Incorporating Japanese data sets early; The long-term benefit to bridging strategies

The development of a Bridging Strategy is a key component of any successful development program aimed to deliver new medicines to the largest Pharmaceutical markets. Since the implementation of ICH E5 in 1998 on the acceptability of foreign clinical data into regional approvals, many different approaches have been taken by researchers to allow the fastest registration in all markets.

As a globally recognised CRO for the conduct of clinical trials in Japanese subjects, having completed 60+ studies involving this population over the past 12 years we offer unique insight in this area. In this briefing note we provide examples of different approaches client companies have taken to introducing Japanese Subjects into their development programs, the ease and cost effectiveness of these approaches and how your programs could benefit similarly.

At the core of this issue is the "normality" of Japanese subject recruitment outside of Japan. The strict ethnicity criteria (4 grandparents) and non-assimilation into local culture (<5 years ex-Japan) have hindered many CROs from carrying out this type of work, however at Richmond Pharmacology our methods for Japanese subject recruitment have become standard practice and are no longer exceptional.

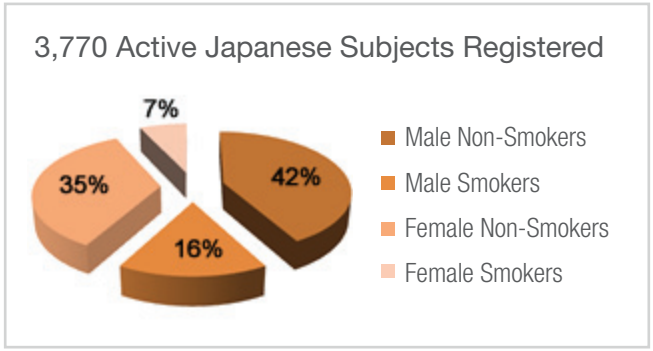
Due to our longstanding commitment to Japanese staffing and culture, we offer sponsors a seamless and wholly beneficial experience when working with us.

Experience

Over the past 12 years, we have observed the changing trends in bridging strategies adopted by both large and small companies.

Our work in earlier years was focused on small cohort PK studies used to support sequential registrations in ICH regions. However over the past 5 years we have seen a shift to parallel and global development methods where incorporation of Japanese, and increasingly non-Japanese Asians, have been made earlier in the programs and in more innovative ways.

By gathering Japanese data sets from Phase I, potential ethnic variations can be detected early on and assist plans for subsequent phases of development to facilitate later entry into the Japanese market. These can be obtained directly in Japan; however with the high attrition rates in early clinical development, this can add significant complexity to established development plans and the costs significantly outweighing the benefits. By implementing a coherent, cost effective and risk adjusted strategy, a small additional investment can lead to significant savings in future programs, greater certainty of decision making and enhancement of a product's market potential.



Study Strategies

The following are examples where client companies have worked with Richmond to integrate Japanese Subjects at early or pivotal stages in their development.

St George's University of London,
Cranmer Terrace, Tooting, London SW17 ORE
T: +44 (0)20 8664 5200 F: +44 (0)20 8664 5201
E: info@richmondpharmacology.com

In each case the success of the strategy was dependent on efficient recruitment of Japanese alongside conventional London based or ethnically specified populations (Caucasians). In all these scenarios, reliable, on-time and cost effective recruitment of Japanese subjects was the cornerstone of success.

Adaptive Trials

Richmond has performed a number of adaptive or umbrella protocols utilising Japanese subjects in the design. Many clients use parallel groups of Japanese and Caucasians in combined SAD and MAD studies, allowing them to accelerate their program without added cost, complexity and delay of performing their Phase I program in Japan. In a further enhancement we commonly incorporate 2-3 groups of Japanese in the MAD phase of a study, generating comprehensive safety, PK and PD ethnic comparisons at 2 or 3 discrete dose levels.

QT Assessments

In a standard 4 period cross-over design TQT study, Richmond incorporates Japanese Subjects with a minimum 40% split of gender in each. This innovative approach allows the client to perform their QT study, generate 2 dose levels of PK data and the thorough ECG information required by Japan's Pharmaceuticals and Medical Devices Agency (PMDA). The design is fully compliant with ICH E14 and is performed at a very modest additional cost to a standard TQT study.

PD Evaluations

In our most challenging recruitment scenario to date, we delivered 52 Japanese and 52 Caucasian Subjects with elevated LDL-C levels in a Single and Multidose PK and Safety Study, with an in-house phase of 34 days. Both ethnicities were delivered simultaneously the same time frame with <14days interval between Cohorts.

The study was completed on time within 6 months from initiation, and had an excellent retention rate with no Japanese volunteers withdrawing consent.

Enriched PK/PD

All of these approaches to incorporating Japanese subjects can be enhanced by effective PK/PD population analyses; enabling high quality independent Japanese data sets to enrich the analysis and acceptability of marketing applications to the PMDA.

Cost Effectiveness

Japanese subjects cost approximately 30% more to recruit than our normal healthy volunteers, however through careful integration into existing programs the additive cost will be significantly less than a separated PK comparison performed during Late Phase Clinical Research.

Conclusions

- Innovative and adaptive bridging strategies can be highly cost effective when efficiently delivered.
- Product values and decision making will be enhanced by early evidence of ethnic similarity or divergence.
- Integrating Japanese Subjects into the development plan will accelerate the program, and will save cost and time in global development programs.
- Richmond Pharmacology has the track record, experience and expertise to empower bridging strategies.

Our innovative solutions can add value to your global development.
Contact our BD team to discuss your requirements or to arrange a visit to our trials unit.

St George's University of London,
Cranmer Terrace, Tooting, London SW17 ORE
T: +44 (0)20 8664 5200 F: +44 (0)20 8664 5201
E: info@richmondpharmacology.com