NOVOTECH
The Asia Pacific CRO

Asia Pacific, a hub for clinical trials in NAFLD

February 2018

Summary and report background

This report aims at highlighting the benefit of conducting non-alcoholic fatty liver diseases clinical trials in the Asia Pacific region based on epidemiology data, key opinion leaders experience' and connections with the industry, as well as information from Novotech's network in relation to standard of care and patient recruitment rates.

Non-alcoholic fatty liver diseases (NAFLD) are one of the most common liver disorder in developed countries and are particularly prevalent in Asian countries, especially in South Korea and Taiwan. Over a third of all industry-sponsored clinical studies initiated during the period (2015-2017) involved sites located in a country in which Novotech operates.

Information from Novotech's network suggests that Thailand and Hong Kong are also promising locations to look at to run trials in NAFLD based on investigators' engagement, number and profile of patients routinely seen during clinic visits.

This report is based on preliminary feasibility findings collected by Novotech as well as on information available publicly on clinicaltrial.gov and other private databases.

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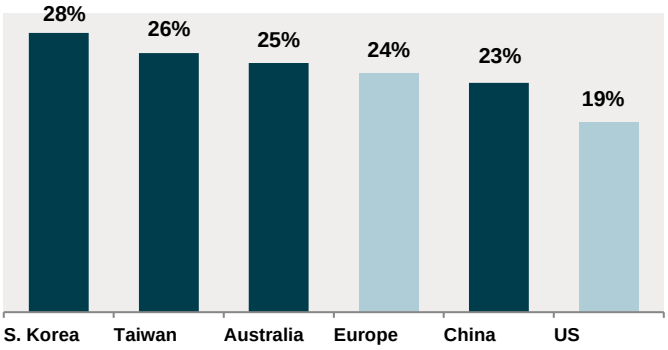
1.0 Epidemiology of NAFLD

Non-alcoholic fatty liver diseases are one of the most common liver disorder in developed countries, and are particularly prevalent, along with various other liver diseases, in Asian countries.

Information from the IPD database showed that prevalence of NAFLD exceeds that of Europe and the US in a number of Asian countries and in South Korea and Taiwan in particular (up to 28% of the population).

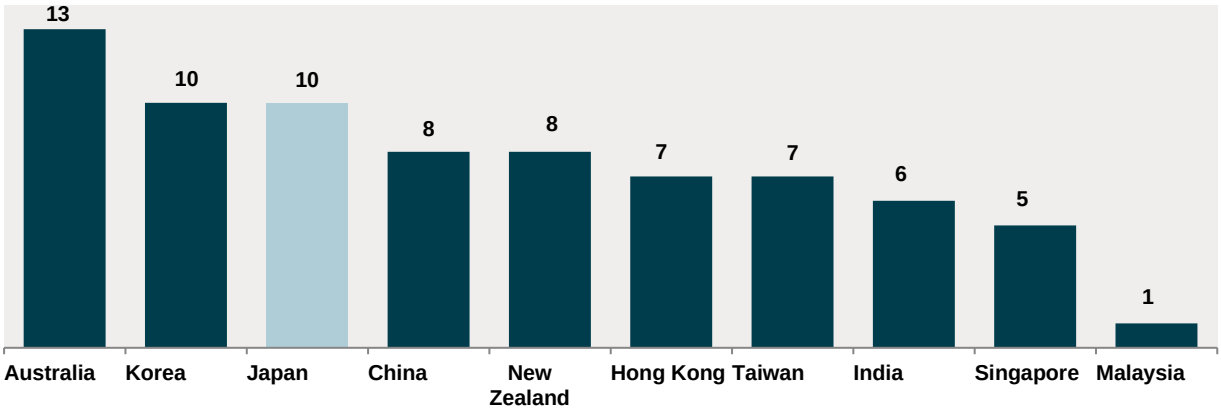
NAFLD prevalence rates in a selection of Asia Pacific countries, US and Europe (source IPD)



2.0 Clinical activity in Asia-Pacific

From the 195 industry-sponsored clinical studies initiated between 2015 and 2017, over a third involved a country in which Novotech operates, with Australia, South Korea and Japan being the most frequent countries involved in NAFLD studies with sites in Asia Pacific, with 13 and 10 studies initiated respectively.

Top 10 countries in Asia Pacific in relation to the number of NAFLD studies initiated between 2015 and 2017



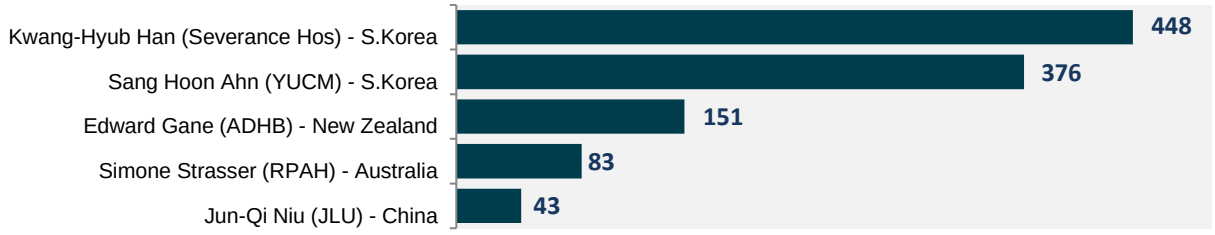
Countries in which Novotech operates

3.0 Key sites and investigators

Asia Pacific includes some of the most active key opinion leaders and investigators in the field of hepatology, some of whom participated in key early and late phase trials for both multinational pharmaceutical companies and biotechnology companies. From the sites below, Novotech has worked with SNUH and SGH and has extensive experience with the Prince of Wales Hospital in Hong Kong, having conducted three studies in NASH with investigators from this site.

Top 5 sites in Asia (exc Japan) in NAFLD trials (# studies) (Source Citeline)

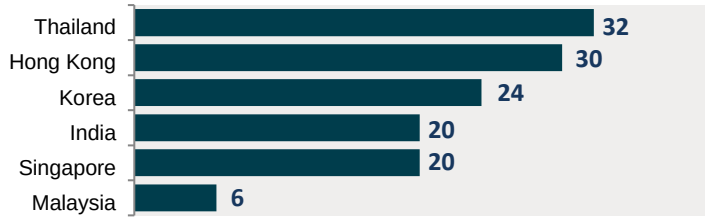
Top 5 investigators in Asia Pacific in hepatology trials and number of scientific publications (Source Pubmed)



4.0 Recruitment and SOC data from Novotech network

Data collected from clinical investigators in Novotech's network (n=25) in 2017 suggests that clinicians routinely see between 50 to 150 patients each year with NASH depending on the site surveyed, with co-infection with HBV being frequently observed (up to 30% of cases).

Est. average number of NASH patients a sample of Asia-based clinical investigators could recruit during a 12 months enrolment period (n=25)



TOTAL Average 22 patients/year

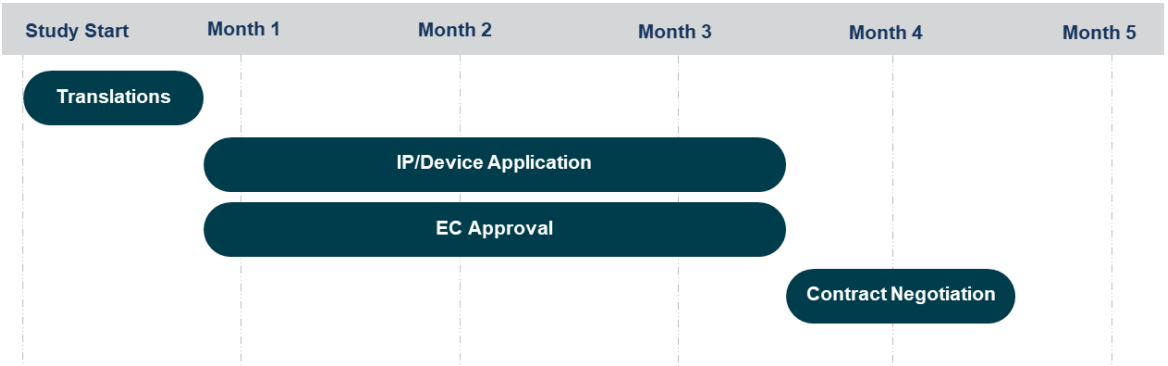
More specifically looking at site feedback from Hong Kong and Thailand, diagnosis of NASH mostly relied on abdominal ultrasound, fibroscan or elastography with a standard of care based on dietary control with supplement of liver tonic, lipid lowering agent, Vitamin E and/or Pioglitazone in most cases.

5.0 Regulatory timelines in Thailand and Hong Kong

Regulatory regimes in Asia Pacific are heterogeneous. Institutional Review Board approvals, regulatory, import licensing and contract negotiations are undertaken simultaneously in some countries and sequentially in others. Thailand and Hong Kong are amongst countries offering quick study start-up timelines, with about 4 to 5 months between EC approval submission and contract negotiation.

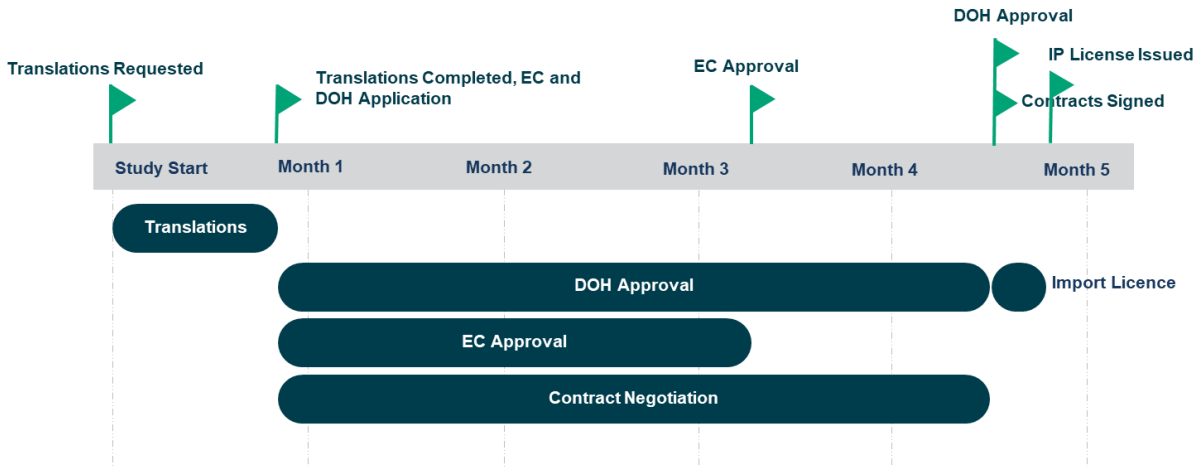
Study start-up in Thailand

The Thai FDA is responsible for Investigational Product (IP) and Medical Device import licensing but is not responsible for study approval, and each EC application is site specific.



Study start-up in Hong Kong

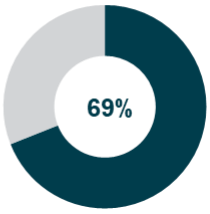
Subject information sheet and ICF documents need to be in English and Traditional Chinese and all trials must be approved by Department of Health. There are 6 clusters of Ethic Committees, the EC submission being conducted through the Principal Investigator.



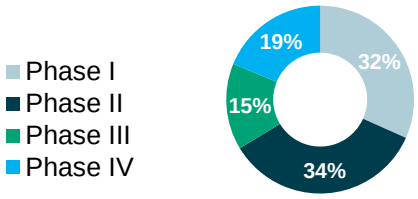
About Novotech

Novotech is internationally recognized as the leading regional full-service contract research organization (CRO) in the Asia Pacific region. Novotech provides clinical development services across all therapeutic areas and has been instrumental in the success of hundreds of Phase I - IV clinical trials.

69% of clients are repeat customers



Project types in hepatology (split by phase)



Novotech has conducted over 35 projects in hepatology, including in NASH, hepatocellular carcinoma, and hepatitis, in both early and late phase clinical trials.

Full service CRO with on-the-ground operations in Australia, New Zealand, India, South Korea, Taiwan, Thailand, Malaysia and Singapore, the Philippines, Hong Kong and China.

340+ full-time employees

Extensive therapeutic area experience handling clinical studies with small and mid-size biotechnology companies across all phases of clinical trials

Managed around 700 projects including APAC component of pivotal trials for multiple FDA, EMA registered products since 2001

State of the art technology solutions including CTMS (Oracle Siebel), eDC (Medidata Rave, Oracle Inform), eTMF (SureClinical) and Safety (Oracle Argus)

Established in 1996, with head office in Sydney, Australia

Recipient of the 2017 Frost & Sullivan award for **Asia Pacific Biotech CRO Company of the Year**