

## A Questionnaire On Adoptive Cell Therapy Among Syrian Medical Students

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### 1. Abstract

Adoptive Cell Therapy (ACT) is a type of immunotherapy, in which immune cells are implanted in patients to help them cure diseases (such as cancer). It is a new technique that has proven its effectiveness in treating different types of cancer, especially melanoma, breast cancer, and colon cancer. It has many factors that distinguish it from other cancer treatments, such as its selectivity towards cancer cells without harming normal body cells, therefore less side effects.

We aimed in this questionnaire to evaluate the knowledge of medical students in Syria on this new technique, it included (822) participants, mainly students and graduates from medical faculties and others who have interests in the medical field or are informed about it. The questionnaire involved questions about ACT, if the participants were familiar with it or heard of it before, if they were familiar with other cancer treatments, and many other questions. It was evident from the results that the participants were more familiar with chemotherapy and trusted it the most, as for ACT, few have heard of it, and many thought it is unlikely to be applied in Syria due to many obstacles.

### 2. Introduction

Adoptive Cell Therapy (ACT) is a type of immunotherapy, in which immune cells are implanted in patients to help them cure diseases (such as cancer). Many types of immune cells can be used in Adoptive cell therapy, they can be either taken from the patient's own blood, tumor tissue, or from another donor. They are then grown in large numbers in vitro and activated using different techniques. After that they are infused back in the patient's body to help fight the cancer cells.

It had been noticed that in vitro modifying of the immune cells such as T-cells would make them more effective and selective to the antigens of the tumor cell. While the treatment is still under study, each year new discoveries are being made involving it and more obstacles are being overcome. [1-3]

#### 2.1. Adoptive Cell Therapy with Genetically Engineered T-Cells

T-cells can recognize tumor cells with TCR (T-cell receptor), but this action is not effective enough to stop the tumor spreading or killing the cancer cells. Scientists found that the anti-tumor action can be improved when TCRs are genetically engineered.

Another way has been discovered to improve the effectiveness of T-cells, which is replacing the TCR with CAR (chimeric antigen receptor), then cultivating the engineered cells in large numbers and implanting them back in the patients. These new cells can immediately recognize cancer cells and attack them. [4-6]

#### 2.2. Adoptive Cell Therapy with Tumor-Infiltrating Lymphocytes (Tils)

Tumor infiltrating **lymphocytes** are white blood cells that leach and invade the tumor. TILs express the body's natural response against a cancerous tumor, through their ability to identify cancer cells, which possess TAAs (tumor-associated antigens) and then destroy them as if they were foreign bodies.

TIL can be isolated from a fresh tumor sample and cultivated in large numbers in vivo. This technique has been very effective in the treatment of metastatic melanoma, and it can be used in many tumors and conditions such as colon cancer. [7-9]

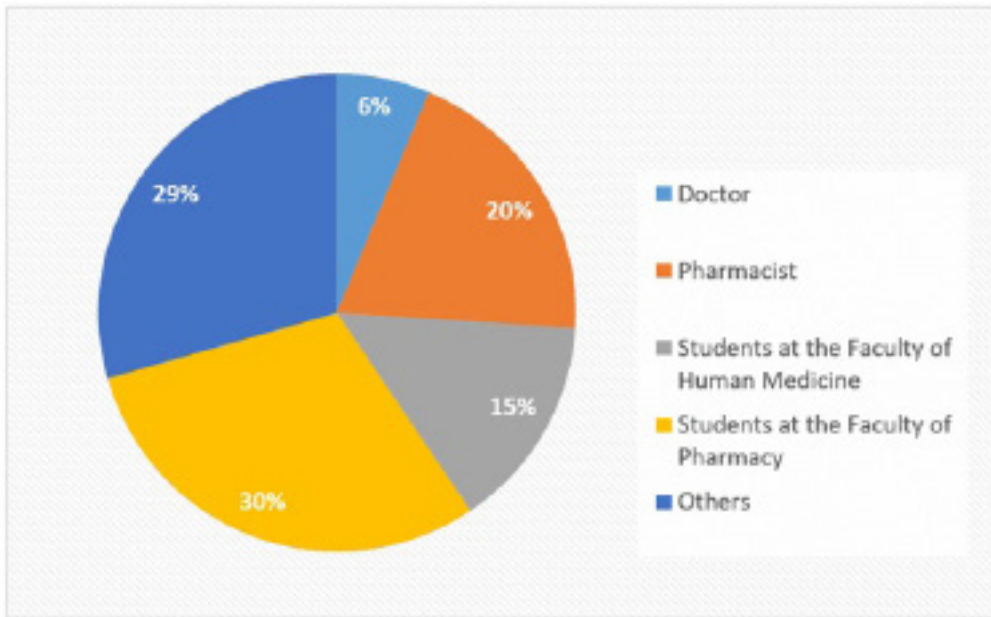


Figure 1: Academic specialization of the participants.

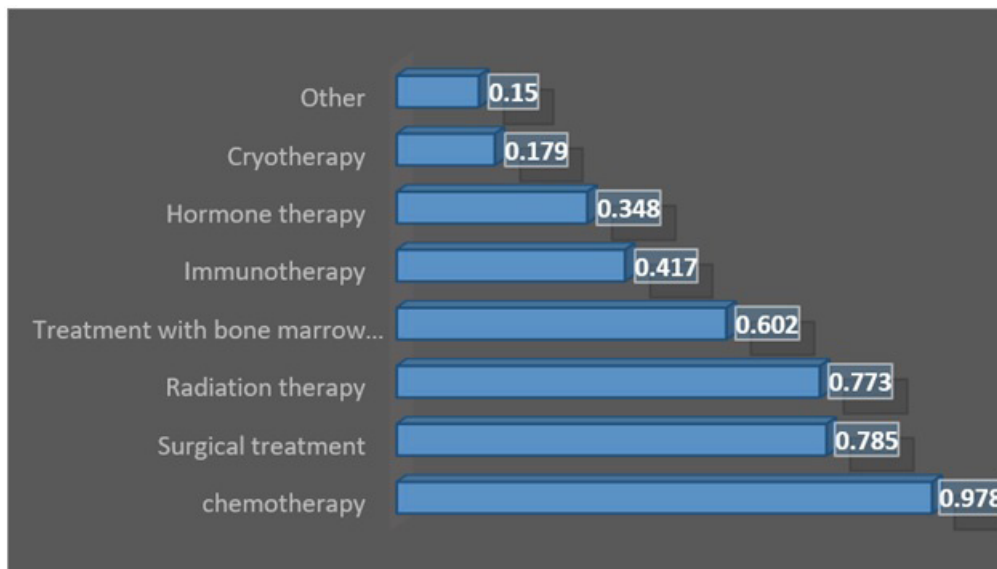


Figure 2: Cancer treatments the participants are familiar with

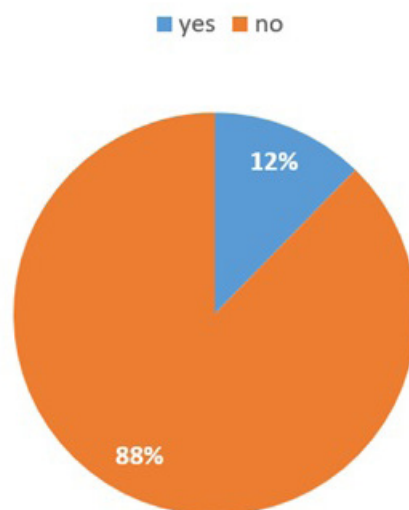
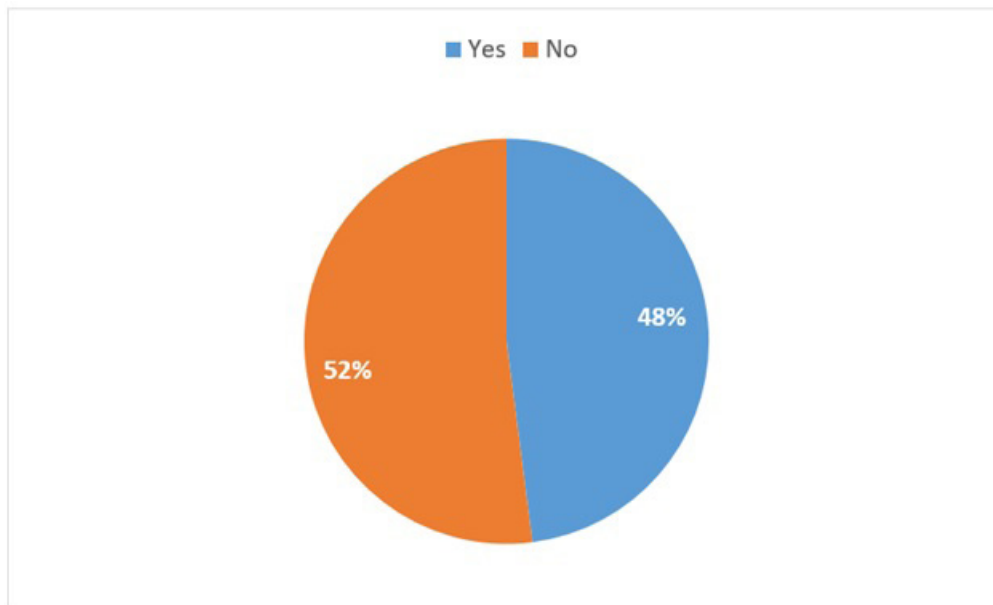
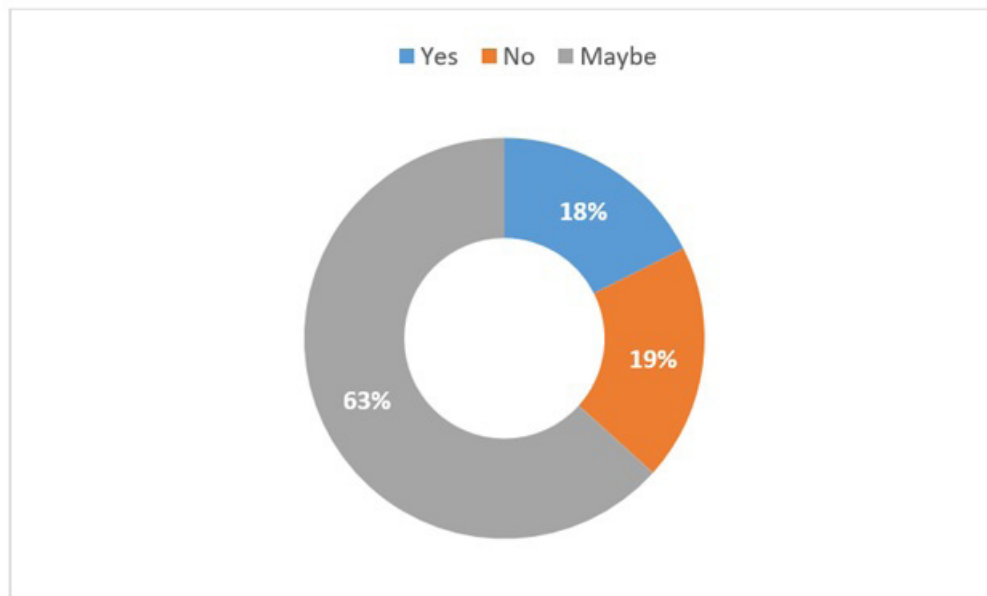


Figure 3: Percentage of participants that have heard about/are familiar with ACT



**Figure 4:** Percentage of participants who find ACT as a viable treatment



**Figure 5:** Percentage of participants that believe ACT is applicable in Syria

### 2.3. Treating with Adoptive Cell Therapy Using Peripheral Blood Mononuclear Cells (Pbmcs)

PBMCs have been used as a source for the cells used in ACT for 3 decades because they are easy to isolate, and available in abundance. They develop from different cells, including lymphocytes (T cells, B cells, and the natural killer cells), monocytes, and the dendritic cells. They can be activated using more than one method, like genetic modification. By activating these cells using high doses of IL-2, we get lymphokine-activated killer cells (LAK), which are used to create the cytokine-induced killer cells (CIK's). [10]

### 2.4. Adoptive Cell Therapy with Cytokine-Induced Killer Cells (CIK's)

CIKs are considered the grandchild of LAKs, since they are easier

to get and more effective, and do not show any toxicity for normal tissue cells. Studies have confirmed that these cells can be used to treat colorectal cancer safely, guaranteeing a good effect. [11,12]

### 2.5. Adoptive Cell Therapy with Natural Killer Cells:

Natural killer cells belong to the innate immune system which form the most important defense line for humans against pathogens and mutant cells, and the significant feature for these cells, is expressing CD56 and/or CD16 but without the complex TCR-CD3.

These cells can recognize mutant or pathogen cells through specific antigens, whereas they can coordinate their job through the integration between the activating and deactivating signals of the receptors found on their surface, which lead to activating the natural killer cells.

These activating and deactivating receptors are considered responsible for these cells' ability to recognize abnormal cells and kill them, they are also responsible for the cells' inability to kill normal cells. [13-15]

### 3. Material and Methods

We made an electronic questionnaire about adoptive cell therapy and other cancer treatments in general, it included hundreds of participants (822 participants), mainly students and graduates from medical faculties (pharmacy, medicine, dentistry, medical engineering) and others who have an interest in the medical field or are informed about it [16].

### 4. Results

And the results were as shown below:

Percentage of participants according to their academic specialization:

1. The category "other" includes dentistry which reached 70%, medical engineering which reached 15%, and college students whom are interested in medical affairs and modern therapy techniques reached a percentage of 15%.
2. The participants were asked about the different cancer treatments they were familiar with and the results are represented in the diagram below: And as we can see –as expected- that chemotherapy is the most commonly known therapy in Syria, followed directly by surgical treatment, which is followed by radiation therapy.
3. The participants were then asked if they knew about ACT, or if they heard of it before, and as we can see, the majority have not heard about this treatment technique before:
4. Then we asked the participants who answered "yes" to the previous question, what exactly do they know exactly about this technique and the extent of their knowledge of it: And the majority of their answers (92%) said that their knowledge of it was shallow and limited on some general information about this technique, since they don't know the complete procedure, but only that it is one of the immunological techniques used for cancer treatment.
5. After that we made a discussion for the participants, and we asked them based on their point of view, what is the most effective cancer treatment technique used nowadays? And we noticed that chemotherapy took first place according to the participants based on trust and effectiveness, followed by surgical treatment, then radiation therapy, and finally immunotherapy.
6. We created a definition for ACT: Adoptive cell therapy is a form of immunological technique for cancer treatment, in which lymphocytes are isolated, proliferated, and modified in vitro until it gains the ability to recognize tumor cells and target them, after that, the modified lympho-

cytes are injected back into the patient's body where they attack the tumor and treat it. After that, we asked them, if they expect ACT to be a significant technique and a new hope for cancer treatment, and the results were as shown below:

7. We asked the participants about their opinion on the possibility of applying ACT in Syria, and the answers were as shown below:
8. We discussed the obstacles that can face the possibility of applying ACT in Syria. with the participants. In their opinion, the biggest and most important obstacle was the high material cost of this technique and the lack of experts and equipment in the country due to war circumstances; they also confirmed that the lack of scientific research and interest in researchers has a big effect on this issue.

### 5. Conclusion

Adoptive cell therapy is a new promising strategy to reactivate the immune system to fight cancer cells. Third world countries lack the new techniques to make a research on humans, so we aimed of this questionnaire to measure the knowledge of Syrian society, especially health practitioners and medical students, about adoptive cell therapy to treat different types of cancer

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