PORT Phase II Trial of Pembrolizumab and Radiotherapy in Cutaneous T cell lymphoma

ELIGIBILITY CRITERIA (summarised)

INCLUSION

- Age ≥ 18 years
- Diagnosis of Stage IB - IVB CTCL Mycosis Fungoides (MF)/Sézary Syndrome (SS)
- Have relapsed, are refractory or progressed after at least one systemic therapy
- Skin biopsy at the time of or within 6 months prior to study entry
- Have at least 1 cutaneous lesion suitable for palliative radiotherapy
- Have in addition at least 1 measurable lesion with a minimum mSWAT score of 10, or 2 or more cutaneous tumours, which will not be irradiated but must be measurable to assess the abscopal effect of the treatment
- Have a minimum wash-out and adverse event (AE) recovery period from previous treatments
- Have ECOG performance status of 0 or 1
- Demonstrate adequate organ function
- Female patients of childbearing potential should have a negative urine or serum pregnancy within 72 hours prior to receiving the first dose of study medication
- Female patients of childbearing potential must have a negative urine or serum pregnancy test
- Willing to comply with the contraception requirements
- Written informed consent

EXCLUSION

- Received chemotherapy or targeted small molecule therapy within 4 weeks prior to study entry or has not recovered from adverse events due to agents administered ≥4 weeks earlier
- Is currently or has participated in an IMP or device study within 4 weeks prior to the first dose of study medication
- Received any other monoclonal antibody within 4 weeks prior to the first dose of pembrolizumab or has not recovered (≤ grade 1 or to baseline level) from adverse events due to agents administered >4 weeks earlier
- Active autoimmune disease requiring systemic treatment within the past 3 months or history of clinically severe autoimmune disease, or any other syndrome that requires systemic steroids or immunosuppressive agents.
- Has a diagnosis of immunodeficiency or is receiving systemic corticosteroid / immunosuppressive therapy within 7 days prior to the first dose of pembrolizumab
- Prior therapy with anti-PD-1, anti-PD-L1, anti-PD-L2
- Has known history of, or any evidence of active, non-infectious pneumonitis
- History of other pulmonary disease such as interstitial lung disease, emphysema or chronic obstructive pulmonary disease
- Has a known history of HIV
- Has a known history of active TB, Hepatitis B/C, or any psychiatric or substance abuse disorders that would interfere with the requirements of the trial
- Has received a live vaccine within 30 days prior to the planned start of study medication
- Patients who have previously received a solid organ transplant

EXPLORATORY BIOLOGICAL STUDIES

Immune monitoring of primary tumour

- Baseline PD-L1 expression
- Immune cell infiltration

Peripheral blood mononuclear cell phenotyping

- Assessment of changes in the immune status of peripheral blood, in comparison to the intratumoural microenvironment, by analysis of mononuclear immune cell phenotypic markers by flow cytometry
- Analysis of plasma HMGB-1 isoform levels as a biomarker of immunogenic cell death following pembrolizumab and radiotherapy (RT)
- Functional analysis of isolated cell populations to determine any effect of pembrolizumab and RT on peripheral cell-mediated immune function
- DNA extraction for T cell receptor sequencing to assess diversity and clonality of T cell clones, in parallel with tissue for similar analysis
- RNA storage for evaluation of immune signatures for responders and non-responders
- Analysis of T cell reactivity against neo-antigens and other tumour associated antigens

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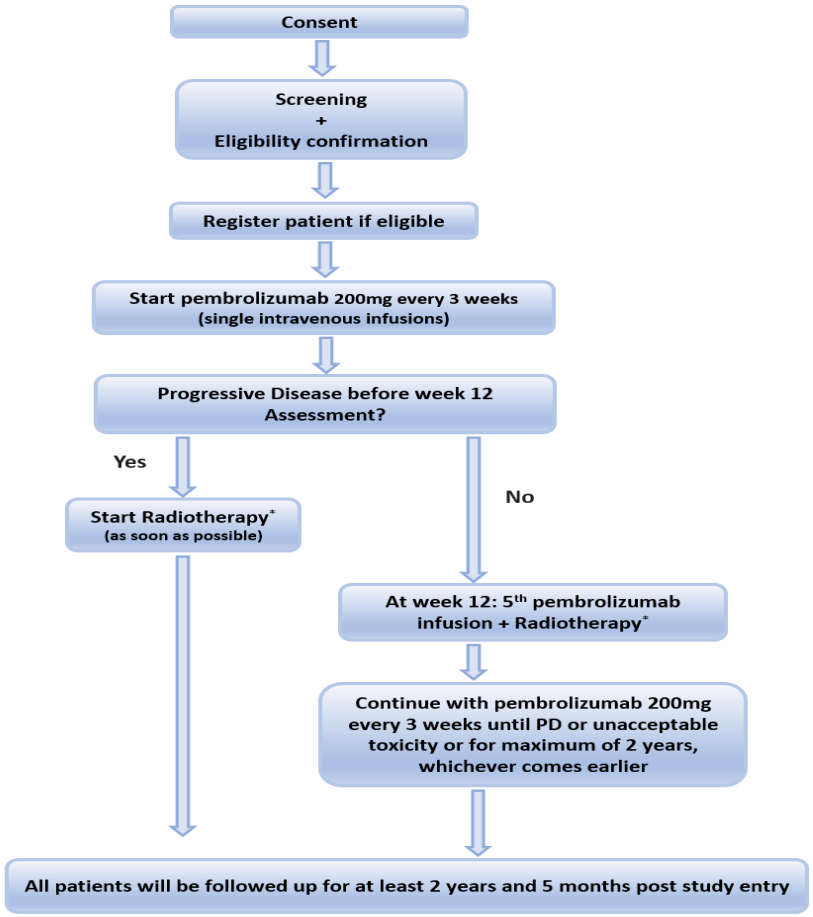

* Radiotherapy will be given as 12Gy in 3#

PRIMARY OBJECTIVES

- To determine whether the addition of radiotherapy to pembrolizumab results in improved response rates
- To investigate immune biomarkers of response to pembrolizumab in combination with radiotherapy

PRIMARY ENDPOINTS

Global assessment of overall response of the combination of pembrolizumab plus radiotherapy at 24 weeks, after the commencement of pembrolizumab

SECONDARY ENDPOINTS

- Response after 12 weeks of pembrolizumab
- Change (improvement) in response
- Duration of response
- Time to next treatment
- Abscopal effect (measured by regression of pre-defined lesions which have not been irradiated)
- Safety and toxicity
- Progression-Free & Overall Survival

TARGET ACCRUAL / NUMBER OF SITES

- 46 Patients recruited over a period of 3 years, and would be followed up for at least 2 years and 5 months after study entry
- 12 identified sites to be open

TRIAL STATUS

- Currently In-Set-Up
- Proposed Dates:
  - EC Submission: REC Provisional Favourable Opinion given
  - 1st Site open (proposed date): July 2018
- CRN Adopted
- Wales Research Directory adopted
- Fully funded
- HRA Outcome of Initial Assessment received
- ClinicalTrials.gov number – NCT03385226

CHIEF INVESTIGATOR
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