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AACR 2020 preview – no Tigit, but plenty of novel mechanisms

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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.*)

Selected clinical data on targeted therapies				
Project	**Mechanism**	**Company**	**Detail**	**Abstract**
CKI27 + defactinib	Braf/Mek + FAK inhibitors	Verastem	Phase I in Kras mutant cancers	CT143
WNT974	Porcupine inhibitor	Novartis	Phase I study	CT034
Ricolinostat	HDAC6 inhibitor	Bristol-Myers Squibb	Abraxane combo in metastatic breast cancer	CT107
KA2507	HDAC6 inhibitor	Karus	Phase I study	CT151
EOS100850	A2A antagonist	Iteos	First-in-human study	CT152
RGX-104	LXR agonist	Rgenix	Docetaxel combo dose escalation	CT146
Orelabrutinib (ICO-022)	BTK inhibitor	Innocare	–	CT132
Amelie (almonertinib)	3rd-gen EGFR TKI	Jiangsu Hansoh	T790M+ve NSCLC (Apollo trial)	CT190
Poziotinib	EGFR & Her2 TKI	Spectrum	Exon 20 mut NSCLC (data from failed cohort 1)	CT081

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

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				
Project	**Mechanism**	**Company**	**Detail**	**Abstract**
LN-144 or LN-145	TILs	Iovance	Opdivo combo in NSCLC, cites "durable complete responses"	CT056
GC027	Anti-CD7 Car-T	Gracell	First-in-human allogeneic Car-T in T-cell ALL	CT052

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.

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

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