**Figure 2.** Summary of key practical aspects of the Clinical Evaluation of the DOSe of Erythropoietin (C.E.DOSE) trial.

**POTENTIALLY ELIGIBLE**
- Male/ female ≥ 18 years
- Subjects with ESKD and anemia, receiving renal replacement therapy (low or high flux bicarbonate dialysis, hemofiltration, hemodiafiltration, on-line hemodiafiltration, acetate-free biofiltration)
- Subjects without contraindications to ESA treatment or already receiving treatment with any ESA

**RANDOMIZATION VISIT (time 0)**
- Written informed consent
- Patient clinical history
- Randomization and treatment allocation
- Blood chemistry: red blood cells count, HCT, MCV, MCH, MCHC, RDW, MPV, Pct, PDW, platelets
  - lipid profile, glycemic profile, assessment of liver and kidney functions
- Assessment of hemoglobin levels
- Measurement of systolic and diastolic blood pressure, measurement of heart rate
- Assessment of comorbidities
- Detailed information on dialysis (nPCR, Kt/V, dry weight, interdialytic weight gain, dialysis blood flow rate, duration and type of dialysis, type of filter)
- Detailed information on intradialysis and/or house cointervention on ESKD
- Detailed assessment of concomitant medication use (trade name, dose, indication)
- Quality of life questionnaire

**FOLLOW-UP VISIT AT MONTHS 1, 2, 3**
- Blood chemistry: Htc, MCV, MCH, MCHC, platelets
  - Measurement of systolic and diastolic blood pressure, measurement of heart rate
- Detailed information on dialysis (nPCR, Kt/V, dry weight, interdialytic weight gain, dialysis blood flow rate, duration and type of dialysis, type of filter)
- Detailed information on intradialysis and/or house cointervention on ESKD
- Detailed assessment of concomitant medication use (trade name, dose, indication)
- Assessment of haemoglobin level after treatment allocation. For Hb level <9.5 g/dL or >12.5 g/dL (double measurement) ESAs’ dose will be changed according to clinical practice (gradual increase or decrease by 25%). For example look at the therapeutic algorithm (related to erythropoietin or darbepoietin that can be extended to other epoietin) in the protocol.

**FOLLOW-UP VISIT AT MONTHS 6, 12, 18, 24, 30, 36, 42, 48**
- Blood chemistry: red blood cells count, HCT, MCV, MCH, MCHC, RDW, MPV, Pct, PDW, platelet
  - lipid profile, glycemic profile, assessment of liver and kidney functions
- Assessment of haemoglobin levels
- Measurement of systolic and diastolic blood pressure, measurement of heart rate
- Detailed information on dialysis (nPCR, Kt/V, dry weight, interdialytic weight gain, dialysis blood flow rate, duration and type of dialysis, type of filter)
- Detailed information on intradialysis and/or house cointervention on ESKD
- Assessment of haemoglobin level after treatment allocation. For Hb level <9.5 g/dL or >12.5 g/dL (double measurement) to change ESAs’ dose according to clinical practice (gradual increase or decrease of 25%). For example look at the therapeutic algorithm (related to erythropoietin or darbepoietin that can be extended to other epoietin) in the protocol.
- Quality of life questionnaire

**MONITORING OF SAFETY AND EFFICACY**
- Open central monitoring of safety and efficacy by an independent Data Safety and Monitoring Committee (DSMC) and blinded qualitative monitoring of outcome by an End-point Committee