ALMAC

Partnering to Advance Human Health

Almac Clinical Technologies: Adaptive Trial Designs and Complex Innovative Designs

Almac has extensive experience with IXRS® implementation of Clinical Trials involving Adaptive Designs, including Complex Innovative Designs and Master Protocols (Basket, Umbrella, Platform Trial Designs).

Almac In-House Experts on Adaptive Trial Implementation:

Almac Biostatistics Group
Almac is uniquely positioned to have a dedicated Biostatistics Group who are 100% focused on Randomisation IXRS Implementation. The Biostatistics Group is comprised of a team of experienced Biostatisticians and Randomisation List Analysts. The Almac Biostatistics Group are available to provide consultancy advice (based on extensive experience and detailed knowledge and understanding of regulatory guidance / literature) on randomisation methodology selection, blinding considerations, and IXRS implementation around various types of Adaptive Trial Designs.

Adaptive Trial Design Centre of Excellence:
To ensure that your Adaptive Trial Design is implemented efficiently and effectively to meet your protocol's requirements and expectation, Almac has a cross-functional team of experts in place to provide advisement and oversight of your adaptive trial design across all phases of the study and all functional areas.

The Centre of Excellence team is comprised with representatives from Biostatistics, Software Development, Testing, Project Management, IXRS Design, Data Integrations, Quality Assurance, Contracts / Proposals, and Medication Management. This team will collaborate with your team in determining the optimal implementation approach through engaging you with the important considerations and satisfying all your key questions.

The Centre of Excellence will guide you with Best IRT Practices for:

- **Entire IRT Life Cycle:**
  - Design (Requirements Gathering)
  - Implementation and Testing
  - Maintenance

- **Every aspect of the IRT:**
  - Subject Management
  - Treatment Management
  - Medication Management
  - Data Integrations
  - Reporting

> "With over 20+ years of experience collectively, Almac Clinical Technologies is uniquely positioned to offer clients dedicated expertise on randomisation IXRS implementation."

Adaptive trial designs

Common adaptive trial designs / design adaptations that Almac routinely execute include:

- Dropping / adding of treatment arms
- Modifications to the allocation ratio
- Dose finding cohort studies
- Combined Phase IIa/IIb and II/III designs
- Sample size re-assessments
- Bayesian response-adaptive algorithms
- Custom algorithms
- Complex Innovative Designs
- Master Protocol (Basket / Umbrella / Platform Trial Designs)

Real-Time / Seamless Implementation:
The IXRS typically includes a Real-Time Adaptation Feature that allows the designated Client user(s) to specify the required randomisation adaptation (e.g., close existing treatment group(s), open new treatment group(s), adjust treatment ratio, etc.). Based on the user's selection, the IXRS executes the randomisation adaptation seamlessly (in real-time). The adaptations can be managed at the global level or at the sub-group level (e.g. independently for each sub-group, sub-protocol, biomarker, etc.).

Biostatistics / Technical Consultancy:

- IXRS implementation considerations (real vs. near-real time)
- Randomisation implementation:
  - List-based
  - Algorithm-based

Almac has various randomisation adaptation approaches for IXRS implementation (including both list-based and algorithm-based methodologies). A few general approaches include:

- **Switch list:** Several randomisation lists prepared to cover all possible adaptations; the IXRS randomises with the appropriate list based on current IXRS Adaptation Feature settings.

- **Modify list:** prepare a single randomisation list accounting for all possible treatment arms (existing arms and unknown arms); the IXRS utilises records based on the current IXRS Adaptation Feature settings.

- **Algorithm approach:** Treatment group inclusion / allocation ratio / treatment assignment probabilities are adapted or modified per current IXRS Adaptation Feature settings.

Complex innovative designs / Master protocols:
Almac's team of experts are proficient in the implementation of Complex Innovative Designs / Master Protocols such as Basket, Umbrella, and Platform Trial Designs. Master Protocols are designed with multiple sub-studies / sub-protocols / sub-groups (one or more investigational treatments and / or one or more disease subtypes) and require adaptations to be managed independently within each sub-group within the IXRS. As these complex designs often involve new (unknown) treatments perpetually being introduced throughout the trial, Almac ensures that these common adaptations occur in the IXRS randomisation scheme seamlessly.

On-Boarding new medication type(s) within complex innovative designs / Master protocols:
While introducing new treatments within the IXRS randomisation scheme can occur seamlessly for complex designs, introducing the associated new medication types can pose a challenge to for real-time implementation. New medication types often require coordination with clinical supply company(s) and various actions to be performed (e.g. the new medication(s) need to be packaged and labelled, shipped to sites, etc.). To overcome these hurdles for rapid adaptation, the Almac COE and Biostats team will partner with you to craft an onboarding strategy, inclusive of steps for introducing new treatments / medications (e.g. timing, coordination of packaging / labelling / distribution of new medication(s), site / IRB approval, etc.).

Bayesian Response Adaptive Randomisation:
Adaptive trial design protocols may include Bayesian Response Adaptive Randomisation (BRAR) methodology, where treatment assignment probabilities are updated continuously based on the accumulating subject response data. Typically, the BRAR algorithm is hosted by a (third-party) Bayesian Statistical Consulting company who is responsible for designing / executing the BRAR algorithm and providing updated treatment assignment probabilities. Data integrations between the BRAR algorithm's host and the IXRS are required for automatic utilisation of the updated treatment assignment probabilities for randomisation. Almac has experience with setting up these types of data integrations with leading Bayesian Statistical Consulting firms.

General randomisation recommendation (for Adaptive designs / Complex innovative designs):
- To build the IRT Randomisation Scheme with flexibility
- To allow for seamless adaptations throughout the study with the IRT's ability to:
  - Add new investigational arms
  - Drop existing investigational arms
  - Change ratios / probabilities / targets
- To NOT have to amend IRT randomisation scheme for each adaptation

almacgroup.com

GET IN TOUCH

Global HQ
+1 215 660 8500

UK HQ
+44 28 3835 2121

Asia HQ
+65 6309 0720

Japan
+81 367 218720

clinicaltechnologies@almacgroup.com