Bayesian adaptive designs for phase 1 studies in healthy volunteers

**Objectives:**
- Assess the performance of an innovative (Adaptive) approach that includes Bayesian adaptive designs in healthy volunteers. (Several dose response curves investigated)
- Comparison with a more traditional approach (sequential)

**Study designs:**
- Single ascending dose
- Leap Frog design

**Improvements:**
- Standardization of the prior

**Endpoints:**
- Quality: Focus on the variance and bias in the estimate of MTD
- Efficiency: Number of subjects Duration of the trials
- Safety: Number of overdose subjects

**Methods**

<table>
<thead>
<tr>
<th>Traditional (Sequential)</th>
<th>Innovative (Adaptive)</th>
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<tbody>
<tr>
<td>MTD</td>
<td>0/5/6 subjects with OLE</td>
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<tr>
<td>Escalation</td>
<td>Modified Fibonacci</td>
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<tr>
<td>Cohort</td>
<td>6A+2P</td>
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<tr>
<td>Dose levels</td>
<td>3-4 candidate doses</td>
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**Abbreviations:**
- MTD = Maximum Tolerated Dose
- An = Active
- OLE = Dose Limiting Event
- P = Placebo
- CV = Coefficient of variation

**Approaches (SAD):**
- Traditional (Sequential) 6+2

**Approaches (Leap Frog):**
- Traditional (Sequential) 6+2

**Results**

- **SAD**
  - Relative Error vs. % maximum tolerated dose (MTD - flat)
  - Relative Error vs. % estimated MTD
  - RMSE vs. % maximum tolerated dose (MTD - flat)
  - RMSE vs. % estimated MTD

- **Leap Frog**
  - Relative Error vs. % maximum tolerated dose (MTD - flat)
  - Relative Error vs. % estimated MTD
  - RMSE vs. % maximum tolerated dose (MTD - flat)
  - RMSE vs. % estimated MTD

**Conclusions**

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<tbody>
<tr>
<td>MTD estimated more often</td>
<td>A fewer number of subjects</td>
<td>A fewer number of overdose subjects</td>
<td>For Safety only, Leap frog is not necessarily better than SAD</td>
<td>A new methodology to define the priors: avoid MCMC, a clear meaning of the priors</td>
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