

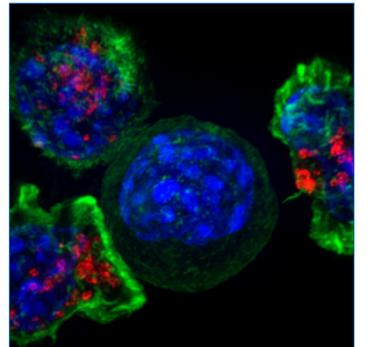
# CYTOKINE RELEASE SYNDROME REACTION: THE CLINICAL PHARMACIST IN THE CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY TEAM

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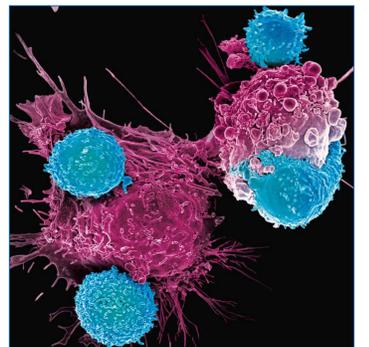
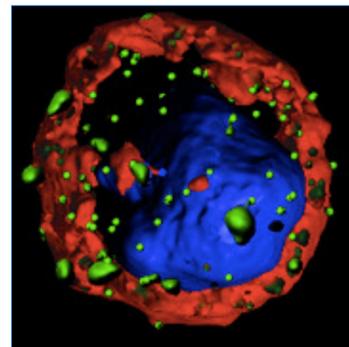
## Background and Importance:

Chimeric antigen receptor (CAR) T cell therapy is being studied for the treatment in hematologic malignancies. CARs are synthetic receptors that reveal the specificity, purpose and metabolism of T cells. The first step in making CAR- T cells is to insert a gene into the cell, in order to express a new antigen binding site on its surface and to redirect the T cell to the new target. Since CAR- T is a personalized therapy, the medicine should be administered to the patient for whom it was intended. For this reason, the clinical pharmacist plays a key role in clinical surveillance, care coordination, and patient education.



## Aim and Objectives:

The aim of this work is to frame the pharmacist as risky manager for this reason, he's involved in a CAR-T multidisciplinary team composed by figures able to take care of cancer patients. Beyond the implementation of the hospital circuit, the pharmacist is essential in the follow-up of the patients after the administration, in consideration of the complexity of the side effects, as well as in the antidote management.



## Material and methods:

Cytokine release syndrome (CRS) is one of the most common side effect in the CAR-T therapy, in which there is a fast release of cytokine involved in the inflammatory process. It seems that the onset of CRS is related to the efficacy of the therapy, even though this side effect is extremely dangerous and it's on-target. Pharmacist should managed the CRS by ensure the supply of tocilizumab, one monoclonal antibody against interleukin-6 (IL-6) as antidote in label or siltuximab, off-label.

## Results:

Nowadays, 6 patients are treated with CAR- T cell therapy and safety outcomes are ongoing. All of them has CRS reactions and received tocilizumab.

**Conclusion and relevance:** Based on these results, the immediate availability of antidote and treat on time the CRS reactions (mandatory activity for the pharmacist) by ensuring the therapeutic and safety benefits for the patients. This shows the essential role of the pharmacist to cover the risks of this kind of therapy and to reduce the seriousness of side effects in an innovative therapy like CAR-T cells.

| CRS Parameter      | Grade 1  | Grade 2                                     | Grade 3   | Grade 4  |
|--------------------|----------|---|---|--|
| <b>Fever</b>       | T > 38°C | T > 38°C                                    | T > 38°C  | T > 38°C   |
| <b>Hypotension</b> | None     | Not requiring vasopressor                   | Requiring a vasopressor with or without vasopressin                             | Requiring multiple vasopressor (excluding vasopressin)                           |
| <b>Hypoxia</b>     | None     | Requiring low-flow nasal cannula or blow-by | Requiring high-flow nasal cannula, facemask, nonrebreather mask, or Venuri mask | Requiring positive pressure (eg CPAP, BiPAP, intubation, mechanical ventilation) |

