions or complications were analyzed. Four parameters were selected in the final model: response sensitivity to rhEPO (Sen). delay to response (Del), RBC life span (Lif) and natural Hgb decrement (Dec). Parameters were obtained by sequential search algorithm. Parameters used in prediction were obtained individually from data earlier than prediction time.

Results :

1) Overall fit(~12wk):

Parameter	Mean	CV
Sen(g/dl/wk/3u)	0.00912	0.44
Del(wk)	0.5916	1.56
Lif(wk)	6.43	0.40
Dec(g/dl/wk)	0.12	1.29

Mean Absolute Residual = 0.155 g/dl
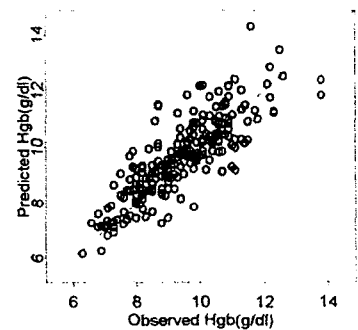
2) Prediction(6~12wk):

Mean Absolute Prediction Error = 0.639g/dl, 6.5%

Conclusion : The prediction error of this model is considered small enough to use in clinical settings. Maintenance dose of rhEPO can be determined as follows:

Maintenance Dose = {(Target Hgb - Baseline Hgb)/Lif + Dec}/Sen (u/kg thrice weekly)