Evaluate Vantage

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Prame looks like the real deal

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But can the novel antigen be targeted effectively? Immatics reckons it can, with the right dose and the right manufacturing process.

When Roche launches a diagnostic for a novel cancer antigen the endorsement, in terms of target validation, counts for a lot. And this is precisely the endorsement that Prame, a target around which excitement had been building over the past year, got this morning.

True, the Roche assay is not intended to guide the type of pharmacological treatment, but rather to assess whether a tumour is malignant. But the development comes just a day after Immatics reported the biggest and most promising clinical dataset with a Prame-targeting therapy to date – a happy coincidence for the German cell therapy player.

The Immatics results came from phase 1 cohorts of a study of the anti-Prame engineered T-cell receptor IMA203, and represented an important update to a dataset that had piqued interest at last year's SITC meeting. They were enough to send the group's Nasdaq stock up 12% yesterday, and enable it to close a $110m secondary share offering.

Roche, meanwhile, today launched the Prame (EPR20330) Antibody, which runs on the company's IHC/ISH instruments, and is intended for use specifically on tissue samples from patients with suspected melanoma. Roche says that, because Prame is expressed in most melanomas, the assay can be used to differentiate between benign and malignant lesions.

Focus on melanoma

A day earlier Immatics' data pointed in a similar direction. Though Immatics cited Prame's highly cancer-specific expression on many solid cancers, including lung and ovarian, its update suggested that IMA203's best activity was in melanoma, including cutaneous and uveal subtypes. Prame is shorthand for "preferentially expressed antigen of melanoma".

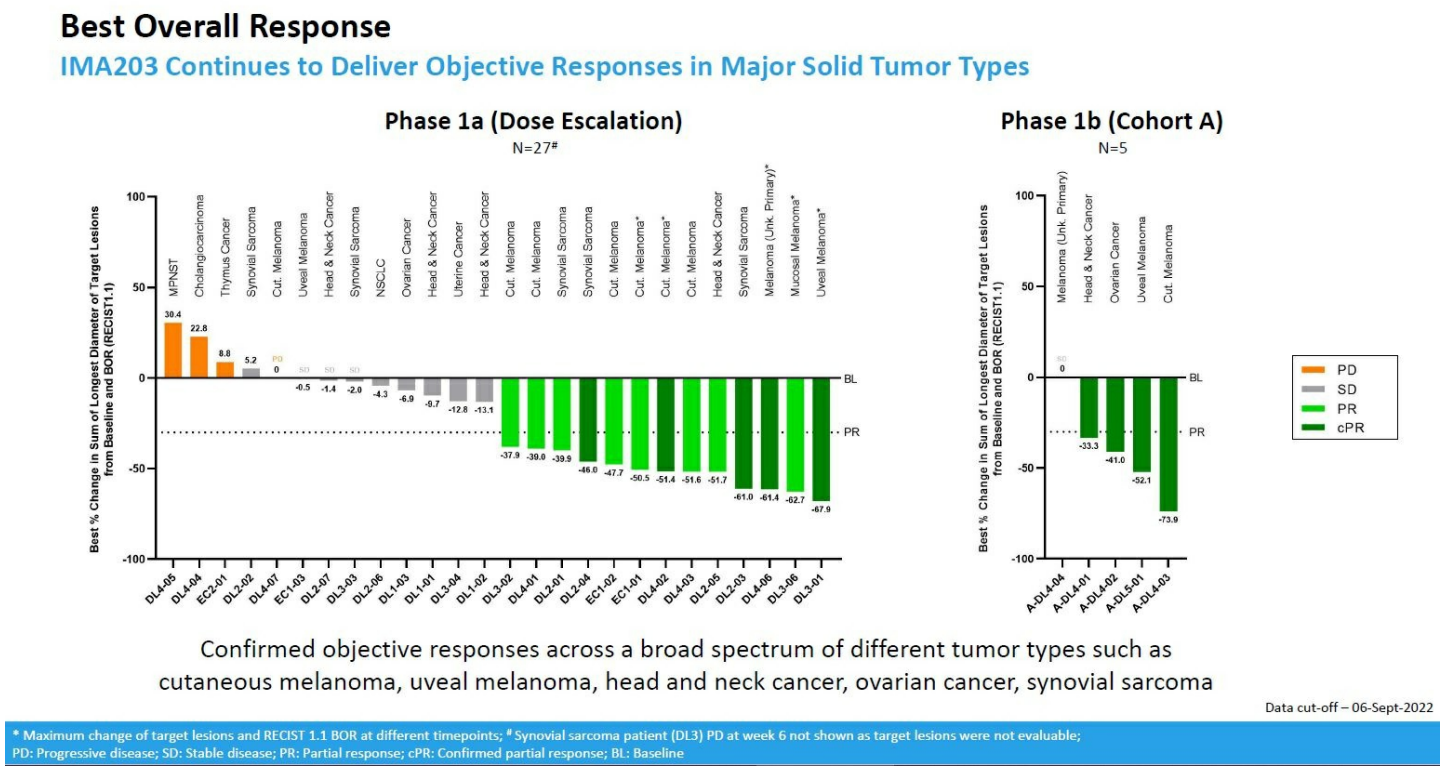
A year ago the phase 1 trial in question had yielded eight remissions among 16 evaluable patients on the first three dose levels of IMA203; four quickly relapsed. Yesterday the result was updated for a fourth dose, and with that initial dose-escalation cohort now at 27 evaluable subjects the ORR at six weeks stood at 48%.

The bad news is that relapses here were still a problem: six weeks later the confirmed ORR was just 19%, or 29% among six subjects at dose level 4.

However, the good news came from a separate dose-expansion group using a new manufacturing process, in

which three of four dose level 4 patients had confirmed remissions at week 12 – as did one patient treated with an even higher, exploratory dose.

Thus Immatics was able to make a headline claim that treating patients at dose level 4 or higher resulted in a confirmed ORR of 50%, or 80% if looking just at the second cohort, in which all responses were ongoing at the September 22 cut-off. Prame, it said, was now clinically validated as a multi-tumour target.



Confirmed objective responses across a broad spectrum of different tumor types such as cutaneous melanoma, uveal melanoma, head and neck cancer, ovarian cancer, synovial sarcoma

Data cut-off – 06-Sept-2022

* Maximum change of target lesions and RECIST 1.1 BOR at different timepoints; # Synovial sarcoma patient (DL3) PD at week 6 not shown as target lesions were not evaluable;
PD: Progressive disease; SD: Stable disease; PR: Partial response; cPR: Confirmed partial response; BL: Baseline

The other thing in Immatics' favour, and which backs its claim that Prame is not expressed especially well in normal tissue, is safety. There are few off-tumour effects in its trial, and cytokine release and neurotoxicity appear at relatively low levels.

If this is the case one obvious question is why no one before Immatics has been able to seize on the potential of Prame, which has been studied by industry for some time. Immatics says ATR203 has improved affinity thanks to enhanced pairing of TCR chains, as well as high avidity and low off-target toxicity.

The group has not finished yet. The first patient was treated in August with an improved version of ATR203 coded IMA203CD8, and initial data are due next year. Competitors, including Immunocore, which disappointed at Esmo, and Biontech, which did a Prame deal with Medigene in February, will pay attention.

Selected projects targeting Prame				
Company	**Project**	**Modality**	**Clinical trial**	**Note**
Immatics	IMA203	eTCR (HLA-A*02-specific)	NCT03686124	Oct 2022: 53% ORR, including 50% confirmed ORR at ph2 dose or above
Immatics	IMA203CD8	As above, but adds CD8 co-receptor to allow CD4+ T cells to be utilised		First patient treated Aug 2022; data 2023
Immunocore	IMC-F106C	Immtac (HLA-A*02:01-specific)	NCT04262466	Disappointed at Esmo 2022: 23% ORR, vs 38% cited in abstract
Medigene	MDG1011	eTCR (HLA-A*02:01-specific)	NCT03503968	Feb 2022: 1 short-term remission in 8 evaluable patients
Neximmune	NEXI-001	WT1, Prame & cyclin A1 vaccine	NCT04284228	Data due in Q4 2022
Mana Therapeutics	Mana-312	WT1, Prame & Survivin vaccine	NCT04679194	No news since 2021 series A
Bellicum	BPX-701	eTCR (HLA-A*02:01-specific; rimiducid-activated suicide switch)	NCT02743611	Deprioritised
GSK	GSK2302032A	Prame vaccine	NCT01853878	Discontinued
Mannkind	MKC1106-PP	Prame & PSMA vaccine	NCT00423254	Discontinued
Biontech/ Medigene	MDG1014	eTCR (PD-1/4-1BB switch receptor)	NA	Deal in Feb 2022
GSK/ Adaptimmune	Unnamed	eTCR	NA	$4m preclinical development milestone in 2021
Myrio (formerly Affinity Bio)	Unnamed	Bispecific T-cell engager	NA	Preclinical
Source: Evaluate Pharma & clinicaltrials.gov.				