Immunocine Cancer Center

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Participant Inclusion Criteria

In order to be eligible to participate in this treatment plan, an individual must meet all of the following criteria:

i. Provision of signed and dated informed consent form.

ii. Stated willingness to comply with all procedures and availability for the duration of the treatment.

iii. Male or female, aged 18 years and older.

iv. Diagnosed with a solid cancer deemed to be of poor prognosis, refractory, late stage, and/or with limited treatment options, as determined by a qualified oncologist. Patients with typically good standard of care options must have either: (a) failed such therapy after a reasonable trial period, (b) declined such therapy for documented reasons unrelated to this treatment, or (c) are pursuing such therapy concurrently with this treatment.

    - B Cell cancers may be considered if there is a sizeable mass capable of being biopsied, pathologically confirmed to be at least 50% malignant, and the rest of treatment is considered feasible and safe (case-by-case determination).

v. A cancerous lesion must be at least 2cm in any 1 diameter, and able to be biopsied. *Not required if previous tumor sample was collected and cryopreserved elsewhere and can be transported to Immunocine.*

    vi. Multiple lesions may be added together to reach the 2cm minimum.

    vii. A biopsy must be predicted to be at least 50% tumorous material.

    viii. Ability to adhere to the bi-weekly injections of IDCT vaccine regimen.

ix. For females of reproductive potential: use of highly effective contraception (defined as methods with a failure rate of less than 1% per year when used consistently and correctly) for at least 1 month prior to screening and agreement to use such a method during study participation and for an additional 12 weeks following discontinuation of last vaccination. Must have a negative serum pregnancy test prior to first treatment.

x. For males of reproductive potential: use of condoms or other methods to ensure effective contraception with partner during study participation and for an additional 12 weeks following discontinuations of last vaccination.

xi. Adequate kidney, liver, bone marrow function, and immune function, as follows:

- Hemoglobin ≥ 8.0 gm/dL
- Absolute neutrophil count (ANC) ≥ 1,500 cells/mm3
- Platelet count ≥ 75,000 /mm3
- Total bilirubin ≤ 1.5 times upper limit of normal (ULN),
- Aspartate transaminase AST (SGOT) and alanine aminotransferase ALT (SGPT) ≤2.5 times the ULN
- Albumin >2g/dL
- White blood count ≥ 3,000/uL and ≤ 11,000/uL
- Acceptable clotting abilities
- PT: 10-16 seconds
- PTT: 26-45 seconds

xii. Able to comply with the requirement to be off strong immunosuppressive drugs (as defined in Appendix A) for at least 21 days before IDCT and during the IDCT process, as determined by the treating physician.

- Note that this is a requirement before IDCT treatment and not medical review.
- This does not necessarily include all chemotherapy and/or radiation as not all are detrimentally immunosuppressive.

xiii. ECOG performance status ≤ 3, preferably ≤ 2.

xiv. No concomitant lymphohematopoietic pathologies that would interfere with Dendritic Cell procurement, maturation, loading or T cell activity.

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Participant Exclusion Criteria

An individual who meets any of the following criteria will be excluded from IDCT treatment:

i. Tumors deemed unable to be biopsied.

- Potentially overcome if previous cancer tissue has been stored to preserve mRNA.

ii. No tumorous lesion either separate or in aggregate with other lesions would reach 2cm.

iii. The presence of tumorous lesions within the brain.

- Note that this does not necessarily include lesions within the skull, and the risk of 50% pseudoprogression will need to be evaluated by the medical team.

- Certain brain cancers can be treated if resected and cryopreserved at home, a post-op scan reveals minimal residual disease in the brain cavity, and the rest of treatment is considered feasible and safe (case-by-case determination).

iv. The presence of tumorous lesions within the heart.

v. If cancer is estimated to occupy more than 30% of the airway space.

vi. If the estimation of an enlargement of any lesion would cause an emergent medical situation (e.g. the spine is of considerable note).

- If lesion ≤ 7cm in 1 direction; estimate UL of 50% increase.
- If lesion ≥ 7.5cm in 1 direction; estimate UL of 25% increase.
- Note that this does not preclude the potential of pain or side effects, but focuses on emergent, potentially catastrophic outcomes.
- Risk can often be preventively mitigated with localized radiation.

vii. Female patients who are pregnant breast feeding or of childbearing potential without a negative pregnancy test prior to baseline. Post- menopausal women must be amenorrheic for at least 12 months to be considered of non-childbearing potential.

viii. Non-B Cell hematological malignancies, or B Cell cancers that do not fall within inclusion considerations.

ix. Bone disease must be carefully analyzed by a qualified physician, especially if involvement of the spine is suspected. Patients with bone disease are excluded if they meet at least 3 of the following criteria:

- ECOG performance status of 4, possibly 3 depending on other factors
- Serum calcium level above 10.2mg/dL
- Evidence of kidney failure as defined by [specific parameters]
- Documented low pain threshold based on standardized assessment
- Limited mobility requiring assistance for daily activities
- High risk of pathological fracture with 25% lesion expansion, as determined by imaging
- High risk of spinal nerve compression with 25% lesion expansion, as determined by imaging

i. Cancers of the eyes

ii. Cancers of the testicles

iii. Autoimmune disorders are not necessarily a disqualifier but can be. Some guidelines are below:

Autoimmune Disorders and IDCT Treatment

Regarding autoimmune disorders, several conditions are compatible with IDCT treatment while others are contraindicated. **Type 1 Diabetes, Vitiligo, and Celiac Disease** are generally acceptable for IDCT treatment without additional restrictions. **Psoriasis** is treatable provided it is not severe, active, or recently active, and will require rheumatologist involvement during treatment. **Sjogren's Syndrome** may also be treatable with rheumatologist oversight. **Rheumatoid Arthritis** patients may be eligible for treatment on a case-by-case basis depending on severity and medications, with rheumatologist involvement required. **Hashimoto's Disease** is treatable if the thyroid is absent, and **Crohn's Disease** is acceptable if the affected bowel has been removed, both requiring rheumatologist consultation. **Lupus** patients may be eligible for Dendritic Cells only treatment, determined on a case-by-case basis, with rheumatologist involvement. **Multiple Sclerosis, Graves Disease, and Myasthenia Gravis** are contraindicated for IDCT treatment under all circumstances.

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Appendix A: Strong Immunosuppressive Drugs

This appendix defines medications considered "strong immunosuppressive drugs" for the purposes of criterion xii in the Participant Inclusion Criteria. Patients must discontinue these medications at least 21 days before IDCT treatment and avoid them during the IDCT process, as determined by the treating physician.

Categories of Strong Immunosuppressive Drugs

1. High-Dose Systemic Corticosteroids

- Prednisone >10 mg daily (or equivalent)
- Dexamethasone >1.5 mg daily
- Methylprednisolone >8 mg daily
- Hydrocortisone >40 mg daily

2. Calcineurin Inhibitors

- Cyclosporine
- Tacrolimus (FK506)

3. Antimetabolites

- Methotrexate
- Azathioprine
- Mycophenolate mofetil
- 6-Mercaptopurine

4. Alkylating Agents

- Cyclophosphamide
- Chlorambucil

5. Biologics and Targeted Immunosuppressants

- TNF inhibitors (adalimumab, etanercept, infliximab, certolizumab, golimumab)
- Interleukin inhibitors (anakinra, tocilizumab, ustekinumab, secukinumab)
- T-cell inhibitors (abatacept)
- JAK inhibitors (tofacitinib, baricitinib, upadacitinib)
- mTOR inhibitors (sirolimus, everolimus)

6. Immunomodulators

- Leflunomide
- Fingolimod
- Dimethyl fumarate

Chemotherapy Agents and Immunosuppression

Given the specific context of cancer treatment, below is a categorization of chemotherapy agents by their immunosuppressive potential at standard therapeutic doses. Low-dose regimens may be considered on a case-by-case basis by the treating physician.

Strongly Immunosuppressive Chemotherapies (Contraindicated for 21+ days before IDCT)

1. **Alkylating Agents (at standard doses)**
   - Cyclophosphamide >500 mg/m²
   - Ifosfamide >1 g/m²
   - Busulfan
   - Melphalan >100 mg/m²
   - Dacarbazine

2. **Purine Analogs**
   - Fludarabine
   - Cladribine
   - Pentostatin

3. **Anti-metabolites (at standard doses)**
   - Cytarabine >1 g/m²
   - Gemcitabine >800 mg/m²
   - Clofarabine
   - Nelarabine

4. **Intensive Combination Regimens**
   - BEACOPP
   - ICE
   - DHAP
   - Hyper-CVAD
   - R-CHOP within 21 days of IDCT

5. **Platinum Compounds (at high doses)**
   - Cisplatin >75 mg/m²
   - Carboplatin AUC >6

6. **Other Strong Immunosuppressants**
   - Temozolomide
   - Bendamustine
   - Doxorubicin >50 mg/m²

Moderately Immunosuppressive (Require Case-by-Case Assessment)

- 5-Fluorouracil standard dose
- Capecitabine standard dose

- Paclitaxel/Docetaxel standard dose
- Gemcitabine ≤800 mg/m²
- Platinum compounds at lower doses
- Anthracyclines at lower doses (e.g., doxorubicin ≤50 mg/m²)

Potentially Compatible with IDCT (Less Immunosuppressive)

- Hormone therapies (e.g., tamoxifen, aromatase inhibitors, LHRH agonists)
- Many targeted therapies (e.g., EGFR inhibitors, PARP inhibitors, CDK4/6 inhibitors)
- Low-dose metronomic chemotherapy regimens
- Certain immunotherapies (case-by-case assessment)

Radiation Treatments Considered Strongly Immunosuppressive

- Total body irradiation
- Extended field radiation involving significant bone marrow reserves
- High-dose radiation to lymphoid tissues (>30 Gy)
- Radiation to >30% of total bone marrow
- Any radiation therapy completed within 3 days of IDCT initiation

Assessment and Monitoring

Patients who have recently taken strong immunosuppressive drugs will require assessment of immune function prior to IDCT treatment, including but not limited to:

1. Complete blood count with differential
2. Lymphocyte subset analysis (if clinically indicated)
3. Immunoglobulin levels (if clinically indicated)

The treating physician has final authority to determine whether a patient's medication regimen and immune status are compatible with IDCT treatment.