Evaluate Vantage

December 04, 2020

Sutro bucks the folate trend

Jacob Plieth

Competing folate receptor-targeting projects have recorded one failure after another, but Sutro scores a phase I win.

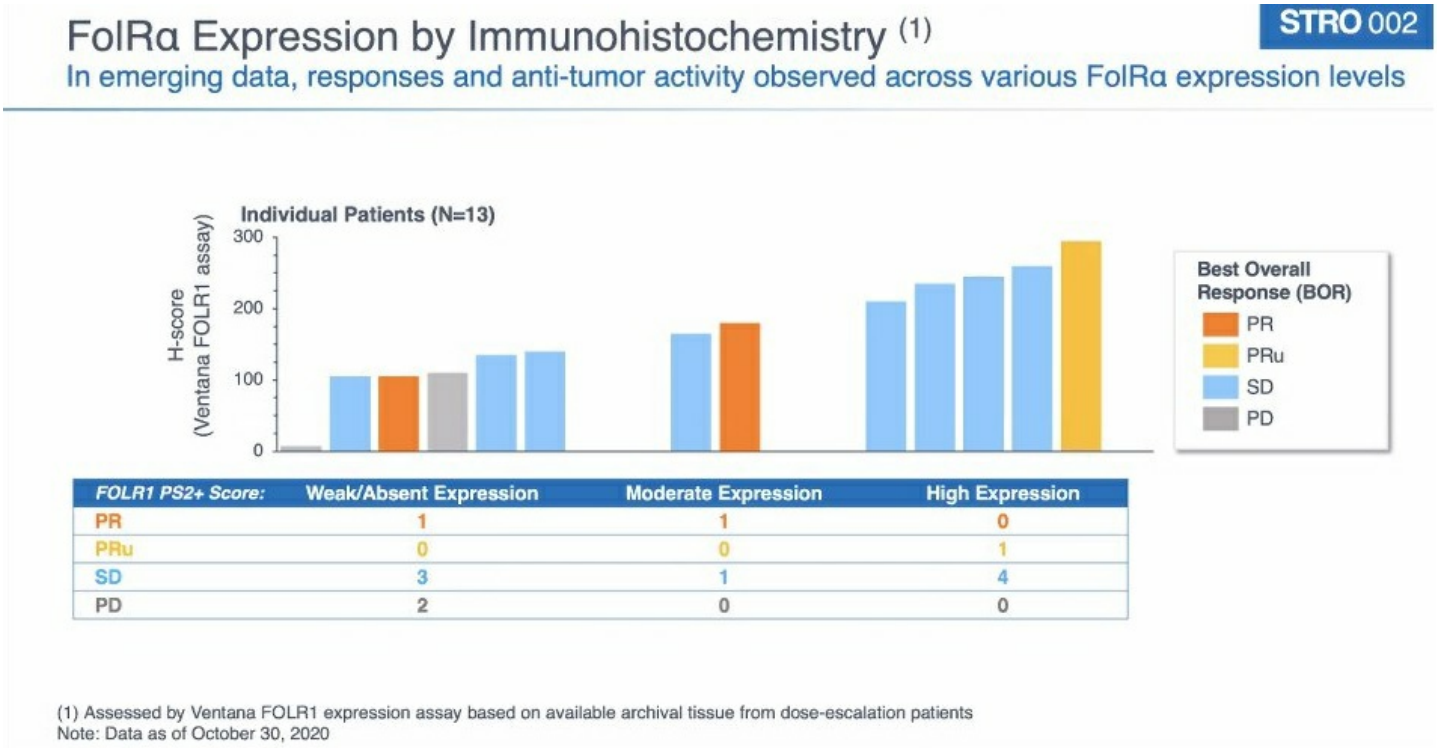
Not only does yesterday's early clinical success for Sutro's STRO-002 appear to validate the group's lead wholly-owned project, it comes in direct contrast to virtually every other company that has attempted its mechanism of action.

The most recent to fail with this mechanism, targeting the folate receptor, was Immunogen, and before that Eisai and Endocyte had crashed and burned. But Sutro says a heavily pretreated population of 31 ovarian cancer patients in a dose-escalation trial has yielded a win for STRO-002, with a 32% overall response rate, including one complete remission.

A blemish on this dataset is grade 3 or 4 neutropenia, which occurred in over half the patients studied. Despite being hailed as a highly targeted, tumour-specific approach, hitting folate receptor α (FRα) has frequently been accompanied by toxicities.

Interestingly, the population that Sutro enrolled – ovarian cancer patients who had received a median of six prior therapies – had not been preselected for FRα expression.

And data on how FRα expression correlated with efficacy appear to be inconclusive: among 13 patients who had their FRα levels tested there were two partial remissions in those with weak, moderate or absent FRα, while in five high expressers there was only one PR and four stable diseases.



Source: Sutro presentation.

Though Sutro claimed that this demonstrates STRO-002's activity across various expression levels, it said it would begin a trial in FRα-selected endometrial cancer patients next year.

For dose-expansion in ovarian cancer, at 4.3mg/kg and 5.2mg/kg, the company plans to collect tissue samples at enrolment and assay these to determine if a FRα-selection enrichment strategy is needed. This will "inform regulatory discussions ... and identify the broadest population that may benefit from STRO-002", it said yesterday.

To enrich or not to enrich?

Preselection for FRα expression is important considering Immunogen's phase III disappointment with mirvetuximab soravtansine last year, also in ovarian cancer (*Immunogen fails to leap Forward, March 1, 2019*).

This study failed in all-comers, but Immunogen claimed to have seen a benefit in a FRα-high subgroup, and has continued development in a trial that preselects for FRα positivity. Mirvetuximab, like STRO-002, is an antibody-drug conjugate.

Other FRα-targeting late-stage failures include Endocyte's vintafolide and Eisai's farletuzumab, though the later has not formally been discontinued. The industry pipeline reveals projects using this mechanism in mid-stage development at Marker Therapeutics and Epsilogen, a private UK company formerly known as Igem Therapeutics.

Sutro's success against the odds could give these and others a second wind.

Selected folate receptor α (FRα) targeting projects in clinical trials			
Project	**Company**	**Mechanism**	**Trial detail**
Phase III			
Mirvetuximab soravtansine	Immunogen	Anti-FRα MAb-drug conjugate	Soraya, in high FRα expression (failed in all-comers)
Phase II			
TPIV200	Marker Therapeutics	Anti-FRα cancer vaccine	Two ongoing trials (one terminated)
IGEM-F	Epsilogen	Anti-FRα MAb	Status unclear
Farletuzumab / MORAb-202	Eisai	Anti-FRα MAb	Most recent ph2 completed Aug 2020 (failed ph3)
Phase I			
STRO-002	Sutro Biopharma	Anti-FRα MAb-drug conjugate	32% ORR in 31 unselected ovarian cancer patients
CT900	Carrick Therapeutics	Anti-FRα thymidylate synthase inhibitor	Status unclear
Source: EvaluatePharma.			