Next week’s virtual meeting could resuscitate Ox40 agonists, but an important omission will disappoint.

Unveiling of the presentation titles for the first instalment of this year’s AACR meeting has revealed two surprises: the absence of keenly awaited clinical data on Roche’s anti-Tigit MAb tiragolumab, and the presence of a trio of studies on Ox40, an immuno-oncology target that had earlier fallen out of favour.

The latter feature first-in-human data from one of Glaxosmithkline’s major oncology hopes and a bispecific from Alligator Bioscience, as well as early data from Moderna’s Ox40L-producing mRNA project. And there are plenty of other novel targets to whet investors’ appetites, but the absence of Tigit will be a major disappointment.

Investors in other Tigit-focused biotechs, including Arcus, Compugen and Iteos, had been keenly awaiting the early tiragolumab data for evidence to back Roche’s decision to launch a phase II/III programme that now comprises three Skyscraper studies in 1,060 subjects.

Tiragolumab’s nearest rival, Merck & Co, subsequently put its competitor, MK-7684, into four new trials. However, not only does AACR have nothing on tiragolumab, there are no presentations obviously highlighting any Tigit-targeting projects.

(After this story was published Roche told Vantage that the tiragolumab data presentation was now planned for AACR II on June 22-24.)
The 2020 instalment of AACR was to have started on Friday, but the Covid-19 pandemic has caused the organisers to turn the meeting into two virtual events.

The first, next Monday and Tuesday, will feature most of the clinical presentations, which AACR says it wanted to get out in a timely manner, and it is this meeting for which abstract titles have been made available. AACR II will be a separate three-day virtual meeting in June, the abstracts for which will go live on May 15.

Among other novel approaches featuring in clinical presentations at AACR I will be an anti-LIF-1 MAb from Northern Biologics that had been optioned to Celgene, but whose future under Bristol-Myers Squibb is uncertain; an anti-CLDN6/9 conjugate from Abbvie; and Immutep’s soluble Lag3 protein.

The focus on Ox40 will come as a surprise to those who had already written off this approach. At the 2016 Esmo meeting Pfizer’s PF-04518600 and Astrazeneca’s MEDI0562 showed disappointing remission rates as monotherapies.
## Selected clinical data on biologicals

<table>
<thead>
<tr>
<th>Project</th>
<th>Mechanism</th>
<th>Company</th>
<th>Detail</th>
<th>Abstract</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSK3174998</td>
<td>Ox40 agonist</td>
<td>Glaxosmithkline</td>
<td>First-in-human study +/- Keytruda (Engage-1 trial)</td>
<td>CT150</td>
</tr>
<tr>
<td>mRNA-2416</td>
<td>Ox40L mRNA</td>
<td>Moderna</td>
<td>A phase I/II dose escalation</td>
<td>CT032</td>
</tr>
<tr>
<td>ATOR-1015</td>
<td>CTLA-4 x Ox40 bispecific</td>
<td>Alligator</td>
<td>First-in-human study</td>
<td>CT145</td>
</tr>
<tr>
<td>COM701</td>
<td>Anti-PVRIG MAb</td>
<td>Compugen</td>
<td>Antitumour activity as monotherapy and in Opdivo combo</td>
<td>CT031</td>
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<tr>
<td>MSC-1</td>
<td>Anti-LIF-1 MAb</td>
<td>BMS/Northern Biologics</td>
<td>Phase I dose escalation</td>
<td>CT147</td>
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<tr>
<td>SC-004</td>
<td>Anti-CLDN6/9 ADC</td>
<td>Abbvie</td>
<td>First-in-human study in epithelial ovarian cancer</td>
<td>CT124</td>
</tr>
<tr>
<td>Pepinemab (VX15)</td>
<td>Anti-SEMA 4D/CD100 MAb</td>
<td>Vaccinex</td>
<td>Bavencio combo in NSCLC (Classical-Lung study)</td>
<td>CT191</td>
</tr>
<tr>
<td>Eftilagimod alpha</td>
<td>Soluble Lag3</td>
<td>Immutep</td>
<td>Keytruda combo in NSCLC or H&amp;N (Tacti-002 study)</td>
<td>CT202</td>
</tr>
<tr>
<td>Actimab-P</td>
<td>Anti-CD33 MAb-Ac-225 conjugate</td>
<td>Actinium/Astellas</td>
<td>Phase I in mCRPC</td>
<td>CT122</td>
</tr>
<tr>
<td>Tecentriq + Xtandi</td>
<td>Anti-PD-L1 + AR inhibitor</td>
<td>Roche</td>
<td>Imbassador-250 trial vs Xtandi in 3L mCRPC</td>
<td>CT014</td>
</tr>
<tr>
<td>Geptanolimab</td>
<td>Anti-PD-1 MAb</td>
<td>Genor Biopharma</td>
<td>Phase II trial in alveolar soft part sarcoma</td>
<td>CT197</td>
</tr>
<tr>
<td>Camrelizumab</td>
<td>Anti-PD-1 MAb</td>
<td>Jiangsu Hengrui</td>
<td>Apatinib combo in SCLC (Passion trial)</td>
<td>CT083</td>
</tr>
<tr>
<td>AK104</td>
<td>PD-1 x CTLA-4 bispecific</td>
<td>Akeso</td>
<td>Chemo combo in 1L gastric or GEJ cancer</td>
<td>CT120</td>
</tr>
</tbody>
</table>

Among preclinical presentations the SERD theme will get an airing, with data from Astrazeneca and Roche, as will Kras, via posters on Novartis’s SHP2 inhibitor and a pair of Boehringer Ingelheim assets targeting Kras and Sos1. Kras data should be of interest to Mirati, which slumped yesterday on a short report from Kerrisdale Capital.

In terms of share price appreciation AACR has already produced one winner: Iovance’s multi-billion dollar valuation put on another 17% on April 14 when the title of its TIL study revealed “durable complete responses” in NSCLC. The inference was that there were at least two CRs, and as the trial recruited up to 20 subjects that meant a rate of at least 10%.

However, nothing is known about how the remissions were evaluated, when they occurred or how durable they were; indeed, since the single-arm study combines TILs with Opdivo, IL-2 and two chemotherapies, it seems difficult to put any benefit specifically down to Iovance’s TILs.

## Selected clinical data on cell therapies

<table>
<thead>
<tr>
<th>Project</th>
<th>Mechanism</th>
<th>Company</th>
<th>Detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>LN-144 or LN-145</td>
<td>TILs</td>
<td>Iovance</td>
<td>Opdivo combo in NSCLC, cites “durable complete responses”</td>
</tr>
<tr>
<td>GC027</td>
<td>Anti-CD7 Car-T</td>
<td>Gracell</td>
<td>First-in-human allogeneic Car-T in T-cell ALL</td>
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</tbody>
</table>

Instead, the most intriguing cell therapy presentation at AACR might be first-in-human data from Gracell’s allogeneic anti-CD7 Car-T project GC027. Very little is known about Gracell, a Chinese company founded by the former chief executive of the controversial company Cellular Biomedicine Group, but it raised $85m in a series
B round, and claims to have a one-day Car-T manufacturing process.

Among technical questions, it is not clear how GC027, which targets T-cell leukaemia, might avoid fratricide problems. Perhaps all will be revealed next week.

<table>
<thead>
<tr>
<th>Project</th>
<th>Mechanism</th>
<th>Company</th>
<th>Detail</th>
<th>Abstract</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZD9833</td>
<td>SERD</td>
<td>Astrazeneca</td>
<td>-</td>
<td>1042</td>
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<tr>
<td>RG6171</td>
<td>SERD</td>
<td>Roche</td>
<td>-</td>
<td>DDT02-05</td>
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<tr>
<td>TNO155</td>
<td>SHP2 inhibitor</td>
<td>Novartis</td>
<td>Will structure be revealed?</td>
<td>DDT03-02</td>
</tr>
<tr>
<td>BI-3406 &amp; BI</td>
<td>Kras &amp; SOS1 inhibitors</td>
<td>Boehringer Ingelheim</td>
<td>Preclinical combo with Mek inhibitors or irinotecan</td>
<td>1091</td>
</tr>
<tr>
<td>1701963</td>
<td></td>
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</tr>
<tr>
<td>SNDX-5613</td>
<td>Menin-MLL1 antagonist</td>
<td>Syndax</td>
<td>Preclinical data in MLL-r and NPM1 mutant leukaemias</td>
<td>DDT01-01</td>
</tr>
<tr>
<td>BAY 2416964</td>
<td>AhR inhibitor</td>
<td>Bayer</td>
<td>Preclinical data on first AhR inhibitor to enter phase I</td>
<td>DDT01-02</td>
</tr>
<tr>
<td>IPN60090</td>
<td>Glutamase inhibitor</td>
<td>Ipsen</td>
<td>Preclinical data in KEAP1/NFE2L2 mut NSCLC &amp; ASNS-low HGSOC</td>
<td>DDT01-03</td>
</tr>
<tr>
<td>ABBV-184</td>
<td>Anti-Survivin bispecific</td>
<td>Abbvie</td>
<td>-</td>
<td>DDT03-01</td>
</tr>
<tr>
<td>RBN-2397</td>
<td>Parp7 inhibitor</td>
<td>Ribon</td>
<td>-</td>
<td>DDT02-01</td>
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</tbody>
</table>

**Selected preclinical data**

**AACR I takes place in virtual format on April 27-28; the full abstract texts will go live at 12:01am on April 27.**

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