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The safety of fat-derived cells combined with a cancer-killing vaccine in patients with advanced solid tumors

Submission date
10/10/2018

Recruitment status
No longer recruiting

Registration date
22/10/2018

Overall study status
Completed

Last Edited
21/08/2019

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Some viruses called oncolytic viruses can specifically target tumor cells, but not healthy cells and tissues. However, the patients' immune system can eliminate most of the injected viral particles. This clinical study aims to overcome this issue by mixing the oncolytic viral particles with some of the patient's cells called stem cells. The stem cells would make the oncolytic viruses invisible to the patient's immune system during transport to the tumor sites. This study will evaluate the safety of the stem cells incubated with oncolytic virus in patients with advanced tumors. This study aims to recruit 30 patients with advanced tumors. The goal is to
evaluate the safety of this novel treatment approach in patients with advanced tumors. This study will also evaluate the anti-tumor effects of this treatment.

Who can participate?
Adults over the age of 18 who have advanced tumors

What does the study involve?
Participants are asked to join this study in their oncologist's clinic. Participants must pass the screening criteria for this study. Participants will be treated once and all treatment procedures will be completed within 3 hours. Patients will receive a combination of systemic intravenous and /or regional intratumoral deployment by a single injection. The study lasts one year in total. Participants are asked to give 7 small blood samples at the beginning, during and at the end of the study to test for the blood levels for virus DNA and specific proteins. Participants also complete online questionnaires every week during the study period.

What are the possible benefits and risks of participating?
There may or may not be immediate direct benefit to those taking part. There should be benefits to future treatment protocols for cancer therapies. The main risk of this treatment would be chills, low-grade fever and other flu-like symptoms in the first 8-24 hours. Therefore, doctors will continue to follow routine safety procedures to monitor participants for 24 hours following treatment.

Where is the study run from?
This study is being run by the Cell Surgical Network (USA) and takes place in two clinical centers located in Rancho Mirage, CA and Beverly Hills, CA (USA)

When is the study starting and how long is it expected to run for?
December 2015 to July 2017

Who is funding the study?
Cell Surgical Network (USA)

Who is the main contact?
1. Dr. Elliot Lander, MD (elliot@cellsurgicalnetwork.com)
2. Dr. Mark Berman, MD (mark@cellsurgicalnetwork.com)

Contact information

Type(s)
Scientific

Contact name
Dr Boris Minev

Contact details
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United States of America
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Additional identifiers

Protocol serial number
SI-01

Study information

Scientific Title
The safety of autologous adipose derived SVF combined with the ACAM2000 (Vaccinia) vaccine in patients with advanced solid tumors

Study objectives
Oncolytic viruses can target advanced solid malignancies with increased uptake and replication of the virus in cancer tissue. However, the patients' immune system can neutralize most of the viral particles after deployment. We suggest that the oncolytic viral particles taken up by autologous stem cells would be invisible to the host immune system during transport to the tumor sites. Stem cells also exhibit a natural tropism towards cancer and can be exploited to carry the viral payloads directly to the cancer microenvironment, thus eluding the host immune system. This study evaluated safety of autologous Stromal Vascular Fraction (SVF) cells incubated with oncolytic vaccinia virus in patients with advanced solid tumors.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Institutional Review Board (IRB) of the International Cell Surgical Society (ICSS), 28/08/2015, approval number ICSS-2015-007

Study design
Interventional open-label non-randomised study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Advanced solid tumors

Interventions
Patients were treated with autologous stromal vascular fraction (SVF) derived from autologous fat incubated for 15 minutes to 1 hour with oncolytic vaccinia virus ACAM2000. Patients received a combination of systemic intravenous and/or regional intratumoral deployment, which included intra-peritoneal or intra-nodal injections. The dose range for ACAM2000 in this trial was between $1.4x10^6$ pfu and $1.8x10^7$ pfu.
The total duration of the study was 3 years and 19 days.
Adverse events will be monitored throughout the study until resolution. In addition, all patients will respond to a weekly questionnaire answering specific questions on their current condition. Participants will be asked to give 7 small blood samples at the beginning, during and at the end of the study to test for the blood levels for virus DNA and specific proteins.

Intervention Type
Biological/Vaccine

Primary outcome(s)
Safety of autologous adipose-derived stromal vascular fraction (SVF) combined with oncolytic vaccinia virus ACAM2000 in patients with advanced solid tumors, assessed using:
1. Patient interviews, weekly throughout the study period
2. Physical examinations at 1 day, 1 month, and 3, 6 and 12 months after treatment

Key secondary outcome(s))
1. Anti-tumor effects of the SVF/ACAM2000 administration, assessed at 3, 6 and 12 months after treatment using:
1.1. Physical examination
1.2. Imaging
2. Anti-vaccinia and anti-tumor immune responses following administration of SVF/ACAM2000, assessed at 1 day, 1 month, and 3, 6 and 12 months after treatment using:
2.1. Blood sample analysis for plasma cytokines
2.2. Flow cytometry

Completion date
19/07/2018

Eligibility

Key inclusion criteria
1. Ability to understand and the willingness to sign a written informed consent
2. Histologically proven diagnosis of advanced (AJCC, 7th addition: stage III or IV) or aggressive (published disease-specific survival rates less than 20% at 5 years following best currently available therapies) solid organ cancer
3. Have no continuing acute toxic effects of any prior therapy, including but not limited to:
3.1. Biological therapy
3.2. Radiotherapy
3.3. Chemotherapy
3.4. Surgical procedures
All such effects must have resolved to Common Terminology Criteria for Adverse Events (CTCAE, Version 4.0) Grade ≤1. Any other
surgery (except biopsies) must have occurred at least 28 days prior to study enrollment
4. Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 2
5. Have a life expectancy of at least 3 months
6. Adequate organ and marrow function
7. Women of child-bearing potential and men with partners of child-bearing potential must agree to use adequate contraception (hormonal or barrier method of birth control, or abstinence) prior to study entry, for the duration of study participation, and for 90 days following completion of therapy. Should a woman become pregnant or suspect she is pregnant while participating in this study, she should inform her treating physician immediately
8. Women of child-bearing potential has negative pregnancy test prior to initiating study drug dosing
9. Be willing and able to comply with scheduled visits, the treatment plan, imaging and laboratory tests

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
26

Key exclusion criteria
1. Current or anticipated use of other investigational agents or marketed anticancer agent while on study
2. Received chemotherapy or radiotherapy within 4 weeks prior to entering the study or has not recovered from adverse events due to agents administered more than 4 weeks earlier
3. Patients who are less than 4 weeks from surgery (except biopsies) or have insufficient recovery from surgical-related trauma or wound healing

4. Have known immune system disorders (including acquired immunodeficiency syndrome (AIDS), HIV infection or hepatitis B or C). Eligible patients must have a negative HIV test result within 4 weeks prior to study initiation
5. Receiving additional immunosuppressive therapy or any steroids (except concurrent corticosteroid usage if no more than 20 mg per day, prednisolone equivalent is applied)
6. Received prior gene therapy or therapy with cytolytic virus of any type
7. Have clinically significant cardiac disease (New York Heart Association Class III or IV) including pre-existing arrhythmia, uncontrolled angina pectoris, and myocardial infarction one year prior to study entry, or Grade 2 or higher compromised left ventricular ejection fraction
8. Pulse oximetry oxygen saturation <90% at rest
9. Dementia or altered mental status that would prohibit informed consent
10. Severe or uncontrolled medical disorder that would, in the investigator's opinion, impair ability to receive study treatment (i.e. ncontrolled diabetes, chronic renal disease, chronic pulmonary disease or active, fever, systemic and/or uncontrolled infections, psychiatric illness /social situations that would limit compliance with study requirements)
11. Be receiving concurrent antiviral agent active against vaccinia virus (e.g., cidofovir, vaccinia immunoglobulin, imatinib, ST-246) during the course of study
12. Have known allergy to ovalbumin or other egg products
13. Have clinically significant dermatological disorders (e.g., eczema, psoriasis, or any unhealed skin wounds or ulcers) as assessed by the Principal Investigator during screening and during the study
14. Have a history of allergy to iodinated contrast media
15. Have an active dental infection or recent dental work within 2 weeks of deployment
16. Known brain metastases
17. Pregnant or nursing
18. Condition does not seem to be one that can be improved with SVF/ACAM2000 as determined by one or more of our physician team

Date of first enrolment
01/12/2015

Date of final enrolment
19/07/2017

Locations

Countries of recruitment
United States of America

Study participating centre
California Stem Cell Treatment Center
72-780 Country Club Drive
Suite 301
Rancho Mirage, CA
United States of America
92270

Study participating centre
Cell Surgical Network
120 S Spalding Dr., Suite 300
Beverly Hills, CA
United States of America
90212

Sponsor information

Organisation
Calidi Biotherapeutics

Funder(s)

Funder type
Not defined

Funder Name
California Stem Cell Treatment Center

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	19/08/2019	21/08/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes