Evaluate Vantage

November 01, 2019

Upcoming events – key tests approach for Kadmon and Surface

Lisa Urquhart

Kadmon awaits key graft-versus-host disease data, and Surface Oncology's change of tack comes under the spotlight.

Welcome to your weekly roundup of approaching clinical readouts. The end of this year will be hugely important for Kadmon, which is to make a decision on whether to file its lead asset, the Rock2 inhibitor KD025, in chronic graft-versus-host disease (GVHD).

The call will hinge on the first readout from its 126-patient phase II Rockstar trial, evaluating KD025 in chronic patients who have had at least two prior forms of treatment. Kadmon is expected only to disclose whether the trial met the hurdle for filing, with more detailed data due next year.

Patients in the uncontrolled two-cohort study are receiving a 200mg dose of KD025 once or twice daily, and the primary endpoint is six-month overall response rate (ORR); clinical significance would be reached with an ORR of ≥30% in either study arm.

However, to compete with Johnson & Johnson/Abbvie's Imbruvica, which has shown an ORR of 67% in chronic GVHD, KD025 would need to get closer to the 58% ORR it showed in phase II.

GVHD, which can occur in patients who have undergone transplants, comes in two forms: acute, when the attack begins soon after transplant, and chronic, starting 100 days after transplant. The standard of care for both types is steroids.

Incyte's Jak inhibitor Jakafi recently got the go-ahead in steroid-refractory acute disease. Imbruvica is indicated for chronic GVHD, also after steroids, while Jakafi is in a phase III trial, Reach 3, in steroid-refractory chronic GVHD, with data due next year.

KD025 has a chance to make an impact if its clean safety profile in phase II can be replicated in Rockstar: Imbruvica and Jakafi are both linked with infections, which has not been seen with the Kadmon project, Cantor Fitzgerald analysts noted. They added that KD025's lower ORR versus Imbruvica could be down to the latter having been studied in a more severe patient population.

Still, the GVHD market could soon get more crowded, with Incyte also testing its next-generation Jak, itacitinib, in acute and chronic disease (*Upcoming events – Roche braves liver cancer and Incyte looks for a new Jak, October 11, 2019*).

Selected graft-versus-host disease treatments*				
Project	**Company**	**Mechanism of action**	**2024e sales ($m)**	**Status**
KD025	Kadmon	Rock2 inhibitor	473	Phase II
Jakafi	Incyte	Jak1 & 2 inhibitor	216	Marketed
Temcell HS	Mesoblast	Mesenchymal stem cell therapy	209	Marketed
ATIR101	Kiadis Pharma	T-lymphocyte cell therapy	189	Filed
Alzumab	Equillium	CD6 antibody	59	Phase II
Itacitinib	Incyte	Jak1 inhibitor	35	Phase III
ALPN-101	Alpine Immune Sciences	ICOS/CD28 antagonist	44	Phase I
Thymoglobulin	Sanofi	T-cell inhibitor	29	Marketed
Temcell HS	JCR Pharmaceuticals	Mesenchymal stem cell therapy	27	Marketed
**Sales by indication. Source EvaluatePharma.*				

Surface tension

Surface Oncology floated in 2018 largely on a wave of enthusiasm about CD47 antagonism, but subsequent events have taken the shine off this approach, and its stock now stands 90% off its $15 IPO price. Fortunately, the company has a Novartis-partnered clinical asset, SRF373/NZV930, to which it has been able to switch attention.

SRF373 is an antibody against CD73, and its phase I study is expected to yield results by the end of 2019. While the trial's main aim is to demonstrate tolerability, the 344 patients enrolled have several types of advanced cancers, and investors will fix on overall remission rates as an early sign of efficacy.

Making sense of the data and parsing the contribution of SRF373 could be easier than in other combo studies. As well as testing SRF373 in combination with Novartis's anti-PD-1 MAb spartalizumab and/or its A2a antagonist NIR178, the Surface project is given to a separate cohort as monotherapy.

The thinking behind SRF373 is that in cancer cells CD73 acts as an enzyme to stimulate production of adenosine, which in turn has an immunosuppressive action. SRF373 hits membrane-bound and soluble CD73.

Though only a handful of competing projects are in the clinic, Surface investors have some baseline expectations. Astrazeneca's oleclumab has been tested alone or in combination with Imfinzi, and the combo yielded partial responses in 5% of colorectal and 10% of pancreatic cancer subjects. And Bristol-Myers Squibb's BMS-986179 plus Opdivo gave a 12% ORR across various tumour types.

Over $500m in potential milestones is due from Novartis, so the phase I readout is Surface's most important near-term catalyst. CD47 meanwhile, has quietly been shelved on the grounds of toxicities and an "evolving competitive landscape".

Selected anti-CD73 MAbs			
Project	**Company**	**Status**	**Results?**
Oleclumab	Astrazeneca	Several ph2 monotherapy & Imfinzi combo studies	Data at Asco 2018
CPI-006	Corvus	Monotherapy & Keytruda combo; ph1 started Apr 2018	Data at SITC 2019
BMS-986179	Bristol-Myers Squibb	Monotherapy & Opdivo combo; ph1 started Jun 2018	Data at AACR 2018
SRF373	Surface Oncology/Novartis	Monotherapy & spartalizumab/NIR178 combos, & triplet; ph1 started Jun 2018	First data H2 2019
TJD5	I-Mab/Tracon	Monotherapy & Tecentriq combo; ph1 started Aug 2019	Data possible 2020
IPH5301	Innate Pharma	Preclinical	Preclinical data AACR 2019
Source: EvaluatePharma & company statements.			