

## The Science of CAR-T Cell Therapy <sup>[1]</sup>



### **CAR-T cell therapy: The living drug<sup>1</sup>**

CAR-T cell therapy is a targeted, personalised therapy that contains patients' autologous T cells reengineered to fight cancer. This living drug continues to exist in the body and combat cancer long after its infusion.

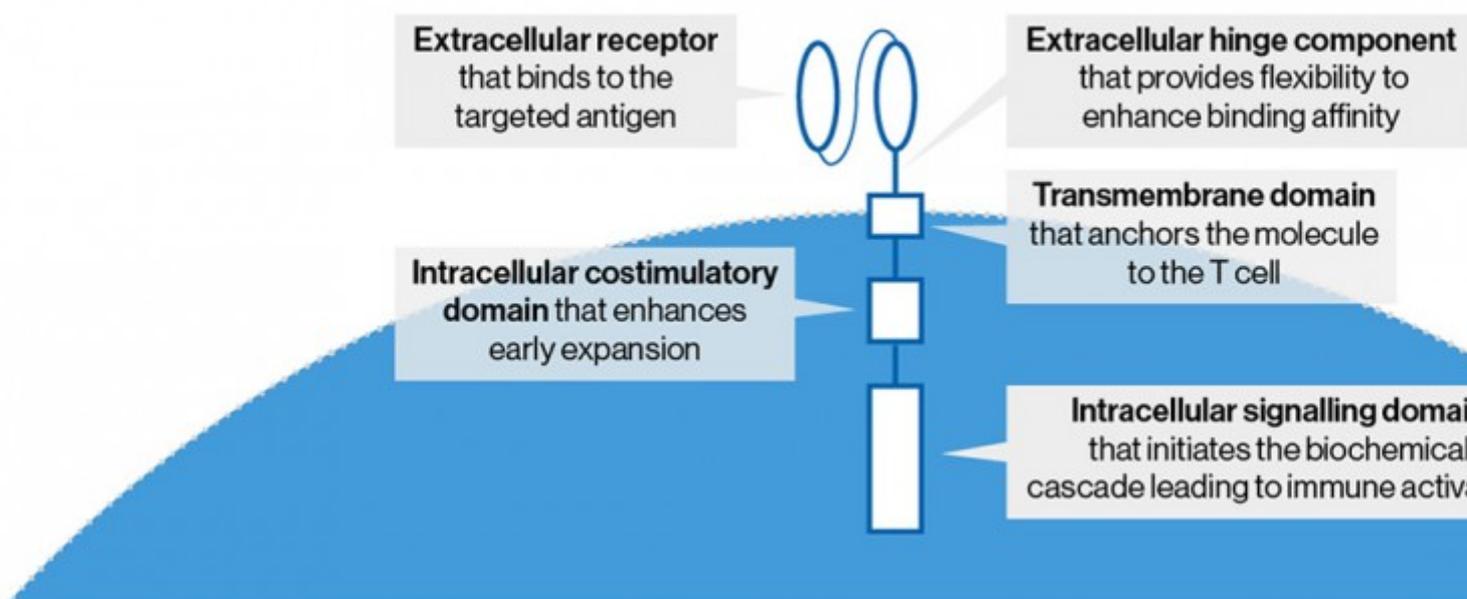


**Personalised:** Establishes individual treatments for individual patients<sup>1</sup>

	<p><b>Reengineered:</b> Harnesses the power of our existing defense mechanisms to fight cancer<sup>1</sup></p>
	<p><b>Persistent:</b> Provides hope for long-lasting efficacy to relapsed or refractory patients who need it most<sup>1</sup></p>

## The structure of CAR-T cells<sup>1</sup>

CAR-T cell therapy contains patients' autologous T cells that are modified to express the CD19 chimeric antigen receptor (CAR), which helps eliminate B cells, including those that are malignant. Current CAR-T cell therapies contain CARs composed of five parts. Please see the diagram and accompanying text below to learn more about the function of each component.



1. **Extracellular receptor** that binds to the targeted antigen
2. **Extracellular hinge component** that provides flexibility to enhance binding affinity
3. **Transmembrane domain** that anchors the molecule to the T cell
4. **Intracellular costimulatory domain** that enhances CAR-T cell persistence
5. **Intracellular signaling domain** that initiates the biochemical cascade leading to

immune activation

## Costimulatory domains

CARs can have different costimulatory domains. Two such costimulatory domains are 4-1BB and CD28. See the table below for some characteristics of 4-1BB- and CD28-containing CARs.

<b>4-1BB</b>	<b>CD28</b>
Enhances <b>CAR-T cell expansion</b> and <b>long-term persistence</b> <sup>2,3</sup>	Enhances <b>early and rapid CAR-T cell expansion</b> in vivo and in vitro <sup>2,6</sup>
Demonstrated induction of central memory T-cell differentiation for <b>improved proliferative potential</b> in vitro <sup>3,4</sup>	Correlated with effector memory T-cell differentiation for <b>immediate protection</b> in vitro <sup>3</sup>
May help <b>prevent CAR-T cell exhaustion</b> <sup>1,5</sup>	Provides <b>limited long-term persistence</b> and can <b>cause rapid CAR-T cell exhaustion</b> <sup>5</sup>

To learn more broadly about the field of cell and gene therapy and the difference between the two, please [click here](#) [2].

## Potentially definitive treatment<sup>1</sup>

The CAR-T cell therapy patient population is often heavily pretreated and in need of an effective, durable treatment option. CAR-T cell therapy is a breakthrough treatment that offers a unique approach to fighting cancer.<sup>7</sup> Patients may not require another treatment after CAR-T cell therapy, especially if they achieved a complete response or complete remission (CR).<sup>1</sup>

Deeper responses to CAR-T cell therapy correlate with durable efficacy. For patients with leukaemia, minimal residual disease negative (MRD-) status is tied to positive outcomes.<sup>8</sup>

## Identifying appropriate patients

CAR-T cell therapy offers a new treatment option for some patients who have not responded (refractory) following therapy or who have relapsed following two or more prior therapies, including stem cell transplant (SCT). Patients who are not suitable for SCT due to performance status, comorbidities, or inability to achieve CR may be eligible for CAR-T cell therapy.<sup>1,9</sup>

**Selecting appropriate patients is important, as the following characteristics may impact how patients respond to CAR-T cell therapy<sup>10,11</sup>:**



Age<sup>10</sup>

	Number of prior therapies <sup>11</sup>
	Performance status <sup>10</sup>

Some benefits of CAR-T cell therapy include the fact that patients do not need to be in CR to initiate treatment and that no donor is required for treatment.<sup>1</sup>

## Manageable safety profile<sup>1</sup>

CAR-T cell therapy has a different side effect profile than other treatment options. Please [click here](#) <sup>[3]</sup> to view the treatment landscape. Possible side effects of CAR-T therapy include cytokine release syndrome, neurotoxicity, and hypogammaglobulinemia. Although these side effects can be serious, they are often transient and are typically manageable.

CAR-T cell therapy is not known to be associated with some serious long-term side effects, such as graft-vs-host disease or hair loss.

Some patients who received CAR-T cell therapy reported improvements in quality of life and were able to return to normal activities shortly after infusion. Research into future generations of CAR-T cell therapies aims to further improve upon the efficacy and safety profile of this drug class.<sup>12</sup> Please [click here](#) <sup>[4]</sup> to view the future of CAR-T cell therapy.

## Next: The Process ? <sup>[5]</sup>

### Disclaimer:

### References:

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