Evaluate Vantage

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Another immuno-oncology mechanism threatens to disappoint

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As J&J tears up a licensing deal with Alligator, CD40 agonism might join the likes of Ox40 and IDO as an immuno-oncology approach that has failed to deliver.

It is easy to see today's ending by Johnson & Johnson of a collaboration with Alligator Bioscience covering ADC-1013 as the axing of an asset to which the pharma group had devoted little attention, and indeed Alligator describes it as a "strategic portfolio decision".

However, the reason might stem from last month's Asco meeting, at which the asset, a CD40 agonistic MAb, posted disappointing early data. This could spell bad news for Alligator and raise questions about this approach; the Swedish group, which now needs to find either a new partner or the cash to develop ADC-1013 itself, fell 40% this morning.

ADC-1013 is Alligator's lead asset, so it is understandable that the company put on a brave face, describing the J&J partnership as having made good progress since being signed in 2015. "Considering recent development in the CD40 field we are certainly optimistic about the future of this compound," it said in a statement.

Closer inspection of the facts reveals less grounds for optimism, however. Results of a phase I study in 95 solid tumour subjects, presented at Asco, showed just a single partial remission in a patient with renal cell cancer.

Leerink analysts at the time contrasted this with Apexigen's similarly acting APX005M, which at the AACR meeting put up a 54% overall remission rate in first-line pancreatic cancer on top of gemcitabine or Abraxane and without Opdivo. In combination with Opdivo APX005M showed 17% ORR in a melanoma trial.

CD40 is an immune system co-stimulatory protein, so the aim in engaging it to treat cancer is to stimulate the immune system without causing severe adverse events. Agonising CD40 remains a pipeline focus for several other groups, perhaps most notably Roche and Seattle Genetics.

Selected approaches targeting CD40 in cancer		
Project	**Company**	**Note**
Phase II		
APX005M	Apexigen	Promising data at AACR 2019
RG7876/selicrelumab	Roche	Phase I/II combo trial ends Nov 2019
Phase I		
ADC-1013/JNJ-64457107	Alligator Bioscience	Early data at Asco 2019; J&J terminated deal Jul 2019
ABBV-428	Abbvie	CD40/anti-TAA bispecific; phase I ends Aug 2019
CDX-1140	Celldex Therapeutics	Phase I ends mid-2020
SEA-CD40	Seattle Genetics	Phase I ends mid-2021
MEDI5083	Astrazeneca	CD40L fusion protein; preclinical data at AACR 2019
Preclinical		
CD40 & 4-1BB Duobody	Biontech/Genmab	IND planned 2019
rMVA-CD40L	Bavarian Nordic	CD40L vaccine; early data at AACR 2019
HERA-CD40L	Apogenix	Hexavalent CD40 agonist
CD40 agonist project	Immunext	
Source: EvaluatePharma. Note: CD40 agonist MAbs unless specified; excludes non-oncology applications and CD40-blocking approaches for autoimmune diseases.		

Apart from the early data from Apexigen and Alligator, there do not appear to be any other clinical results from other CD40 approaches. However, clinicaltrials.gov notes that studies of Roche's selicrelumab and Abbvie's ABBV-428 are due to end this year.

Leerink analysts have suggested that the better early efficacy of Apexigen's APX005M versus Alligator's ADC-1013 might be down to the former's tight binding to the FcyRIIb receptor, leading to better crosslinking and enhanced CD40 agonism.

It is also apparent that if CD40 agonism has merit it is as part of a combination, though Biontech, for one, has argued that a simple combination of two MAbs is not enough. Alligator ended June with $37m in the bank, and without re-engineering ADC-1013 it might struggle to find a new partner.