



NOVOTECH™

The Asia Pacific CRO

**CLINICAL TRIAL LANDSCAPE OF
ENDOMETRIAL CANCER IN
ASIA-PACIFIC**

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EPIDEMIOLOGY OVERVIEW

Background

Endometrial cancer (EC) is a gynaecological cancer with a growing prevalence globally. As EC is the most frequent type of uterine cancer, it is sometimes referred to as uterine cancer itself or cancer of the corpus uteri as it arises from the epithelial lining of the uterine cavity. Adenocarcinomas of the endometrium account for more than 80% of all EC types (such as Endometrioid adenocarcinoma, Serous adenocarcinoma, Adenosquamous carcinoma etc) [1]. Excess bodyweight (responsible for about a third of uterine corpus cancers), abdominal fatness, menopausal oestrogen therapy, early age at menarche and late menopause, nulliparity, polycystic ovarian syndrome, and tamoxifen use are all risk factors for EC, which accounts for the bulk of uterine corpus malignancies. Lynch syndrome and diabetes are also known risk factors. In 2020, cancers of the corpus uteri ranked as the sixth most frequent cancers among women globally.

Disease Prevalence

According to Globocan cancer statistics, over 410,000 new cases and close to 100,000 deaths due to cancers of the corpus uteri were observed in 2020 [2]. According to the International Agency for Research on Cancer, the incidence rate of EC is fast increasing and is expected to rise by more than 50% globally by 2040. The global ASIR (age-standardized incidence rate) of EC increased by 1% per year between 1990 and 2019 [3].

In the US, there were over 800,000 women living with uterine cancer in 2018, with new cases and mortalities projected to reach 66,570 and 12,940 respectively in 2021. The ASR of incidence was 28 per 100,000 women per year while the ASR of mortality was 5 per 100,000 women per year based on 2014–2018 cases and deaths [4]. For the year 2020, Globocan reported more than 60,000 new cases of cancer of corpus uteri accounting for about 3% of all new cancers in the country [5].

In 2020, Globocan reported a total of 417,367 new corpus uteri cases, with Asia accounting for about 40% of these new cases. China, where EC is the third most common female malignancy, accounted for nearly half of the new cases in Asia (81,964). The 2020 ASIR and ASMR (age-standardized mortality rate) were 7.6 and 1.4 per 100,000 female population respectively in China [6]. Although EC is most frequent in postmenopausal women, there is an increasing proportion of younger women being diagnosed in China. Indeed, according to a recent study, nearly 40% of women living with EC in China were diagnosed before their menopause, compared to less than 25% for Caucasian women [7,8].

In Hong Kong, 1,165 new cases of cancer of the corpus uteri were diagnosed in 2018, with the majority cases (760) observed in women aged 45–64. The ASR of incidence for 2018 for this cancer was 17 per 100,000 female population, a significant increase compared to 2011 (11 per 100,000) [9].

In Australia, Globocan reported 3,055 new cases of corpus uteri in Australia in 2020, with an ASIR and ASMR of 13.9 and 1.9 per 100,000 females respectively. Being the most frequent form of uterine cancer, EC accounted for two thirds (349 deaths) of all uterine cancer deaths (524) in 2018, with the 2018 ASMR being 2.1 women per 100,000 [10].

In South Korea, Globocan reported 3,425 new cases of corpus uteri in South Korea in 2020 with an ASIR and ASMR of 8.1 and 0.8 per 100,000 females respectively. During the period between 1999 and 2015, EC incidences have been increasing, with the ASR of incidence rising from 2.4 in 1999 to 5.7 in 2015. The EC incidence has followed a rising trend in all age groups during the last 5 years of the study period [11].

In India, Globocan reported 16,413 new cases of the corpus uteri with an ASIR of 2.4 per 100,000 women and 6,385 deaths with an ASMR of 0.9 per 100,000 women in 2020. The rise in EC in India is mainly attributed to evolving lifestyle and reproductive profile (such as younger age at menarche, late age at menopause, infertility etc) of women in urban areas [12].

In New Zealand, the EC incidence has increased by about 40% in the last four decades. New Zealand has an ASIR of 12 to 20 cases per 100,000 women each year. Based on data from New Zealand Cancer Registry between 1996 and 2012, a total of 5,486 EC cases were reported among all women, with a total of 1,920 EC related deaths. There were 4,228 non-Maori non-Pacific, 655 Maori, and 603 Pacific cases respectively. The average ASIR for all women was 14.5 per 100,000, and an ASMR of 4.7 per 100,000 women. Pacific women had the highest incidence rates, which grew the fastest (increasing from 2 per 100,000 to 24 per 100,000) in those under 50 years during the study period [13]. According to Globocan, there were 724 new cancers of corpus uteri in 2020 which accounted for 2% of all new cancers.

In Thailand, the EC incidence increased from 2.9 to 4.3 per 100,000 women-years between 1997 to 2012 [14]. According to Globocan, Thailand had a total of 4,524 new cases of corpus uteri, accounting for a little more than 2% of all new cancers in Thailand, with 1,382 related deaths in 2020 [15].

In Singapore, EC is the fourth most common cancer diagnosed in females [16]. The 2018 ASR of incidence for EC was 19.1 per 100,000 female population [17]. According to Globocan, there were 775 new cancers of corpus uteri in 2020 which accounted for about 3% of all new cancers [18].

In Malaysia, cancers of the corpus uteri are one of the ten most common cancers, with Globocan reporting 1,401 new cases in 2020, constituting roughly 3% of all new cancers [19]. From 2012 to 2016, there were 2,898 new cases constituting 4.5% of 63,733 female cancers. The ASIR for this period was 4.6 per 100,000 Malay, 6.8 per 100,000 Chinese, and 5.5 per 100,000 Indian females respectively [20].

In the Philippines, EC is the eighth most common cancer. Globocan reported 4,374 new cases in 2020 constituting roughly 3% of the 153,751 new cancers in the country [21].

Table 1: Corpus uteri cancer - Incidence, Mortality and Prevalence in selected regions

Region	New cases			Deaths			5-year Prevalence (all ages)	
	Number	ASIR	(%)	Number	ASMR	(%)	Number	Prop. (Per 100 000)*
World	417,367	8.7	2.2	97,370	1.8	0.98	1,415,213	36.62
Asia	167,310	6	1.8	40,995	1.4	0.71	508,022	22.41
China^a	81,964	7.6	1.8	16,607	1.4	0.55	244,822	34.7
Australia	3,055	13.9	1.5	571	1.9	1.2	12,291	96.01
New Zealand	724	17.7	2	167	3.2	1.6	2,795	113.99
South Korea	3,425	8.1	1.5	426	0.8	0.48	12,196	47.63
Singapore	775	16.4	3.3	169	3.1	1.4	2,906	104.23
Malaysia	1,401	8.3	2.9	433	2.5	1.5	4,546	28.89
Thailand	4,524	7.6	2.4	1,382	2.1	1.1	14,206	39.64
Philippines	4,374	8.7	2.8	1,306	2.6	1.4	12,417	22.76
India	16,413	2.4	1.2	6,385	0.94	0.75	43,484	6.56
US	61,738	21.4	2.7	11,460	3.1	1.9	241,265	144.28

Source: Globocan 2020

* Proportions per 100 000

ASIR - age-standardized incidence rates per 100,000

ASMR - age-standardized mortality rates per 100,000

^aIncludes Taiwan and Hong Kong

STANDARD OF CARE

Most ECs with an early diagnosis are treated with surgery alone (hysterectomy). Other common treatment options include chemotherapy, or hormone treatments depending on the histology, disease location, and extent or bulk of disease [22]. While surgery alone helps in managing low risk disease, adjuvant vaginal brachytherapy is indicated for high-intermediate risk endometrial cancers to maximise local control and minimise side effects that may affect patients' quality of life. Recent large, randomised trials also support the use of pelvic radiotherapy for high-risk endometrial cancers of stage I-II [23].

Despite promising outcomes in patients with early-stage disease, those with metastatic or recurrent disease forms have limited options (with paclitaxel/carboplatin combination as a standard of care). Hence treating these patients presents a clinically difficult scenario, with an overall poor survival, forcing doctors to rely heavily on off-label drug use recommended in the National Comprehensive Cancer Network (NCCN) guidelines.

Due to this, the current development efforts seem greatly focused on improving oncologic outcomes in patients with advanced/recurrent disease. In line with this goal, investigators have been exploring novel immunotherapy combinations as second line therapies particularly in biomarker select populations [24]. In this emerging category, the immune

checkpoint inhibitors such as the recently approved pembrolizumab appear poised to change the current chemotherapy dominant treatment landscape for ECs with high mutation burden [25].

Recent advancements such as the biomarker testing and the first immunotherapy drug approval for EC are also leading to a revival of interest among other drug developers who have otherwise been historically lethargic in seeking drug approvals in this indication area. This is reflected by a greater number of drug candidates entering the late-stage pipeline and the explosion of clinical trials involving immunotherapy drugs.

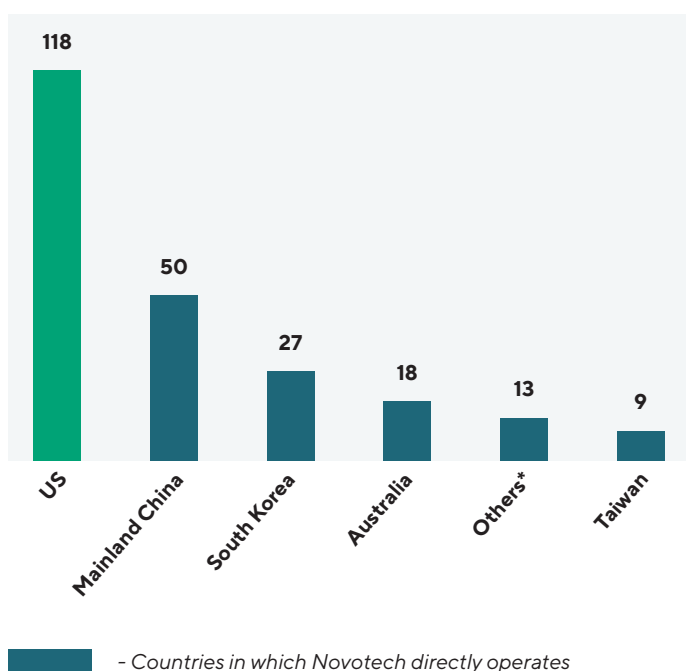
In addition to immunotherapies which target novel proteins and molecular pathways, there are also other new treatment forms such as DNA vaccines, cell therapies, novel antibodies, antibody drug conjugates (ADC), oncolytic virus therapy and immunomodulator proteins being investigated in clinical trials [26].

To conclude, molecular biomarker signatures will be the key in identifying the target patient population most likely to benefit from these novel therapies, as predicted by several Key Opinion Leaders (KOLs) in this field. These will go a long way in positively impacting the disease's current treatment paradigm, competitive landscape, and the goal of addressing unmet needs of patients [27].

CLINICAL TRIAL LANDSCAPE

Biopharma companies have initiated over 180 clinical trials in Endometrial cancer since 2018, with the Asia Pacific region involved in more than 40% of the trials. Clinical trials in Asia-Pacific predominantly involve Mainland China, South Korea and Australia with fewer competing trials compared to the US, but also involve more than 10 sites from India, Singapore, New Zealand, Hong Kong, Thailand and Malaysia combined. (Figure 1).

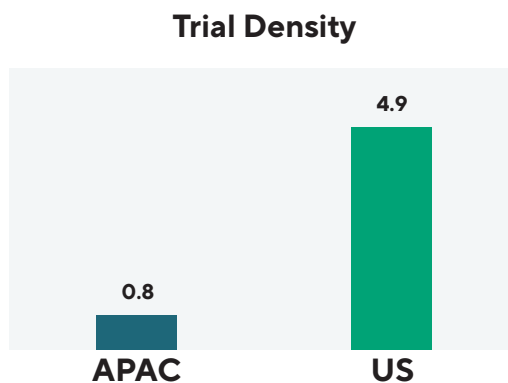
Figure 1: Top countries in Asia-Pacific based on the number of studies in Endometrial cancer initiated by Biopharma companies since 2018 [28].



Note: Others* includes India (4), Singapore (3), New Zealand (2), Hong Kong (2), Thailand (1) and Malaysia (1)

Due to its large population and lower volume of studies, the Asia-Pacific region has lower competing trial risk with a trial density about 6 times lower than the US (Figure 2).

Figure 2. Comparison of the trial density* for industry-sponsored Endometrial cancer clinical trials in the US and Asia-Pacific [28]



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

Trials running in the Asia-Pacific region since 2019, show recruitment durations about 30% shorter than trials in the US (Figure 3). In addition, these trials in the Asia-Pacific region recruited about twice faster than the US (0.7 and 0.4 patient per site per month respectively) (Figure 4).

Figure 3. Comparison of median patient enrolment duration (in months) for Endometrial cancer clinical trials in the US and Asia-Pacific since 2019 [28]

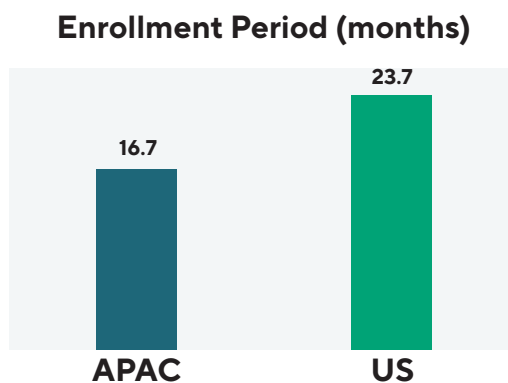
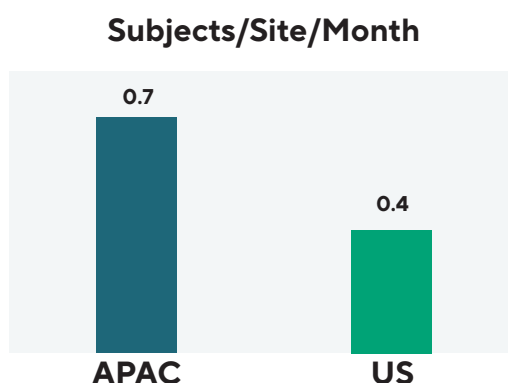


Figure 4. Comparison of median patient recruitment rate (in subjects per site per month) for Endometrial cancer clinical trials in the US and Asia-Pacific since 2019 [28]



KEY OPINION LEADERS IN ENDOMETRIAL CANCER

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 gynecologic 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. LINDA MILESHKIN

Peter MacCallum Cancer Centre – AUSTRALIA

Professor Linda Mileshkin is the Deputy Director of Medical Oncology at PeterMacCallum Cancer Centre. She is particularly interested in the treatment of gynaecological and lung cancers, as well as the care of cancer patients. She is currently working on several clinical research initiatives involving gynaecological and lung cancers, and early phase trials in a variety of tumour types. She has participated as the Principal Investigator for over 10 trials, involving sponsors like Pfizer Inc, AstraZeneca Plc, BeiGene Ltd and Apollomics Inc among others. She has more than 100 published papers to her credit.

Prof. SANG-YOON PARK

National Cancer Center – SOUTH KOREA

Professor Park Sang Yoon is the Principal Scientist at the Centre for Uterine Cancer, National Cancer Center Korea. Dr. Park is an avid researcher who has participated in numerous clinical studies linked to gynaecological cancers and has published his research extensively in international journals (more than 25 papers during last 5 years). He has been a Principal Investigator in 10 trials involving sponsors such as F. Hoffmann-La Roche Ltd, AstraZeneca Plc, Pfizer Inc and Amgen Inc among others.





Prof. PENG-HUI WANG

Taipei Veterans General Hospital – TAIWAN

Dr. Peng-Hui Wang is the Chief, Division of Gynecology, Department of Obstetrics and Gynecology, Taipei Veterans General Hospital. Dr. Wang's key scientific interests include gynaecological cancer sialylation, minimally invasive surgery and hormone research. He has almost 400 published papers to his credit, the majority of which he supervised. He is an Editor or Deputy Editor and peer-reviewer for several journals, including the Journal of the Chinese Medical Association, the Taiwanese Journal of Obstetrics and Gynecology, and Minimally Invasive Surgery, as well as a member of the editorial board for several journals devoted to gynaecological oncology research. He has been the Principal Investigator in 2 trials and has worked with sponsors such as OncoQuest Inc and Merck & Co Inc.

A/Prof. DAVID S PTAN

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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 11 publications in leading journals such as the British Journal of Cancer and Lancet Oncology.



A/Prof. KAREN K.L. CHAN

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Dr. Karen Chan is currently a clinical associate professor at the Department of Obstetrics and Gynaecology, University of Hong Kong. Dr. Chan is interested in both clinical and basic research, primarily in gynaecological malignancies, in addition to her clinical work at a tertiary gynaecological oncology referral centre. Her study focuses on finding successful ovarian cancer treatment techniques with fewer side effects, such as using traditional Chinese medicine or selective hormone therapy. She is on the editorial boards of the Journal of Paediatrics, Obstetrics and Gynecology, ISRN Obstetrics and Gynecology, and Scientifica. She also serves as a reviewer for several international journals and has more than 50 publications to her credit.





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For more information, visit <https://novotech-holdings.com/>

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