Evaluate Vantage

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AACR – Combinations, oncolytic viruses and more

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With all the abstract titles for the American Association for Cancer Research meeting now available, as well as the texts of the non-clinical presentations, biotech investors have a good idea what to expect when the meeting kicks off tomorrow.

Much focus could fall on combinatorial approaches, especially that of Lilly's abemaciclib, while with the recent approval of Merck KGaA/Pfizer's Bavencio investors will be keen to pick apart the Merkel cell cancer study due for presentation on Monday. There is even a supporting role for oncolytic virus approaches, which also hold most promise in combination (see table below).

The most important oncolytic virus presentation seems to be on Viralytics' Cavatak, with results of a phase I study combining it with Yervoy due on Tuesday. Response durability will be analysed to see if the melanoma study backs the theory that virus-infected cells increase a tumour's immunogenicity, making it liable to immune checkpoint blockade.

Transgene is presenting a preclinical poster on its own oncolytic virus that also seems to support combination with PD-1 or CTLA-4 blockade.

Immuno-oncology combos

That said, other combinatorial approaches might get more attention, especially those involving IDO inhibition, with Bristol-Myers Squibb investors looking for read-across from a trial of BMS-986205 with Opdivo to back the company's recent acquisition of Flexus, which has given it an alternative IDO inhibitor to combine (*AACR – Rags to riches to rags again, March 3, 2017*).

Beyond IDO three presentations investigate combining abemaciclib with a PD-L1 blocker, anti-ERK1/2 or Mek inhibitor – the last in a clinical study. Abemaciclib most recently improved progression-free survival in the Monarch-2 trial in HR-positive, Her2-negative breast cancer, and is expected to be launched in 2018.

Bavencio, as Merck KGaA/Pfizer's avelumab is now known, recently became the fourth MAb targeting the PD-1/PD-L1 interaction to be approved, getting the US green light for the orphan indication of Merkel cell carcinoma. Its Merkel cell trial might thus be of academic interest, though safety will be scrutinised as investors await progress in more lucrative cancer types.

The texts of AACR abstracts detailing clinical trials do not become available until 4:30pm Eastern time tonight. Accordingly, investors are still none the wiser about some studies, including that of Corvus's A2a antagonist – an approach more commonly associated with failing to deliver in Parkinson's disease.

A separate clinical trial, due for unveiling at AACR on Sunday, concerns Novocure's wearable Optune device, which delivers low-intensity electric fields. Investors will look for the magnitude of the benefit Optune shows in final results of a trial whose interim data were good enough for US approval in glioma (*Interview – Novocure plays the fields, February 9, 2016*).

Selected abstracts for 2017 AACR meeting			
Project	**Company**	**Abstract detail**	**Abstract no**
Abemaciclib + anti-PD-L1	Lilly	Anti-PD-L1 combo	583/17
Abemaciclib + LY3214996	Lilly	Anti-ERK1/2 combo	317/3
Abemaciclib + PD-0325901	Lilly	Embargoed clinical trial - Mek inhibitor combo	CT046
Opdivo	Bristol-Myers Squibb	Embargoed clinical trial - 5yr follow-up from CA209-003 NSCLC study	CT077
Opdivo + Yervoy	Bristol-Myers Squibb	Embargoed clinical trial - 2yr OS update from Checkmate-067	CT075
BION-1301	Aduro	First-in-class fully blocking anti-April MAb	2645/4
Cabiralizumab	Five Prime	Anti-CSF-1R approach	1599/7
COM701	Compugen	Anti-PVRIG approach	581/15
FPA154	Five Prime	Anti-GITR approach	613/17
INCAGN1876	Agenus	Anti-GITR approach	3643
Cavatak + Yervoy	Viralytics	Embargoed clinical trial - oncolytic virus combination	CT114
NKTR-214	Nektar	CD122-biased cytokine agonist synergistic with radiotherapy	1604/12
Avelumab	Merck KGaA/Pfizer	Embargoed clinical trial - Merkel cell carcinoma	CT079
STRO-001	Sutro Biopharma	CD74-targeting antibody-drug conjugate	67/18
Optune	Novocure	Embargoed clinical trial - wearable device in GBM	CT007
on/off CAR switch tech	Bellicum	Use in activating or ablating CAR-T cells	LB-184/7
BPX-701	Bellicum	Go-switch activated anti-PRAME engineered TCR	3745
UCART22	Cellectis	Allogeneic anti-CD22 CAR in relapsed leukaemia	3763/19
Self-deliverable siRNA	Mirimmune (RXI Pharmaceuticals)	Suppression of PD-1 to improve CAR-T cell activity	5650/4
mRNA administration	Moderna	mRNAs encoding IL-36γ, IL-23 and Ox40L	1607/15
CA4948	Curis	IRAK4 inhibitor	127/23
TG6002	Transgene	Armed oncolytic virus boosted by checkpoint blockade	4563/8

With clinical data still under wraps numerous preclinical presentations have caught the attention of analysts and physicians.

For instance, early data on Aduro's BION-1301 will be important since this project is a first-in-class MAb fully blocking April, a ligand associated with BCMA, with potential in multiple myeloma. For signs of activity against novel immune targets early data will be discussed on PVRIG, courtesy of Compugen's COM701, and GITR (Five Prime's FPA154 and Agenus's INCAGN1876).

And, as before, novel adoptive cell therapy approaches will play an important role, with Bellicum's on/off switch technologies featuring in two AACR presentations. At a recent investor webinar Dr Marcela Maus, a prominent

cell therapy specialist at Massachusetts General Hospital, cast doubt on the utility of these suicide genes.

Be that as it may, all the leading CAR-T players are on the lookout for novel technologies of this type, and AACR is bound to provide plenty of food for thought.

This story was amended to correct the Transgene entry. The AACR meeting this year takes place in Washington, DC, and begins on April 1.

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