133 Molesworth Street
PO Box 5013
Wellington 6140
New Zealand
T+64 4 496 2000

20 June 2022

s 9(2)(a)

By email: s 9(2)(a)
Ref: H202206798

Tēnā koes 9(2)(a)

Response to your request for official information

Thank you for your request under the Official Information Act 1982 (the Act) to the Ministry of Health (the Ministry) on 23 May 2022. You specifically asked:

> *How many immunotherapy drugs to treat cancer are approved in New Zealand at the moment?*
> *How many are in process to be approved?*
> *How many clinical trials with immunotherapy drugs to treat cancer are happening in New Zealand at the moment?*
> *Which types of immunotherapy are being tested in these clinical trials?*
> *How many people are participating on these clinical trials?*
> *Where are these clinical trials happening?*

On 30 May 2022, the Ministry contacted you to clarify what you defined as "immunotherapy drugs" as there were potentially a large number of medicines and clinical trials within scope. The next day you advised you were seeking data from the last three years and interested in following immunotherapy drugs used on cancer treatments: Adoptive Cell Therapies, Monoclonal Antibodies, Oncolytic Virus Therapy, Cancer Vaccines, and Immune System Modulators. As such please find a response to each part of your request below:

> *How many immunotherapy drugs to treat cancer are approved in New Zealand at the moment?*

This information is publicly available in the New Zealand Formulary (https://nzf.org.nz/). In section 8 on malignant disease and immunosuppression, please refer to the subsection on drugs affecting the immune response: https://nzf.org.nz/nzf_4719.

> *How many are in process to be approved?*

Applications for medicine approval from Medsafe can be viewed here: www.medsafe.govt.nz/regulatory/DbSearch.asp. Please select application and restrict using the dates and other fields if required.

> *How many clinical trials with immunotherapy drugs to treat cancer are happening in New Zealand at the moment?*

The Ministry provides Secretariat support to the Health and Disability Ethics Committees (HDECs). The Health and Disability Ethics Committees (HDECs) are Ministerial committees (established under section 11 of the New Zealand Public Health and Disability Act), whose function is to secure the benefits of health and disability research by checking that it meets or exceeds established ethical standards. The Ministry undertook a search of our Ethics databases with key terms and of the clinical trials captured, some may have concluded, some may be ongoing, and some recent ones may have not begun. The Ministry cannot provide the total number of clinical trials currently happening as this would require substantial research and collation. As such this part of your request is refused under section 18(f) of the Act.

You may however be interested in searching through the Australian New Zealand Clinical Trials Registry at: https://anzctr.org.au/ through keyword searches.

Which types of immunotherapy are being tested in these clinical trials?

For details of the trials in the past three years, please refer to the attached documents. Please note document 1 titled *MDF Immunotherapy Studies* contains studies from the Ministry's old system that was active from 2012 to 2021 and document 2 titled *ERM Immunotherapy Studies* contains studies on the new system active from September 2021. Information deemed out of scope of your request has been excluded.

How many people are participating on these clinical trials?
Where are these clinical trials happening?

The information does not exist in the requested format. The Ministry's Ethics database is a repository of applications made to HDECs before the clinical trial has begun recruitment and is not a live monitoring system of a clinical trial's recruitment progress. Post-approval, applicants are required to submit an annual progress report which includes recruitment numbers of the preceding year. The information in each of these annual reports is filed under the main application and is not readily available under keyword searches for collation or comparison.

HDECs do not review where in New Zealand clinical trials are happening and the Coordinating Investigator of a clinical trial may add or remove sites at their discretion without HDEC approval. The Ministry cannot provide the total number of participants currently on immunotherapy trials or their locations as this would require substantial research and collation of each study's initial application and progress reports to generate. As such these parts of your request are refused under section 18(g) and 18(f) of the Act.

Under section 28(3) of the Act, you have the right to ask the Ombudsman to review any decisions made under this request. The Ombudsman may be contacted by email at: info@ombudsman.parliament.nz or by calling 0800 802 602.

Please note that this response, with your personal details removed, may be published on the Ministry website at: www.health.govt.nz/about-ministry/information-releases/responses-official-information-act-requests.

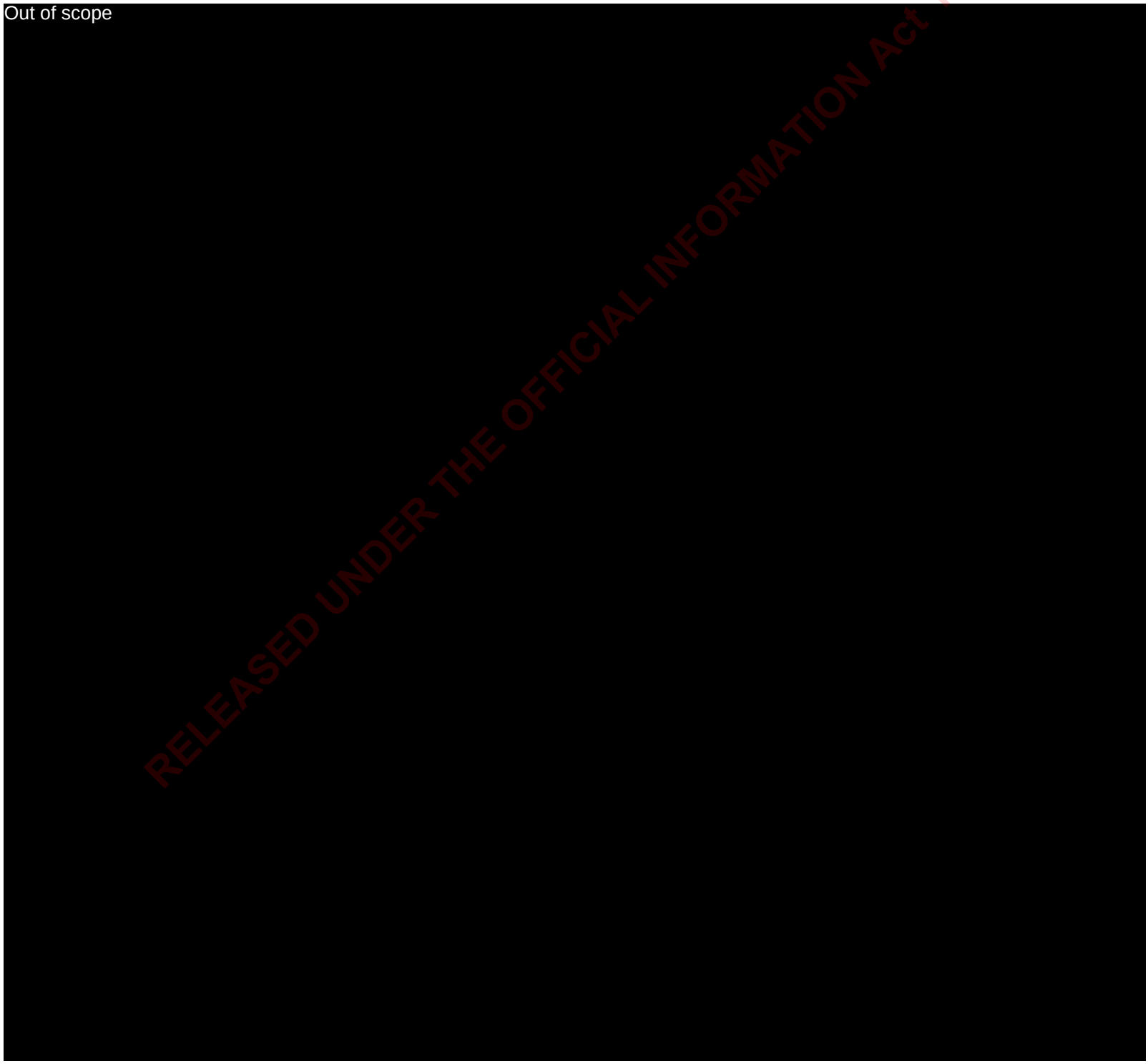
Nāku noa, nā

Ruihua Gu
Acting Group Manager, Quality Assurance and Safety
Health System Improvement and Innovation

Test Search

This report was based on the following criteria:

- Filter fields: **Review Committee Is (Central Health and Disability Ethics Committee,Northern A Health and Disability Ethics Committee,Northern B Health and Disability Ethics Committee,Southern Health and Disability Ethics Committee), MDF.ClosedMeeting - value Is (No), MDF.ProjectSummary Contains 'immunotherapy', Project Title Contains '', Review Status Is (Approved,Assigned to Committee,Declined,PA Response Assigned,Provisionally Approved,Review Complete,Submitted by Applicant,Validated), Application Type Is (Amendment,ESOP,Expedited Review,Final Report/Summary of Results,Full Review,Notification of Conclusion or Early Termination,Progress Report,Protocol Deviation,RED MDF,Tissue Bank), Review Date Received > No Date**
- Output fields: **Review Date Received, Review Reference, Project Title, Application Type, Review Status, A9.StudyObjective, A8.ScientificBasis, MDF.ProjectSummary**



Out of scope

							This is an open label (participantâ€™s treatment is known) study that will evaluate the efficacy and safety of NKTR-214 combined with nivolumab (immunotherapy drug), compared with the Investigatorâ€™s choice of a tyrosine kinase inhibitor (sunitinib or Cabozantinib), in previously untreated participants with intermediate and poor-risk advanced Renal Cell Carcinoma RCC. After screening to

14/03/2019 12:30	19/NTB/37	CA045-002	RED MDF	Approved			determine their eligibility to take part, the participants will be randomly allocated (in 1:1 ratio) to receive: 1)NKTR-214 0.006 mg/kg combined with nivolumab 360 mg (intravenously, every 3 weeks) OR 2)The Investigatorâ€™s choice of either Sunitinib 50mg (orally once daily for 4 weeks, then 2 weeks off) or Cabozantinib 60mg (orally once daily). Participants will be treated until a maximum of 2 years (NKTR-214/nivolumab group only), disease progression, death, unacceptable toxicity, symptomatic deterioration, achievement of maximal response, the Investigatorâ€™s decision to discontinue treatment, patient decision to discontinue treatment or withdraw consent, lost to follow up, or Nektar Therapeutics decides to terminate the study. Treatment may continue beyond progression if there is clinical benefit as determined by the Investigator. Response and progression will be determined by blinded independent radiology review using Response Evaluation Criteria in Solid Tumours (please see protocol for details). The study will also evaluate overall and progression-free survival, incidence of adverse events and other parameters related to RCC.
							This is a study for patients with Advanced Hepatocellular Carcinoma (HCC).

31/01/2020 15:37	20/NTA/6	GT-30 Personalised Neoantigen DNA Vaccine + IL-12 for Advanced HCC	RED MDF	Approved			Since many patients currently do not respond adequately to immunotherapies, the Investigational Product is a DNA vaccine which has been personalized to express tumour specific antigens to generate improved immune cell infiltration to tumour cells. The IP (GNOS-PV02 + INO-9012), in combination with the immunotherapy Pembrolizumab, could lead to improved clinical outcomes. The first primary objective is to determine safety and tolerability of GNOS-PV02 + INO-9012 delivered by injection followed by electroporation through CELLECTRA 2000 (a device that delivers four small electric charges through 3 needles to help entry of the DNA into cells). This will be assessed through adverse event reporting. Other objectives are to evaluate the immune response following treatment through blood tests and the anti-tumour activity through radiographic imaging and survival. For study enrolment, HCC patients that are not amenable to curative treatment are referred to ADHB Liver Research Unit. Since this is a second-line study, patients will be initiated on a first-line therapy (Sorafenib or Lenvatinib). During this time, a tumour biopsy tissue sample will be provided to the Sponsor lab for manufacturing the DNA vaccine. At the discretion of the

							treating physician, patients can discontinue the first-line therapy and begin receiving GNOS-PV02 + INO-9012 and Pembrolizumab according to the dispensing schedule. Safety and efficacy testing are listed in the protocol schedule of assessments and include physical exam, vital signs, blood testing and radiographic imaging. Treatment will continue whilst clinician considers that patient is incurring clinically meaningful benefit up to a maximum of 2 years.
14/07/2020 14:05	20/CEN/150	A Phase 2, multicenter, single-arm, open-label study to evaluate the efficacy and safety of AK104 in subjects with recurrent or metastatic cervical cancer	RED MDF	Approved			This Phase 2 global multicentre study will evaluate efficacy, safety, tolerability, pharmacokinetic (PK) and immunogenicity of an investigational immunotherapy drug AK104 in approximately 40 women aged â‰¥18 years of age with previously treated recurrent or metastatic cervical carcinoma. Volunteers will be screened for up to 28 days prior to study drug administration to confirm their eligibility. It is an open-label study, which means the participants and their doctors will know what treatment the participants receive. All eligible participants will receive AK104 infusions every 2 weeks until unacceptable toxicity, disease progression (worsening), participantâ€™s withdrawal, or for a maximum of 24 months, whichever is earlier.

							Participants may be permitted to continue their treatments beyond initial disease progression if the Investigator decides the subject will benefit from continued treatment. After the study treatment all participants will be followed for overall survival by phone call every 3 months until death, withdrawal of consent, or end of the study. The study will continue be until all subjects have died or a minimum of 12 months after the last subject is enrolled, whichever occurs first.
13/08/2020	20/CEN/191	PIVOT-12	RED MDF	Approved			This is an open label (participantâ€™s treatment is known) study that will evaluate the efficacy and safety of bempegaldesleukin plus nivolumab (immunotherapy drug), compared with nivolumab after complete resection of melanoma in patients at high risk for recurrence. After screening to determine their eligibility to take part, the participants will be randomly allocated (in 1:1 ratio) to receive one of two treatment arms: â€¢ Arm A: bempegaldesleukin plus nivolumab every 3 weeks (q3w) â€¢ Arm B: nivolumab monotherapy every 4 weeks (q4w) Randomization will be stratified by: â€¢ PD-L1 status by Dako PD-L1 PharmDx 28-8 assay: PD-L1 â‰¥ 1% vs PD-L1 < 1% vs indeterminate/not

							evaluable â€¢ Stage: IIIA(LN metastases > 1 mm)/IIIB vs IIIC vs IIID/IV Patients will be treated for approximately 1 year (maximum of 17 cycles for Arm A and 13 cycles for Arm B) or until disease recurrence, death, unacceptable toxicity, decision by Investigator to discontinue treatment, decision by patient to discontinue treatment or withdraw consent from the study, patient is lost to follow-up, or decision by Nektar Therapeutics to terminate the trial.
							This is an open-label, multi-cohort phase II study designed to evaluate the safety and efficacy of targeted therapies or immunotherapy as single agents (or in specified combinations) in patients with unresectable, locally advanced or metastatic solid tumours determined to harbour specific oncogenic genomic alterations. The genomic alterations required for study enrollment will be identified using Next Generation Sequencing (NGS) performed at a local accredited diagnostic laboratory or alternatively, at an overseas central laboratory (Foundation Medicine, Cambridge, MA, USA). The study cohorts are: - Cohort A: Entrectinib in patients with ROS1 fusion-positive tumours - Cohort B: Entrectinib in patients with NTRK1/2/3 fusion-

13/10/2020 15:58	20/CEN/228	BO41932: Tumour-agnostic Precision Immuno-oncology Phase II Platform Trial (TAPISTRY)	RED MDF	Approved			positive tumours - Cohort C: Alectinib in patients with ALK fusion-positive tumours - Cohort D: Atezolizumab in patients with tumour mutational burden (TMB)high tumours - Cohort E: Ipatasertib in patients with AKT1/2/3 mutant-positive tumours - Cohort F: Trastuzumab emtansine in patients with HER2 mutant-positive tumours - Cohort H: GDC-0077 in patients with PIK3CA multiple mutant positive tumours The overarching structure of the TAPISTRY study is a platform interventional study in which patients with solid tumours will be treated with a drug or drug regimen tailored to their NGS assay results at screening. The adaptive trial design allows for additional cohorts to be added to address various identified somatic mutations or other biomarkers via future protocol amendments. Each cohort may have separate endpoints, screening, and treatment requirements. Patients may continue to receive study treatment until disease progression, loss of clinical benefit, unacceptable toxicity, patient or physician decision to discontinue or death.
							This is a Phase 3, randomised open label study to evaluate the antitumour activity of the study drug cosibelimab (CK-301) in combination with chemotherapy compared

							to chemotherapy alone using Overall Survival (OS). Cosibelimab is a new immunotherapy drug which targets PD-L1. It is an anti-PD-L1 antibody, and could prevent PD-1/PD-L1 binding and reactivate the anti-tumor immune response. Approximately 560 participants with advanced or metastatic non-squamous, non-small cell lung cancer (NSCLC) who have not previously received systemic therapy will be enrolled worldwide. The study consists of 3 periods: Screening (up to 28 days), Treatment (3-week cycles), Follow up (minimum 30 days after End of Treatment). Participants will be randomised into 2:1 ratio to one of the 2 groups: - Group 1: CK-301 treatment with chemotherapy treatments - Group 2: Chemotherapy treatments alone The number of cycles of treatment the participants receive will depend on how well they tolerate the study treatments as well as their disease progression. The investigator may modify the dose or discontinue one or more of the study treatments based upon any side effects experienced by the participants.
14/05/2021 14:49	21/NTB/126	CK-301-301: Phase 3 study on Cosibelimab (CK-301) in Participants with Non-Small Cell Lung Cancer	RED MDF	Approved			
							Durvalumab is an immunotherapy for the treatment of cancer. As

							of November 2020, Durvalumab is approved in multiple countries for non-small cell lung cancer (NSCLC) and extensive-stage small cell lung cancer (ES-SCLC) under the brand name IMFINZI injection as an intravenous (IV) infusion over 60 minutes. The purpose of this study is to establish the subcutaneous (SC) dose level of Durvalumab that is comparable to the currently approved IV administration to provide equivalent treatment whilst reducing the time a patient spends in hospital and eliminating the hospital burden associated with IV administration. This is a multicentre study that will be conducted across various sites in several different countries. The study will be comprised 2 parts and will include up to 124 patients with Stage III NSCLC and Stage IV SCLC, using treatment regimens approved by regulatory authorities for Durvalumab IV administration. Every patient will receive up to 12 doses (1 dose per treatment cycle) of Durvalumab, administered as a combination of both IV and SC. The dosing groups will be enrolled sequentially and subsequent dosing groups will only proceed if there are no significant safety
20/05/2021	21/NTB/131	D9072C00001: A Study of Subcutaneous Durvalumab in Patients with Non-Small Cell and Small Cell Lung Cancer	RED MDF	Approved			

							concerns based on previous groups.
10/06/2021	21/NTB/151	dMMR colorectal cancer South Island	RED MDF	Approved			3000 patients per year are diagnosed with colorectal cancer (CRC) in New Zealand. 15% can carry a DNA mutation which affects DNA repair which can lead to development of cancer, called deficient mismatch repair (dMMR). dMMR correlates to microsatellite instability high (MSI-H) which describes a state of increased accumulated mutations, hence terms are used interchangeably. dMMR carries a worse prognosis in metastatic CRC, but there are new immunotherapy drugs such as pembrolizumab that are more effective in dMMR CRC than traditional chemotherapy. All CRC diagnoses from 1/7/2018 to 30/6/2019 will be requested from the National Cancer Registry. This time frame has been chosen as it encompasses a year starting 1 month after testing for MMR/MSI in patients with CRC was mandated by the Ministry of Health. National Health Index numbers for all diagnoses of CRC in this time frame will be requested, and those patients residing in the South Island will be analysed for the purposes of this research. It is estimated that about 900 patients will be included. The research project aims to estimate the proportion of metastatic CRC in the South Island that has

							dMMR or MSI-H. The South Island population was chosen for pragmatic reasons as there is a shared electronic health record system, meaning that the data required can be extracted from a single source. Other aims are to estimate the proportion of CRC (including non-metastatic) in the South Island with dMMR/MSI-H, to estimate the proportion of patients with dMMR/MSI-H or metastatic CRC with a BRAF mutation, to estimate the proportion that are tested for dMMR/MSI-H and BRAF, and to estimate the proportion with dMMR/MSI-H but without a BRAF mutation that are referred to a genetics service.
07/07/2021 10:50	21/CEN/182	COG ANBL19P1	RED MDF	Approved			In this study, researchers want to find out if the combination of chemotherapy drugs irinotecan and temozolomide with immunotherapy can be given safely to patients with high-risk neuroblastoma (NBL) when given following Consolidation therapy. The aim of the study is also to see how the cancer responds to the study therapy and to understand immune response in patients receiving this treatment. This combination of chemo- and immunotherapy has been used before in the settings of relapsed/refractory disease (COG ANBL1221) and showed to be active and

							well tolerated. The addition of irinotecan and temozolomide to immunotherapy in the frontline Post Consolidation settings is considered experimental. If participants are able to tolerate the study therapy then future studies may test if addition irinotecan and temozolomide to immunotherapy is superior to standard immunotherapy.
09/08/2021	21/CEN/227	Healthy donor blood for immunotherapies	RED MDF	Approved			Immunotherapies use the immune system to treat a variety of conditions such as cancer, autoimmune diseases, infections and allergies. The Malaghan Institute of Medical Research is committed to performing immune system research with the goal of developing immunotherapies to lower the burden of these diseases in NZ. Before we can test new immunotherapies on precious tissue samples from patients, we need to do extensive research using tissue samples from healthy volunteers. This will allow us to optimise and validate both scientific techniques and clinical study protocols. This study aims to provide the foundation for current and future immune system research and immunotherapy development by optimising all of the necessary protocols through the collection, storage and research use of healthy donor peripheral blood

Test Search

This report was based on the following criteria:

- Filter fields: **A6.ClosedMeeting - value Is (No), A8.ScientificBasis Contains 'immunotherapy', Project Title Contains '', Review Status Is (Approved,Assigned to Committee,Declined,PA Response Assigned,Provisionally Approved,Review Complete,Submitted by Applicant,Validated), Application Type Is (Amendment,ESOP,Expedited Review,Final Report/Summary of Results,Full Review,Notification of Conclusion or Early Termination,Progress Report,Protocol Deviation,RED MDF,Tissue Bank), Review Date Received > No Date**
- Output fields: **Review Date Received, Review Reference, Project Title, Application Type, Review Status, A9.StudyObjective, A8.ScientificBasis, MDF.ProjectSummary**

Review Date Received	Review Reference	Project Title	Application Type	Review Status	A9.StudyObjective	A8.ScientificBasis	MDF.ProjectSummary
16/11/2021 11:23	2021Â FULLÂ 11729	GO43643: An Open-Label Study Evaluating the Efficacy and Safety of Mosunetuzumab in Combination with Polatuzumab Vedotin in	Full Review	Approved	The primary analysis of the study will test the equality of Progression Free Survival (PFS) distribution in mosunetuzumab plus polatuzumab vedotin versus R-GemOx. The primary endpoint is PFS, defined as the time from randomization to the first occurrence of disease progression, as determined by the Independent Review Facility (IRF) with use of the Lugano 2014 Response criteria, or death from any	Refer Protocol v1 from page 28 Diffuse-large B-cell lymphoma is the most common aggressive form of non-Hodgkinâ€™s lymphoma (NHL; Armitage and Weisenburger 1998). Additionally, each year, around 3% of FLs transform into a higher-grade NHL, most commonly DLBCL (Lossos and Gascoyne 2011), leading to histologic transformation in one-third of patients in 10 years. These transformed follicular lymphoma (trFL), as well as the high-grade form of FL, namely FL3B, are treated with the same standard therapies as high-grade lymphomas. While a majority of patients are cured with the combination of chemoimmunotherapy, the management of R/R disease can be challenging. For these patients, high-dose chemotherapy followed by ASCT offers an additional chance for a cure, but more than half of the patients who are considered for ASCT will experience R/R disease due to insufficient response to salvage therapy or relapsed disease after ASCT (Seyfarth et al. 2006; Gisselbrecht et al. 2010). Moreover, older and more frail patientsare often	

		Participant with Aggressive B-Cell Non Hodgkin's Lymphoma			cause, whichever occurs first. For participants who have neither progressed nor died as of the clinical cutoff date (CCOD) for analysis, PFS will be censored on the date of last disease assessment when the participant is known to be progression-free. For participants who do not have any evaluable post-baseline tumor assessments, PFS will be censored on the date of randomization.	in relation for ASCT Mosunetuzumab (RO7030816; BTCT4465A), is a full length, humanized anti-CD20/CD3 bispecific IgG1 antibody (Atwell et al. 1997; Spiess et al. 2013) engineered for minimal binding to fragment crystallizable (Fc)-ï § receptors. CD20 is a validated target in B-cell NHL, which provides a rationale for the development of a Tï€cell-recruiting bispecific antibody targeting CD20 for the treatment of these diseases. Mosunetuzumab has shown single-agent activity in indolent and aggressive NHL (aNHL), and has a manageable safety profile, which makes it an attractive agent to evaluate in combination with other agents. Mosunetuzumab administered as a single agent has shown an acceptable safety profile and promising activity in a Phase I/II clinical trial (Study GO29781) in participants with B-cell NHL. Polatuzumab vedotin in combination with BR is approved for the treatment of R/R DLBCL in many countries, including the European Union and the United States.	
						While most Ovarian Cancer (OC) patients achieve a complete remission, the majority (>85%) will recur. Almost all patients will ultimately develop a platinum-resistant disease, with about 30% demonstrating platinum resistance at the time of first recurrence. Median overall survival for those with platinum-resistant recurrent ovarian cancer	

						(PRROC) is typically <12 months. There are many approved treatment options available for PRROC patients, however there is no ideal therapy established yet. Chemotherapy has modest activity in PRROC, and overall survival is poor. Single-agent chemotherapy (paclitaxel, topotecan or liposomal doxorubicin) is preferred with or without bevacizumab. Weekly paclitaxel +/- bev is considered the preferred regimen, though only approximately 30% of PRROC patients are clinically eligible for bev. Pembrolizumab combined with chemotherapy with or without anti-angiogenic therapy (bevacizumab, lenvatinib) has shown promising activity in recurrent ovarian cancer improving both Objective Response Rate(ORR) and Progression-Free Survival(PFS). In Keynote-100, pembrolizumab showed a modest monotherapy activity (ORR was 8.6% in platinum resistant-recurrent subgroup). Multiple trials are exploring the augmentation of chemotherapy efficacy and ways to overcome drug resistance by combining standard chemotherapy with immunotherapy. AURELIA study: Weekly paclitaxel plus bevacizumab was the most active of the combination regimens, and is thus considered an ideal option, although not all patients with PRROC are eligible for bevacizumab treatment. JAVELIN
23/11/2021 14:27	2021Â FULLÂ 11416	MK3475-B96 Pembrolizumab/placebo plus paclitaxel with or without bevacizumab for platinum-resistant recurrent ovarian cancer	Full Review	Approved	To compare pembrolizumab plus paclitaxel with or without bevacizumab to placebo plus paclitaxel with or without bevacizumab, with respect to progression-free survival (PFS) per RECIST 1.1 as assessed by the investigator Hypothesis (H1): pembrolizumab plus paclitaxel with or without bevacizumab is superior to placebo plus paclitaxel with or without bevacizumab, with respect to PFS per RECIST 1.1 as assessed by the investigator for participants with PD-L1 positive tumors (Combined Positive Score [CPS] â‰¥1) Hypothesis (H2): pembrolizumab plus paclitaxel with or without bevacizumab is superior to placebo plus paclitaxel with or without bevacizumab, with respect to PFS per RECIST 1.1 as assessed by the investigator for all participants Endpoints: PFS:	

					The time from randomization to the first documented disease progression or death due. to any cause, whichever occurs first.	200 Ovarian: The PD-L1 subgroup analysis revealed that for the avelumab plus PLD arm, patients with PD-L1+ tumors had a higher ORR (18.5%) than those with PD-L1â€“ tumors (3.4%). Wenham MISP: In the Ph2 of paclitaxel as a pembrolizumab combination partner, it was noticed substantial efficacy improvement in PRROC. 51% ORR with combination compared favorably to the 30% expected with paclitaxel alone. Zsiros MISP:There was substantial synergistic activity between antiangiogenic therapy and immunotherapy with the combination of pembrolizumab, bevacizumab and metronomic cyclophosphamide. The combination therapy of PD-1/PD-L1 inhibitors and chemotherapy (with or without an antiangiogenic therapy) has the potential to be superior to chemotherapy alone. Details please refer to PR page 34-35.	
						Lung Cancer Classification and Treatment Lung cancer is an extremely heterogeneous family of diseases, commonly classified according to histological type. This classification is important for treatment and predicting outcomes of the disease. Almost all lung cancers are carcinomas â€“ malignancies arising from epithelial cells. For therapeutic purposes, two broad classes are distinguished: non-small-cell lung carcinoma (NSCLC, accounting for ~85%	

						2 cases) and small cell lung carcinoma (SCLC, ~15% of cases). Treatment for lung cancer depends on the specific cancer cell type, how far it has spread, the presence of targetable mutations, and the patientâ€™s performance status. Common treatments include surgery, chemotherapy, and radiation therapy. Molecularly targeted therapy and immunotherapy are growing in importance for advanced lung cancer. Lung surgery (tumour resection) remains the treatment of choice for NSCLC patients diagnosed at an early stage, as these tumours are not usually sensitive to chemotherapy and/or radiation. In contrast, SCLC typically responds well to chemotherapy and/or radiation, but has usually metastasized widely by the time of diagnosis, making surgery ineffective. Although surgical resection is potentially effective in lung cancer patients diagnosed at an early stage, 80% of patients are diagnosed at a late stage when their tumours have already spread. Metastasis of lung tumours therefore presents a major challenge to treatment and patient survival. Radiotherapy is often given together with chemotherapy, and may be used with curative intent in people with NSCLC who are not eligible for surgery. For potentially curable SCLC cases, chest radiotherapy is often recommended in addition to chemotherapy. Chemotherapy regimens for lung cancer depend on the tumor type SCLC is

treated primarily with chemotherapy and radiation, even in relatively early-stage disease. In advanced NSCLC, chemotherapy can improve survival and is used as first-line treatment, provided the person is well enough. Typically, two drugs are used, one of which is usually cisplatin or carboplatin. Other commonly used drugs are gemcitabine, paclitaxel, docetaxel, pemetrexed, etoposide or vinorelbine. Several drugs that target molecular pathways in lung cancer are now available, especially for the treatment of advanced disease in NSCLC. Molecularly targeted therapies directed against receptor tyrosine kinases (RTKs) lead to moderate improved responses in subsets of adenocarcinoma patients harbouring activating genomic alterations in the corresponding kinase genes, including EGFR, ALK, and ROS1. For squamous carcinoma patients there are fewer actionable mutations (i.e., FGFR1, PI3K and DDR2) and targeted agents have been less successful. Immunotherapy may be used for both SCLC and NSCLC. Multiple checkpoint inhibitor antibodies have been approved in the last 5 years. They are typically used in patients with advanced disease, and are often used in combination with chemotherapy or after chemotherapy fails. The antibodies approved to date inhibit the PD-1/PD-L1 axis, and target the PD-1 receptor on immune cells (nivolumab, pembrolizumab) or the PD-L1 ligand

14/01/2022 18:54	2022Â EXPÂ 11383	Lung Cancer Genetics and Epigenetics study	Expedited Review	Declined	1) We will establish a blood-based DNA signature (that combines methylation and mutation markers) that can be used to identify lung cancers with high sensitivity and specificity. To achieve this, we will carry out sequencing-based analysis of critical gene mutation and DNA methylation landscapes of lung cancers patient blood and tissues from the same patient, blood samples from patients referred to fast track nodule follow up clinics or chest Xray clinics, and blood samples from healthy/non-malignant controls (Lung ctDNA) 2) To identify DNA methylation, gene expression, and targeted mutation differences between lung cancers from responding and non-responding patients to TKI therapy such as anti-EGFR, ALK, ROS1, BRAF, KRAS (Lung Epi Response)	frequently overexpressed by tumour cells (atezolizumab, durvalumab). A major proportion of the patients eventually develops resistance to these treatments. Molecular marker that can predict patient response could substantially improve the outcome for lung cancer. Recent studies have indicated epigenetic changes could provide promising molecular tool to track drug-tolerant phenotype and predict treatment resistance. Use of liquid biopsy DNA molecular testing in early detection and patient monitoring of lung cancer The survival outcomes for NZ lung cancer patients are among the poorest in the world. Lung cancer represents 18% of all cancer-related deaths in NZ, more than any other tumour type, with stark inequalities between MaÌ„ori and non-MaÌ„ori (15,16). The recently proposed national low-dose computed tomography (LDCT) lung cancer screening programme marks an important step towards improving survival outcomes for lung cancer patients and addressing inequities in healthcare delivery. Although LDCT is a powerful technology, it has relatively poor specificity. Initial studies in LDCT showed that 96% of LDCT positive patients are confirmed false-positive upon subsequent biopsy, necessitating â€œNodule Follow-Upâ€ clinics to monitor indeterminate nodules. Further, LDCT struggles to

						distinguish between indolent lesions that are unlikely to progress within a patientâ€™s lifetime (e.g. in situ and minimally invasive adenocarcinomas) and clinically significant disease, leading to an over-diagnosis rate of 18%. In a population screening setting, this modest performance will result in uncertainty and over-treatment for large numbers of people. Moreover, LDCT screening requires costly diagnostic equipment and specialist operators, creating a substantial economic and infrastructural burden, with the added potential of further increasing rural-urban inequities. Indeed, a recent NZ analysis showed that LDCT screening is unlikely to be cost-effective for all sociodemographic groups. To mitigate these issues of access, cost and accuracy of screening, we propose to develop a sensitive, accessible and cost-effective blood-based test (molecular liquid biopsy) approach that can detect lung cancers at early stages and could be used to monitor patients during therapy and predict response. These molecular liquid biopsy approaches use the circulating tumour DNA (ctDNA) fraction of cell-free DNA or circulating tumour cells (CTCs) isolated from plasma. ctDNA in particular showing great promise as a dynamic molecular monitoring tool for cancer. The aim is to improve the diagnostic performance of the proposed LDCT-based national lung cancer screening programme, in order to reduce the healthcare burden and

						outcomes. The ctDNA test is a minimally invasive, highly specific technology that identifies the presence of tumour from plasma derived DNA. Its development represents a major step towards improving the diagnosis and management of cancer , with applications including: earlier stage of diagnosis; detection of molecular relapses to allow more salvage therapies; tracking response to treatment; and the detection of molecular targets to enable targeted therapy. Tumour-derived DNA is distinguished from background normal DNA in plasma by the presence of distinct somatic DNA alterations, typically mutations and DNA methylation changes. Although ctDNA analysis panels consisting of common pathogenic mutations display high sensitivity for late-stage disease and exceptional overall specificity, they have only modest sensitivity for the detection of early-stage disease. However, recent data demonstrates that high sensitivity can be achieved through the use of richer panels comprising both DNA methylation and mutation markers. We and others have shown that alterations in DNA methylation are not only tissue- and cancer-type specific, but, because of their abundance, also enable earlier tumour detection with >95% sensitivity and specificity for all stages of cancer. In a recent landmark study (n=123,000), a tumour-specific

						could detect lung and other cancers at least 4 years before the standard of care practice.	
17/02/2022 16:32	2022Â EXPÂ 12181	Patient adherence to Hymenoptera venom immunotherapy	Expedited Review	Approved	The aim of the study is to ascertain the adherence rate to Hymenoptera venom immunotherapy and examine the factors that may influence adherence.	Hymenoptera venom immunotherapy (VIT) is a highly effective treatment in reducing the risk of anaphylaxis and death from insect stings and improving the quality of life in people at risk. The level of protection from anaphylaxis during VIT is >95% with wasp stings and >90% with bee stings after the maintenance dose is achieved. In the case of a systemic reaction to a sting during or after completion of VIT, the reaction is usually milder than before treatment and are rarely severe. Most VIT studies concluded that a minimum of a five-year treatment is superior to shorter duration for long-term effectiveness. Life-long therapy should be considered in high risk individuals, such as those with very severe index reactions, adverse reactions during VIT, high exposure risk or comorbidities such as systemic mastocytosis. Adherence to therapy is therefore crucial in achieving successful outcomes. There have been many studies that found low rates of patient adherence to aeroallergen immunotherapy (AIT) regardless of the route and location of treatment administration. However, adherence data on VIT is limited. One prospective study demonstrated that 94.7% and 83.7% of patients still continued VIT after three and five years respectively. In this study, the	

						majority of patients (61%) had access to a local allergy centre where they completed the full VIT course. Of interest, out-of-region patients who underwent maintenance VIT in non-specialised settings were also observed to have similar adherence rates. Another prospective study on a highly mobile military population found the contrary. Only 35% of 76 patients were still undergoing imported fire ant subcutaneous immunotherapy after 1 year of maintenance VIT. The main reported reasons for discontinuation in these studies included lack of compliance to appointments, inconvenience, onset of a new disease, adverse reactions, cost, and fear. Little is known about patientsâ€™ adherence to Hymenoptera venom immunotherapy and the factors influencing adherence in the New Zealand context.	
						Use of liquid biopsy DNA molecular testing in early detection and patient monitoring of lung cancer: The survival outcomes for NZ lung cancer patients are among the poorest in the world. Lung cancer represents 18% of all cancer-related deaths in NZ, more than any other tumour type, with stark inequalities between MaÌ„ori and non-MaÌ„ori (15,16). The recently proposed national low-dose computed tomography (LDCT) lung cancer screening programme marks an important step towards improving survival outcomes for lung cancer patients and addressing inequities	

in health care delivery.

Although LDCT is a powerful technology, it has relatively poor specificity. Initial studies in LDCT showed that 96% of LDCT positive patients are confirmed false-positive upon subsequent biopsy, necessitating â€œNodule Follow-Upâ€ clinics to monitor indeterminate nodules. Further, LDCT struggles to distinguish between indolent lesions that are unlikely to progress within a patientâ€™s lifetime (e.g. in situ and minimally invasive adenocarcinomas) and clinically significant disease, leading to an over-diagnosis rate of 18%. In a population screening setting, this modest performance will result in uncertainty and over-treatment for large numbers of people. Moreover, LDCT screening requires costly diagnostic equipment and specialist operators, creating a substantial economic and infrastructural burden, with the added potential of further increasing rural-urban inequities. Indeed, a recent NZ analysis showed that LDCT screening is unlikely to be cost-effective for all sociodemographic groups. To mitigate these issues of access, cost and accuracy of screening, we propose to develop a sensitive, accessible and cost-effective blood-based test (molecular liquid biopsy) approach that can detect lung cancers at early stages and could be used to monitor patients during therapy and predict response. These molecular liquid biopsy approaches use the circulating tumour

						DNA (ctDNA) fraction of cell-free DNA or circulating tumour cells (CTCs) isolated from plasma. ctDNA in particular showing great promise as a dynamic molecular monitoring tool for cancer. The aim is to improve the diagnostic performance of the proposed LDCT-based national lung cancer screening programme, in order to reduce the healthcare burden and improve lung cancer outcomes. The ctDNA test is a minimally invasive, highly specific technology that identifies the presence of tumour from plasma derived DNA. Its development represents a major step towards improving the diagnosis and management of cancer , with applications including: earlier stage of diagnosis; detection of molecular relapses to allow more salvage therapies; tracking response to treatment; and the detection of molecular targets to enable targeted therapy. Tumour-derived DNA is distinguished from background normal DNA in plasma by the presence of distinct somatic DNA alterations, typically mutations and DNA methylation changes. Although ctDNA analysis panels consisting of common pathogenic mutations display high sensitivity for late-stage disease and exceptional overall specificity, they have only modest sensitivity for the detection of early-stage disease. However, recent data demonstrates that high sensitivity can be achieved through the use of richer panels
					1) We will establish a blood-based DNA signature (that combines methylation and mutation markers) that can be used to	

01/04/2022 09:26	2022Â EXPÂ 12566	Lung Cancer Epigenetics and Genetics Study	Expedited Review	Provisionally Approved	identify lung cancers with high sensitivity and specificity. To achieve this, we will carry out sequencing-based analysis of critical gene mutation and DNA methylation landscapes of lung cancers patient blood and tissues from the same patient, blood samples from patients referred to fast track nodule follow up clinics or chest Xray clinics and blood samples from healthy/non-malignant controls. 2) We aim to establish a panel of epigenetic and genetic analysis for advanced prediction of responder and non-responder patients in lung cancer. For this, we aim to identify DNA methylation, gene expression and targeted mutation differences between lung cancers from responding and non-responding patients to TKI therapy such as anti-EGFR, ALK, ROS1, BRAF, KRAS.	comprising both DNA methylation and mutation markers. We and others have shown that alterations in DNA methylation are not only tissue- and cancer-type specific, but, because of their abundance, also enable earlier tumour detection with >95% sensitivity and specificity for all stages of cancer. In a recent landmark study (n=123,000), a tumour-specific methylation signature could detect lung and other cancers at least 4 years before the standard of care practice. Lung Cancer Classification and Treatment: Lung cancer is an extremely heterogeneous family of diseases, commonly classified according to histological type. This classification is important for treatment and predicting outcomes of the disease. Almost all lung cancers are carcinomas â€“ malignancies arising from epithelial cells. For therapeutic purposes, two broad classes are distinguished: non-small-cell lung carcinoma (NSCLC, accounting for ~85% of cases) and small-cell lung carcinoma (SCLC, ~15% of cases). Treatment for lung cancer depends on the specific cancer cell type, how far it has spread, the presence of targetable mutations, and the patientâ€™s performance status. Common treatments include surgery, chemotherapy, and radiation therapy. Molecularly targeted therapy and immunotherapy are growing in importance

for advanced lung cancer. Lung surgery (tumour resection) remains the treatment of choice for NSCLC patients diagnosed at an early stage, as these tumours are not usually sensitive to chemotherapy and/or radiation. In contrast, SCLC typically responds well to chemotherapy and/or radiation, but has usually metastasized widely by the time of diagnosis, making surgery ineffective. Although surgical resection is potentially effective in lung cancer patients diagnosed at an early stage, 80% of patients are diagnosed at a late stage when their tumours have already spread. Metastasis of lung tumours therefore presents a major challenge to treatment and patient survival. Radiotherapy is often given together with chemotherapy and may be used with curative intent in people with NSCLC who are not eligible for surgery. For potentially curable SCLC cases, chest radiotherapy is often recommended in addition to chemotherapy. Chemotherapy regimens for lung cancer depend on the tumor type SCLC is treated primarily with chemotherapy and radiation, even in relatively early-stage disease. In advanced NSCLC, chemotherapy can improve survival and is used as first-line treatment, provided the person is well enough. Typically, two drugs are used, one of which is usually cisplatin or carboplatin. Other commonly used drugs are gemcitabine, paclitaxel, docetaxel, pemetrexed, etoposide

						02 Lung Cancer. Several drugs that target molecular pathways in lung cancer are now available, especially for the treatment of advanced disease in NSCLC. Molecularly targeted therapies directed against receptor tyrosine kinases (RTKs) lead to moderately improved responses in subsets of adenocarcinoma patients harbouring activating genomic alterations in the corresponding kinase genes, including EGFR, ALK, and ROS1. Immunotherapy may be used for both SCLC and NSCLC. Multiple checkpoint inhibitor antibodies have been approved in the last 5 years. They are typically used in patients with advanced disease, and are often used in combination with chemotherapy or after chemotherapy fails. The antibodies approved to date inhibit the PD-1/PD-L1 axis, and target the PD-1 receptor on immune cells (nivolumab, pembrolizumab) or the PD-L1 ligand frequently overexpressed by tumour cells (atezolizumab, durvalumab). A major proportion of the patients eventually develops resistance to these treatments. Molecular marker that can predict patient response could substantially improve the outcome of lung cancer. Recent studies have indicated epigenetic changes could provide a promising molecular tool to track drug-tolerant phenotype and predict treatment resistance.	
						Acute Rheumatic Fever (ARF) is an autoimmune	

						A Streptococcus infection, characterised by autoimmune attack of the joints and, more seriously, the heart valves as part of carditis. Repeated bouts of ARF can lead to chronic damage in heart valves, also known as Rheumatic Heart Disease (RHD), a condition that affects an estimated 33 million people worldwide and results in 275,000 global deaths per year. There are large ethnic disparities in the disease burden of ARF and the subsequent RHD in New Zealand, with these diseases disproportionately born by MÄ ori and Pacific people. The disease mechanisms (pathogenesis) of RHD is poorly understood, and there is no effective immunotherapy treatment available. This is in contrast to other autoimmune disease such as rheumatoid arthritis and systemic lupus erythematosus for which there are a suite of biological agents available to manage the immune-driven symptoms. Current knowledge of ARF pathogenesis suggests that antibodies and specific immune cells (T-cells) of the immune system become dysregulated. They start targeting proteins in the heart in error, and this causes progressive damage and inflammation which contributes to the scarring of heart valves that can eventually lead to heart failure. The â€˜triggerâ€™ and molecular mechanisms that cause the immune system to become dysregulated remain
07/04/2022 11:38	2022Â FULLÂ 11877	Visualising the Immunology of Rheumatic Heart Valves (VIV-Study)	Full Review	Approved	The aim of this study is improve understanding of of immune activities in rheumatic heart disease. This will encompass two main objectives: 1. Profile circulating immune cells in blood of RHD patients 2. Visualise the immune cells in valve tissue removed during surgery in the same patients.	

						Prior studies of valve tissue from RHD patients have identified antibodies and T-cells in the tissue using conventional H&E (Haematoxylin and Eosin) staining and immunofluorescence microscopy . However, there is a lack of studies applying contemporary microscopy techniques to examine the structure and immune cell infiltrate in RHD tissue. Furthermore, there are limited studies that have simultaneously characterised immune cells in circulation (blood) alongside those that are present in affected tissue (heart valves).	
						The international standard of care for treating early stage endometrial cancer (EC) is surgery, which typically involves total hysterectomy and removal of the fallopian tubes and ovaries. The prognosis for patients with early stage disease treated with surgery alone is generally good. However, when patients have high-risk features, such as nodal involvement or late stage disease, the prognosis is poor, with 5-year overall survival rates ranging from 47-69%. People with known high-risk features are often treated with adjuvant chemoradiation therapy (PORTEC-3 regimen) after surgery, which includes sequential delivery of pelvic chemoradiation followed by 4 cycles of carboplatin plus paclitaxel chemotherapy. This regimen became standard of care in Australia and New	

						Zealand after a trial conducted by the New Zealand Gynaecological Oncology Group (ANZGOG) and international collaborators demonstrated that the PORTEC-3 regimen significantly improved failure-free and overall survival compared to the previous standard treatment of pelvic radiotherapy alone, with the biggest impact seen for stage III patients.
20/04/2022 20:51	2022Â FULLÂ 11761	ADELE: Adjuvant tislelizumab plus chemotherapy in high risk endometrial cancer	Full Review	Approved	The principal aim is to determine if patient outcomes can be improved by adding immune checkpoint inhibitor therapy (tislelizumab) to standard adjuvant therapy for high-risk endometrial cancer. This new type of therapy may improve the immune system's ability to attack cancer cells for some types of endometrial cancer. The primary objective is to determine failure free survival at one year after treatment. Secondary objectives include the feasibility of administering the study treatment, the effects of the study treatment on patient reported outcomes, failure free survival at 6 months post-treatment, overall survival time, and the frequency and severity of study-related side effects. Tertiary objectives will look at the associations between clinical outcomes and potential predictive or prognostic biomarkers.	Despite treatment with primary surgery, adjuvant chemotherapy and radiotherapy, people with high-risk endometrial cancer (EC) are still at significant risk of relapse. Treatment options following relapse are limited, and the median survival after relapse is approximately 12 months. Several studies have recently shown that adjuvant treatment with immune checkpoint inhibitors (ICIs) may improve outcomes for high-risk patients. ICIs are a type of drug that blocks proteins called checkpoints that are made by immune system and cancer cells. When not blocked, these checkpoints help regulate immune responses, but can also prevent the bodyâ€™s immune system from killing cancer cells. Blocking checkpoints with ICIs may improve the immune systemâ€™s ability to prevent the growth of cancer cells, which may be particularly effective for some molecular sub-types of EC which are considered high-risk, such as microsatellite unstable (MSI-H) or mismatch repair deficient (dMMR),

						approximately 20% of EC. The ANZGOG PHAEDRA trial demonstrated that patients with advanced EC of these molecular sub-types have a durable response rate to ICIs of 40-50%. Radiation and chemotherapy induce cell damage that may have immune-stimulating properties which can synergise with immunotherapy, providing rationale for combining these treatments in all EC, including those with high-risk molecular sub-types. In the adjuvant settings of melanoma and non-small cell lung cancer, introducing ICI early in the treatment course of solid tumours is associated with sustained responses. Two lung cancer trials, PACIFIC and IMPower, showed a better response to ICIs when given concurrently with chemotherapy in less responsive molecular subsets of lung cancer, or as maintenance treatment following chemoradiation. These factors provide the rationale for testing a combination of these treatments to improve the effectiveness of adjuvant therapy for high-risk endometrial cancer in the ADELE trial.	