Pulling back the curtain on Astrazeneca’s Car-T work

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Astra’s stealthy move into cell therapy has yielded a truly novel cancer target, and the company could be in clinical trials soon.

Astrazeneca is not alone among big pharma groups to have come late to cell therapy, but the mists around its work here are slowly clearing. What could become Astra’s first clinical-stage Car-T therapy is AZD0754, and it targets the Steap2 antigen, a document seen by Evaluate Vantage reveals.

It is still unclear whether AZD0754 is an allogeneic Car-T therapy, but it is likely to play into the hot and largely untapped space of solid tumours: Steap2 is an antigen overexpressed in prostate cancer. And, while many chase tried and tested cancer targets, Astra is going for true novelty, as no other industry project against Steap2 is near the clinic.

Indeed, the only other company working on Steap2 might be Regeneron, according to a patent filing describing MAbs, antibody-drug conjugates and bispecifics against Steap2. Perhaps tellingly, the patent cites Astra’s Medimmune unit; back in 2016 Regeneron and Medimmune struck a deal to develop anticancer ADCs.

AZD0754

Now an apparently internal document detailing Astra’s early oncology clinical trials programmes has revealed the existence of the anti-Steap2 Car-T therapy AZD0754.

At the time of going to press the company had not responded to Vantage’s questions about the status of this project, its possible uses and plans for clinical trials. At present AZD0754 has no entry on clinicaltrials.gov, and it is unclear when it might enter human studies, but the fact it features in a list of clinical programmes suggests that trials might not be far off.

For a long time Astra was, like Roche, a big pharma cancer player that avoided making a big push into cell therapy, preferring to focus on antibodies and bispecifics. And, beyond a 2015 clinical collaboration to combine Imfinzi with a Juno Car-T therapy, Astra has said little publicly about progress.

But work behind the scenes has ramped up recently, with Fierce Biotech reporting in August that this was focusing on allogeneic therapies and solid tumours. Astra’s cell therapy unit is up and running; a study leader is in place, and a recruitment drive has been mounted, according to posts on LinkedIn.

Roche too has slowly turned away from its earlier reluctance, like Astra focusing on off-the-shelf therapies, and
this year it has struck cell therapy deals with Adaptimmune and Poseida. This kind of push comes in stark contrast to GSK, which in short order has ended collaborations with Lyell, Adaptimmune and Immatics in what looks like an exit from cell therapy.

**Steap2**

Expression of Steap2, which stands for six-transmembrane epithelial antigen of the prostate-2, is increased in prostate cancer, suggesting that this protein might drive the cancer’s progression.

A related antigen, Steap1, is the target for a handful of clinical projects, most notably perhaps Amgen’s AMG 509. There is no clinical work against Steap2, though AZD0754 might soon change this.

<table>
<thead>
<tr>
<th>Project</th>
<th>Company</th>
<th>Mechanism</th>
<th>Status</th>
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<tbody>
<tr>
<td>VTP-850</td>
<td>Vaccitech</td>
<td>Prime-boost immunotherapy against PSA, PAP, Steap1 &amp; 5T4</td>
<td>Ph1/2 in prostate cancer</td>
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<tr>
<td>AMG 509</td>
<td>Amgen (ex Xencor)</td>
<td>Anti-Steap1 T-cell engager</td>
<td>Ph1 in prostate cancer</td>
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<tr>
<td>AZD0754</td>
<td>Astrazeneca</td>
<td>Anti-Steap2 Car-T therapy</td>
<td>Preclinical</td>
</tr>
<tr>
<td>Unnamed</td>
<td>Regeneron (ex Astrazeneca?)</td>
<td>Anti-Steap2 MAb, ADC or T-cell engager</td>
<td>Not formally in development (patent only)</td>
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<tr>
<td>Vandortuzumab vedotin (RG7450)</td>
<td>Roche</td>
<td>Anti-Steap1 ADC</td>
<td>Discontinued in 2017</td>
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*Source: Evaluate Pharma, clinicaltrials.gov & company documents.*