NOVOTECH™
The Asia Pacific CRO

SOLID TUMORS - ASIA PACIFIC – CLINICAL TRIAL LANDSCAPE

CONTENTS

1. EPIDEMIOLOGY

DISEASE BACKGROUND

A solid tumour arises from an abnormally growing mass of cancer cells in organ systems and is free of fluid or cysts. About 90% percent of adult cancers are solid tumours, which may develop in the breast, lung, prostate, colon, melanoma, bladder, kidney, and other areas of the body, with the two basic types being sarcomas and carcinomas. According to statistics, solid tumours account for around 40% of all malignancies in children, with brain tumours reported as the most prevalent and dangerous type of solid tumour.[1] In addition to having a distinct presentation than blood cancers, solid tumours may also need a different course of treatment, which could involve chemotherapy, radiation therapy, and surgery. [2] In order to match treatments to patients' mutations, genomic profiling is increasingly employed for solid tumours in adults, as well as for paediatric brain tumours and blood malignancies. However, due to the variety and rarity of these diseases, genomic fingerprinting has proven difficult for children with solid tumours, resulting in the treatments remaining non-specific. [3] Survival rates for patients with solid tumors may depend on the patient's age, time of diagnosis, health status, co-morbidities, stage and the type of cancer.

PREVALENCE

According to GLOBOCAN, there were over 8.2 million new cases and over 5 million deaths due to solid cancers in Asia, with the region accounting for half of the new cancer cases and 60% of the world's deaths in 2020.

The selected locations of the Asia Pacific region (which include China, India, South Korea, Japan, Australia, New Zealand, Malaysia, Singapore, Thailand and the Philippines), emerged as a hub to an overwhelming cancer population, accounting for over 50%, 45%, 35% and 65% of the global incidence of lung, colorectal, breast and stomach cancers respectively, in 2020. In this region, breast, lung, colorectal and stomach cancers also showed the highest age-standardized incidence rates (ASIR) of 38, 25, 19 and 16 per 100,000 population respectively, in 2020. Lung, colorectal and stomach cancers were also the three top cancer indications where the ASIR even exceeded or was similar to that of the world incidence.

The other top solid tumor indications where the Asia Pacific locations showed higher incidence rates include cancers of the prostate, cervix uteri, liver, oesophagus and thyroid with ASIRs of around 14, 13, 12, 10 and 7 per 100,000 population respectively, in 2020. Cancers of the liver, oesophagus, thyroid and cervix uteri were also the indications where the Asia Pacific locations accounted for the majority of the new cases (61%, 70%, 50% and 45% respectively) reported worldwide in 2020.

Additional solid tumor indications where the Asia Pacific locations have shown a higher percentage share of the globally reported incidence include those of the nasopharynx (58%), gall bladder (56%), lip and oral cavity (50%), pancreas (41%), ovary (41%), brain/CNS (41%), larynx (41%), with ASIRs ranging between 2 and 6 per 100,000 among all these cancer types. [4]

Globally, the burden of cancer is rising, and during the next 20 years, the absolute cancer burden is predicted to rise multi-fold. One of the major world regions whose incidence and mortality rates are expected to rise dramatically is Asia, with China alone predicted to witness close to 7 million new cases and 5 million deaths from cancer in 2040. This alarming trend has boosted the need for novel drug therapies for solid tumors in Asian patients.[5]

The table 1 summarizes the estimated incidence, mortality and 5-year prevalence of top solid tumors in selected Asia Pacific locations, for 2020.

Table 1: Estimated Incidence, Mortality and 5-Year Prevalence of top solid tumor cases in selected Asia Pacific locations, both sexes, all ages (excl. NMSC) - 2020

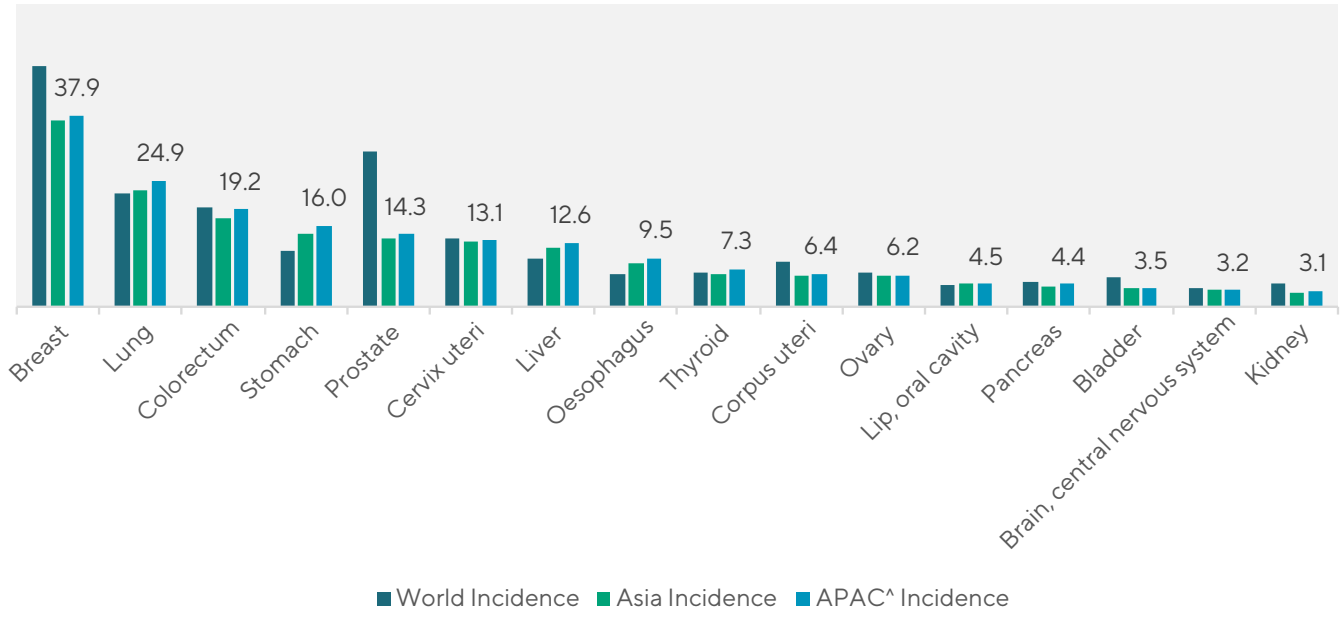
Cancer	World Incidence	APAC ^ Incidence	% Share of APAC^	ASR*	APAC^ Mortality	APAC^ 5-Y Prevalence
Lung	2,206,771	1,121,791	50.8	24.9	939,236	1,303,222
Colorectum	1,931,590	866,547	44.9	19.2	427,078	2,288,483
Breast	2,261,419	797,248	35.3	37.9	254,080	2,570,761
Stomach	1,089,103	718,444	66	16	489,872	1,254,494
Liver	905,677	550,060	60.7	12.6	506,738	617,790
Oesophagus	604,100	423,618	70.1	9.5	379,786	459,957
Prostate	1,414,259	311,753	22	14.3	95,986	1,007,722
Thyroid	586,202	293,036	50	7.3	18,138	964,435
Cervix uteri	604,127	269,849	44.7	13.1	151,964	693,278
Pancreas	495,773	203,159	41	2.5	193,643	154,208
Lip, oral cavity	377,713	189,518	50.2	4.5	98,603	451,551
Corpus uteri	417,367	134,505	32.2	6.4	30,766	417,110
Kidney	431,288	133,236	30.9	3.1	67,884	353,195
Ovary	313,959	128,686	41	6.2	85,349	332,377
Brain, CNS	308,102	126,820	41.2	3.2	103,416	334,905
Bladder	573,278	123,673	21.6	3.5	69,750	458,841
Nasopharynx	133,354	77,556	58.2	1.9	44,767	229,858
Larynx	184,615	74,865	40.6	1.7	41,503	199,856
Gall bladder	115,949	64,717	55.8	1.4	48,643	76,207
Melanoma of the skin	324,635	34,092	10.5	0.8	9,975	110,803

Source: GLOBOCAN2020

**** Age standardized rate of incidence per 100,000 population***

^ APAC includes China, India, South Korea, Japan, Singapore, Malaysia, Australia, New Zealand, Thailand and The Philippines

Figure 1: Incidence rates* of solid tumors, by region, 2020



Source: GLOBOCAN2020

**** Age standardized rate of incidence per 100,000 population***

^ APAC includes China, India, South Korea, Japan, Singapore, Malaysia, Australia, New Zealand, Thailand and The Philippines

2. STANDARD OF CARE

Systemic anti-cancer therapy (SACT), radiotherapy, and other treatment modalities—either separately, in combination, or sequentially—are frequently used to treat solid tumors. Multiple types of SACT such as cytotoxic, endocrine therapy, targeted therapy and immunotherapy are being employed in different settings (e.g., adjuvant, neoadjuvant, locally advanced and palliative). [6]

The effectiveness of anti-cancer treatment and patient outcomes have considerably improved due to the rapid growth of cancer immunology and immunotherapy, and have completely changed how solid tumours are treated since the discovery of immune checkpoint inhibitors in the 1990s. Immune checkpoint inhibitors and other immunotherapies have emerged as the primary lines of treatment for more than ten distinct solid tumour cancers, including breast cancer, skin cancer, bladder cancer, and hematologic malignancies, over the past 15 years. For certain malignancies, immunologic methods are now even more crucial than chemotherapy. Oncology care has undergone a dramatic revolution due to the advancement of immunotherapy.[7]

Standard treatment guidelines have been published by reputable bodies like the NCCN (National Comprehensive Cancer Network) and ESMO (European Society for Medical Oncology), for multiple cancer types. However, there are inter-ethnic pharmacogenetic variances that account for changes in both the pharmacokinetics (PK) and pharmacodynamics (PD) of medications, which in turn contribute to variations in therapeutic responses, in addition to the regional and ethnic variations in prevalence of cancer. In order to find the treatments that may provide the best possible therapeutic outcomes, limit toxicity, and improve cancer survival in Asia, it is therefore necessary to include a representation of Asian patients in clinical studies. [8]

For certain cancer types, the ESMO Clinical Practice Guidelines have been customized to harmonise optimal, evidence-based oncology practice across Asia, through the Pan-Asian Guidelines Adaptation (PAGA) project. This project born of out of an active collaboration between ESMO and the oncology societies of China (CSCO), India (ISMPO), Indonesia (ISHMO), Japan (JSMO), South Korea (KSMO), Malaysia (MOS), Philippines (PSMO), Singapore (SSO), Taiwan (TOS), and Thailand (TSCO) aims to consider Asian ethnic, scientific, socioeconomic, and local practice characteristics, to build consensus towards Pan-Asian adaptation of three to four ESMO Clinical Practice Guidelines, which are then published in ESMO Open and presented at the ESMO Asia Congress.

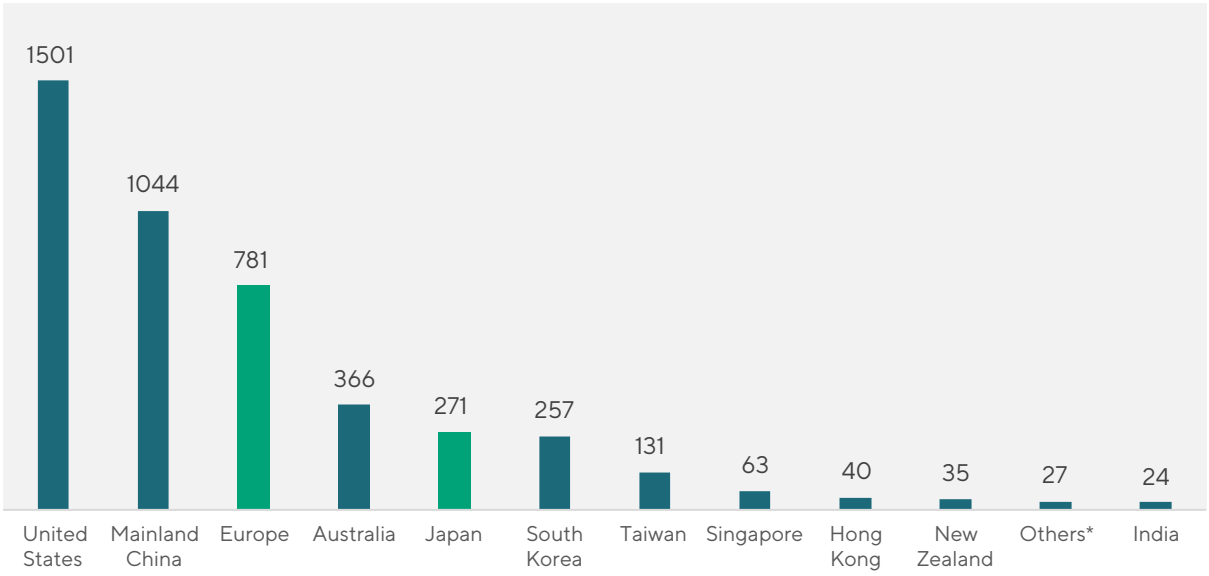
ESMO-PAGA are available for a range of cancers such as Renal Cell Carcinoma (2021), Squamous Cell Carcinoma of the Head and Neck (2021), localised colon cancer (2021), early breast cancer (2019), intermediate and advanced/relapsed HCC (2019), locally advanced unresectable NSCLC (2019), metastatic NSCLC (2018), metastatic gastric cancer (2018), metastatic oesophageal cancer (2018) and metastatic colorectal cancer (2017).[9]

Similarly, oncology thought leaders from China, Japan, South Korea, and Taiwan, as well as members of the NCCN Guidelines Panel, provide modified regional adaptations of the NCCN Guidelines to help clinicians choose effective and suitable treatment options in Asian locations. Bladder cancer, kidney cancer, and non-small cell lung cancer are among the cancer types for which amended NCCN Guidelines have been published. [10]

3. CLINICAL TRIAL LANDSCAPE

Biopharma companies initiated over 4,000 solid tumor clinical trials globally since 2016, with the Asia-Pacific region involved in over 40% of the trials. Trials in Asia-Pacific predominantly involve Mainland China, Australia, Japan, South Korea, and Taiwan with fewer competing trials compared to the US and Europe. (Figure 2).

Figure 2: Top locations in Asia-Pacific, Europe, and the US, based on the number of studies on Solid tumors initiated by Biopharma companies since 2016. [11]



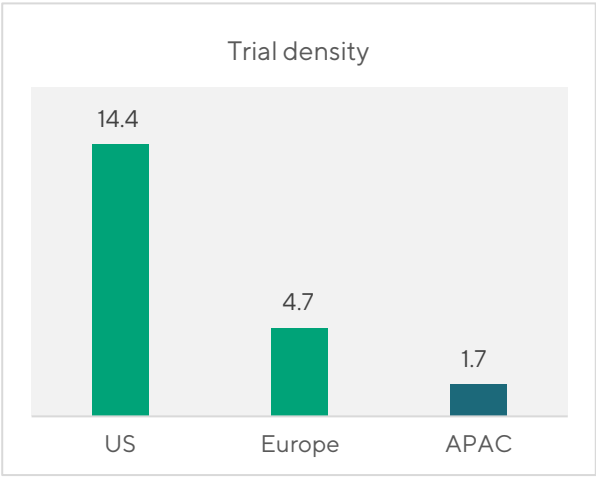
- *Locations in which Novotech directly operates*

Source: GlobalData, Extracted date: 14th July 2022

**others include Malaysia (11), Thailand (10) and the Philippines (6)*

Due to its large population and lower volume of studies, the Asia-Pacific region has lower competing trial risk with a trial density about 8 times lower than the US and about 3 times lower than Europe. (Figure 3).

Figure 3. Comparison of the trial density* for industry-sponsored Solid tumor clinical trials in the US, Europe, and Asia-Pacific. [11]



**Trial density is the number of recruiting sites for industry-initiated trials per million urban population*

Source: GlobalData, Extracted date: 14th July 2022

Trials initiated in the Asia-Pacific region since 2016, show median recruitment durations about 22% shorter than trials in Europe and about 20% shorter than trials in the US (Figure 4). In addition, these trials in the Asia-Pacific region recruit, on average about twice faster than Europe and the US (0.5, 0.3, and 0.2 patients per site per month respectively) (Figure 5).

Figure 4. Comparison of median patient enrolment duration (in months) for Solid tumor clinical trials in the US, Europe, and Asia-Pacific since 2016. [11]

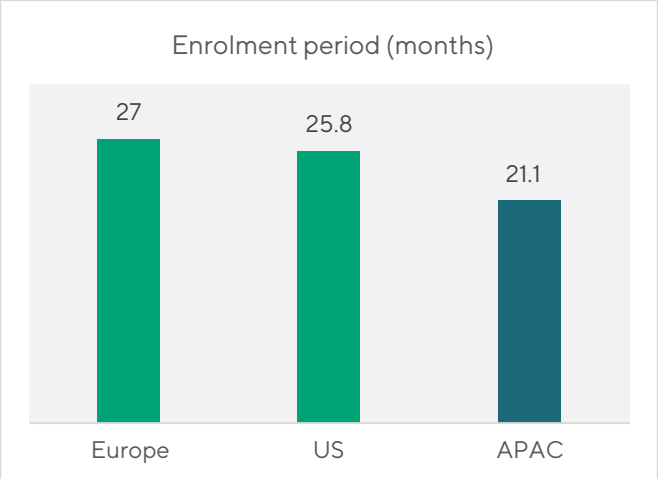
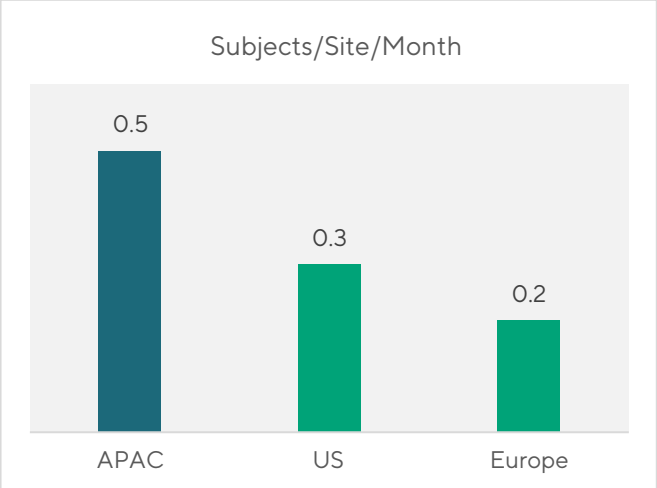


Figure 5. Comparison of median patient recruitment rates (in subjects per site per month) for Solid tumor clinical trials in the US, Europe, and Asia-Pacific since 2016. [11]



Source: GlobalData, Extracted date: 14th July 2022

4. KEY OPINION LEADERS IN SOLID TUMORS

Dr.PETER KAR HAN LAU
Peter MacCallum Cancer Centre – **AUSTRALIA**

Peter Lau is a Medical Oncology Consultant at Peter MacCallum Cancer Centre based in Melbourne, Victoria. His areas of interests lie particularly in the application of immunotherapy and molecular targeted therapies in solid cancers. He has participated as clinical trial investigator for multiple Phase I-III melanoma and skin cancer trials and has worked with sponsors such as BeiGene Ltd, Bristol-Myers Squibb Co and Ono Pharmaceutical Co Ltd among others. He has participated in over 25 publications.

DR BAEK-YEOL RYOO
Asan Medical Center **– SOUTH KOREA**

Dr. Baek Yeol Ryoo is a Professor in Oncology, UUCM, AMC, South Korea. His clinical areas of interest include Stomach Cancer, Liver Cancer, Gastrointestinal Stromal Tumor, Gastrointestinal Sarcoma and Neuroendocrine Tumor. He has participated in close to 40 clinical trials and he served as a Principal Investigator in about 10 of them. He has worked with sponsors such as AstraZeneca Plc, Merck KGaA, F. Hoffmann-La Roche Ltd, Bristol-Myers Squibb Co and Exelixis Inc to name a few. He has co-authored more than 180 peer reviewed articles in the past 15 years.

Prof. XIAOHUA WU
Fudan University Shanghai Cancer Center – **CHINA**

Xiaohua Wu, is a Professor and Chair of the Gynaecologic Oncology department of Fudan University Shanghai Cancer Center. Dr. Wu's main research interests include molecular biological mechanisms (gene, protein, cell), pre-clinical and clinical management of gynaecologic cancers. He has been a Principal Investigator in over 25 domestic and international clinical trials involving sponsors such as Shenzhen Chipscreen Biosciences Co Ltd, Shanghai Haihe Biopharma Co Ltd, MacroGenics Inc, BeiGene Ltd and Apollomics Inc. He led large-scale, multi-center translational research related to BRCA gene mutations in Chinese high-grade serous ovarian cancer patients and has participated in about 35 publications.

Prof. FENG JIFENG
Jiangsu Cancer Hospital **– CHINA**

Feng Jifeng is Professor of Medical Oncology and Director of the National Pharmaceutical Clinical trials institute in Jiangsu Cancer Hospital. He is Editor-in-chief of the *Journal of International Translational Medicine*. Prof. Feng is the co-author of over 100 scientific publications, and was involved in over 130 clinical studies, mostly in solid tumor trials, for Innovent Biologics, Teligene, RemeGen, and Hutchison MediPharma.

Prof. CHENG ANN-LII
National Taiwan University College of Medicine – **TAIWAN**

Professor Cheng Ann Lii is a distinguished Professor, Attending Physician, Vice superintendent and Director of the NTU Cancer Center at National Taiwan University. His areas of interest include oncology, internal medicine and general medicine, nuclear medicine, hematology, and translational research for endemic cancers. Dr.Cheng has actively contributed towards basic and translational research in hepatocellular carcinoma and has co-authored over 300 peer reviewed publications. He was involved in over 80 clinical studies, including 40 solid tumor studies for Celgene, Boehringer Ingelheim, MSD, BeiGene, Innopharmax, and Taiwan Liposome Company.

Prof. STEPHEN CLARKE
Royal North Shore Hospital **– AUSTRALIA**

Prof. Clarke is a Professor of Medicine at the University of Sydney and Director of Cancer Services at Northern Sydney Local Health District (Australia). He is an advisor to the Department of Veterans Affairs as well as a member of the Repatriation Pharmaceutical Review Committee. Prof. Clarke is the co-author of over 100 publications. He was involved in over 40 clinical studies, including more than 30 solid tumor studies, for BMS, ASLAN Pharmaceuticals, Array BioPharma and Alder Biopharma.

A/Prof. DAVID S P TAN
NUS Yong Loo Lin School of Medicine – **SINGAPORE**

Dr. David Tan is an Associate Professor, Dept of Medicine, Yong Loo Lin School of Medicine. His primary clinical and research interests include gynaecological (ovarian, cervical, endometrial) cancers, particularly on the development of biomarkers and novel anti-cancer therapeutics. He has been a Principal Investigator for 12 trials with sponsors such as AstraZeneca Plc, Clovis Oncology Inc, and Byondis BV among others. He has participated in more than 10 publications in leading journals such as the *British Journal of Cancer and Lancet Oncology.*

A/Prof. HERBERT LOONG
Prince of Wales Hospital **– HONG KONG**

Dr. Herbert Loong is the Assistant Professor in the Department of Clinical Oncology, CUHK and the Deputy Medical Director of the Phase 1 Clinical Trials Centre, CUHK. He is also the Convenor of the Adult Sarcoma Multi-Disciplinary Tumour Board at Prince of Wales Hospital. Dr Loong's specific areas of interest include Sarcoma Medical Oncology, Neuro-oncology, Thoracic Oncology, Melanoma and Early Phase Clinical Trials. He has been a Principal Investigator in 10 clinical trials for sponsors such as Pfizer Inc, Arcus Biosciences Inc, Imugene Ltd and MacroGenics Inc among others, and has participated in 13 publications.

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For more information, visit https://novotech-cro.com

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