Evaluate Vantage

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# Idera’s reinvention takes a hit

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**The company’s lead, tilsotolimod, is meant to turn cold tumours hot, but it was investors who became frosty last week in response to mid-stage clinical results.**

This summer’s phase II setback in the rare disease dermatomyositis left Idera’s investment case focused on immuno-oncology. The strategy was dealt a blow on Friday when mid-stage results for the group’s lead asset, tilsotolimod, underwhelmed.

Idera’s problem is that a phase III trial of tilsotolimod is already under way in the same setting, in combination with Yervoy in melanoma subjects who have progressed after checkpoint blockade. With $82m in the bank at the end of September the group will have been looking for a share price uplift to enable another equity raise; instead its stock crashed 40% on Friday.

Investors are thus no clearer as to what shape the company’s reinvention plan might take. At one point this year Idera was to have been merged with Biocryst, another biotech struggling to reinvent itself, but that move fell apart shortly after the dermatomyositis setback.

Both the dermatomyositis project, IMO-8400, and tilsotolimod are toll-like receptor agonists, but the latter specifically hits TLR9. Idera’s TLR9 research had once been licensed for oncology use to Merck KGaA, but the German group canned the deal in 2011.

The phase II results revealed on Friday, from the Illuminate-204 study, related to tilsotolimod plus Yervoy given to 34 evaluable melanoma subjects who had relapsed on checkpoint blockade.

**(Briefly) turning tumours hot**

At first glance the data looked impressive, comprising a 32% overall response rate, including two complete remissions. Comparable response rates in this setting range from 10.5% to 21% for Opdivo plus Yervoy.

However, in Idera’s case all but four of the 11 responding patients relapsed, including three remissions that lasted for just three months or so. On an investor call the company sidestepped the question of median response duration at the study’s current data cut, and refused to be drawn on what duration would be needed for the result to be considered clinically relevant.

Instead, it made much of the disease control rate seen in the trial, and the fact that five of the enrollees had already failed Yervoy monotherapy; two of these responded. Moreover, the response of one of the two initial complete remitters is still ongoing two and a half years from enrolment.

Thus the results do hint at tilsotolimod's ability to turn cold tumours immunogenic, but without longer follow-up the long-duration complete responder can be dismissed as a mere outlier. This is the second time Illuminate-204 has disappointed: at Asco a 38% overall response rate sent Idera down 4% (*Asco 2018 – Toll like receptors join the immuno-oncology combo parade, June 5, 2018*).

Idera said checkpoint inhibitors had transformed front-line melanoma treatment, but that refractory patients represented a significant population that it would target with tilsotolimod. Its pivotal study aims to recruit some 300 subjects by the end of next year, and to treat them with tilsotolimod plus Yervoy or Yervoy alone.

Interim phase II data were clearly aimed to increase confidence in the pivotal plan, but in the event all they have done is add doubt, since the more robust setting of phase III will likely yield a weaker result.

| Stage | Study name | Setting | Status | Trial ID |
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| Phase II | Illuminate-204 | Yervoy or Keytruda combo (single arms) | Interim data Dec 2018 | NCT02644967 |
| Phase III | Illuminate-301 | Yervoy combo vs Yervoy | Full recruitment by end 2019 | NCT03445533 |