Asco 2020 - Bavencio “cure” suggests another cancer target for immunotherapy

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The Merck KGaA/Pfizer drug is said to have cured 52% of women with a rare gynaecological cancer, one of whom subsequently gave birth.

Merck KGaA/Pfizer’s Bavencio looks to have succeeded in a rare cancer type with little competitor involvement. A late-breaking Asco presentation of the investigator-sponsored Trophimmun trial has revealed that eight of 15 women with gestational trophoblastic tumours (GTTs) that were resistant to chemotherapy were “likely cured” after receiving Bavencio.

The investigators, from Institut de Cancérologie des Hospices Civils de Lyon, France, said Trophimmun was the first study of an immunotherapy in GTTs. The cancer accounts for less than 5% of gynaecological tumours, and arises from malignant transformation of trophoblasts, which are cells originating from the placenta.

The single-cohort trial enrolled 17 women with GTTs who were no longer responsive to chemotherapy, and 15 of these were treated and assessable. Seven of the 15 developed resistance to Bavencio, but the other eight responded, and remained relapse-free at 29 months’ follow-up despite discontinuing the anti-PD-L1 antibody.

Patients with GTTs normally relapse within six months, but if they are progression-free after a year, and monitoring of the hormone hCG has concluded, they are considered cured. In Trophimmun seven of the responders saw their levels of hCG, a biomarker of GTT, normalise while taking Bavencio, while the eighth did so after coming off the drug.

First pregnancy

What is more, one of the responders later became pregnant and delivered a healthy baby. This, the investigators said, was “the first report of a normal pregnancy after a curative treatment with an immunotherapy agent”. As for toxicity, Bavencio was said to be more tolerable than chemotherapy, and to spare patients the toxicity of the latter.

Despite saying that the eight responders could “likely” be considered cured, the authors say more evidence is needed before calling Trophimmun a practice-changing study. To this end Trophamet, a first-line GTT trial testing Bavencio plus chemo, is enrolling.

The scientific rationale behind using an anti-PD-(L)1 drug like Bavencio is that GTTs overexpress PD-L1. Indeed, PD-L1 expression is thought to be the way in which immune tolerance is developed in a pregnancy.
On an Asco press call the Trophimmun paper’s lead author, Dr Benoit You from the Centre de Référence des Maladies Trophoblastiques, said he had examined data on over 100 GTT patients, and all were PD-L1 expressers at ≥50%.

Accordingly, “we did not select patients based on PD-L1 expression because we know all [GTT] patients will have PD-L1 overexpressed tumours”, he said. “We thought we should take all patients.” Dr You added that he did not yet know why some subjects did better than others, but said further analysis would be done to try and determine this.

**Why so few?**

Given this strong biomarker correlation it seems surprising that so few anti-PD-(L)1 drugs have been tested against GTT. Not only that, but there appears to be no primary pharma industry involvement here.

Three other anti-PD-(L)1 antibodies, Merck & Co’s Keytruda, Bristol-Myers Squibb’s Opdivo, and Jiangsu Hengrui’s Airuka, are in trials against this cancer, but all the studies are sponsored by academia.

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<td>Bavencio</td>
<td>Merck KGaA/Pfizer</td>
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*Source: clinicaltrials.gov & Asco.*

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